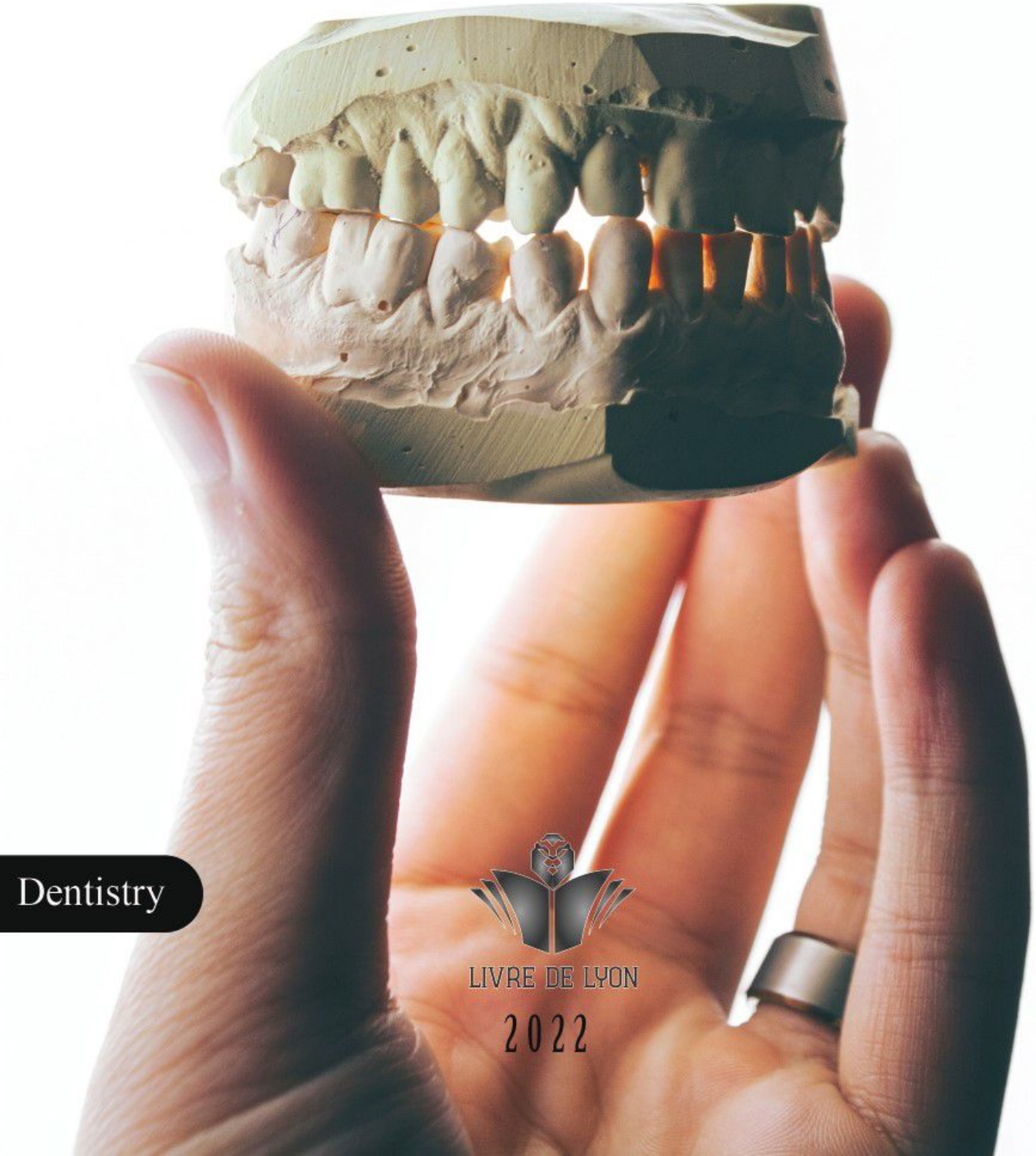
Reviews in Dentistry

Methodology, Research and Practice

Editor

Assoc. Prof. Dr. Fariz Salimov



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PREFACE

Dear colleagues

Today, there are many different developments in dentistry. Academic physicians, who follow the developments and examine them, strive to make usable of all these informations in clinics.

We hope that our academic physicians, who share their researches in this book, which is based on the principle of "Success is not a coincidence", will continue to contribute to science.

Best regards..
Assoc Prof. Dr. Fariz Salimov

CHAPTER I

PROSTHETICS REHABILITATION IN PEDIATRIC DENTISTRY

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1. Introduction

The treatment methods that can be applied in hereditary partial or total deciduous tooth deficiencies in children, deciduous tooth formation anomalies due to genetic diseases, loss of deciduous teeth due to trauma or caries, or material losses related to deciduous teeth are fixed and removable appliances. The use of these appliances varies according to the case. (1)

Tooth deficiencies (anodontia, oligodontia, hypodontia) or tooth loss are accepted as an important health problem with emotional, social and psychological consequences that affect the child's nutrition, aesthetics and self-confidence. (2) Premature tooth loss in children; It is caused by systematic diseases such as dental caries (rampant, early childhood and bottle caries), traumatic injuries, Papilion le fever. Congenital deficiency

of teeth is systemic diseases such as cleft lip and palate, ectodermal dysplasia. Prosthetic rehabilitation of children, to restore chewing function, appearance; to protect and develop phonation; to prevent the development of harmful oral habits; and helps to minimize possible psychological disturbances. There are different treatment modalities for prosthetic rehabilitation in children and youth, such as removable partial dentures, full dentures, overdenture dentures, implant-supported or nance dentures, stainless steel crowns, polycarbonate, composite strip crowns, adhesive prostheses, post-core restorations.(3)

The consequences of premature tooth loss

Early tooth loss can cause loss of space in the mixed dentition, which can lead to misalignment of the teeth. Premature loss of primary incisors or molars can lead to harmful oral habits such as anterior or lateral tongue thrusting, respectively. (4)

Congenital absence of anterior teeth, dental trauma or tooth loss due to dental caries may occur. This situation can cause psychological trauma in children. This can lead to a feeling of rejection or inadequacy about their personal appearance. (5)

Missing teeth, especially in the anterior areas, can cause incorrect speech. Missing incisors often cause problems in the child's pronunciation of letters such as "t", "d", "n" and in some languages "l". (6)

Other than that, the effects of tooth deficiency or loss are: reduced chewing efficiency, aesthetic problem, loss of vertical dimension of occlusion, loss of alveolar ridge height. (7) In many children with early childhood caries; strip crowns, zirconium crowns or stainless steel crowns are among the treatment options. These treatment options lead to a better speech pattern in the anterior teeth. In the posterior teeth, it increases the chewing efficiency. It also restores the appearance and self-confidence of children. (8)

Prosthetic treatment is based on the results of the clinical examination and is ideally part of a comprehensive treatment plan. The clinical examination of the child is carried out in the usual way. The radiographic examination includes panoramic radiographs, so that the different developmental stages of all teeth can be seen. This information helps the prosthodontist to estimate the approximate time and sequence

of eruption of permanent teeth, as well as to decide whether the patient presents an indication for dentures.

The following procedure is recommended in the treatment plan: (9)

1. The developmental status of the teeth;

2. Caries-risk assessment;

3. The patient's oral hygiene;

4. Expected parental compliance and possibility of recall;

5. The patient's ability to cooperate for treatment.

The treatment options for prosthetic rehabilitation of pediatric patients are as follows (10):

1. Removable partial dentures

2. Complete dentures

3. Partial dentures fixed with orthodontic bands or Nance dentures

4. Various crowns such as stainless steel crowns, polycarbonate, composite strip crowns

5. Resin bond and resin bonded fixed dentures

8. Nutritional plates for babies

9. Obturators used in patients with cleft palate-lip

10. Speech prosthesis for velopharyngeal deficiency or velopharyngeal

11. Osseointegrated implants.

1.1.Partial removable dentures in children:

It should be planned taking into account the growth and development of the child. The design of the dentures should be such as to allow modification when teeth erupt or are displaced. However, if edentulous (or dental prosthesis) is prolonged, it causes alveolar process narrowing and vertical alveolar defects in tooth-deficient areas, eruption of the anagonist permanent teeth, and tipping of adjacent teeth. (11)

Tissue supported partial dentures; it is indicated when a child has been edentulous for a long time, when we expect bone resorption and remodeling immediately after extraction or traumatic tooth loss. They are also indicated in severe cases of hypodontia, congenital genetic conditions (such as ectodermal dysplasia), or after cyst/tumor surgeries. Especially in cases of hypodontia, dentures at an early age restore lost appearance, speech and chewing functions. Such positive changes can increase the child's selfconfidence and help to establish appropriate nutrition chewing. The use of tissue supported prosthesis does not prevent maxillary or mandibular growth. (12)

Retention of tissue-supported prostheses in children is most commonly achieved by the elongated body of the acrylic base of the prosthesis resting on the alveolar crest and palate. Clasps are used only when necessary because of the force they exert on the teeth, but some orthodontic springs can be incorporated into the denture design (if needed) to facilitate the required tooth movement.(13)

In recent years, polyamide based prostheses have been used more frequently in pediatric dentistry, especially due to their high elasticity and good aesthetics. Their high adaptability and elasticity have made them especially suitable for use in the period of primary and mixed dentition. (14)

While the retention of tooth supported dentures is ensured by minimizing contact with the mucosa as much as possible with dental clasps and occlusal rests, the rigidity of the prosthesis is provided by the supporting metal main binder. (15)

While taking impressions in child prostheses, impression trays in various sizes should be selected and the edges should be waxed and

the impression should be taken. Fast setting alginate should be used in children younger than 6 years of age. In older children, the 2nd impression can be taken with silicone material.

While taking the measurement, the assistant should take the measurement overflowing from the posterior palatal area with a mirror or tongue depressor. The clasp design clasps must enter the undercut areas for retention.

Circumforentinal and adams clasps are used in removable child prostheses. Circumforentinal (which surround the tooth) clasps can be used on primary canines or molars. Their retention can be increased with composite resins. However,"adams" clasps are the most preferred of all clasps. Adams clasps can be bent easily, they are compatible with occlusion, and they are among the clasps with the best retention. All clasps and arch wires are made from 0.028 -0.030 stainless steel orthodontic wires. (13)

All designed prostheses should be such that they allow oral care of both the artificial tooth and the child, and should not damage the surrounding tissues.

Regular check-ups should be called every 3- 6 months and changes should be made to suit and adapt to the child's growth and development. (16)

Loss of anterior teeth in children and adolescents is mostly the result of complications from injury and/or previous trauma (such as ankylosis or root resorption). The central maxillary incisors are the teeth most commonly affected by trauma. (17) A non-invasive long-term intermediate restoration should be designed in childhood, and particularly in adolescence, until the implant is indicated. Implant treatment should be postponed until adulthood due to the risk of complications such as implant infraposition. (18)

1.2.Complete dentures in children:

Total edentulism in children is usually seen due to the syndrome (such as ectodermal dysplasia, le fevre syndrome). In this case, children often need full dentures to restore primary and permanent teeth. Children with ectodermal dysplasia, in particular, continue to exhibit normal facial

growth except for alveolar bone deposition. There is a need to periodically re-make the prosthesis and customize the prosthesis aesthetically to the child's current stage of dental and facial development. (19) In general, it is difficult to record a centric relationship in children because they do not have the same muscle structure, TMJ functions or growth maturity as adults.(20)

1.3.Resin-bond or resin-bonded fixed prostheses:

For the preservation of pulp and periodontal health and tooth structure, composite-resin body prostheses should be the first choice as much as possible. Retention and resistance are provided only by tooth preparation at enamel level, etching the enamel with acid and cementation with adhesive resin cements. Adhesive prostheses are indicated for congenital single tooth deficiency, tooth lost due to trauma, teeth with adequate clinical crown length; It is contraindicated in cases of extensive caries or malposition in the abutment tooth, in children who cannot perform oral and dental care adequately.(21)

The advantages of adhesive bridges are that they protect the tooth structure, can be done without local anesthetic, are aesthetic and can be repaired in any fracture. They also tend to prevent pressure from the mucosa and alveolar ridge (as opposed to tissue supported partial dentures), thus reducing the risk of alveolar bone resorption and possible complications for future implant treatment. Careful planning is required to properly distribute chewing pressure to adjacent teeth. (22)

The most common causes of resin bonded bridge failure are breakage, discoloration and abrasion of intrafiber bonds, particularly in areas where the fibers are exposed to the oral cavity. Most of the studies show that the success of the adhesive bridge is around 72-74% after 3-5 years.(23)

It has been reported that anterior restorations are expected to last longer than posterior restorations and the survival rate of resin bridges in the maxilla is higher than in the mandible (81% versus 56% after 2.5 years).(24)

1.4.Stainless Steel Crowns (SSC)

Stainless steel crowns first emerged as a full crown treatment option in the 1950s. These nickel-chromium crowns were known to cause a variety of undesirable clinical symptoms, mostly due to the allergenic potential of nickel. Since then, the design of the crowns and the metals used have changed significantly.(25) Nowadays, stainless steel crowns consist of a mixture of metals containing iron, chromium, carbon and 9% nickel, similar to orthodontic braces.(26) Longevity of the crown depends on following appropriate protocols for crown placement, particularly with regard to the margins. If possible, the crown should be based on a healthy tooth margin, otherwise amalgam or glass ionomer restorative material. Studies have shown that these two materials show the least amount of microleakage.(27) Probably the biggest problem with stainless steel crowns is their poor aesthetic appearance, which limits their use to restoration of first and second molars.(28) It was stated by the British Association of Pediatric Dentistry in 2008 that restorations with SSC could be preferred. In the systematic analysis published by Innes et al. in 2015, evidence was revealed that SSC is the most appropriate restoration method, the effect of which is compared with traditional methods. Although its durability, long life and preventing the recurrence of caries are the biggest advantages of SSC, studies have shown that the aesthetic expectations of patients and their parents cannot be met. Since these restorations did not meet the expectations in terms of aesthetics, various materials such as resin composite were tried to cover the buccal and occlusal surfaces, but these studies were not successful in clinical terms. (29) The aesthetics of the applied dental treatments is one of the most important factors for parents. For this purpose, single-faced crowns, strip crowns and SSC veneer crowns have been developed. Although these new materials contributed aesthetically, they caused some gingival problems.(30)

1.5.Zirconium crowns

It was first introduced in the field of dentistry in 2001. However, the material itself has been used in medicine in orthopedic practice during hip

surgeries since the 1960s. The zirconia used in dental crowns is yttrium stabilized zirconia.(31) Yttrium stabilized zirconia has the highest flexural strength of all zirconia-based materials, as well as high chemical and erosion resistance. In addition, the material is biocompatible, hypoallergenic and has similar durability to natural enamel. Because they are not adjustable (unlike stainless steel crowns), zirconia crowns for milk teeth come prefabricated with certain features. It is therefore important to do a trial run using a mock-up crown prior to cementation to ensure proper tooth preparation, margin and occlusion.(32) Unlike traditional ceramic, zirconia crowns for primary teeth show low wear on opposing teeth. Zirconia and stainless steel crowns have the lowest wear rates among full pediatric dental crown materials. Prefabricated zirconia crowns with excellent aesthetic appearance, good durability and longevity make them fully usable in both anterior and posterior restoratins.(33)

In addition to the advantages of zirconium crowns, it is more difficult to adapt due to its thicker structure than SSC and it is not possible to make any corrections on it. Due to this thickness, more material needs to be removed during tooth preparation, which turns into a major disadvantage against stainless steel crowns. Another disadvantage is that zirconium crowns have to be completely replaced when broken and repair is not possible.(30)

1.5.Dental implants in pediatric patients

Implant applications are routinely performed in adult individuals, in the bones that have completed their development. Implant application can be a treatment option in cases of edentulism due to agenesis, trauma and congenital syndromes or early tooth loss in children and young patients. (34)

Removable partial dentures are the most commonly used treatment option in children with missing teeth. However, removable partial dentures increase the risk of caries and alveolar bone resorption, and may cause periodontal disorders. Some of the use of removable partial dentures. Due to the difficulties, families and pediatric patients want to start using fixed prosthesis with implant applications as soon as possible.(35)

While placing the implant in adult patients, attention is paid to the quality and width of the bone tissue, the treatment plan, the surgical operation to be applied, optimal prosthesis planning and long-term good oral hygiene. Since growth and development continues in pediatric patients, it may not be predicted how the compatibility of the implant with the jaw bones and periodontal tissue will continue after implant applications.(36)

It has been concluded that implants behave like ankylosed teeth in patients in their growth and developmental age, and alveolar development is restricted because they do not show lifelong eruptions as in adjacent teeth and cause occlusion disorders. In addition, it has been reported that osseointegrated implants do not show any displacements in the sagittal or transverse direction during the development of the jaws.(37) As a result of these studies, it is recommended not to apply dental implants before permanent dentition and skeletal growth are completed in young individuals in order to prevent implant-supported crowns from remaining in infraocclusion.(38) However, the existence of reports stating that there are serious changes in the craniofacial dimensions following permanent dentition in young individuals and a continuing eruption of the teeth in the post-adolescent period, and despite this, successful implant applications have led researchers to make clinical applications related to implant application in young patients. (34)

With growth, the implants placed on both sides of the midpalatal suture are separated from each other. If placed implants intersect with the midpalatal suture, it limits transverse growth. An implant placed in the maxillary posterior region of a young patient may become embedded in the maxilla as a result of vertical growth and may even form an antrum in the maxilla.(39)

Recommendations for implant applications for healthy children: (40)

1. Implant applications should be postponed until the age of 18 for both girls and boys.

2. Adequate follow-up of patients undergoing implant treatment must be done.

3. In implant applications, the location of the implant to be applied, the age and gender of the patient, and the stage of skeletal growth and development of the patient are the most important factors.

4. It is recommended that growth and development must be completed for implant application, except for some patients with ectodermal dysplasia (ED).

According to Guckes et al., children's alveolar bone volume may not allow implants to be placed in ideal positions to provide adequate prosthetic support. Congenital anodontia is a rare condition and is usually seen together with inherited syndromes. Anodontia of the jawbone is most commonly seen in cases of ectodermal dysplasia (HED) of the hypohidrotic type. Anodontic patients should be tried to be treated with optimal treatment options in terms of both appearance and function throughout their growth and development periods. (41)

2.Conclusion

Most of the parents are negligent about the restoration and care of their primary teeth and they do not know much about this issue. This usually results in the extraction of decayed primary teeth with excessive crown destruction or insufficiency of restorative treatment. As a result, the number of children needing prosthetic restorations is increasing. At this stage, prosthetic rehabilitation, restoring masticatory function, maintaining and improving phonation; prevent the development of harmful oral habits; and it is necessary to minimize possible psychological disturbances. In addition, prosthetic rehabilitation of children with significant edentulism helps normalize the function of chewing and perioral muscles, while providing growth and development of basal bones. The treatment plan should be tailored to the individual. During the use of these prosthetic restorations, it is recommended that the patient maintain adequate oral hygiene and come to regular controls.

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CHAPTER II

SURFACE TOPOGRAPHY OF DENTAL IMPLANTS

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1. Machined surfaces

Machined surface implants were the first dental implants used in dentistry. Nowadays, it is used as a control group in the studies of surface topography. Machined implant surfaces are polish and there is no roughening on surfaces other than the grooves in the macro structure of the implant. Therefore, osseointegration process is longer than roughened surfaces (Jenny et al., 2016). Adding or subtracting roughening processes In order to increase the bone-implant contact; By adding or substracting roughening processes to turned (polished) implant surfaces, the expected time for osseointegration is reduced by increasing the surface area (Le Guéhennec, Soueidan, Layrolle, & Amouriq, 2007).

First dental implants had polished surfaces and today they are used in control groups for various surface researches. Having no roughening beside some macro grooves osseointegration times are very long for polished titanium surfaces (Jenny et al., 2016). To increase bone-implant interface, some increase or decrease of those grooves quantity were done to rough surfaces. Osseointegration process was critically reduced(Le Guéhennec et al., 2007).

In recent years, surface technology is focused on chemical as much as physical properities. Survival rates and healing periodes were significantly

improved by changing surface chemical characteristics and micro and nano topographies (Wennerberg & Albrektsson, 2009)1064 had to be disregarded because they did not accurately present in vivo data on bone response to surface topography. The remaining 120 papers were read and analysed, after removal of an additional 20 papers that mainly dealt with CaP-coated and Zr implants; 100 papers remained and formed the basis for this paper. The bone response to differently configurated surfaces was mainly evaluated by histomorphometry (bone-to-implant contact.

2. Blasted surfaces

Adding or substracting roughening processes are used to increase surface interface(Le Guéhennec et al., 2007). Substracting process works by extracting a layer from implant surface or by deforming the core material. Sand-blasting is used for mechanicly roughening process. This process is usually done with aluminum oxide(Al_2O_3), zirconium oxid (ZrO_2),titanium oxid(TiO_2) or ceramic particles.

