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Research on causes, treatment, prevention of dental caries

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Abstract. Dental caries is a disease which is affected by many factors, mainly bacteria, and eventually leads to the dissolution and damage of the hard tissue of the teeth. Dental caries has become one of the most common diseases affecting children worldwide, and it is on the rise, seriously endangering children's oral, general and mental health. Traditional clinical treatment methods mainly use filler therapy and root canal therapy, but these are invasive and dependent on patients' compliance. There are many therapies that are less invasive and more suitable for children being researched and applied clinically. It is worth noting that for caries, early prevention is more