In recent years sand-blasted surfaces were compared with rough surfaces. Because of increased surface space %BIC is found higher in sand-blasted surfaces. Aparicio et al. discovered that after sand-blasting with alumina paricles of 425-600 um, surface roughness (Sa) was found between 4.15-0.26 um (Aparicio, Padrós, & Gil, 2011). In another in vivo research Bachelli et al. sand-blasted implant surfaces with ZrO2 particles and found surface roughness (Sa) between 8.15- 0.78 um (Bacchelli et al., 2009). But it was also noted that increasing surface roughness would also increase bacteria adhesion and periimplantitis risk.

3. Acid-etched surfaces

Apart from mechanical abrasion with sand-blasting, acid and titanium composed alkali compounds were used for modifying surface topograpy, energy and wettability (Liu, Chu, & Ding, 2004)especially as hard tissue replacements as well as in cardiac and cardiovascular applications, because of their desirable properties, such as relatively low modulus, good fatigue strength, formability, machinability, corrosion resistance,

and biocompatibility. However, titanium and its alloys cannot meet all of the clinical requirements. Therefore, in order to improve the biological, chemical, and mechanical properties, surface modification is often performed. This article reviews the various surface modification technologies pertaining to titanium and titanium alloys including mechanical treatment, thermal spraying, sol-gel, chemical and electrochemical treatment, and ion implantation from the perspective of biomedical engineering. Recent work has shown that the wear resistance, corrosion resistance, and biological properties of titanium and titanium alloys can be improved selectively using the appropriate surface treatment techniques while the desirable bulk attributes of the materials are retained. The proper surface treatment expands the use of titanium and titanium alloys in the biomedical fields. Some of the recent applications are also discussed in this paper. © 2004 Elsevier B.V. All rights reserved.","author":[{"dropping-particle":"","family":"Liu","given":"Xuanyong","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Chu","given":"PaulK.","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Ding","given":"Chuanxian","non-dropping-particle":"","parse-names":false,"suffix":""}],"container-title":"Materials Science and Engineering R: Reports","id":"ITEM-1","issue":"3-4","issued":{"date-parts":[["2004"]]},"page":"49-121","title":"Surface modification of titanium, titanium alloys, and related materials for biomedical applications","type":"article-journal","volume":"47"},"uris":["http://www.mendeley.com/documents/?uuid=0cf6209c-c77b-4454-b242-d5e5d99442c6"]}],"mendeley":{"formattedCitation":"(Liu, Chu, & Ding, 2004. Acid is also used for removing debris from the surface. The most used chemical agents are hydochloric acid(HCl), hydrofloric acid (HF) and sulfuric acid (H_2SO_4).

Acid is not always used for removing debris from the surface. Surface rougness can also be modified by acid improving cell adhesion and bone formation. Strong acids as HF, HNO3, H2SO4, HCl are used seperatly or in combination which is named dual acid etching (Jemat, Ghazali, Razali, & Otsuka, 2015). Chou et al. conducted a research comparing machined surface with dual etching technique (HF and HCL/H_2SO_4)

It was found that acid etched surfaces had better reverse tork value and better osseointegration (Chou & Chang, 2002).

Chemical modification using hydrofluoric acid is a known method of biochemical fusion between implant surface and bone matrix. HF acid removes oxidation layer on the implant surface to create titanium flourid molecules($TiOF_2$) (Lee JH, 2017). It is well known that $TiOF_2$ has an affinity to calcium and phosphat ions and also catalyzes bone formation. In some researches flourid modified surfaces led to better bone healing periods (Scarano et al., 2020), (Nakagawa et al., 2001).

4. Blasted and acid-etched surfaces (Sand Blasted Large-Grit Acid Etched)

Combination of sand-blasting and acid-etching in combination is a commonly used method for surface modification in last years. The reason they work well together is because sand-blasting is optimal for mechanical modification of implant surface and acid removes blunt corners and increase protein adhesion for early healing period (Wennerberg & Albrektsson, 2009)1064 had to be disregarded because they did not accurately present in vivo data on bone response to surface topography. The remaining 120 papers were read and analysed, after removal of an additional 20 papers that mainly dealt with CaP-coated and Zr implants; 100 papers remained and formed the basis for this paper. The bone response to differently configurated surfaces was mainly evaluated by histomorphometry (bone-to-implant contact.

First in vivo research was conducted in 1991 by Buser et al. in this combination method. Electro-roughening was compared with sand-blasted and acid-etched surfaces and Ra values were found between 0.6-50 um. The higher %BIC value was found in sand-blasted and acid-etched surfaces. In another research Buser et al. compared rough surfaces , dual-etched surfaces, TPS and sand-blasted acid-etched surfaces for reverse tork values. Ra values were 0.15 um, 1.3 um, 3.1 um, 2 um. The highest reverse torque was in sand-blasted acid-etched surfaces altough the roughness value was not so high in comparison (Buser et al., 1999).

In another research roughened-acid-etched surfaces were compared with sand-blasted acid-etched surfaces. Surface roughness and osseointegration time were studied in sand-blasted group for reverse torque value. Measured in optic profilometer Ra values were in turn 0.90 um and 1.53 um In a study done in pigs, after 10 weeks of healing period reverse torque value was higher in sand-blasted acid-etched group (Szmukler-Moncler, Testori, & Bernard, 2004).

Sand-blasted acid-etched surfaces (SLA) were much more successful histologically and histomorphometricaly in osseointegration, bone-implant interface, reverse torque value (Wennerberg & Albrektsson, 2009)1064 had to be disregarded because they did not accurately present in vivo data on bone response to surface topography. The remaining 120 papers were read and analysed, after removal of an additional 20 papers that mainly dealt with CaP-coated and Zr implants; 100 papers remained and formed the basis for this paper. The bone response to differently configurated surfaces was mainly evaluated by histomorphometry (bone-to-implant contact. To further this success, physical and chemical surfaces should be modified by changing surface wettability and hidrophilia. Therefore SLA group is usually used as control groups (Abdel-Haq, Karabuda, Arisan, Mutlu, & Kürkçü, 2011)Kruskal-Wallis test and Spearman rank correlation test. Results: All implants reached to a strong primary stability with a mean 36.13 ± 2.47 and 35.47 ± 2.85N/cm ITV. In the surgical stage, RFA values for SLA and modSLA implants were found to be 72.27 ± 3.17 and 71.6 ± 2.87, respectively. After 3 weeks of healing, mean BIC% (80.64 ± 13.89% (Qamheya et al., 2018)chemical, and osseointegration characteristics of a sandblasted acid-etched surface (SLA group (Almas, 2019).

5. Coated surfaces

Adding process is coating titanium with other materials superficially or thoroughly. (Jemat et al., 2015). This approach aimed to replicate bone biochemical and nano structure. These coating materials include some agents, medicines, proteins and growth factors. Clinical purpose of this studies is replicating naturel osseointegration, improving periimplanter

soft tissue integration, and blocking bacterial invasion (Smeets et al., 2016) hydrophilicity, and outer coating of dental implants in order to enhance osseointegration in healthy as well as in compromised bone. In the first part, this paper discusses dental implants that have been successfully used for a number of years focusing on sandblasting, acid-etching, and hydrophilic surface textures. Hereafter, new techniques like Discrete Crystalline Deposition, laser ablation, and surface coatings with proteins, drugs, or growth factors are presented. Conclusion. Major advancements have been made in developing novel surfaces of dental implants. These innovations set the stage for rehabilitating patients with high success and predictable survival rates even in challenging conditions.","author":[{"dropping-particle":"","family":"Smeets","given":"Ralf","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Stadlinger","given":"Bernd","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Schwarz","given":"Frank","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Beck-Broichsitter","given":"Benedicta","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Jung","given":"Ole","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Precht","given":"Clarissa","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Kloss","given":"Frank","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Gröbe","given":"Alexander","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Heiland","given":"Max","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Ebker","given":"Tobias","non-dropping-particle":"","parse-names":false,"suffix":""}],"container-title":"BioMed Research International","id":"ITEM-1","issued":{"date-parts":[["2016"]]},"publisher":"Hindawi Publishing Corporation","title":"Impact of Dental Implant Surface Modifications on Osseointegration","type":"article-journal","volume":"2016"},"uris":["http://www.mendeley.com/documents/?uuid=2c86a98c-f897-4f8c-b251-60a4357f5118"]}],"mendeley":{"formattedCitation":"(Smeets et al., 2016.

Coating techniques are titanium plasma spray (TPS), hydroxyapatite(HA), alumina, biomimetic calsium phosphate (CaP). Impregnation techniques are ion deposition, oxidation, ion implantation, sputter scattering, thermal evoperation (Albrektsson & Wennerberg, 2019)bone tissue is formed around titanium implants to shield them from the tissues. Oral implant surfaces may be characterized by microroughness and nanoroughness, by surface chemical composition and by physical and mechanical parameters. An isotropic, moderately rough implant surface such as seen on the TiUnite device has displayed improved clinical results compared to previously used minimally rough or rough surfaces. However, there is a lack of clinical evidence supporting any particular type of nanoroughness pattern that, at best, is documented with results from animal studies. It is possible, but as yet unproven, that clinical results may be supported by a certain chemical composition of the implant surface. The same can be said with respect to hydrophilicity of implant surfaces; positive animal data may suggest some promise, but there is a lack of clinical evidence that hydrophilic implants result in improved clinical outcome of more hydrophobic surfaces. With respect to mechanical properties, it seems obvious that those must be encompassing the loading of oral implants, but we need more research on the mechanically ideal implant surface from a clinical aspect.","author":[{"dropping-particle":"","family":"Albrektsson","given":"Tomas","non-dropping-particle":"","parse-names":false,"suffix":""},{"dropping-particle":"","family":"Wennerberg","given":"Ann","non-dropping-particle":"","parse-names":false,"suffix":""}],"container-title":"Clinical Implant Dentistry and Related Research","id":"ITEM-1","issue":"S1","issued":{"date-parts":[["2019"]]},"page":"4-7","title":"On osseointegration in relation to implant surfaces","type":"article-journal","volume":"21"},"uris":["http://www.mendeley.com/documents/?uuid=7f9a5b84-0c61-4d15-b4db-0e2b7a9b298c"]}],"mendeley":{"formattedCitation":"(Albrektsson & Wennerberg, 2019.

For a long time, titanium plasma spray (TPS) was used to acquire 40-50 um coating on implant surface with CaP. The biggest concern was the seperation of the whole coating and consisting a space between coating-implant surface. CaP coating is widely used in othopedic

surgery (Junker, Dimakis, Thoneick, & Jansen, 2009)human reports and studies presenting bone-to-implant contact percentage or data regarding mechanical testing. Results: For recently developed and marketed oral implants, 29 publications and for experimental surface alterations 51 publications fulfilled the inclusion criteria for this review. Conclusions: As demonstrated in the available literature dealing with recently developed and marketed oral implants, surface-roughening procedures also affect the surface chemical composition of oral implants. There is sufficient proof that surface roughening induces a safe and predictable implant-to-bone response, but it is not clear whether this effect is due to the surface roughness or to the related change in the surface composition. The review of the experimental surface alterations revealed that thin calcium phosphate (CaP.

HA coating is very similar to calcium and phosphor reservuar. In 2013 Esposito M. et al. defined multiphosphonic acidic molecules as hydroxyapatite crystals (SurfLink, Nano Bridging Molecules, Gland, Sweden). In a conducted study with 32 patient through one year implant survival rate was 100% and marginal bone level loss was only 0.27 mm (Esposito M., 2013).

6. Oxided surfaces

All titanium implants have natural oxide layer. This layer was made in suitable heat and electrolite enviroment. When galvanic current is used for creating the oxide layer, implant surface would thicken from 5nm to 1 mm. (Wennerberg & Albrektsson, 2009)1064 had to be disregarded because they did not accurately present in vivo data on bone response to surface topography. The remaining 120 papers were read and analysed, after removal of an additional 20 papers that mainly dealt with CaP-coated and Zr implants; 100 papers remained and formed the basis for this paper. The bone response to differently configurated surfaces was mainly evaluated by histomorphometry (bone-to-implant contact. Qamheya et al. studied HF modification in thermal oxidation and oxidation on sand-blasted surfaces. Study consisted in vitro and in vivo parts. In vivo part conducted by using implants in sheep iliac bones. ITV, RTV, BIC%, RFA

values were measured for early and late period of healing. They found no difference between HF added group and SLA group (Qamheya et al., 2018)chemical, and osseointegration characteristics of a sandblasted acid-etched surface (SLA group.

In 2006 Choi et al. found positive corelation between thickness of oxidied implant in different voltages and tissue integration. SEM and optic profilometer were used for surface topography. Yüzey topografisinin karakterizasyonu için SEM ve optik profilometre kullanılmıştır. In implants oxidied with 500V, Ra value was found 5.2 um, It was 3.8 um for 550V and 0.8 um for 300V Reverse torque value and BIC% were found much higher in 500-550V group than 300-400V (Choi et al., 2006).

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CHAPTER III

INFRAOCCLUSION IN PRIMARY TEETH AND CURRENT TREATMENT APPROACHES

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1.Introduction

Infraocclusion is a clinical term that describes teeth that lie below the occlusal plane in the dental arch (1). Various terms are used in the literature for this condition, including secondary retention, reinclusion, impaction, reimpaction, and submerged tooth. In recent years, the usage of the term infraocclusion is preferred more frequently, and it is suggested that this situation is caused by the good expression of the clinical appearance (2). Infraoccluded teeth are often accompanied by ankylosis. The mechanism of formation of ankylosis is not fully elucidated. It is thought that ankylosis, which causes fusion between the cementum and the alveolar bone while the adjacent teeth continue to erupt, prevents the eruption of the tooth, and infraocclusion occurs as a result of the tooth being fixed (3). Since the alveolar bone cannot achieve its normal development and growth at the site of ankylosis, the occlusal level of these teeth remains lower than the adjacent teeth (4).

In the literature, classifications are made for infraocclusion detected using various methods such as the visual method, panoramic and cephalometric radiographs, study models, and intraoral photographs (5).

Although infraocclusion has been classified in various ways, the most preferred classification is by Brearley and McKibben (6). In this classification, infraocclusion is evaluated as mild if the occlusal level is 1 mm below the occlusal level of the adjacent tooth, moderate if the occlusal plane is on the same level as the contact point of the adjacent tooth, and severe if the occlusal level is below the contact point of the adjacent teeth(7).

2.Etiology

Although the etiology of infraocclusion is not exactly known, ankylosis is thought to be the main etiological factor (8). Apart from ankylosis, other etiological factors causing infraocclusion are stated as a genetic effect, the absence of a permanent successor, the local failure of alveolar bone growth, periodontal ligament injury, and local metabolism disorders that cause the periodontal ligament to be affected (9).

There are familial studies in the literature showing that genetic factors have an effect on the etiology of infraocclusion (10,11). In the study by Dewhurst et al., in which they investigated the presence of familial transmission in the etiology of infraocclusion in two different monozygotic twins aged 9 and 12, it was stated that the affected teeth and infraocclusion severity were similar between the twins (12). Via et al. reported the presence of infraocclusion in 30 (1.3%) of 2342 children in their study. Moreover, the prevalence of infraocclusion among siblings was 44% in 18 of the 30 children with a sibling who had infraocclusion in the same study(11).

Having one infraoccluded tooth increases the incidence of infraocclusion in other teeth. This suggests the effect of genetic factors in infraocclusion (8,13).

In a study of 100 people in which they investigated the relationship between infraocclusion and other dental anomalies in 1998, Bacetti reported that permanent tooth germ deficiency was the highest compared

to other anomalies, and its incidence with infraocclusion was 14%. In the same study, microdontia of the maxillary lateral incisors and palatal displacement of the maxillary canines were associated with infraocclusion, while a rate of 13% was reported for both. Moreover, infraocclusion cases were found to be associated with anomalies such as enamel hypoplasia and the ectopic eruption of permanent first molars (14).

3.Prevalence

While the prevalence of infraocclusion in primary teeth varies between 1.3% and 38.5% in studies (15), it differs according to countries. This rate was reported as 5.8% in Italy, 24.8% in Israel, 9.2% in the US, 8.9% in Switzerland, and 21.8% in Spain (10,14,16,17). The variability of the prevalence of infraocclusion between populations is explained by the difference in the age groups of children and the diagnostic criteria used in these studies (9).

In epidemiological studies investigating infraoccluded teeth, there is no consensus about the most frequently affected teeth (13). While most studies report the primary second molars as the teeth with the highest rates of infraocclusion (2,18), on the contrary, there are studies showing that primary first molar teeth are more frequently in infraocclusion (7,16). In the epidemiological study conducted by Kural, it was reported that the number of primary first molars with infraocclusion increased from the age of 3, and the number of primary second molars with infraocclusion increased from the age of 5 and reached a maximum in children aged 8-9 years. This situation was associated with the absence of teeth in the mouth as a result of the eruption of premolar teeth resorbing the roots of primary teeth (16). Ersin et al. reported 24 (42.9%) primary first molars and 32 (57.1%) primary second molars out of 56 infraoccluded teeth they detected in 21 patients with a mean age of 9.4 years. They associated this situation with the earlier ankylosis of the mandibular primary first molar, its mild infraocclusion, and its usually timely loss. On the other hand, they stated that the mandibular primary second molars showed severe infraocclusion, and this prevented the eruption of permanent teeth (2).

4.Clinical And Radiographic Diagnosis

Infraoccluded teeth can usually be diagnosed during a clinical examination. The first striking finding during a clinical examination is the positioning of the affected tooth on a more gingival level than the adjacent teeth (19). Additionally, the other clinical findings are the tipping of the adjacent teeth towards the tooth in infraocclusion and the overeruption of the opposing teeth to restore occlusal contact (9).

The case that the sound heard in the percussion test applied to the infraoccluded tooth is characterized by a sharper and harsher sound compared to the adjacent tooth is an indicator of ankyloses (20).However, percussion tests used in the detection of ankylosis can sometimes provide misleading results (13). Anderson et al. reported that for percussion tests to be reliable, at least 20% of the root surface should be ankylosed (21). Other studies have found that 10% or more of the root surface must be ankylosed in order for dental immobilization to be observed clinically(22,23).

The absence of mobility in an infraoccluded tooth despite root resorption in the radiographic examination of the tooth is a finding of ankylosis that should be considered. The occurrence of ankylosis in a small area complicates the diagnosis with conventional two-dimensional radiographs. As ankylosis progresses, the radiopacity of the roots decreases, preventing them from being distinguished from the surrounding bone (13). Angular bone defects observed in the interproximal bone between the infraoccluded tooth and the adjacent teeth are among other diagnostic features of ankylosis that can be seen radiographically (24). The continuing eruption of the adjacent teeth leads to an increase in the severity of the defect (25).

In infraocclusion cases, some changes are seen in the dental arch, adjacent teeth, or opposing teeth. In their study examining the effects of infraocclusion on the dental arch, Becker et al. detected changes in the arrangement of the transeptal fibers that connect adjacent teeth in the alveolar bone and run parallel to the occlusal plane. They stated that tension occurs in the transeptal fibers between the infraoccluded

teeth and adjacent teeth, and this creates a center of rotation and causes the adjacent teeth to tip over (26). A reduction in the length of the dental arch as a result of the tipping of the adjacent teeth into the space is encountered in 28-43% of infraocclusion cases and most commonly in the infraocclusion of the mandibular second primary molars (13).

In the case of the unilateral infraocclusion of primary teeth, the midline of the tooth usually tends to shift towards the affected arch side, and a midline mismatch occurs. This is because the mesiodistal dimension of the permanent premolar is smaller than the primary tooth (27,28).

Severe infraocclusion may lead to the incomplete vertical development of the alveolar bone, lack of normal mesial drift, non-response to orthodontic forces, the eruption of the affected primary and permanent teeth, the tipping of the adjacent teeth, lateral open bite, and more severe crossbite (1,13). Kurol and Thilander, on the other hand, stated that the vertical bone loss observed in primary teeth with infraocclusion improved with the eruption of permanent teeth, and this had no long-term effect on occlusion (4).

5.Current Treatment Approaches

The early detection of infraocclusion plays an important role in deciding on the treatment plan and minimizing problems that may occur in the future (25). Things to be evaluated before treatment planning in individuals with infraoccluded primary teeth are as follows:

- Presence or absence of permanent tooth germ
- Infraocclusion severity
- Ankylosis onset time
- Progression rate of infraocclusion (9).

The treatment approach is divided into two permanent teeth and non-permanent teeth (1).

5.1 *Treatment Of Infraoccluded Primary Molars With Successor*

The main goal in the treatment of infraoccluded primary teeth with permanent tooth germ is the normal eruption of the underlying permanent tooth (29,30). It has been reported that the roots of infraoccluded primary teeth with permanent tooth germ are usually resorbed, and the eruption of permanent teeth occurs without any problems. Studies have shown that a six-month delay in the exfoliation of the infraoccluded tooth relative to the contralateral tooth is acceptable (13,19).

It is the onset time of ankylosis that paves the way for the development of infraocclusion that should be determined first before planning treatment (13). The occlusal level of teeth with late ankylosis is slightly lower than the adjacent teeth. In this case, the normal exfoliation processes of teeth should be followed until they are completed (25). Prefabricated stainless metal crowns or composites can be used on the teeth to prevent the elongation of the opposing teeth and the tipping of the adjacent teeth. Additionally, the restoration can protect the approximal surfaces and the occlusal vertical dimension (30). Although the rate of resorption is slow in ankylosed teeth, in the case of the rapid progression of infraocclusion, the extraction of the tooth and subsequent placement of space maintenance should be considered (1). Moreover, the decision to extract may be indicated in cases such as the ectopic eruption of permanent teeth, the failure of root resorption, the delayed eruption of primary teeth by more than six months, and the significant overturning of the adjacent teeth that cause occlusal incompatibilities (19).

A late diagnosis of cases with early-onset ankylosis may cause the adjacent teeth to tip towards the infraoccluded teeth and the overeruption of the opposing teeth. Treatment planning includes the correction of occlusal problems and space losses that occur following the extraction of the infraoccluded primary tooth with orthodontic interventions (13).

5.2 *Treatment Of Infraoccluded Primary Molars Without Successor*

In infraoccluded teeth that do not have permanent tooth germ, the patient's malocclusion is evaluated, and the progression rate of the infraocclusion, age at diagnosis, and root resorption play a role in the decision to extract the tooth or keep it in the mouth (19).

The presence of ankylosis, which predisposes teeth to the development of infraocclusion, and the absence of permanent tooth germ are common conditions (25). If the root resorption rate progresses slowly in the teeth where ankylosis occurs in the late period, the primary teeth can be left in the mouth and act as a natural form of space maintenance (19). Infraoccluded teeth can be restored with composite, stainless steel crowns, porcelain, and gold onlays to reconstruct the occlusal and approximal surfaces (25). The aim of the treatment is to prevent the resorption of the existing alveolar bone and delay the patient's need for prosthetics (23).

A late diagnosis of early ankylosis increases the risk of occlusal problems (25). Orthodontic treatment is inevitable for the correction of adjacent teeth that are tipped towards the infraoccluded teeth, after which restorative treatments can be applied. Studies have also suggested that proper arch alignment should be provided with orthodontic treatments prior to tooth extraction to facilitate extraction in cases where extraction is required. Therefore, early diagnosis is important to prevent these risks. In infraoccluded primary teeth, the tooth can stay in the mouth for a long time depending on the rate of root resorption and if the progression of infraocclusion is slow (1). Considering the ongoing root resorption in infraoccluded teeth, restorative procedures performed on these teeth are long-term temporary solutions. In cases where root resorption occurs rapidly, the recommended treatment method is the observation and follow-up of the function provided by the restoration during the eruption process of primary teeth (31). In the case of alveolar bone loss in teeth, it is recommended to review the treatment plan and extract the affected tooth(19). If an ankylosed tooth is decided to be extracted, extraction should be performed very carefully to prevent complications such as bone defects and mental nerve damage (27). After the extraction

of the infraoccluded tooth, multidisciplinary clinical approaches are required. These approaches may include closing the extraction space with orthodontic treatment, restoring it with implants or prosthetic applications, or applying space maintenance while preserving the space (1).

When all primary molar teeth with infraocclusion are examined, severe infraocclusion has a rate of 2.5-8.3% and is not encountered very often. Nevertheless, it was observed that the absence of permanent tooth germ underneath accelerates the progression of infraocclusion (13). Although it is aimed to keep infraoccluded teeth in the mouth, in the case of progressive infraocclusion development in the follow-up of cases, the early extraction of the tooth becomes a requirement even though the root resorption rate is slow (25).

Luxation, another treatment approach, is a treatment discussed in the literature (1). This method involves moving the tooth after applying enough force to break the connection between the ankylosed tooth and the alveolar bone so that the periapical blood supply is not disrupted. It is aimed to regain the physiological eruption of the tooth after the treatment(32). Although few successful cases have been reported in the literature, the usage of the technique has become controversial as it may cause pulp necrosis. Therefore, it is used very infrequently (33).

6.Conclusion

The early diagnosis and treatment of infraocclusion detected in children in the primary and mixed dentition periods is important in terms of increasing the chance of success in its treatment. If an infraoccluded tooth is detected, it should be noted that other primary teeth are also at a high risk of infraocclusion. Infraocclusion relative to the adjacent teeth should be recorded to monitor the rate and severity of infraocclusion. Radiographic techniques should be used to detect permanent tooth germs in cases of infraocclusion. In order to reduce the risk of caries in adjacent teeth associated with infraocclusion, oral hygiene education should be emphasized, and protective practices should be performed if necessary. Thus, accurate diagnosis and

treatment will help plan the clinical options with the best prognosis by reducing the need for multidisciplinary treatment approaches such as orthodontic, surgical and prosthetic interventions that may be needed in the future.

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CHAPTER IV

BIOCOMPATIBILITY AND EVALUATION METHODS IN DENTISTRY

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1.Introduction

Biocompatibility is used to express the biological performance of a material placed in living tissue in contact with the organism. When the material is placed in living tissue, some biological tissue reactions may occur as a result of its interaction with the soft or hard tissues of the body. The degree of this interaction depends on the patient, the strength, function and the conditions of the material. Biocompatibility is a dynamic process that can change depending on time and conditions. Changes may occur in the body due to disease or aging during time. However, changes may occur also in the material based on corrosion, fatigue, load, and occlusion or nutrition. Thus, the initial biological response may change over time (1).

The term "biocompatibility" is a very important concept in both medicine and dentistry. Biocompatibility testing is an essential necessity for materials in both fields. Biocompatibility in dentistry is a key functional requirement in terms of patient safety, dentists' safety, regulatory compliance and legality. While the main materials associated with adverse effects in dentistry are polymer-based materials, natural rubber latex, alloys used in prostheses and orthodontics, and amalgam, materials such as eugenol have also been reported to have the ability to create an adverse reaction (2). A material that is considered biologically

compatible should not damage the pulp and soft tissues. However, it should not have carcinogenic potential, should not contain agents that induce allergic responses and toxic substances (3).

Today, standards for biocompatibility tests have been determined by The International Organization for Standardization (ISO) organizations. In general, ISO 10993 series is applicable for medical devices and ISO 7405 is particularly applicable for medical devices used in dentistry (4). In these standards, the preparation of the samples and the tests (cytotoxicity, genotoxicity, carcinogenicity, implantation, irritation, sensitivity and systemic toxicity) to be applied to these samples are determined. In addition, specific standards have been established for preclinical and clinical studies as well as for the analysis and assessment of the risk of producing a biological reaction (5,6). The simplest way of classifying biocompatibility methods is in vitro (primary) testing, in vivo testing on animal models(secondary testing), and clinical trials in humans as usage tests (1,7).

2. Biocompatibility

Biocompatibility is defined as the ability of a biomaterial to achieve its expected property without any unfavorable reaction in the tissue used (7,8,9). The absence of tissue reactions such as systemic and local toxicity, allergic, mutagenic and carcinogenic effects are expected when the material comes into with living tissues as far as biocompatibility is concerned. The biocompatibility of a material depends on the type and the region to which it is applied and its function (10).

Biological compatibility is a property of a material that must continue as long as it remains in the tissue. When material is introduced into a living organism, interactions between the complicated biological system of the host and material occur, resulting in a biological reaction. The body's response to a material is dynamic, as the body can change due to aging or disease, the material can change due to fatigue or corrosion, or the loads applied to the material can change due to alterations in diet or congestion. Therefore, biocompatibility is also a dynamic, ongoing process, and not static (8,11,12).

Any of these variations can change the conditions of an initially favorable and expected biological reaction. In order to be biologically compatible, the material, the function added from the material and the host must be in harmony (8,11,12). While a biomaterial meet all criteria in a particular treatment to show biocompatible property, if it fails in another application and causes an undesirable tissue reaction, then it should be defined as non-biocompatible (9).

Material surface properties such as surface topography (texture, roughness), surface chemistry, wettability or surface free energy are associated with biocompatibility. The surface chemistry of a material affects the affect protein adsorption, adhesion, and cell proliferation and host response. When a biomaterial get in touch with body tissues, proteins from tissue fluids will be adsorbed on the surface of material. This action is specified by the compound of the tissue fluid and the material surface properties mentioned above. Protein adsorption can alter the material surface properties and after exposing the material surface to serum, the surface angle of hydrophilic surfaces may increase and the angles of hydrophobic surfaces may decrease. However, it has been noted that the in vivo foreign body reaction is independent of surface chemistry, and the same response can occur in vivo from all materials based on ceramic, polymeric or metallic, and exhibiting surface properties ranging from hydrophilic to hydrophobic or hard to soft. This has been reported to be due to non-specific protein adsorption (4,13).

In dentistry, in addition to features such as aesthetics, durability and ease of use, biocompatibility should also be considered in terms of the selection of materials. Dental materials are in direct contact with various tissues such as gingiva, tongue, lip and cheek apart from enamel, dentin, pulp and periodontium. In the biological environment; dental material undergoes some changes by different mechanisms such as substance accumulation, deterioration, chemical modification or corrosion. Various components released by dissolution or corrosion of the material can cause local or systemic toxicity in tissues adjacent to the applied site. High concentrations of these components, which can cause damage to the cell structure, can affect various organ functions in different time periods and cause the synthesis of some proteins or inflammatory reactions (1).

According to Shahi et al., a large number of dental materials with the potential to be toxic to humans were also identified, such as restorative and prosthetic materials, intracanal drugs, various implants, linings, and irrigants (14). Systemic reactions take place in tissues and organs distant from the exposure site and were originally discussed for amalgam in the past, but are now also discussed about resin-based composites due to their bisphenol-A content and possible health effects (4). Absorption of organic materials from the unpolymerized material and unbound resin components can infiltrate to the saliva in the initial stage after polymerization, and it has been stated that this situation predisposes both patients and dentists to allergic reactions (3,15). Unreacted monomers separated from resin-based restorative materials have been accepted as a cause of hypersensitivity, systemic and local reactions. Systemic reactions are also generally defined as allergic skin reactions. This showed that it is very important to maximize the degree of conversion to achieve more biocompatible restorative material. It has also been reported that small amounts of formaldehyde can be released from dental polymers as a result of disruption of the oxygen inhibition layer or oxidation of unreacted methacrylate groups. Although the concentrations were below toxic levels, the formaldehyde amount was still detectable after 115 days (3,8).

Although there is a wide variety of restorative biomaterials on the dental market, there are very few that fulfill all the requirements for use as a biomaterial. All materials in current use are considered acceptable for their biocompatibility with local tissues when properly used and placed. The use of a non-biocompatible material as a dental element may result in an increase in the inflammatory response concluding cell death and tissue necrosis. Therefore; chlorhexidine, sodium hypochlorite, ethylene diaminetetraacetic acid -EDTA, casting alloys and impression materials should be considered for potential toxicity such as amalgam and resin composites (3).

The sensitivity given to biocompatible materials for use in dentistry makes biocompatibility testing a necessity to screen compounds before clinical use and to characterize the potential deleterious effects of a material on oral tissues (6).

3. Biocompatibility evaluation methods

Basic principle of biocompatibility tests is to determine whether there is a change in the structure of the biological system with the effect of the material and to reveal whether this effect is reversible. Various methods have been developed and used successfully in order to determine the biological performance of dental materials up to date (1). The application of tests is based first on shorter, in vitro or less expensive screening tests and then on more extensive and time-consuming tests involving the use of animals. If a material is observed to have a biocompatibility complication based on first studies, it may be possible that certain applications will not be considered for further testing (16).

There are national standards for biocompatibility test methods established by The International Organization for Standardization (ISO). ISO 10993-International standards cover medical devices including dental materials, while ISO 7405 specifically covers dental materials (6,17). ISO 7405 has the title preclinical assessment of biocompatibility of medical devices used in dentistry. This ISO document was prepared in conjunction with the World Dental Federation. It deals with preclinical evaluation of materials used in dentistry and supplements ISO 10993. ISO 10993 is a combination and harmonization of International and National Standards and guidelines. The primary objective stated in ISO 10993 is the protection of people. This document is general guidance for the selection of tests prescribed for the evaluation of biological responses related to medical or dental equipment and material safety (6). Murray et al. summarized the recommended standard practices for the biological evaluation of dental materials as follows. Firstly, it is the dental material manufacturer's responsibility to select appropriate tests to the known and assumed toxicity profile of the material or its components and the intended use of the material. The manufacturer may prefer one of three cytotoxicity tests due to experience, cost, or other reason. New materials should first be evaluated using cytotoxicity and secondary tissue screening tests, followed by extensive animal testing and clinical trials. The test result should always be evaluated taking into account the manufacturer's declared use for the material (6).

The biocompability of a material can be tested directly or using an extract. In the first situation, tissue will be directly exposed to the material and in the second, the material will be stored in a liquid at a specific temperature for a certain period of time under certain conditions. This loaded liquid is called as extract and will be used for further tests. The ISO 10993-5 standard also specifies the extraction temperature and time. Four different standard conditions are proposed: 24 hours at 37°C, 72 hours at 50°C, 24 hours at 70°C and 1 hour at 121°C. Considering the different recommended extraction temperatures, 37°C is a strictly physiological temperature and matches the serum extraction medium and cell culture (9,18).

The test methodologies are identified as in vitro tests, animal tests and usage tests (7,8). Newly developed materials must undergo three steps in the order given in humans, from in vitro to animal testing and from preclinical testing to clinical testing (3).

3.1. In vitro tests

In vitro tests are performed under laboratory conditions, outside of living organisms, using cell cultures or their components. These tests do not include many complicated interactions that create the biological response in the body. These tests include the use of physical barriers such as enamel and/or dentin discs, which are strategies to increase proximity to clinical practice (7,8,12,19).

The purpose of in vitro testing is to simulate biological reactions when materials are placed in body tissue. The number of cells exposed to the material, their metabolic function, growth rate, or other cellular functions are the parameters that determine the effect of the material (12, 15). These tests are practicle for investigating new products compared to time-consuming and expensive animal testing (15). In vitro testing has numerous advantages over in vivo testing, such as being faster, relatively simple, and more cost-effective, experimentally controllable, more reproducible results, and no ethical or legal issues (7,12,15). The disadvantages of in vitro testing are that the material is open to discussion regarding its final usage in a biological system and inability to predict the exact tissue response of the material (7).

Cytotoxicity tests are one of the most widely used in vitro tests. Cytotoxicity tests are used to determine the potential harmful effects of dental materials and the compounds released from them on oral tissues in the laboratory environment. In vitro survival and reproduction of parts taken from different tissues of different living things are evaluated (1). Regarding cytotoxicity tests, methods that determine cell viability by analyzing the cells' mitochondrial activity exposed to materials and/or isolated components are the most commonly used methods. Other tests that are assessing the processing of cell death and whether it is owing to apoptosis or necrosis may contribute to an understanding of the intensity of the toxic effects of dental materials, as those that induce apoptosis are considered to be less aggressive compared to materials that induce cell death by necrosis (19). In vitro cytotoxicity assays measure cell viability, metabolic activity or coating efficiency (7). Among the test methods recommended for in vitro cytotoxicity screening; direct cell culture and culture extract testing, barrier screening tests, agar diffusion test, filter diffusion test, dentin barrier test, and Ames test are included (6,17).

3.1.1. Cell culture test

The first step in evaluating a new material is to place the material or its extract in a suitable cell culture in the laboratory and observe the changes in the cells for a few hours to a few days. Cells are placed in a multi-walled culture array or a culture dish and allowed to grow and multiply under special conditions until a uniform cell layer is formed at the bottom of the dish. Human epithelial cells and persistent mouse fibroblasts are routinely used cell lines. The sample of the material or the liquid extract of the material is added to the culture and the containers are allowed to remain in the incubator for up to 3 days. Next, the cultures are subjected to examination with microscope, alterations in cells or cell death are saved and scored to produce a biocompatibility score (16,17).

One of the most important disadvantages of this method is the inability to distinguish between live and dead cells in the absence of

any morphological changes. The number of viable cells can be highly subjective and any artifact complicates the issue further. Other practical complications of cell culture are that cell and colony counts take a long time and are sensitive to minor changes in morphology (6,17).

3.1.2. Barrier screening tests

Barrier testing methods are used to imitate the dentin barrier, testing a material's ability to dissolve dentin and penetrate from dentinal tubules, thus allowing an estimation of material toxicity relavent to diffusion capacity (6). In the barrier test method, various substances that mimic dentin and allow diffusion of test material components such as dentin are used as barriers (10). In this technique, a dentin disc barrier is placed between the material being tested and the cell culture. If the material penetrates the disc, a positive cytotoxic response occurs (17).

3.1.3. Agar diffusion test

This test, also known as agar plating or tissue culture plating, is probably the longest lasting cytotoxicity barrier test method and uses an agar sheet placed over a monoculture cell sheet and the dye used in this study is generally red vital dye (6,17).

It is a test method that evaluates cell activity according to the amount of accumulation in the lysosomes, depending on the permeability of the neutral red dye in the cell membrane as a result of the 24-hour incubation period. The presence of leachable toxicant is manifested by the loss of dye within the cells as the cells are lysed, provided the concentration of the diffused substance and their cytotoxicity are high enough (6, 10). Although it is a simple and inexpensive method, this test is less sensitive because only one side of sample gets in touch with the agar layer that separates the cells and sample. Test material or components that cannot be dissolved or diffused in agar cannot have any effect on cells. In addition, toxic substances should be freely dispersible in the agar and should not react with the agar (9,10).

3.1.4. Filter diffusion test

The Millipore filter method uses cellulose acetate and changes the oral contact state by growing primary cells on one side of the filter and placing the test material in contact with the filter's opposite surface.

In order for the material to have a cytotoxic effect on the cell, it must diffuse through the 0.45 μm filter (6,10,17). The appearance of test filters in cell contact areas of material is recorded according to a scoring system (ISO 7405) to classify the cytotoxic response demonstrated to a test material (6). The only limitation of the test is the requirement to maintain good contact between the sample and the filter. And it must be shown that the released components do not bind to the filter (9).

3.1.5. Dentin barrier test

Unlike other tests, this method can more mimic the oral environment and uses human dentin tissue or bovine dentin discs as a barrier between the monomers released from the dental material and the target cell (1,10). This system, also called the model cavity method, includes measuring the molecule's size and concentration, the diameter, length and density of dentinal tubules, the effect of temperature, and the cytotoxic effects on pulp cells (6,17). Due to the importance of the principle of generalization of in vitro cytotoxicity findings to human in vivo clinical conditions, it is recommended that this technique be preferred over others (ISO 7405) (6).

3.1.6. Ames test

Ames test was developed in the 1970 by Prof. Bruce Ames and the most commonly used method examining the effect of the applied material on the cell DNA. In this test, in which genetically modified bacteria (Salmonella typhimurium) that do not multiply in a special agar culture and do not form colonies in environments that do not contain histidine, mutational differences in the cell are observed. In this test system, mutagenicity is considered as a result of bacterial growth in the presence

of any mutagenic substance, inability of bacteria to grow and form colonies on histidine-deficient culture agar (1,17).

3.2. Animal tests

In animal testing, the material is implanted into an animal's body, usually mammals such as mouse, rat, monkey, cat, dog, rabbit; subcutaneously, intramuscularly or in the bone of experimental animals. After different implantation periods of several materials into the tissues, the tissues are examined macroscopically and microscopically. In the mucous membrane irritation test, the inflammation caused by the material to be tested on the mucosa or abraded skin is evaluated. Then, the histological evaluation of the test material implanted in the experimental animal bone is performed. The use of a mammalian organism in these tests results in many complex interactions between the biological environment and the material (7,10,12,15). However, these studies may ensure more actual scientific data than in vitro and allow assessment of crucial parameters such as material interaction with blood, bone regeneration and chronic inflammatory responses (19). The ISO 7405 guidelines classify the test duration as short term (7 ± 2 days) and long term (70 ± 5 days) (17).

Animal testing allows for more complex reactions and comprehensive biological response to be observed between the recipient and the material being tested. However, these tests are expensive, time consuming, ethically controversial and also controlling variables is difficult. And the species, gender and age of the animal used in the studies may influence test results (7,8,12,15,19).

Furthermore, the explanation of the observed reactions is complicated because several events occur simultaneously, such as trauma and possible local infections from the application of test materials in contact with the animal's tissues. Another challenge found with using animals for research is the identification of adequate control groups that support the interpretation of results with the least possible biases (19).

In irritation and sensitization tests; the severity of the reaction that will occur after the application of the material thought to be an allergen on the oral mucosa, eyes or skin is determined. In dentistry, especially

when it is desired to evaluate the non-specific local toxic effects of implant materials, the test material is implanted directly or in teflon, silicone or polyethylene tubes into the muscle or bone tissues of laboratory animals such as rats and rabbits, or under the skin. These tissues are examined macroscopically and microscopically for a week - several months. The most important advantage of this method is that it does not need to use a large number of animals (1).

3.3. Usage tests

Usage tests are actually clinical trials of a material and accepted as the gold standard and provide definitive results for investigating the material's biocompatibility. The advantage of the usage tests is that the results are clinically relevant and comprehensive. The difficulty to control and interpret, prolonged duration, their high costs**,** and legal and ethical issues are major disadvantages of these tests (7,8,12).

In clinical studies on dental materials; biological parameters such as pulpal and periodontal reactions (acute and chronic inflammations), gingival and oral mucosal irritations are evaluated. It is also possible to include intraosseous implantation tests in this group. These tests use healthy volunteer humans or other primates. Among the primates, mice, rabbits, some dog and monkey species are used the most (1).

Pulp irritation tests are performed by applying the test material to class V cavities opened in human teeth to be extracted for orthodontic purposes or in intact, caries-free teeth of monkeys or other suitable animals. The test material is kept on the teeth for 1 week to several months and the teeth are extracted. Then, these teeth are prepared for histological examination and acute or chronic inflammation and odontoblast reactions occurring in the pulp are evaluated (10). In the gingiva mucosal test, test materials are applied to the cavities extending under the gingiva, and reactions occurring between 7 and 30 days are detected. Endodontic material usage and periapical tissue damage tests are performed on experimental animals. In this method, the test materials are placed inside the tooth root canals prepared for root canal treatment and then histological evaluation is made (10).

At the last stage, the materials are tested on volunteers who have been informed with a consent form. Usage tests, which are difficult to control and evaluate, are quite expensive and time consuming (1).

Retrospective, cross-sectional, and prospective studies are different types of clinical trials. Prospective or longitudinal studies are more representative in terms of determining the biological performance of the material, and there are strategies that can be used to improve their reliability, such as randomization, blinding, placebo groups, and strategies to minimize bias. However, such studies are expensive, take a long time to complete, and may be affected by operator skill, which may be well above or below the clinical average (19). The United States Public Health Service (USPHS) or Ryge criteria are systems by which clinical testing of restorative materials is evaluated prior to commercial sale. This criterion requires placement of test materials in patients and patient informed consent after institutional review board approval. Restorations should be followed for at least one year and a 90% success rate should be achieved (6).

Conclusion

Evaluation of biocompatibility is a complicated process that may involve various complex biological tests, physical property evaluations such as corrosion, and risk-benefit analysis. The most accurate and efficient way to test the biocompatibility of materials is to use a combination of in vitro, animal and usage testing. The tests contribute to the understanding of the biological effects that the material may cause in tissue, but cannot define with 100% certainty about the biocompatibility of the material. Therefore it is crucial to specify materials that pose a potential risk of unfavorable reactions in patients when materials are available on the market.

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CHAPTER V

NONODONTOGENIC TOOTHACHE

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1. Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" by the International Association for the Study of Pain (IASP) (Merskey & Bogduk, 1994). Actual or potential tissue damage emphasizes the subjective character of pain that differentiates it from the mere stimulation of nociceptors.

Pain can also be classified into two extensive categories as protective or maladaptive. Protective pain causes to withdraw from a potential injury; for example, pulling the hand out of a very hot content. It protects the organism from further injury and tissue damage reflexively. This type of short-lasting pain, following a local injury with minimal damage, is known as nociceptive pain (Basbaum & Bushnell, 2009). The inflammation associated with an injury like bone fracture or severe sunburn sensitizes the nociceptive and non-nociceptive nerve endings in the damaged area resulting in signaling in responses to otherwise non-noxious stimuli. This inflammatory pain protects the individual against further possible trauma. Inflammation resolves and pain subsides after healing.

Pain that continues after the injury or other cause of pain has resolved is defined as maladaptive pain. Maladaptive pain is complex and involves

processes as such peripheral nociceptor activation and sensitization, "central sensitization" and changes in peripheral processes such that now a non-nociceptive stimuli evokes a pain sensation. This type of pain usually takes a chronic course and no longer serves as a protective function. The numerous ways has been used to describe pain, since it isdifficult to define, quantify, and understand (Basbaum & Bushnell, 2009).

The human body has specialized neurons,that respond only to a noxious or potentially noxious stimulus. These neurons are very complex in structure and referred to as primary afferent nociceptors. When these primary afferent neurons are stimulated, they synapse with neurons known as second-order pain transmission neurons in the substantia gelatinosa of the dorsal horn of the spinal cord or, in the head and neck region, the trigeminal nucleus caudalis. From here, the signals are transmitted along specialized pathways first to the thalamus, then the brain stem and then to the somatosensory cortex where the location and intensity of the pain are determined. It is important to note that there is no single brain area that processes pain (Apkarian et al., 2005).

In terms for seeking medical care and attention for pain, the orofacial area is one of the most common region for individuals (Sarlani et al., 2005; Annino & Goguen; 2003). Toothache and orofacial pain affect a big part of the population. A study on the frequency of toothache and orofacial pains showed that 7%-32% of the population suffer from tooth pain while 40%-44% from orofacial pain (Pau et al., 2003; Lipton et al., 1993). Besides, chronic orofacial pain is very common in many countries (MacFarlene et al.,,2002; John et al.,,2003;;Dworkin et,al., 1990). It is obvious that tooth pain is caused by situations such as caries, acute pulpal or periodontal diseases and managed by appropriate dental treatment (Annino & Goguen; 2003).

Toothache with pulpal origin is usually described by an aching pain that is challenging to localize with deep and dull characterization. (Ikeda & Suda; 2003). Moreover, the pain may show itself as moderate or severe, continuous or intermittent, localized or diffuse sharp or dull, and may be affected by the position of the patient's body or time of day. (Okeson & Falace; 1997) However, the symptoms of toothache may have their

origin in a nonodontogenic cause in many cases. As a result, it is common for pain in the orofacial region to be confused for a tooth related ache, and similarly, other pains of the head and neck to imitate a pain with odontogenic source. Therefore, pain with an orofacial origin may be a diagnostic dilemma for the dentists (Balasubramaniam et al., 2011). As a result of inaccurate diagnosis, dentists may perform incorrect dental treatment (Ram et al., 2009; Von Eckardstein et al., 2015). Furthermore, the complex and time-consuming diagnosis in these group of patients may cause to risk factors such as anxiety which allow pain to become chronic (Fillingim et al., 2013).

Clinical and radiographic characteristics aid in differentiating between toothache and orofacial pain. Caries, defective restorations, cracked teeth and root fractures are clinical characteristics which are related to odontogenic pain. Furthermore, hypersensitivity, pain on percussion, palpation and during chewing are other important characteristics. Local anesthesia relieve odontogenic pain which is also characterized by being unilateral and localized (Paul, 2014). Differently, nonodontogenic pain is defined as shooting and non-localized which crosses the midline. It may be related to an headache, joint or muscle pain and anxiety. In addition, these patients might demonstrate many tooth extractions and root canal treatment for pain relief (McCarthy et al., 2010).

The diagnosis of nonodontogenic pain is based on careful medical-dental anamnesis, clinical-radiographic examination and provocation tests. Patients should be given enough time to explain their symptoms to detect the origin of pain. Pain is described as heterotopic when the area where it is felt by the patient is not its true source (Sessle, 2000). Central, projected and referred pain are the three types of heterotropic pain. In the event of central pain, a lesion in the brain or brain stem might damage nerve tissue which somatotopically communicates to a specific part of the body. As a result, pain might be felt in orofacial area, even though the origin of pain is located in the central nervous system. In case of projected pain, a nerve is trigerred at some location of its anatomical course, the pain follows the path of the nerve. The pain sensation felt in trigeminal neuralgia in the event of a neurovascular conflict at the dorsal root entry zone may be regarded as such. Referred pain which is the third

type of heterotopic pain is regarded of significance in a lot of the deep pain conditions detected in craniofacial pain (Chichorro et al., 2017).

2.Types of Nonodontogenic Toothache

2.1.Myofascial toothache

Myofascial pain with the origin of masticatory muscles is a commonly detected basic disorder, related to nonodontogenic,toothache and symptoms including dull, aching and diffuse pain which tends to be worsened by mastication or head and neck movements. It was noted that 11% of the patients suffering from myofascial pain, suffer from nonodontogenic toothache and the masseter generally seems as the causing muscle (Pathak et al., 2020).

A diagnostic test can be efficiently performed based on the fact that provocation of myofascial trigger points and reproduction of referral patterns increases the pain. In addition, diagnostic injection eliminates pain (Yatani et al. 2014).

The clinical features of the toothache of myofascial origin are that pain is more regularly aching than that of pulpal pain sensation and the pain is not tend to increase by provocation of the tooth. There is also lack of dental pathology to describe the pain (Soni, 2018).

Behavioural modification such as resting the jaw, massage and soft food diet are helpful for treatment. Physical therapy including exercises, posture correction and heat therapy is also efficient for the treatment. Muscle relaxants and non-steroidal anti-inflammatory drugs showed efficiency for myofascial pain causing nonodontogenic toothache. In addition, acupuncture which has an important effect on temporomandibular disorders, can be considered as an alternative method (Romero-Reyes & Uyanik, 2014).

2.2.Neurovascular toothache

Migraine, cluster headaches and chronic paroxysmal hemicranias involve the orofacial region and may be mistaken as toothache. Migraine is a

debilitating, inherited episodic disease that has a throbbing, spontaneous maxillary pain similar to toothache. The pain becomes worse by the effect of physical activity and its attacks last 4-72 hours (Obermann et al. 2007). Migraine headaches are detected more common in females and 50% begin befote the age of 20 (Steiner et al. 2003). The headache itself is mainly in characterized as unilateral in the frontal, temporal or retrobulbar areas, even hough about 3% of migraine patients will complain of intraoral pain. This situation increases the likelihood that an undiagnosed migraine patient will seek consultation with a dentist or endodontist before seeing their physician or an orofacial pain specialist (Bussone & Tullo, 2006).

"Facial migraines" or neurovascular orofacial pain disorders has many similarities to migraine that occurs in the lower two third part of the face most commonly in the alveolus occasionally with an associated mucosal site (Benoliel et al., 1997). Neurovascular orofacial pain is also more common in women, mostly unilateral in location. A potentially misleading sign is that some of the patients also report dental sensitivity to cold. These patients often have had one or more root canal treartment in the teeth or prior teeth extractions in the painful region without relief of their pain (Czerninsky et al., 1999). The diagnosis of migraine can usually be achieved by patient history but in the case of neurovascukar orofacial pain examination of the patient complaining of undiagnosed intermittent toothache and facial pain should include a through dental, tempromandibular jont and muscle examination, in addition. Once the obvious dental and joint pahology have been eliminated, and the temporal pattern and qualititive of the pain increases the probability of facial or dental migraine the patient shoul be referred to an orofacial pain specialist.

Considering cluster headaches, the pain quality is similar to dental pulpitis and as a result patients may first refer to a dental professional (Benoliel et,al., 1997; van Vliet.et al.,;2003). The pain is defined as episodic, intense periorbital and maxillary pain which lasts 15 to 180 minutes (Hellmann, 2002). Clinical features of chronic paroxysmal hemicranias is described as acute, episodic periorbital and maxillary pain related to dysautonomic characteristics (Yatani et al., 2014). In the

case of toothache of neurovascular origin, which is commonly felt in the maxillary canine and premolar teeth, the pain has no dental cause. Furthermore, the efficiency of local anaesthesia is unpredictable.

Treatment for neurovascular toothache regarding migraine is based on administrations in accordance with the International Classification of Headache Disorders and patients who suffer from it are referred to neurologists, neurosurgeons or headache clinics. Acetaminophen, non-steroidal anti-inflammatory drugs, triptans((for the acute phase),,and topiramate, valproic acid and amitriptyline (as prophylactic treatment) are used for pharmacologic therapy (Pathak et al., 2020; Yatani et al., 2014). Considering cluster headaches;, triptans and dihydroergotamine((for abortive.therapy), oxygen inhalation, corticosteroids (short term), verampil and, divalproex sodium, lithium and topiramate (prophylactic therapy) are used (Yatani et al., 2014; Torelli et al., 2004). Chronic paroxysmal hemicranias have a 100% response to indomethacin. In addition, topiramate seems to be proven promising (Yatani et al., 2014).

2.3.Cardiac toothache

Ischemic cardiac pain is related to referred pain to the left arm, shoulder, throat, neck, ear, teeth and mandible (Mense, 2003). The pain is burning, tight and aggravated by exercise, improves with rest and showed bilaterally characterized symptoms. Misdiagnosis in such cases may lead to unnecessary dental treatment. The origin of the ischemic cardiac pain referred to the orofacial region may be described by the converging mechanisms of the trigeminal nerve (Ishida et al., 1996). Adequate medical and dental anamnesis aids in detecting true cause of the pain. It should be known that patients who have the possibility of ischemic cardiac diseases, may visit dental clinics with complaints of toothache only. The diagnostic test of the cardiac toothache is that reduction of pain is noticed following the administration of sublingual nitroglycerin tablets. Besides, local provocation of the teeth, and local anesthetics and analgesics do not alter the pain (Ravikumar & Ramakrishnan, 2018). Patients diagnosed with cardiac toothache should be referred to the cardiologists. Treatment involves echocardiogram, anti-angina drugs

such as beta-adrenoreceptor blockers or nitric acid, and antithrombotic drugs (Yatani et al., 2014).

2.4.Neuropathic toothache

Neuropathic pain is explained as the pain originating from a defect in the neural structures. The diagnosis of this kind of pain may be challenging to the clinician because of the fact that structurse innervated by these nerves are painful but seems clinically normal (Sajjanhar et al., 2017). Neuropathic toothache can be either episodic or continuous.

2.4.1.Episodic neuropathic toothache

Trigeminal neuralgia including the mandibular nerve is a disorder related to episodic neuropathic toothache in the orofacial region. This kind of pain sensation is felt as a toothache, however is generally experienced in a broader region. Paroxysms are provoked by relatively innocuous peripheral stimulation of the trigger points at intraoral or extraoral regions such as the buccal mucosa in the area of the molar teeth, the lipschin, nares and nasolabial fold (Yatani et al., 2014; , Balasubramaniam et al., 2011). Pain is defined as electric-like, brief and excruciating, and not altered by thermal stimulus (Pathak et al., 2020). Anesthesia of the trigger zone intraorally reduces the paroxysmal pain, but on occasion tooth itself represents a trigger zone and may lead to misdiagnosis and unnecessary root canal treatment (Sajjanhar et al., 2017). Therefore, the absence of dental pathosis must be proved by using clinical and radiological examinations (Matwychuk, 2004; Apicella & Johnson, 2008). Treatment includes carbamazepine as the first , oxcarbazepine as the second and baclofen and lamotrigine as third choices. Microvascular decompression, radiofrequency thermocoagulation and stereotactic radiosurgery are the surgical procedures for the treatment of trigeminal neuralgia (Yatani et al., 2014).

2.4.2.Continuous neuropathic toothache

Herpes zoster infection of the facial region might be related to toothache. Persistent and continuous, pulpitis-like pain and related symptoms seem

in teeth and become intense in a couple of days. Furthermore, post-traumatic trigeminal neuropathy which begins as a consequence of nerve damage during endodontic treatment may be another cause of continuous neuropathic toothache. Neuritic pain and deafferentation pain are the general types of continuous neuropathic conditions that the patients experienced pain sensation in a tooth (Yatani et al., 2014;;Apicella & Johnson, 2008)..The clinical feateures of a neuritic pain are that the pain is burning, non-pulsatile and accompanied by other neurologic symptoms such as paraesthesia. On the other hand, deafferentation pain differs in intensity with no periods of remission, is not changed by local provocation and commonly noted in maxillary canine and premolar teeth of middle-aged women who have a trauma history. Valacyclovir hydrochloride, acyclovir and vidarabine are the drug choices for the pharmacological therapy of continuous neuropathic pain during the herpes zoster infection in acute phase. For other continuous neuropathic painful conditions, first-line drug choices involve administration of topical anaesthetics, tri-cyclic antidepressants and anticonvultants, while second-line drug choices include non-opioids and serotonin and norepinephrine reuptake inhibitors (Yatani et al., 2014).

2.5.Sinus toothache

Because the roots of the maxillary teeth are in close contact with the maxillary sinus cavity, an infection in the teeth or surrounding periodontal tissues could appear as sinusitis; conversely, an infection which originates from the maxillary sinus could appear as odontogenic pain. Patients might present pain which occurs in the maxillary molars induced by cold stimulation or mastication, and dysesthesia may arise with clenching (Osguthorpe & Hadley, 1999). It is generally experienced in multiple teeth which makes it more indicative of a sinusitis pain rather than pain with an odontogenic source (Falk et al., 1986). Symptoms such as cough, ear pain, fatigue, halitosis, headache and nasal congestion might be more detectable as being related to sinusitis (Okeson, 2000). Pain might be evoked by palpation of the infraorbital region, or moving the head to the knees because of gravitional shifting of fluid in the maxillary sinus

(Murphy & Merrill, 2001). During clinical and radiographic examination, the absence of an endodontic or periodontal infection might explain that there is a sinus disease (Rafetto, 1999). Cloudy, congested and opacified appearance on the panoramic radiograph and thickening of the maxillary sinus mucosal membrane with increased fluid levels on computerized tomography scan might indicate sinus infection or inflammation. Histopathological examination are also helpful to detect the origin of the problem (Ha et al., 2019). In the event of sinus toothache, patients are referred to the otorhinolaryngologists and nasal decongestants might be useful in most of the cases (Kretzschmar & Kretzschmar, 2003).

2.6.Neoplastic toothache

Neoplastic toothache might be the earliest symptom of oral cancer. Primary squamous cell carcinoma which is located on the oral mucosa might represent with mimic pain of odontogenic source on the gingiva, vestibule or floor of the mouth (Cuffari et al., 2006). Primary intraosseous carcinoma which occurs in the maxilla or mandible has no relationship with the oral mucosa and may originate from a cyst (Takayanagi et al., 1990). This type of malignancy is rare, however it may be misdiagnosed as having an odontogenic source because localized bone loss might appear as localized periodontal disease in the clinical examination. Nasopharyngeal cancers might show the signs which mimic parotid gland lesions, temporomandibular disorders and trismus of odontogenic origin (Epstein & Jones, 1993; Reiter et al., 2006). This type of neoplasms demonstrate earache, deviation or limitation of the jaw on opening, facial pain and headache which are the symptoms that might be confused with an odontogenic infection. Leukemia and lymphoma which are systemic cancers might show toothache symptoms, because they penetrate gingiva and periosteum that cause localized pain sensation which might be confused with an odontogenic aetiology (Barrett, 1984). Besides, lesions of multiple myeloma rarely expands adjacent to teeth and may lead to a misdiagnosis. Pain has been noted in 39% of the patients in metastatic disease of the jaws (Hirshberg et al., 1994). The pain and clinical characteristics of metastases might be misdiagnosed as that arising from

an odontogenic origin, the prevalent regions being the posterior region mandible, angle of the mandible and ramus. Orofacial malignancies might also mimic odontogenic infections, therefore dentists must be careful when tissue changes occur in intimate proximity to the certain odontogenic structures and clinical characteristics cannot be related to the findings of odontogenic source (Sajjanhar et al., 2017).

2.7.Psychogenic toothache

Psychological problems might induce psychogenic toothache. Many clinicians use the term "psychogenic" as a diagnosis in patients in whom they cannot identify a disease process to explain the symptoms or in patients whose pain has caused a strong emotional component or in patients who have not responded well to somatic treatment. It must be emphasized, on the other hand, that while psychological factors are strongly involved in the expression of all kinds of pain, regardless of etiology or time course, it is rare for pain to be purely due to a psychological disorder (Jaeger & Skootsky, 1987).

This type of pain is defined as continuous and persistent. There are also an uncertain area of pain sensation in the innervation region and bilaterally characterized symptoms. Psychogenic toothache might include multiple teeth and jump from one tooth to another. Because of the similarities of these features to odontogenic pain, leads to misdiagnosis. But, absence or presence of a psychological factor could give a clue about the source of the pain. Psychiatric characteristics such as delusions or hallucinations may also accompany psychogenic pain (Dworkin & Burgess, 1987; Fukuda, 2016). Patients should be referred to neuropsychiatrists, mental health professionals or liaison treatment specialists. Treatment might involve pharmacological therapy such as antipsychotic drugs or antidepressant (Yatani et al., 2014).

In acute pain, these behaviors and their rewards subside rapidly, but in cases of persistent or chronic pain, pain behaviors and operant conditioning become more prominent and may continue even after the noxious stimulus is gone; it is this behavior that often leads some clinicians to doubt the patient's veracity or label them as having psychogenic pain.

Rather than mistakenly calling unidentified pain "psychogenic", the clinician should reconsider pain classification to answer this question. (Fordyce & Steger, 1978).

2.8.Idiopathic toothache

Idiopathic toothache has been described as characterised by continuous pain in the teeth and/or their surrounding tissues with no objective finding at the location of pain and without a known aetiology by the stidies. This type of pain often lasts over 4 or 6 months. Idiopathic toothache and neuropathic toothache are similar to each other, because researches demonstrate that patients who are diagnosed with atypical odontalgia might actually suffer from post-traumatic trigeminal neuropathy, if somatosensory disorders can be showed and if it can be confirmed by other tests. The onset of the pain may develop or coincide within 1 month or so after various dental treatments especially root canal theraphy or extraction or some acute trauma or medical procedures related to the face, increasing the impression that the pain is possibly neuropathic (Clark, 2006; Benoliel, 2012). It is extremely important for dental practitioners to be aware of the existence of these disorders in order to avoid performing unnecessary dental procedures such as endodontic treatment or teeth extractions. It has been postulated that 3% to 7% of endodontic patients may suffer from this type of toothache, especially if they had pain prior to endodontic treatment. (Melis et al., 2003).

Radiographic evaluations in addition to intraoral examinations can usually be unrevealing. If the pain sensation is in a tooth as opposed to an extraction site, responses to percussion, thermal testing, and electric pulp stimulation can be variable. The majority of patients report very little or no relief after the appliation of diagnostic local anesthetic blocks. Irreversible and invasive treatments, such as root canal therapy, exploratory surgery, tooth extraction, or even occlusal adjustments to some degree, are contraindicated (Clark, 2006). The reason is because, despite possible transient relief, the pain is possibly to recur with equal or even greater intensity.

The most common somatosensory disorders are somatosensory gain with regard to painful cold and mechanical stimuli and somatosensory loss with regard to mechanical detection and cold (Pathak et al., 2020; Malacarne et al., 2018). The effect of tri-cyclic antidepressants was demonstrated to be 60%-75% in cases of idiopathic toothache. Serotonin-dopamine antagonists and topical treatment may also be helpful (Yatani et al., 2014).

3.Conclusion

In conclusion, in most cases, it is considered as difficult and a time-consuming task to diagnose and manage patients suffering chronic or unusual pain. Chronic pain management, including orofacial pain, is a rapidly developing specialty in healthcare. It might take years of experience for dentists to gain sufficent insight to diagnose and manage these complex cases.

There are many nonodontogenic pains which occur in the region of teeth and their surrounding tissues and mimic toothache. Dentists must understand the fact that odontogenic pain has a complicated mechanism and other orofacial structures might stimulate it. First, odontogenic pain must be excluded by appropriate medical and dental anamnesis, clinical and radiographic examination. Therefore, misdiagnosis which may be resulted in incorrect dental treatment, is avoided.

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CHAPTER VI

XEROSTOMIA

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Saliva is a mixture of mostly water, also electrolytes, enzymes, and proteins (Guggenheimer and Moore, 2003). Major salivary glands (parotid, submandibular, sublingual) and also 600-1000 minor glands are distributed throughout the mouth secrete saliva (Guggenheimer and Moore, 2003; Wang et al., 2015). Saliva is crucial for the preservation of homeostasis both general and oral (Escobar and Aitken-Saavedra, 2018). Saliva shows antibacterial, antiviral, and antifungal properties. Basal salivary secretion is always present and helps to maintain a steady pH in the oral cavity, protect the integrity of mucosa, and has cleaning action (Golež et al, 2021). Besides that, it contains digestive enzymes and also helps the remineralization of teeth (Hopcraft and Tan, 2010). MUC7 and MUC5b are two types of salivary mucins. Mucins in the saliva provide lubrication, and their properties determine the residual salivary film thickness and composition (Vinke et al., 2021).

Parasympathetic and sympathetic nervous systems innervate salivary glands. Sympathetic and parasympathetic stimulations of the glands lead to more viscous and more watery flows, respectively (Guggenheimer and Moore, 2003).

Acinar cells secrete the primary saliva which has an ionic composition similar to plasma. Ductal cells modify the saliva by reabsorbing the chloride and sodium without water (Navazesh et al., 2008). At rest the majority of saliva is secreted by the submandibular and sublingual glands. In stimulated saliva, %50 of the salivary volume is secreted by the parotid glands (Escobar and Aitken-Saavedra, 2018). Parotid glands'

secretions are sereous whereas secretions that come from submandibular and sublingual glands show mixed (serous and mucous) characteristics (Navazesh et al., 2008). In the whole saliva volume the minor salivary glands do not contribute to a major part (less than %10), but due to their mucous salivary secretions, they have an important role in the lubrication and protection of oral mucosa (Navazesh et al., 2008; Wang et al., 2015). Daily production of saliva is approximately one liter per day. Diurnal rhythms affect the output and fluctuate as much as %50 (Guggenheimer and Moore, 2003). Sleeping time and late afternoon are the periods when a person has the lowest and highest salivary secretion rates, respectively (Wang et al., 2015). Objective decrease of salivary flow rate is called hyposalivation (Ramírez Martínez-Acitores et al., 2020). Subjective complaint of the dry mouth is called xerostomia (Kang and Kho, 2021; Nanditha Kumar et al., 2021; Ramírez Martínez-Acitores et al., 2020)

The word "xerostomia" comes from *xeros* and *stoma* which mean dry and mouth, respectively. The prevalence is reported between %5,5-63 in the literature and is more common in women, elderly people, and individuals housed in long-term care facilities (Delli et al., 2014; Ramírez Martínez-Acitores et al., 2020). The increased prevalence in the older groups may be derived from the chronic conditions/diseases of the older people who have to take xenogenic drugs which may lead to xerostomia (Ramírez Martínez-Acitores et al., 2020). It affects the patient's quality of life. Over %87,6 of people suffer from it and worry if this sensation will be persistent for the rest of their lives.(Escobar and Aitken-Saavedra, 2018) Xerostomia is divided into two different classes as true xerostomia (primaria, xerostomia vera) where salivary glands malfunction is seen, and pseudo/symptomatic xerostomia (symptomatic, xerostomia spuria) where normal secretion of saliva is seen, but patients complain from oral dryness. (Escobar and Aitken-Saavedra, 2018) There is an association between xerostomia and decreased water-retaining ability of mucins in the saliva (Vinke et al., 2021). Frequently in xerostomia patients, no objective sign of hyposalivation is detected and it is thought that their symptoms are caused by the qualitative and/or quantitive changes in saliva composition (Ramírez Martínez-Acitores et al., 2020).

Xerostomia may decrease the taste sensation, chewing, and swallowing which may lead patients to avoid from dry and sticky foods (Cassolato and Turnbull, 2003; Ramírez Martínez-Acitores et al., 2020). Speaking of the patients may alter; cracks and fissures in the oral mucosa, and also halitosis may be seen (Cassolato and Turnbull, 2003). In addition to these, a decrease in saliva may lead to dental caries, oral candidiasis, burning mouth, dysphagia (Golež et al, 2021; Kang and Kho, 2021; Ramírez Martínez-Acitores et al., 2020).

The normal average of stimulated salivary flow rate is between 1,5 and 2.0 mL/min, and the unstimulated salivary flow rate average is approximately 0,3-0,4 mL/min (Guggenheimer and Moore, 2003). Unstimulated salivary rate test is made in the following steps;

1. Patient is advised to stop taking any food or beverage except water before 1 hour from the test session. Also, smoking, coffee intake or chewing gum are prohibited for 1 hour before the test.
2. Patient is informed about the test procedure and asked to rinse his/her mouth with distilled water several times and rest for five minutes.
3. Ask the patient to remain as still as possible in the procedure time.
4. Before starting the time, ask the patient to swallow, after that the time starts and the patient leans to the test tube, lets saliva drain into the tube. Ask the patient to keep not closing his/her eyes during the procedure.
5. When the saliva collection time is ended, ask the patient to collect any remaining saliva in the mouth and spit it into the tube.

The specimen is collected at the first minute of the trial discards and after that 5 minutes of actual trial continues. The collected specimen's volume is calculated and divided into 5 to achieve a liter per minute value (Delli et al., 2014).

Another test is the stimulated whole saliva flow rate, and it is made according to the following steps;

1. Ask the patient to sit still during the procedure.
2. Ask the patient to lean forward over the funnel.

3. Ask the patient to swallow and then start the time.

4. Ask the patient to chew inert gum with the frequency of approximately 70 times per minute.

5. At the end of every 1 min ask the patient to spit the saliva into the tube and to keep chewing without swallowing.

6. Discard the saliva collected at the first two minutes and continue to collect for 3 minutes.

7. At the end of five minutes that start at the beginning of the trial, ask the patient to spit everything (saliva and gum base) into the tube.

8. Weigh up the saliva after putting out the gum base.

Flow rates of individual glands can also be measured. Carlson-Crittenden collector or modified Lashley cup can be used to collect parotid glands' saliva. Sublingual and submandibular glands' secretion can collect with custom-made collectors like Wolff collectors (Navazesh et al., 2008). For assessing minor salivary glands' flow rates, different methods are present. Wang et al. proposed a method where the clinician firstly dried the mucosa carefully, after that a strip of filter paper (1*2 cm^2 in size) was placed on the mucosa, and immediately a light pressure was applied on the film. For 30-second saliva collection continues, after that, the filter paper is removed and placed in an air-tight container to prevent saliva from evaporation. Weight of container and strip is measured before and after the collection. In this method, the minor salivary gland flow rate can be assessed in ml/min/cm^2 unit (Wang et al., 2015). Wang et al. reported salivary flow rates for minor salivary glands located at the lower labial region as 2.10 ± 0.66, the upper labial region as 2.14 ± 0.62, palatal glands as 2.15 ± 0.51, and buccal glands as 2.88 ± 0.72 (Wang et al., 2015).

Lower values than 0,5-0,7 mL/min for stimulated salivary flow rate and lower than 0,1 mL/min lead to the diagnosis of hyposalivation in patients (Ramírez Martínez-Acitores et al., 2020). Patients usually complain from xerostomia when the salivary flow rate falls below %50 of its normal value (Golež et al, 2021). Many short and long-term factors may affect the salivary secretion, and this leads to xerostomia. Three basic causes are situations/diseases that affect the salivary gland

center (Parkinson's disease, menopause, stress, anxiety, Alzheimer' disease and etc), factors that alter the nerve stimulation of saliva (brain tumors, antihistamines, antidepressants, anxiolytics, antimuscarinics, anticholinergics, opioids, smoking, dehydration or etc), alterations of the salivary gland function (obstruction with calculi, glandular tumors, sialoadenitis, rheumatoid arthritis, chemotherapy, uncontrolled diabetes mellitus, radiotherapy, systemic lupus erythematosus and etc) (Escobar and Aitken-Saavedra, 2018). The thickness of the saliva on the intraoral tissues shows different values at different areas, the thinnest location is at the anterior hard palate (~ 10 μm), anterior dorsal of the tongue shows way thicker values (~ 54 μm) (Assy et al., 2020). The different areas of the oral cavity may show different susceptibility to oral dryness due to several factors. The hard palate is more susceptible due to the lower number of minor salivary glands, evaporation, and gravity. Between swallowing episodes gravity forces the saliva pool in the floor of the mouth, and this makes the palate moistened insufficiently especially in hyposalivation cases. Assy et al. found the posterior palate as the driest area in the oral cavity (Assy et al., 2020).

There are various ways for the diagnosis and therapy of the condition, which makes it too difficult to achieve good results for all the cases of xerostomia due to multifactorial etiological factors that may be presented both locally and systemically (Escobar and Aitken-Saavedra, 2018). To diagnose xerostomia, the clinical history is essential. Systemic diseases, medication uses and possible history of radiotherapy must be questioned (Escobar and Aitken-Saavedra, 2018). Palpation of the salivary glands or observation of the clinical possible clinical signs like cracked lips must be checked. Hydration and condition of the oral mucosa, saliva under the tongue, texture, and appearance of saliva must be controlled (Escobar and Aitken-Saavedra, 2018). Oral mucosal wetness and qualitative salivary changes may be some other factors that influence the subjective oral dryness symptoms (Kang and Kho, 2021). Besides computed tomography, ultrasound, blood tests, salivary gland biopsy, sialography, sialometry and scintigraphy, and magnetic resonance imaging may be used as supplementary tools for differential diagnosis (Kang and Kho, 2021; Escobar and Aitken-Saavedra, 2018). The biopsy of both major and

minor salivary glands may reveal inflammatory infiltrations, dilatation of salivary canals, fibrosis, or acinar destruction (Escobar and Aitken-Saavedra, 2018). Sialography is the technique where a radioopaque material from the opening of major salivary gland duct channels into the duct system. It shows possible sialectasis or nodules. The disadvantages of the procedure are that it is an invasive method and also the patient may be allergic to the materials that are used in the procedure (Escobar and Aitken-Saavedra, 2018). Scintigraphy allows the assessment of major salivary glands' function. Technetium-99m pertechnetates ($^{99m}TcO4^-$) used in the technique, salivary glands' uptake, and excretion of the material are measured (Chen et al., 2021).

There are different questionnaires present to assess the severity of the xerostomia in patients, and xerostomia inventory (XI) is one of them. XI was developed by Thomson et al. in 1999 on the participants aged 65 or older (Thomson et al., 1999). It consists of 11 different questions where higher scores are related to more severe symptoms. In this questionnaire, patients may choose one response from five different options as "never" (1 point), "hardly ever" (2 points), "occasionally" (3 points), "fairly often" (4 points), "very often" (5 points). Patients give the answers for the previous 4 weeks before the questionnaire date. The questions are as follows;

1. I sip liquids to aid in swallowing food
2. My mouth feels dry when eating a meal
3. I get up at night to drink
4. My mouth feels dry
5. I have difficulty in eating dry foods
6. I suck sweats or cough lollies to relieve dry mouth
7. I have difficulties swallowing certain foods
8. The skin of my face feels dry
9. The inside of my nose feels dry
10. My eyes feel dry
11. My lips feel dry (Assy et al., 2020).

At the end of the questionnaire, patients' scores due to their answers were calculated (Thomson et al., 2011). This questionnaire was then

shortened and named "Summated Xerostomia Inventory-Dutch Version". In this version, only the questions numbered 2,4,5,7,11 are used.(Van der Putten et al., 2011) In this version, patients may select one answer to this question from the options "never" (1 point), "occasionally" (2 points), and "often" (3 points). The total scores range between 5 and15, and higher scores are an indicator of more severe symptoms. (Freni et al., 2020). Another questionnaire was recently developed to assess dryness feel in different regions of the oral cavity, and it is called "regional oral dryness inventory". In this questionnaire, 9 illustrations showing different locations of the oral cavity are present. The regions for the upper jaw are the upper lip, inside part of the cheeks, anterior part of the palate including the rugae, posterior palate which starts from rugae to the end of soft palate respectively. The lower jaw illustration locations are the floor of the mouth, lower lip, posterior part of the tongue which start from the vallate papilla to the end of the tongue, and the anterior part of the tongue which is the region from the tip to vallate papilla respectively. The last illustration shows the pharynx. At each location, the patient selects one of the five different options as "none" (1 point), slight (2 points), moderate (3 points), excessive (4 points), severe (5 points) (Van der Putten et al., 2011) Bother index is another index that helps to assess dry mouth severity where the clinician asks the patient to rate the severity on a scale from 0 to 10. The questionnaires mentioned in this paragraph are self-reported and subjective tests. Clinical oral dryness score (CODS) is a method that helps clinicians to assess oral dryness. (Jager et al., 2018) In this method, there are 10 features;

1. Mirror sticks to the buccal mucosa
2. Mirror sticks to the tongue
3. Frothy saliva
4. No saliva pooling on the floor of the mouth
5. Tongue shows loss of papillae
6. Altered/smooth gingival architecture
7. Glassy appearance to another oral mucosa especially palate
8. Tongue lobulated/fissured

9. Active or recently restored (in last 6 months) cervical caries (more than 2 teeth)

10. Debris on the palate (excluding under dentures)

Each item is scored one 1 point, and the severity of the condition is assessed by the final total points of the test. A total score between 1 and3 is considered as mild dryness, and needs no treatment. The patient is advised to chew sugar-free chewing gum for 15-20 minutes twice a day to diminish the symptoms and maintain oral health. A score between 4 and 6 is considered moderate dryness, sugar-free chewing gum is also advised in these cases. In these cases, also mild sialogogues may be needed to relieve the symptoms. The reason behind the dryness must be investigated in these patients. Saliva substitutes/topical fluoride or fluoride toothpaste may be appropriate to prevent the formation of new caries. A patient must be controlled periodically to check the symptoms and caries development (Das and Challacombe, 2016). A score between 7 and 10 shows severe dryness. In these patients possible Sjögren's syndrome must be investigated and excluded, the reason behind the condition must be diagnosed. Topical fluorides, saliva substitutes, topical fluorides are usually needed (Das and Challacombe, 2016).

Xerostomia may be delivered from various conditions/diseases like radiotherapy (RT) to the head and neck, autoimmune diseases like Sjögren's syndrome, diabetes mellitus, oral breathing, use of xerostomic medications (Das and Challacombe, 2016; Guggenheimer and Moore, 2003; Ramírez Martínez-Acitores et al., 2020). More than one thousand drugs were reported to cause xerostomia where main medications that may lead to xerostomia are muscarinic receptor antagonists, antipsychotics, benzodiazepines, antihypertensives, antihistamines, tricyclic antidepressants, opioids. Approximately %64 of all dry mouth cases are caused by side effects of medications (Das and Challacombe, 2016). In antihypertensive drugs, diuretics, β-adrenergic blockers, and drug combinations are in strong association with xerostomia (Ramírez Martínez-Acitores et al., 2020). However, a current review is about the salivary flow rate and xerostomia in patients with the usage of antihypertensive drugs. Authors make a conclusion that with the current

findings in the literature it is not possible to say assuredly that patients with antihypertensive drug usage show more xerostomia or hyposalivation than the patients do not take these drugs (Ramírez Martínez-Acitores et al., 2020).

Salivary glands are sensitive to radiation damage contrary to their slowly proliferating and highly differentiated natures. Radiotherapy is a major factor that can lead to xerostomia, more than %80 of the patients who have received RT for head and neck cancer treatment suffer from xerostomia following RT. The hyposalivation is classified as acute and chronic in the patients with head and neck RT. The acute form seems to be related to salivary acinar epithelial cells loss and chronic form is attributed to glandular fibrosis and failure of regeneration of the functional acini (Jasmer et al., 2020). Not just external radiotherapy, but radioactive iodine (RAI) therapy which is used in many patients with differentiated thyroid cancer following surgery may also lead to xerostomia. The incidence of acute and chronic sialadenitis in patients with RAI therapy is %24-67 and %11,65, respectively (Adramerinas et al., 2021). The symptoms of the sialoadenitis sourced from RAI therapy may persist for months and even years (Adramerinas et al., 2021).

Sjögren's syndrome is one of the options which must have come to mind in xerostomia patients and is an autoimmune disease in which inflammation of exocrine glands is seen (Mravak-Stipetić, 2012). The name comes from Henrik Samuel Conrad Sjögren who was a Swedish opthalmologist that correlated the symptoms of xerostomia, polyarthritis, and keratoconjunctivitis sicca (Negrini et al., 2021). It is classified into two different headings as primary or sycca syndrome where the syndrome is limited to the eyes and mouth or secondary Sjögren's syndrome where another autoimmune disease like systemic sclerosis, rheumatoid arthritis, or systemic lupus erythematosus is present (Mravak-Stipetić, 2012). Dryness is also seen in other body parts like the digestive tract, vagina, or airways. It is more common in women than men with a ratio of 9:1. Diagnosis is generally made in the fifth decade. The prevalence is nearly %0,04. %98 of the patients suffering from Sjören's syndrome report ocular or mouth dryness, and %89 of the patients report that they have both of the symptoms. Nearly 1/3 of the patients sufer from recurrent or chronic

enlargement of major salivary glands. Fatigue is another symptom of the syndrome which is seen in %70-80 of the patients. Other non-specific general symptoms include anxiety, sleep disorders, chronic widespread pain, and depression (Negrini et al., 2021).

Xerostomia treatment is depending on the cause and degree of damage of the salivary glands. Saliva stimulants and saliva substitutes may be used in the patients. Chewing and acidic taste is effective in patients with remaining salivary gland function cases. Patients must be warned not to use sweets or sugar products for increased risk of caries. Low laser therapy has stimulative and regenerative effects on salivary glands. Electrical stimulation and acupuncture can also be used in patients with xerostomia (Negrini et al., 2021). Pilocarpine, cevimeline hydrochloride, bethanechol chloride, anetholetrithione are some of the sialogogic drugs that may be used in xerostomia patients to relieve the symptoms (Miranda-Rius et al., 2015). Interferon-alpha (IFN-α) and rituximab are drugs that are suggested in xerostomia related to Sjögren's syndrome. Amifostine is a cytoprotective drug that lowers the cell damage by the radiation in salivary glands when it is administered simultaneously with radiotherapy. In literature, salivary gland transposition to another region for the prevention of the salivary gland from the radiotherapy is also another proposed method to prevent radiation-induced xerostomia (Miranda-Rius et al., 2015).

In conclusion, xerostomia and dry mouth are complicated situations that have a negative influence on the quality of life of the patients and may need treatment. Understanding the possible etiological factors, diagnosis, and treatment options are important for clinicians.

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CHAPTER VII

CURRENT APPROACHES TO CEMENTS USED IN DENTISTRY

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1. Introduction

Cements are used in very small amounts compared to other materials used in dental practice. However, it is considered that they have great importance in terms of usage areas (1). Dental cements are applied in clinics as luting agents and restorative materials. Luting agents are used for bonding to tooth structures the indirectly prepared extraoral restorations and orthodontic attachments, and to fill the gaps between the teeth. Applications of cements to teeth as restorative materials include their use as temporary and permanent fillings or as base and cavity linings for pulp protection under other restorations. In addition to these, they can also be used as pit and fissure sealants (2,3). The chemical structures of cements used for two different purposes are basically similar. While changes are made in the viscosity of the luting cements to provide a better filling and adaptation between the materials applied to the teeth and the dental hard tissues, changes are made in the formulations to increase the durability of the restorative cements.

Restorative dentists have many decisions to make when performing dental procedures. The most difficult of these is the choice of restorative material, which varies according to the patient, oral condition, hard tissue remaining in the tooth, pulpal damage, and many other factors. For example, when an indirect restoration, a stainless-steel crown, is to

be cemented into the patient's mouth, the product of choice should be of low solubility, withstand chewing forces, and have good bonding ability and strength to prevent dislocation. However, the luting cement used for an orthodontic band that needs to be removed from the patient's mouth when the targeted treatment is completed must be weak enough to come off during tape removal, not break, and at the same time be easily removed from the tooth surface (3). The abundance of commercial products available for use in dental procedures makes the selection more difficult for clinicians. In addition, the constant release of new and improved products by dental manufacturers does not make the work of dental practitioners any easier (2,4).

For such reasons, dentists must have good knowledge of cements, which have a wide range of options for different purposes and clinical scenarios. Choosing the right cement is considered one of the necessary procedures for successful dental treatment (5).

2. Properties of Dental Cements

Cements used as a base in the cavity provide the support needed for the healing of the injured pupa and protect the pulp against the stresses that may occur due to the chewing forces in the future (6). Base cements act as an insulator, protecting the pulp against the effects of foods at different temperatures (7) and replacing the dentin tissue removed during caries removal and metal restoration preparation. Base cements must be sufficiently durable during the condensation of the restorative material to be placed on them and must be a minimum of 0.5 mm thick. Base cements that do not have sufficient strength during condensation may break and cause the amalgam to reach and contact the dentin tissue, thereby losing the thermal protection they are intended to provide (6).

When dental cements are intended to be applied for restorative purposes, it should be considered that their strength is lower than other direct restorative materials. These properties cause dental cements to be applied as temporary fillings. They also may apply permanently in areas of low stress in the mouth (3).

The basic requirements expected from luting cements used for the application of indirect restorations to the teeth are different. Some of these are the adequate flow of the dental cement for the restoration to fit the tooth properly, a good seal at the restoration-tooth interface for the longevity of the restoration, and the ability to resist the forces in the mouth.

The fact that the properties expected from cements for different clinical procedures are so high has led to the fact that an ideal cement has not yet been developed. However, cements are expected to respond to the criteria described below.

2.1. Biocompatibility

Considering the intended use of dental cements, they are used on surfaces with large amounts of dentin tissue rather than enamel. In some cases, the thickness of the remaining dentin tissue may be insufficient to protect sensitive tissue such as pulp from external influences. Many of the luting agents used in the cementation of restorations such as crowns, inlays, and onlays have been shown to be cytotoxic at different rates when examined in vitro. (8). In addition, histological studies on this subject have reported that dental cements placed close to the connective tissue causes an early inflammatory response in these tissues (9). These reactions are mostly associated with the initial low pH of acid-based cements and self-etch resin cements or the monomers in resin cements and resin-modified glass ionomer cements (8). An ideal dental cement is expected to have low allergic potential, non-toxicity, and minimal interaction with oral tissues and oral fluids (biocompatibility) (10).

2.2. Inhibition of caries formation and antibacterial effect of cements

Caries formation is the leading cause of failure of cast restorations (10). Preventing the formation of caries is a very complex issue for dentistry. Considering the difficulty of keeping caries-causing microorganisms away from dental tissues in the oral environment, the use of cements with antibacterial effects can be seen as an alternative to prevent of

caries formation (11). It is thought that fluoride-containing cements inhibit bacterial activity (8). Ideal dental cement is expected to have antimicrobial properties that reduce the effect of plaque accumulation on the restoration margins (10).

2.3. Plaque inhibition

Plaque accumulation in dental cements may occur in the area where the dental cement opens into the mouth. Since the cements used as a base are not exposed to the oral environment, the issue of plaque accumulation is more important for luting agents. Dental cements that have a porous structure and cannot be polished cause plaque accumulation more easily. Therefore, polishable resin cements containing organic phases are superior to other products in terms of plaque accumulation (11).

2.4. Interfacial sealing and hypersensitivity

The sealing of the tooth-restoration interface is important in preventing the invasion of bacteria that can cause secondary caries while ensuring that the restoration is resistant to microleakage. In addition, leakage of organisms from the tooth-restoration interface in dental restorations causes a negative pulpal response and reduces the restoration longevity (8, 12). It has been determined that leakage at the restoration interface is the most common cause of failure in endodontically treated teeth (13-15). In order to achieve a successful seal, the dental cement must have a good ability to penetrate and establish close contact with irregularities in both the restoration and dental tissues (8). Adequate sealing of the interface is necessary to maintain the movement of dentin fluids within physiological limits. Sudden changes in normal dentin fluid ratios cause tooth hypersensitivity (16).

3. Mechanical Properties of Dental Cements

An ideal dental cement should have sufficient mechanical properties to withstand functional movements and forces in the mouth as long as

the restoration is used by the patient. In addition, for the restoration to function successfully for a long time, the dental cement must be strong enough to withstand fracture and cyclic fatigue tests (17, 18). Wear, strength (usually in compression or in flexural mode), fatigue resistance, elastic modulus, fracture toughness is used to mechanically describe dental cements (8).

3.1. Solubility

The expected behavior for solubility of an ideal dental cement is its resistance to dissolution and disintegration in water and other solutions. Because the increased solubility will cause more plaque accumulation and adversely affect the marginal integrity of the restoration, especially in agents used as luting (11). An in-vivo study examining the solubility of dental cements in the patient's mouth revealed that zinc phosphate and polycarboxylate cement dissolved more than glass ionomer cement, and in the SEM evaluation, pits and cracks were observed on the surface of polycarboxylate and glass ionomer cement, while more pits were detected on the surface of zinc phosphate cement (19). When the cements are evaluated among themselves in terms of solubility, it is concluded that resin cements are less soluble than other cements (20,21).

3.2. Adhesion

The term adhesion refers to the establishment of molecular interactions by forming an adhesive bond between the tooth substrate and the luting agent brought into close contact with it (22). When conventional cements such as non-adhesive zinc phosphate cement are used as dental cements, the retention of the restoration is dependent on the geometry of the tooth form created during tooth preparation (23).

It is considered that three mechanisms, non-adhesive, molecular, and micromechanical, play a role in the cementation of restorations to teeth (24). Non-adhesive luting cements (e.g., zinc phosphate) fill the gap between the restoration and the tooth and provide adhesion via invasion to small surface irregularities in both substrates (restoration and tooth

surface). Dental cements perform this process at different levels depending on their properties. Therefore, the success of non-adhesive cements depends on the geometric form of the tooth preparation rather than the mechanical properties of the cement itself (23). Molecular adhesion is achieved by van der Walls forces, a weak chemical bond between the tooth and the cement. Dental cements that bond in this way are glass ionomers and polycarboxylate cements. In micromechanical bonding, desired irregularities on bonding surfaces are achieved by sandblasting and phosphoric acid. Resin and resin-modified glass ionomer cements can be given as examples of dental cements that provide bonding in this way (25).

3.3. Wear

The wear that will occur in dental cements may vary according to different parts of the mouth and teeth or the type of restoration applied. Although it is thought that the importance of wear is less in classical and full-crown restorations, the same station is not true for aesthetic restorations. If the preparation margins are located away from the gingival area and near the occlusal stop points, the wear sensitivity will increase. It is considered that composite resin cements have the best wear resistance proporties. In addition, increasing the amount of filler in the composite resin material will reduce the wear (11).

3.4. Viscosity and Film Thickness

The long-term clinical success of dental cements is directly related to film thickness and viscosity (10). The film thickness of dental cement is determined by the average particle size and viscosity it contains (8). Low film thickness is expected from dental cements. The low film thickness ensures better placement of the applied restoration and reduces marginal irregularities. In this way, plaque accumulation, gingival diseases, dissolution of cement, and dental caries are reduced (26). While some cements are thick after mixing, they show good fluidity under settling pressure (pseudoplastic) (8). Pressure applied to cements can alter the flow properties

of these materials. The more pressure is applied, the more fluidity will increase depending on the thixotropic property of the cement (27). When dental cements are used properly, in accordance with the manufacturer's instructions, and without exceeding the recommended working times, they may have a lower film thickness than the ISO standards allow (8).

3.5. Radiopacity

It is of great importance that dental cements are radiopaque in order to detect gaps between the tooth and the restoration, secondary caries, overflow fillings, or missing fillings. Dental cements should have a higher radiopacity than dentin (10,11). As a general rule, the radiopacity of material is thought to depend on the atomic structures of its constituents. High molecular weight components (i.e., metals) will retain more radiation than plastic-derived or water-based materials, showing a greater radiopacity (11).

3.6. Ease of Use

Ease of use, short setting time, and long working time are desirable properties of dental cement. In the past, dental cements, which were produced as powder and liquid, have recently been offered to consumers as capsules or as two pastes mixed in one end. Making the products available in this way ensures that the powder-liquid ratio is adjusted or the mixing is done properly and prevents the consumer from mistakes due to usage (8).

Removing the excess cement from the restoration edges after cementation is another important issue that jeopardizes the life of dental cements. Damage to the surrounding tissues during removal of the cement may increase the contact of the cement edges with blood and saliva at an early stage, increasing the bond strength and erosion of the cement (28,29). In addition, the cement removed after setting reaction may come from a region below the restoration margin. Therefore, residual cements should be removed before full hardening occurs during the setting reaction (10).

3.7. Esthetic

The application of dental cements when used with translucent restorations or where the margins of the restoration are above the gingival margin may compromise patient esthetics. In such cases, resin cements are superior to other cements due to their translucency and excellent color compatibility with dentin and enamel. Glass ionomer, resin-modified glass ionomer, compomer, and self-adhesive resin cements are also considered to have good esthetics. Zinc polycarboxylate, ZOE, and zinc phosphate cements have an opaque appearance. Therefore, in cases where translucent restorations are applied and the restoration margins are in the visible regions, they may not provide a good satisfaction about aesthetic expectations (8,11).

3.8. Shelf Life

Dental cements should retain their mechanical and physical properties for a clinically acceptable time. Changes in the properties of the cement before the specified shelf life may not be noticed by the dental practitioner. Therefore, shelf life is an important issue for dental cements (30).

4. Classification of Dental Cements

If luting cements are classified according to the time they are expected to remain in the mouth; They can be divided into two as temporary and permanent luting cement. Temporary cements should provide hold in the mouth until the next appointment, provide a lower strength compared to permanent cements, and can be easily removed from the relevant surface when desired. In addition, it should not damage the tissue to which it is temporarily attached. Zinc oxide-eugenol (ZOE) and non-eugenol cements and calcium hydroxide pastes are temporary luting cements. Since permanent luting cements are expected to remain in the patient's mouth as long as possible, they are expected to have the properties outlined above that are expected of a cement (8).

Most cements consist of two forms, powder, and liquid. The powder in cements is the base part that can release cations into acidic solutions.

The liquid portion is usually an acidic solution. Cations in the powder react with acid anions to form a salt (31). After a series of reactions, the cured cement is essentially a salt hydrogel matrix around unreacted powder. This matrix is the weakest and most soluble component of uncured cement (25). When cements are classified according to their setting mechanism, zinc phosphate, zinc polycarboxylate, ZOE, glass ionomer, and resin-modified glass ionomer cements are included in this group. The other group is resin cements, compomer, and self-adhesive resin cements cured by polymerization. However, in some cases, resin-modified glass ionomer cements contain polymerized groups, while compomer and self-adhesive resin cements can show acid-base reactions. In such cases, whichever event is more common in the setting reaction of the produced cement, the cement can be included in that group (8).

In addition, Craig classified cements according to their main components, while O'Brien classified them according to matrix type (32,33). Donovan, on the other hand, simply divided cements into two as conventional and contemporary based on knowledge and experience. According to this classification, zinc phosphate, polycarboxylate, and glass ionomer are included in the conventional classification, while resin-modified glass ionomers and resin cements are included in contemporary cements (34).

Finally, cements can be classified as active and passive. While composite resin cements and compomers that interact with dentin by forming a hybrid layer are considered active; cements that are mechanically clamped to rough areas in the tooth structure and restoration bonding surface are considered passive. Although glass ionomers bond chemically to dentin and form an interlayer, they are considered passive because they cannot bond to the restoration surface treated with hydrofluoric acid or silane (8).

5. Zinc Phosphate Cement

Zinc phosphate cements are the cements that have been in use for the longest time. It has been used successfully for many years for the cementation of metal, metal-ceramic and porcelain restorations (25).

The fact that it has been used successfully in dental practice for a very long time has caused this cement to be used as the 'gold standard' in comparative studies. More evidence-based studies have been conducted on zinc phosphate cement than any other cement (35). It has two components, powder and liquid. The powder part consists of zinc oxide (90%) powder containing magnesium oxide (10%) and liquid containing 45-64% phosphoric acid and 30-55% water. In addition, there are 2-3% aluminum and 0-9% zinc in the liquid. Zinc regulates the reaction between powder and liquid and provides appropriate working time. The recommended powder/liquid ratio is 2.5g/3.5ml (33).

The setting time determined by ISO in 2007 for dental cements is 2.5-8 minutes. There are four basic methods for chancing the setting time. The first of these is the reduction of the powder/liquid ratio. In this case, the curing time will be extended, but the pH will decrease. The second method is to perform the mixing process by adding the powder little by little. The third method is to delay the final amount of powder to be added to the mix. The fourth method is to perform the mixing process on a cold glass plate to cool the acid-base reaction, which is an exothermic reaction. The fourth method is the most effective method that can be applied to prolong the setting time. In this method, more powder can be added to the final mix, which improves the physical properties of the cement (36).

Zinc phosphate cements are attached to the surfaces by mechanical rather than chemical bonding. Therefore, the length, surface, and preparation angle of the prepared tooth are of great importance in fixed restorations to be bonded with this cement (33). In addition, in order to use non-adhesive cements in the cementation of ceramic and indirect composite restorations, the retention of the preparation must be good and the restorations must-have durability (23).

Zinc phosphate cement has very low pH values within the first hour after mixing. While the pH of the cement reaches 5 levels in 24 hours, it is neutralized only after 48 hours. These cements are not recommended in situations where pulpal irritation may occur and in deep preparations due to the low pH that exists for a long time (4). In cases where a dentin thickness of less than 1 mm remains between the pulp and the cement,

it has been suggested to use cavity varnish or calcium hydroxide on the preparation surface (37). A resin-based sealant is not preferred as it may adversely affect retention (38).

Water is important for the control of acid ionization. It should not be used in products whose lids are left open for a long time, as the water in the liquid will evaporate. If the liquid of the cement appears cloudy, evaporation of the water should be suspected. Water loss can prolong the setting reaction and vice versa (39,40).

When zinc phosphate cements are applied as a base, they should be mixed until they reach a solid and dry paste consistency. In this way, a strong and hard base material that hardens in a short time is obtained. A permanent restoration can be placed in the same session and a barrier that will protect the pulp both chemically and thermally is obtained. Solid preparation of the cement will be less irritating as it means less liquid to be included (4).

Zinc phosphate cements reach their maximum physical properties within 24 hours. Compared to other cements, their compressive strength is high and their tensile strength is low. Although they have a high modulus of elasticity, they are brittle and hard. Their solubility in water and acid environments is high. Therefore, they require minimal exposure in oral fluids. For this reason, it is suitable to be used as a base in filling materials with good sealing or in well-fitting restorations. Their use may not be the right choice in patients with an acidic diet and suffering from reflux (25).

6. Zinc Polycarboxylate Cement

Zinc polycarboxylate cement was developed in 1968 by a dentist working in Manchester, Dr. Dennis Smith (41). It is the first luting cement that bonds to tooth structures among the cements produced in those years. Its powder is mostly zinc oxide. Its liquid is a high molecular weight polyacrylic acid solution between 30-43%. In addition to zinc oxide, the powder contains 10% magnesium oxide and 4% tin fluoride. Although it contains fluoride, the fluoride release is 10-15% of glass ionomer cement. The fact that fluoride is released in such low amounts does not impart

anti-cariogenic properties to the cement. When zinc polycarboxylate cement is used for cementation, the recommended powder/liquid ratio is determined as 1.5/1. However, when it is desired to increase endurance, this ratio should be changed to 2/1. Working time was determined as 2.5-3.5 minutes at room temperature and setting time as 6-9 minutes (33).

It should be used in recommended powder/liquid ratios. If the mixture is prepared too thick, it indicates that there is insufficient acid to form adequate bonding to the tooth. If the excess liquid is used, the intraoral solubility of the resulting mixture increases significantly. When properly prepared, the mixture has a glossy appearance. It is important that the minimum time elapses between the completion of the mixing and the placement of the cement. The mixture should not lose its glossy appearance during cementation and application (6).

Zinc polycarboxylate cement is chemically bonded to dental tissues by ionic bonds through the interaction between the free negatively charged carboxyl groups in its liquid and the positively charged calcium ions in the tooth structure. The more mineralized the tooth structure, the stronger the bond. When the tooth structure is examined, the enamel is a more mineralized structure than dentin. Therefore, it can be said that it bonds relatively better to the enamel. In addition, this hydrophilic cement can wet the dentin surface (4,33,41,42).

The pH of the liquid of zinc polycarboxylate cement is approximately 1.7 (4). Although more acidic compared to zinc phosphate, the pH rises rapidly and is neutralized. In addition, the fact that these cements have large organic acid molecules prevents the penetration of these molecules into the dentinal tubules (25). In a study evaluating the effects of zinc phosphate and zinc polycarboxylate cement on pulp in deep cavity preparations, it was found that zinc polycarboxylate did not have a significant irritating effect on the pulp. It was concluded that possible irritation was caused by bacteria remaining in the pulp (43).

After cavity and tooth preparation, enamel and dentin surfaces can be covered with a smear layer. In addition, cementing the temporary restoration with zinc oxide-eugenol may cause the preparation to be covered with a thin layer of eugenol. In such cases, the contamination should be removed with 10% polyacrylic acid for 10-15 seconds (6).

Zinc polycarboxylate cements reach their final strength values in a short time. However, the results vary depending on the studies in the literature under different conditions and parameters (25). The compressive strength of zinc polycarboxylate is expressed as half or two-thirds of zinc phosphate, while the tensile strength is considered to be one-third more. The modulus of elasticity is one-third of zinc phosphate cement. They show significant plastic deformation against loading forces (32). Therefore, they are not recommended for cementation of long bridges and in areas with high chewing stress (42).

Considering the clinical applications of zinc polycarboxylate cement, the most important success is a very good pulpal compatibility due to the reasons described previously (44). They are used in sensitive teeth, short fixed restorations, areas subject to low chewing forces, cementation of metal-supported porcelain restorations, bonding of orthodontic bands, as cavity lining and base material, and as temporary restorations (42).

7. Zinc Oxide Eugenol Cement

The powder of zinc oxide-eugenol (ZOE) cement consists of 70% by weight zinc oxide added to rosin to reduce the brittleness of the cured material. The liquid part is the fluid obtained from the clove structure called eugenol. Eugenol, which has a bactericidal effect on its own, increases its bactericidal effect even more when combined with zinc oxide (45).

Zinc oxide-eugenol cements are defined as the least irritating of all dental products. Its pH is approximately 7 and it is argued that it has a sedative effect on the pulp. However, when zinc oxide eugenol cements are used in high concentrations, they can be toxic to the pulp (32). Therefore, direct contact of the pulp tissue with ZOE should be avoided.

Eugenol, which is mixed and applied to the patient's mouth, is released by hydrolysis. The wetness of the dentin causes sufficient eugenol to be released from the mixture at a concentration that kills bacteria but does not damage the pulp. A study on this subject showed that dentin protects the pulp from chemical irritation and there is a correlation between dentin thickness and this protection (46).

Although ZOE does not adhere to dental tissues, they provide a better seal when used in the recommended powder/liquid ratio (47). This marginal covering prevents dietary substrates from reaching the microorganisms under restoration. This causes a decrease in acid production by bacteria and reduced caries formation. By inhibiting bacterial cell metabolism, ZOE reduces the incidence of postoperative sensitivity in patients after treatment.

The hydrolysis of zinc oxide precedes the reaction between the resulting zinc hydroxide and eugenol. This allows the ZOE mixture to harden. The substance that acts as a catalyst in this reaction is water. With this humidity, the reaction occurs faster in a wet environment than in a dry environment (36).

The powder should be added little by little to the liquid while mixing ZOE. A flexible and sturdy spatula should be used during mixing. The resulting mixture is not exothermic, but working conditions should be adjusted by physicians as the humid environment will accelerate the reaction. If the powder/liquid ratio is increased, the mixture is drier and less sticky. It can also be manipulated more easily and is less irritating to the pulp as it contains less free eugenol.

The reaction between zinc oxide and eugenol has been used in dentistry in various fields such as endodontic pastes, root apex filling materials, wound closure after the periodontal procedure, inelastic impression materials, cavity base, and temporary restorations (22).

The main problem for zinc oxide eugenol cements is that residual free eugenol from phenolic hydrogen acts as a free radical scavenger and inhibits proper polymerization, which affects the microhardness and color stability of the resin composites. If a resin-based luting agent is to be used for permanent cementation, the use of temporary luting cements that do not contain eugenol in their formulation is important for the success and longevity of the indirect restoration (39).

8. Glass Ionomer Cement

Glass ionomer cement was introduced in 1969 by Wilson and Kent. The powder of glass ionomer cement is usually calcium fluoro-aluminosilicate

glass. But some mixtures can replace calcium with strontium and lanthanum. Its liquid is polyacrylic acid or other alkenoic acids such as itaconic acid or maleic acid. Tartaric acid can sometimes be added to improve transport properties (6,25).

Application forms of glass ionomer cements can be classified as follows (48,49).

Type I: Cements for bonding crowns, bridges, and brackets

Type II: Restorative cements

Type III: Base material and cements used as pit and fissure sealants

Type IV: Cements used as root canal filling paste

One of the most important properties of glass ionomer cements is their ability to bond to the tooth structure. The hydrogen bond formed between the carboxyl group of the polyacid and the calcium in the dental hard tissues forms the basis of the chemical bonding. In addition, it was determined that the glass ionomer cement showed a micromechanical penetration (50). The presence of a tooth-like coefficient of thermal expansion of glass ionomers reduces microleakage, minimizing the postoperative sensitivity that may occur in the patient after the procedure (51). One of its biggest advantages is that it can be absorbed onto hydrophilic surfaces. Thus, the gap between the restoration and the tooth can be completely closed (52).

The compressive strength of glass ionomer cements is higher than zinc polycarboxylate and zinc phosphate cements (42). Contamination of cement with water and saliva during application will adversely affect its mechanical properties. If the marginal fit of the restoration is weak, it may move from the restoration site as a result of water absorption and deterioration (52).

As with any acid-base reaction cement, saliva contamination should be avoided to prevent material loss due to erosion of the cement as a result of early dissolution (25). Some researchers have suggested temporary closure with a varnish, arguing that some ions are still in soluble form during the formation of the glass ionomer cement matrix (53). Other researchers have argued that there are risks of dehydration and microcracking in glass ionomers that have been insulated for a long time. In extreme dryness, cracks and crevices occur, discoloration and

edge leakage begin. They also commented that the use of a waterproof varnish and resin sealant to cover the exposed cement was unnecessary. Therefore, isolation in the oral environment for more than 10 minutes is not recommended (49,54,55).

In addition to chemically bonding to calcified tissues such as enamel and dentin, glass ionomer cements can also adhere to stainless steel, gold, platinum, amalgam, and composite. Their biological compatibility is good. They are well tolerated by the pulp (56). They adapt well to the gingiva. It has anti-cariogenic properties because it contains fluoride. This property of glass ionomer cement is due to fluoride release and storage. Fluoride replaces hydroxyl ions in the structure of hydroxyapatite, forming fluorapatite, which is extremely resistant to caries. Fluoride also inhibits enzymes involved in plaque metabolism. The fluoride gained by the enamel from the glass ionomer cement continues for 6 months, even if the restoration is removed. Fluoride release has been shown to be pH-dependent. In addition, glass ionomer cements show fluoride uptake (fluoride charge) after topical fluoride application. The choice of this material as the bonding agent may be an important issue for the patient with high caries potential (57). Glass ionomer cements are sensitive to moisture, with moisture contamination the hardness of the material decreases, and its dissolution increases. They have low resistance to abrasion, tensile and tensile forces. Its aesthetic appearance and color stability are not good (58).

Some cases have been reported to cause postoperative sensitivity when glass ionomer cement is used as an adhesive agent, particularly in deep preparations with minimal dentin thickness. This may be due to the low initial pH of the cement and its slow curing reaction. In order to protect against possible pulpal damage, very deep cavities and preparations should be covered with calcium hydroxide. The prepared dentin surface can be cleaned mechanically with pumice, but the smear layer should not be removed to prevent the dentinal tubules from opening. After cleaning, the dentin should be rinsed and dried, but excessive drying should be avoided. A slightly damp surface appearance is sufficient to help minimize sensitivity (6).

9. Resin-Modified Glass Ionomer Cement

These cements were introduced in the late 1980s to combine the known and desirable properties of glass ionomer cement with the high strength and low solubility properties of resins (59). The powder part consists of fluoroaluminosilicate glass powders. The liquid part consists of HEMA (2-Hydroxyethyl methacrylate), methacrylate groups (Bis-GMA), polyacrylic acid, tartaric acid, and 8% water. The methacrylate groups provide polymerization of the cement, while the polyacrylic acid is responsible for reacting with the glass for the acid-base reaction. HEMA holds the resin and acid components together in an aqueous solution and takes part in the polymerization reaction. In an acid-base reaction with water, it ionizes the acid so that the reaction can start. Other components in the cement are polymerization activators and stabilizers (60).

An additional light-curing reaction has been added to the acid-base curing reaction in light-cured resin-modified glass-ionomer cements. The continuation of the acid-base reaction in the matrix formed as a result of light polymerization causes better hardening and higher resistance of the cement (61). Resin modified glass ionomer cements are known to be fluoride reservoirs like conventional glass ionomer cements. Resin-modified glass-ionomer cements contain 23% fluorine and their fluoride release and recharge capacity are higher than conventional glass ionomer cements (62). When evaluated in terms of their biological compatibility, they are considered to be biocompatible (56,58). However, residual monomer (HEMA) release may occur even if polymerization is provided in accordance with company instructions. This may adversely affect pulp biology at various levels, from sensitivity to inflammation, and may lead to allergic reactions and contact dermatitis. As a result, the biocompatibility of resin-modified glass-ionomer cements are lower than that of conventional glass ionomer cements due to the HEMA it contains (63). Due to their resin substructure, they provide a better aesthetic result than conventional glass ionomers. Although their compressive strength is the same as conventional glass ionomer cements, their tensile strength is twice that of conventional glass ionomer cements. Their resistance to

abrasion is better than conventional ones. Chemically bonds to tooth structures like conventional glass ionomer cements. It is less soluble in the oral environment than conventional glass ionomer cements. They are easy to manipulate and have long working times.

Resin modified glass ionomer cements have some disadvantages as well as advantages. As a result of polymerization shrinkage, microleakage, and thus postoperative sensitivity and discoloration may occur (56,58). Another disadvantage is that they contain HEMA, which has a hydrophilic structure. HEMA is a material that has a tendency to absorb water and is responsible for water absorption, subsequent plasticity, and hygroscopic expansion. Initial water absorption can compensate for polymerization shrinkage stresses, but continued water absorption leads to significant dimensional change. Cement that changes in size under restoration may cause fractures and cracks in the restoration over time. Therefore, its use in all-ceramic feldspathic restorations is contraindicated. In addition, it has been observed that post cementation applied to non-vital teeth increases the risk of fracture in tooth roots due to enlargement (61). It is frequently used in cavity lining material, base material, permanent cementation of restorations, and bonding of core and orthodontic bands (33).

10. Poly-Acid Modified Composites (Compomer)

Compomers, also known as polyacid modified composite resins, emerged in the late 1990s and are defined as a combination of composite resin (comp) and glass ionomer (omer). This restorative material contains dimethacrylate monomers with two carboxyl groups and ion-releasing glass-like fillers found in resin-modified glass ionomer cements. In addition to these, there are reaction initiators, stabilizers, and pigments (64). It contains 20-30% glass ionomer cement and 70-80% composite resin (49,65).

The physical properties of compomers are more similar to composite resins than glass ionomers. The compressive and flexural strengths of compomers are higher than RMGI but lower than resin composite (66). Compomers contain 13% fluorine and fluorine releases are also very low (62). Fluoride charge occurs but less than conventional glass ionomer (67).

11. Resin Cements

Methacrylate-based resin cements have been used for many years as liner and base materials, as well as for cementation of indirect restorations (32, 4). Although resin cements have basically the same content as composite resins used for restorative purposes, they contain less (50-70% by weight) glass and silica fillers than restorative composites (42). In addition, the distribution of filler material and initiator content has been changed so that they have lower film thickness, appropriate curing and working time (22). Resin cements are classified into three categories according to their curing mode as self-cured (class I), ligth-cured (class II) and dual-cured (class II). Most of the resin cements available on the market are dual-cured resin cements in which chemical and photoactivation mechanisms are combined. Resin cements with this feature not only offer a comfortable working time, which is characteristic of light-cured composite resin materials, but also provide a safe conversion safety with their self-cured properties even in areas where light cannot reach (8).

Resin cements are divided into three categories according to their use and bonding procedures: 1-etch-and-rinse cements, 2-self-etch cements, 3-self-adhesive resin cements (68). Etch-and-rinse cements are the most clinically reliable and long-lasting, as well as the most technically complex resin cements. While the adhesive stages applied to the tooth surface can be 3 stages such as applying acid, primer and bonding agents; After the acid is applied, there can be 2 stages with the presence of primer and bonding agents in a solvent in a single bottle (69,70). The acid (conditioner) usually consists of 30-40% phosphoric acid. It removes the smear layer and smear plugs and demineralizes intertubular dentin to a depth of 5-10 μm leaving hydrated collagen bundles, exposing Type 1 collagen in dentin. The acid is washed off with water and the tooth surface is carefully dried or left moist, depending on the solvent content of the adhesive (71,72). While hydrophilic primary resins are hydrophilic for exposed collagen fibrils, they are hydrophobic for copolymerization with adhesive resin. Bonding acts as a bridge between the resin-based composite and the hybrid layer. The three-stage etched and washed cements showed excellent bond strength both in-vivo and in-vitro (73).

However, their multi-step and technical precision complicate their use by dental practitioners. In order not to reduce the bond strength, each step should be applied at the times specified by the manufacturer and saliva contamination should be prevented (32). It has been reported that they cause postoperative sensitivity (74,75).

In self-etch resin cement systems, there can be 2 stages or it can also be in the form of 1 stage. It performs acidic resin primer, enamel and dentin etching and priming. Their pH is between 1-2. The bond or adhesive resin acts as a bridge between the hybrid layer and the resin-based luting cement. It has been reported that the postoperative sensitivity decreases with the use of self-etch resin cements (76). Although resin cements containing these bonding systems are more preferred by dentists due to the low application steps, it has been reported that they show weaker bond strength than cements that are etched and washed on the enamel surface. It has been reported that caution should be exercised when used with chemical or light-cured cements, since the acidic primer may inhibit the amine catalyst in the luting cement. It has been reported that this can inhibit resin polymerization. Therefore, it is not recommended to use single-stage binder systems with resin-based cements (77).

Cementation of inlay-onlay restorations, fixed crowns and bridges, application of prefabricated metal and fiber posts into the canal and fixation of orthodontic brackets to the tooth surface are performed successfully with this type of cement. Apart from this, they are mandatory cements to be used in the cementation of low strength ceramic restorations and indirect composite restorations (8,74). However, when restoration thicknesses are thicker than 2mm, the exposure time of the resin cement to light should be extended beyond the manufacturer's recommended times (75).

The organic matrix of resin cements usually contains dimethacrylate monomers and oligomers. High molecular weight molecules such as Bis-GMA, UDMA and ethoxylated Bis-GMA (Bis-EMA) are combined with smaller molecules derived from ethylene glycol dimethacrylates (diethylene glycol dimethacrylate) to achieve a high degree of conversion with low volumetric shrinkage. Resin cements, which are known to have

less filler content than restorative composites in order to obtain fluidity and a thin film layer, contain silane radiopaque glasses such as barium, strontium or zirconia as well as silica filler particles. It is known that the average filler size is 0.5-8.0 μm.

Both pastes contain pigments and opacifiers. Some adhesive resin cements have their own proprietary monomers, such as MDP. The resin catalyst paste contains benzoyl peroxide, a self-curing activator. Camforquinone and a tertiary amine are added to one of the pastes to initiate the light reaction of resin cements. The amine in the resin cement gives positively charged ions and also acts as an accelerator in the production of free radicals to initiate the polymerization reaction. The presence of amines in the structure of resin cements is of concern because it can cause adverse clinical outcomes. It has been clinically experienced for years that amines degrade over time and change the color of cements. In addition, when used with an acidic adhesive system, contact with acid renders amines inactive. In the absence of light activation, the polymerization of the cement cannot be initiated by the inactive amines. This situation, which negatively affects the degree of conversion of the resin cement, may increase the risk of debonding of the restoration (8). Trying to solve this problem, some manufacturers add chemical activators to traditional 2-stage and 1-stage systems. These activators consist of catalysts that react with acid monomers to form free radicals. These free radicals initiate the chemical polymerization of composites (75). After the resin cements have hardened, the resulting product is actually a polymer, not a cement. However, the term cement is used to describe the function, not the chemistry, of the product (36).

Resin cements are versatile as it is a material that can be used for both liner, base and cementation. In addition, it has high compressive and tensile forces, low solubility and high aesthetic properties compared to other cements. Therefore, it occupies a large place in the dental market. In addition to these features, the main disadvantages are that it is difficult to remove the excess from the restoration tooth interface, requires technical sensitivity during its use, is more expensive than other cements, this process is difficult when the restoration needs to be removed, and they are sensitive to moisture (78).

12. Self-Adhesive Resin Cement

Self-adhesive resin cements have been developed in line with clinicians' desire to reduce adhesive procedures during resin cement use and to prevent contamination that may occur during long-term adhesive application (79). Self-adhesive resin cements are hybrid materials developed in some cases by combining the properties of conventional dental cements, composite resins and self-etch adhesives (80).

One of the components in self-adhesive resin cements consists of mono-, di- and/or multi-methacrylate monomers used in resin-based dental materials. These are generally Bis-GMA, urethane oligomers of Bis-GMA, UDMA, HEMA, Glycerol dimethacrylate (GDMA), TEGDMA, trimethyloylpropane trimethacrylate (TMPTMA) and others. Acid-functional monomers are currently used for demineralization and bonding on tooth surfaces, mainly methacryloxyethyl trimellitic anhydride (4-META), pyromellitic glycerol dimethacrylate (PMGDM), (meth)acrylate monomers with phosphoric acid groups, 2-methacryloxyethyl phenyl hydrogen phosphate (Phenyl-P) is 10-methacryloxydecyl dihydrogen phosphate (MDP). In addition to these, new phosphate-based acidic-functional monomers continue to be developed, especially for demineralization of enamel. The concentration of the acidic functional monomer in these materials should be low enough to prevent excessive hydrophilicity in the formed polymer, but high enough to cause sufficient demineralization to bond to enamel and dentin tissue. Ensuring this balance is important for the stabilization of the cement. The fillers used consist of selected combinations of barium fluoroaluminoborosilicate glass, strontium calcium aluminosilicate glass, quartz, colloidal silica, ytterbium fluoride, and other glass fillers. The average total filler particle content in self-adhesive resin cements is in the range of 60-75wt% (79).

Self-adhesive resin cements, which are specifically designed to interact with the dentin surface without requiring any surface preparation, bond with dental hard tissues chemically and micromechanically (81). In the bonding mechanism, the adhesive substrate simultaneously demineralizes the smear layer and the underlying dental hard tissue and infiltrates

the formed gaps. Multifunctional monomers react with hydroxyapatite in dental hard tissues. When phosphorylated methacrylates come into contact with the water in the tooth, an average pH value of 1.5-3 occurs. Like self-etch adhesives, they etch enamel and dentin, and the cement penetrates etched tooth surfaces. When the cement is polymerized, a micromechanical bond is formed with the tooth (79).

In self-adhesive resin cements, etching of dentin is easier than enamel at low pH, which is formed as a result of chemical reactions. Therefore, self-adhesive resin cements bond to dentin better than enamel. However, etching the enamel with phosphoric acid before applying these cements positively increases the bond strength of the enamel. However, the same positive development cannot be achieved when dentin is pre-etched. Because it has been shown that self-adhesive resin cement cannot penetrate a thick collagen network formed after phosphoric acid (82,83).

Self-adhesive resin cements do not have any of the multiple steps required for etch-and-rinse cements. Therefore, they eliminate the technical sensitivity. Although their bond strength is lower than that of etch-and-rinse adhesive cements, they are similar to self-etch cements. Self-adhesive resin cements were found to provide more retention compared to resin modified glass ionomer cements. In addition, its use with all-ceramic restorations shows positive results. Because these restorations require more removing the dental hard tissue from the teeth than metal restorations to increase the strength of the ceramic. However, self-adhesive resin cements improve retention and support ceramic restoration, thanks to their good bonding to the tooth. In addition to these properties, self-adhesive resin cements are easy to use, have better physical properties than conventional cements, resist compression, have good microhardness, they have sufficient film thickness for single crown cementations (81).

The most recently developed self-adhesive resin cements are preferred by dental clinicians due to their resin cement structure and easier application. However, these newly introduced products need to be supported by clinical studies to decide whether they are at the level of resin cements.

13. Conclusion

Today, there is no ideal dental cement that clinicians can use for all conditions and patients. Dental materials are changing rapidly and new materials are introduced to the market before the evaluation processes of the previous ones are completed. The dental material market is a manufacturer driven rather than clinician demand.

There is no guarantee that products released with improved properties will result in good clinical performance. Long-term clinical follow-up studies are needed to evaluate these results. For this reason, working with old materials that have proven their reliability as well as their supposed properties are a good option for dentists. It is also very important for clinicians, as practitioners, to have a good understanding of the indications and limitations of dental cements and to interpret them with the patient's situation.

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CHAPTER VIII

CAVITY LINER AND BASE MATERIALS IN RESTORATIVE DENTISTRY

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1. Introduction

Tooth tissue has three main components: enamel, dentin and pulp. Dentin and pulp tissue are two tissues that are both anatomically and functionally interconnected. It is important to protect the pulp tissue from caries, mechanical forces, chemical stimuli caused by bacteria and restorative materials and thermal injuries. The aim of restorative dentistry is to protect this tissue, to maintain the vitality of the tooth and to complete the lost tooth structure.

In deep caries lesions, pulp preservation becomes more important as the cavity preparation goes deeper. Conventional restorative materials may be insufficient to provide these properties. Thefore, cavity liner and base materials have been developed to fulfill this task (1). The most important criterion for pulp preservation is the remaining dentin thickness, depending on the depth of the cavity preparation. The remaining dentin thickness has excellent buffering capacity to neutralize the effects of cariogenic acids (2). It may be necessary to place protective materials on the pulp in order to protect the pulp tissue from chemical, thermal, electrical, mechanical effects and to encourage tertiary dentin formation. Linings and base materials used for this purpose under restorations are common practice and they continue to be an important part of restorative procedures (3, 4).

2. Cavity Liners

Liners have been introduced as products applied as a very thin layer to the restoration-tooth interface to protect the pulp and dentin from the potential toxic effects of restorative materials and by-products of microorganisms (2). Cavity primers are classified as solution primers (varnishes) 2-5 μm and suspension primers 20-25 μm. Varnishes are applied to the cavity preparation in a thin layer and by evaporation of the solvent, they close the dentinal tubules. For this reason, varnishes can be considered as a lining material because they seal the dentin (3). However, it is contraindicated when using composite resin in the upper restoration. They can provide insulation and thermal protection against first-time electrification in metallic restorations to be made on dentin, amalgam fillings, and indirect restorations (1).

Suspension linings are a thin (20–25 μm) film layer that acts as a barrier between the dentin and the restorative material. They provide a therapeutic effect, but do not provide mechanical support (3). When too much dentin is lost due to caries, the use of suspension linings alone is insufficient in terms of thickness, hardness and strength (5).

3. Cavity base materials

Base materials are applied on the axial pulp wall of 1-2 mm thickness. They replace lost dentin and provide mechanical support in deep cavity preparations. It protects the pulp against thermal stimuli. They provide local stresses to be distributed from the upper restoration to the underlying dentin surface. It helps to resist breakage of fine dentin on the pulp during amalgam condensation procedures and cementation of indirect restorations (2).

Although common generalizations have been made about cavity lining and base materials since they have similar usage purposes, they are not the same in every case (1). Improvements in lining and base materials and a better understanding of pulp biology have changed the indications for use of these materials. The properties of materials currently available and how they interact with pulp tissues are important factors in the

decision of clinicians when to use a liner or base material and which products to choose (5,6).

In this section, pulp covering materials, their intended use and physical properties will be reviewed and the issues related to their clinical use will be discussed.

4. Intended Uses

One of the functions of enamel and dentin is pulp insulation. Most restorative materials cannot insulate like enamel and dentin. Recently, composite resin materials with improved aesthetic, mechanical and physical properties have become popular in order to anatomically restore lost tooth tissues. However, composite resin restorations have disadvantages such as secondary caries, restoration fracture, erosion, marginal deterioration and postoperative sensitivity (7). It is generally accepted that postoperative hypersensitivity remains a concern for resin-based restorations and poses a hazard to biological pulp tissue (7,8). The main causes of hypersensitivity are polymerization shrinkage, monomer dissolution, and acidic fluid accumulation between the restoration and dentin. So it is microleakage (7). Microleakage is affected by the thermal expansion difference between the restorative material and the tooth surface, polymerization shrinkage, the structure of the enamel prisms, the application procedure of the material, and the finishing and polishing processes. Bacteria in the oral cavity may enter the restoration and tooth interface and cause postoperative sensitivity, marginal discoloration, secondary caries, pulp inflammation, and pulp necrosis. Postoperative hypersensitivity can be defined as pain in a tooth or sensitivity to hot, cold and sweet stimuli that persists for a relatively long time after temporary restoration. To prevent such problems, 1-1.5 mm protective material should be applied to the dentin surface to protect the pulp before permanent restoration is made (5,7).

When using a liner or base, it should be considered that the interface between the material and dental tissues is dynamic and not static. The interaction between the two, how the body will respond to the foreign substance and how the material will resist degradation by the body is

important. Possible reactions can be classified as toxic, inflammatory, allergic or mutagenic. The pulp has the ability to make more dentin (reparative, tertiary dentin) against various irritations such as a result of caries, cavity preparation or interaction between tooth tissue and restorative material. The response of the pulp-dentin complex is thought to depend on the remaining dentin thickness (5). In cases where the dentin thickness remains 0.5 mm or the pulp is opened, protecting the pulp with a protective material is important for the continuation of tooth vitality. The remaining dentin thickness should be approximately 2 mm or equivalent thickness of protective material should be available. Although this thickness is not always possible, 1-1.5 mm insulation thickness can be considered as a suitable thickness.

In addition to thermal protection, lining materials, to prevent micro-leakage between tooth tissue and restoration, to prevent microorganisms from reaching the pulp, to occlude dentin tubules against postoperative sensitivity, to provide support that can replace dentin in deep cavities, to prevent very thin dentin (0.5 mm) in deep cavities, or to encourage the formation of reparative dentin by covering the pulp tissue are used (3). Conventional coating materials include zinc oxide ogenol (ZOE), calcium hydroxide, glass ionomer and resin-modified glass ionomers (RMGI). Calcium hydroxide is considered the gold standard and has long enjoyed high popularity among clinicians (1,3). With the development of glass ionomer cements, the tasks of lining and base materials began to convergePreviously, a calcium hydroxide liner was placed in deep cavities. Then, base material began to be placed on it to provide mechanical support and to distribute the forces. Today, light-cured calcium hydroxide and glass ionomers are used as both lining and base materials. (1). Conventional glass ionomer and resin modified glass ionomer cement are widely used due to their ability to adhere to tooth surfaces, fluoride release and anticariogenic properties. Their ease of use, rapid hardening, low coefficient of thermal expansion and biocompatibility have made them popular as lining and base materials (9).

The development of a biocompatible calcium silicate material (mineral trioxide aggregates, tricalcium silicates, etc.) marked a turning point in the development of a unique material category (9).

The prognosis of treatment in pulp covering is greatly affected by the type of covering material used. An ideal pulp covering material should be well bonded to dental hard tissues and be biocompatible. Biocompatibility refers to the ability of a material to perform with an appropriate host response without adverse effects. Good biocompatibility is an important prerequisite for the use of biological materials in living organisms (2,5). Other desirable properties are good bond strength, marginal sealing, insolubility in tissue fluids, easy handling and manipulation, short curing time, suitable mechanical properties, radiopacity, antimicrobial activity and low cost (10). Recently, new calcium silicate materials such as MTA, Biodentin, TheraCal have been developed for this purpose (11).

5. Zinc Oxide Eugenol (ZOE)

Zinc Oxide Eugenol (ZOE) is an unsaturated aromatic phenol whose powder part consists of 70% zinc oxide (ZnO), and its liquid part is produced from clove oil. ZnO is a white, odorless moisture-affected powder. Assumed to be the least irritating dental material used for over the century. (5).

ZOE formulations are used in dentistry as linings, base cements and temporary restorative materials. ZOE also serves as cementation of temporary restorations, root canal filling, surgical dressing and impression material. However, its use for direct pulp capping is controversial (6). Thanks to its sedative, analgesic and antibacterial properties, ZOE is an ideal base material for the treatment of pulp symptoms such as reversible pulpitis (12). Although it has a pH of about 7 and has a sedative effect on the pulp, high concentrations of ZOE are toxic. Therefore, the ZOE should not be placed in direct contact with the pulp. They can be easily removed over the teeth and provide a perfect seal against leakage. ZOE karışımlarından salınan öjenolün dentine nüfuz ettiği gösterilmiştir. It has been shown to adversely affect the physical properties and polymerization of composite resins (13). Compared to glass ionomer cements, it has good sealing potential, although it is less resistant to chewing pressure. To strengthen its physical properties, resin, fused silica, quartz, aluminum,

cotton fibers, calcium, phosphate and ethyl cellulose are added to the powder. Polystyrene or ethoxy benzoic acid is added to the liquid (14).

6. Zinc Phosphate (ZOP)

Zinc phosphate cement (ZOP) is the oldest luting cement introduced by Dr Otto Hoffman in the 1800s. Similar to ZOE, it has two components as powder and liquid. Powder consists of zinc oxide (90%) and (10%) magnesium oxide and other oxides, while liquid phosphoric acid consists of aluminum phosphate (acts as a buffering agent) and water. ZOP cement is highly resistant to pressure. It has sufficient working time (2.5-8 minutes) (15). Water affects the rate of the acid-base reaction. Increasing the amount of water results in a reduction in both compressive and tensile strength and a longer curing time (5,16). Fine-grained zinc phosphates are used for bonding permanent metallic restorations and cementation of orthodontic bands, while medium-grained ones are used in clinical applications as heat-insulating base material (2). Bonding to enamel and dentin is provided by mechanical principles. Its biocompatibility is low and due to the presence of acids in its structure, it has the potential to cause pulp inflammation in deep cavities. At first, the pH rises rapidly, reaching 4.2 after 3 minutes of mixing, and reaching PH 6 after 1 hour (2). Disadvantages of ZOP cements are solubility in oral fluid, low hardness, high risk of sensitivity due to low initial pH, and lack of anti-cariogenic effect (2,15). Despite many disadvantages, it has good clinical performance as a base material (2).

7. Zinc polycarboxylate (ZPC)

Zinc polycarboxylate (ZPC) cement was first described by Smith in 1968. ZPC is also known as zinc polyacrylate. Similar to ZOE and ZOP, it has two components as powder and liquid. The powder consists of zinc oxide and magnesium oxide, while the liquid contains a 35-40% aqueous solution of polyacrylic acid. They belong to the class of materials known as acid-base reaction. It is prepared by mixing modified zinc oxide and pure zinc oxide with a small amount of magnesium oxide and melting

the mixture at 1100-1200 °C. This process reduces the reactivity of zinc oxide to acid so that in clinical use the cement hardens slowly enough to be mixed and placed (5,17). It is similar to ZOP in durability and ZOE in biocompatibility. The pH of the liquid is about 1.7, and the free acid is quickly neutralized after mixing.

ZPC cements have been widely used in cavity linings, placement of crowns and bonding of orthodontic appliances (16-18). ZPC and glass ionomer cements are two types of polyelectrolyte cements commonly used as adhesives in dentistry. Due to their hydrophobic properties, they can wet dentin and enamel surfaces and bond chemically. The binding is the result of the reaction between the carboxyl groups of the cement and the calcium in the tooth structure. Therefore, the more mineralized the tooth structure is, the stronger the bond is formed (19).

Its disadvantages are low operating time (1–2 minutes) and low compressive strength (40–70 MPa). An attempt has been made to overcome these disadvantages by adding various fillers to ZPC cement (19). It has been shown that when potassium nitrate is added, ZPC becomes an effective lining material and has no adverse effects on pulp viability. Both ZOP and ZPC are acidic, help remove the smear layer formed during cavity preparation and are easy to adapt to the cavity. When used as a base material, ZPC allows an immediate final restoration to be placed on top of it (5).

8. Calcium hydroxide (CH)

Calcium hydroxide (CH) was introduced in 1921 and is considered the "gold standard" of direct pulp capping materials in dental practice. CH has two well-known important advantages: its antibacterial effect is excellent and promotes dentin bridge repair. CH is believed to affect pulp repair through one or more mechanisms of action (6). It dissociates into calcium and hydroxyl ions. Hydroxyl ions inhibit the enzymatic activities of microorganisms with high pH (approximately 12). The release of calcium ions is essential for the mineralization process (19). The high pH of calcium hydroxide stimulates dentin formation by irritating the pulp tissue. It is known that various proteins are involved in the dentin matrix

during dentinogenesis. At least two of these proteins, Bone Morphogenic Protein (BMP) and Transforming Growth Factor-Beta One (TBF-β1) are known to exhibit the ability to stimulate pulp repair (6).

Besides, it has some negative features. CH dissolves over time, does not bind to dental hard tissues, has insufficient mechanical resistance and poor sealing properties. Another disadvantage is the appearance of so-called "tunnel defects" that allow bacterial invasion in the reparative dentin formed under calcium hydroxide (3).

Various forms of conventional CH are available. These are aqueous solutions, primers, cements and resin fillers. After application of aqueous suspensions of CH, the solvent is removed, leaving a layer of calcium hydroxide. It has been modified with a varnish to improve the use and viscosity of the CH used as a primer. Calcium hydroxide cements are two separate tubular systems. One tube contains CH and the other salicylate. Visible light-cured CH primer contains CH, barium sulfate, visible light-activated initiators and urethane dimethacrylate resin (2,3).

One-component visible light-cured CH was developed to overcome the disadvantages of chemically cured CH. Acid and water solubility properties are increased. The polymeric resin content of the material allows bonding between the overlying composite restoration. However, it has been reported that the degree of ion release of light-cured calcium hydroxide compounds is lower than that of chemical-cured compounds, and their alkalizing and antimicrobial properties are lower (2,3,21). Although CH is widely used by clinicians, its effect on clinical success in selective or gradual deep caries lesion treatments is examined; it was found to be moderate for primary teeth and low for permanent teeth (22).

9. Glass Ionomers (GI)

Conventional glass ionomers were first introduced by Wilson and Kent in 1972. GI is available in powder and liquid form. The powder is an acid-soluble calcium fluoroaluminosilicate glassAfter the powder and liquid are mixed, the acid corrodes the silica. It results in the dissolution of calcium, aluminum, sodium and fluoride ions. Fluoride is released

from the hardened material and provides anticariogenicity (2,5). Glass ionomers are available in different forms of use in powder-liquid, paste-paste and capsules. The ability of glass ionomers to bind to dental tissues is a chemical linkage that occurs through the chelation of carboxyl groups of acid polymer chains with calcium ions in enamel and dentin (23). It has a similar expansion coefficient with tooth tissueTherefore, it helps to reduce microleakage and postoperative sensitivity (5). Gradually improved properties of moisture-affected GI (24). Although they have similar contents, they are classified according to different application methods.

Type I: Bonding cement (crown-bridge, orthodontic bracket)

Type II: As a restorative material (Aesthetic and Strengthened)

Type III: Used as fast-setting base material and fissure sealant (23,25).

The two main properties that make GI cement the most acceptable restorative material for direct pulp capping and indirect pulp capping treatment are its good adhesion to enamel and dentin, and fluoride release. In this way, it helps to reduce dentin hypersensitivity (2).

Short working time, long curing reactions, poor resistance to abrasion, susceptibility to moisture contamination, and dehydration in the early stages of the curing reaction are disadvantages of conventional GI (25). Resin-modified glass ionomers (RMGI) have been introduced to improve mechanical properties, shorten curing time, and reduce moisture sensitivityFor deep restorations that are close to the pulp but do not expose the pulp, an RMGI liner may be the primary choice. These materials are very dimensionally stable, bind to dentin and release fluorine. They also reduce stress on the tooth and can prevent microleakage (2,24).

10. Cements with Calcium Silicate Content

Preservation of dental pulp vitality and healing of the dentin layer can be achieved by direct pulp capping procedure. Successful direct pulp capping treatment preserves pulp vitality and functionality and promotes new dentin bridge formation. The size and depth of the caries lesion, the presence of microorganisms, the age of the patient and the type of biomaterial used also play an important role in the prognosis and success of the procedure

(26). In vital pulp treatments, pulp coating materials increase the biological responses of pulp cells and support tertiary dentinogenesis by stimulating odontoblast secretory activity (26). Calcium hydroxide, zinc oxide eugenol, resin modified glass ionomer cement, adhesive systems, enamel matrix derivative, collagen, formocresol and hydroxyapatite have been suggested as pulp coating materials. However, lack of adhesion to dentin and resin restorations, poor mechanical properties, bacterial infiltration, tunnel defects in dentin bridges and pulp resorption led clinicians to seek new biomaterials. Recently, hydraulic calcium-silicate cements derived from the original Porland cement have been introduced. Porland cement consists of lime, silica, alumina, iron oxide and other compounds (27). Porland cement also contains arsenic, which raises great concerns about its use because of its toxic effects. Porland cement and Mineral Trioxide Aggregate (MTA) have similar compositions, while other materials (biodentin) are modified or hybrid materials for mechanical and biological enhancements (26). Calcium silicate-based cements are widely used in endodontic procedures involving pulp regeneration and hard tissue repair, such as pulp capping, pulpotomy, apexogenesis, apexification, perforation repair, and root tip filling (28). The setting reaction, known as hydration, can occur in wet environments. The curing reaction refers to the reaction of calcium silicate with water-forming calcium-silicate hydrate and calcium hydroxide (29). In recent years, materials containing calcium silicate have been used for this purpose.

10.1 Mineral Trioxide Aggregate (MTA)

Mineral trioxide aggregate (MTA) was introduced in 1993 and was the first calcium silicate cement used in endodontic treatment (30). It is used in various clinical applications such as apexification, root perforations, internal and external resorptions, root canal filling material. The bioactivity of this material, stimulation and regeneration of the dentin-pulp complex, prevention of bacterial leakage, low solubility, ability to release calcium hydroxide, and curing reaction in moist environment have made it available as a pulp-coating agent (31). The main components of MTA are tricalcium silicate, tricalcium aluminate, tricalcium oxide and silicate oxide. Originally

produced MTA was gray in color, but white MTA was developed due to aesthetic concerns. Although there is no difference between the two MTA forms in terms of physical properties and biocompatibility, it is seen that iron oxide, aluminum oxide and magnesium oxide are higher in gray MTA in terms of content. The color change is thought to be the result of iron oxide reduction. White MTA has also been reported to have an overall smaller particle size than gray MTA (32). Analysis of the structure of the white and gray versions of MTA revealed that both materials were similar to Portland cement, but bismuth oxide was added to render the materials radiopaque for dental use (33). MTA is in the crystalline phase before the hydration reaction. It has been reported that it mainly exists in the form of calcium oxide and amorphous calcium phosphate in this phase, and when powder-liquid is mixed, it hardens after the hydration reaction and becomes a colloidal gel. Initially, CH and calcium silicate hydrate are formed and eventually turn into a weakly crystalline and porous solid gel. Due to the formation of calcium precipitate, the ratio of calcium silicate decreases. The precipitated calcium produces CH which is the reason for the high alkalinity of MTA after hydration (34). The pH of MTA was determined as 10.2 immediately after its preparation; it has been stated that this rises to 12.5 within three hours after curing (34). When the powder is mixed with sterile water at a ratio of 3/1, the working time is approximately 5 minutes and the total hardening time is 165 ± 5 minutes (35). Although MTA remains the best hydraulic calcium-silicate material in its class, there are some disadvantages. Disadvantages of MTA are the difficulty associated with clinical use, long curing time, inability to remove from treated areas (no known solvent), low levels of arsenic release (not clinically contraindicated), tooth discoloration, and high cost. In order to eliminate the undesirable properties of MTA and improve pulp response, new materials based on second generation tricalcium silicate have been developed (26,28,31).

10.2 Biodentine

Biodentine is a newly developed based on tricalcium silicate (Ca3SiO5) new material. It consists of powder and liquid form. The powder form

is made of tricalcium silicate, calcium carbonate and zirconium oxide; the liquid form consists of hardening accelerator calcium chloride and superplasticizer polycarboxylate. Liquid is dropped into the powder in the disposable capsule and mixed for 30 seconds in an amalgamator until it reaches a paste-like consistency. It has improved physical properties and curing time has been reduced to 12 minutes compared to Portland cements (36,37). Initial setting time is 9-12 minutes and final setting time is 45 minutes. This cure time is an improvement over other calcium silicate materials. This is because calcium chloride is added to the mixing fluid. (30-32,35,38).

Biodentin is denser and less porous than MTA due to its low water content in the mixing stage. This results in less microleakage and bacterial infiltration (39). Biodentine has a wide range of applications including endodontic repair (root perforations, apexification and retrograde filling material in endodontic surgery) and pulp capping. It can be used as a direct pulp coating and dentin replacement material in restorative dentistry (38,40). Biodentine provides stimulation of growth factors that activate dentineogenesis and differentiation of odontoblasts. By increasing the secretion of TGF-B1 (growth factor) from pulp cells, it causes angiogenesis, aggregation of progenitor cells, cell differentiation and mineralization (32). It has been stated that it has bioactive properties, promotes hard tissue regeneration, and does not show any signs of moderate or severe pulp inflammation response. Its clinical ease of use and superior mechanical properties, sealing properties, antibacterial properties seem to meet therapeutic and restorative requirements (39). However, it has disadvantages such as higher cost and longer curing time compared to calcium hydroxide (41). To overcome the water-based chemistry of biodentin and its poor micromechanical bonding to the overlying resin restoration, TheraCal LC has been introduced as a light-curable resin-modified tricalcium silicate pulp capping material (36,42).

10.3 TheraCal LC

Resin-based materials are a group of commonly used dental materials in different compositions (43). TheraCal LC is produced as a lining material

used under pulp coating material and restorative material. It is a light-curing hybrid material in paste form based on calcium silicate. TheraCal LC contains radiopaques as Portland type III cement (45%), silica (7%), resin (43%), bismuth oxide (3%), and barium sulfate (3%) (42). The goal in the development of this material was to take advantage of tricalcium silicate biocompatibility and proven bioactivity by reducing the setting time of calcium silicates. Light-cured resin-containing material can be used as a direct pulp coating agent, as a protective lining/base under restorations in deep preparations (44).

There are still concerns about pulp cell toxicity caused by TheraCal. This is because it contains Bisphenol A-glycidyl methacrylate (Bis-GMA) and urethane dimethacrylate (UDMA) resin monomers (43%) (45,46). The resin monomers included in TheraCal may not polymerize during light curing. Free monomers have a detrimental effect on pulp cells. Therefore, it is recommended to deposit and polymerize Theracal in thin layers of 1mm (45). The controversial biological properties of TheraCal indicate that it is toxic to pulp fibroblasts and has a higher inflammatory effect and a lower bioactive potential than Biodentine (44,47). TheraCal LC has been extensively studied both in vitro and in vivo since its introduction and different results were found. The researchers recommended that its use be limited to indirect pulp capping (36).

10.4 TheraCal PT

Theracal LC is an easy-to-use material based on tricalcium silicate modified with light-curing resin. However, it has controversial biological properties, making it not recommended as a pulp coating material. Recently, Theracal PT, a dual cure, resin-modified calcium silicate material designed for vital pulp treatments, has been introduced into clinical use. It is in paste/paste form and has a dual cure setting reactionIt contains SG-Mix cement, Bis-GMA, barium zirconate, ytterbium fluoride, initiators. According to its manufacturer, it is primarily indicated for pulpotomies but can also be used for direct and indirect pulp capping. There are not enough studies on this subject due to its new release (36,47).

11. Conclusion

There are some factors that affect the success of vital pulp treatment. These factors are harmful stimuli in the cavity, bleeding control of the exposed pulp, disinfection protocols, an ideal pulp covering material and stimulation of tertiary dentin formation (2,3,46).

Historically, calcium hydroxide (Ca(OH)2) has been considered the gold standard. However, there are also disadvantages such as insufficient adhesion to the dentin walls, multiple tunnel defects in the formed dentin bridges, and poor sealing ability. Therefore, today, calcium hydroxide is being replaced by new generation calcium silicate materials.

The role of calcium silicates is gradually increasing due to their high biocompatibility, better quality dentin bridge construction and sealing. Current findings confirm that both MTA and Biodentine are reliable materials for inducing dentin bridge formation while preserving a vital pulp in direct and indirect pulp capping procedures. In vitro and in vivo futher studies are required to confirm the clinical significance and efficacy of the next generation light-cured resin-modified calcium silicates. Therefore, the cytotoxicity of these materials, the quality of the induced dentin bridge, the bond strength to the tooth structure should be the subject of future studies (19,32,46).

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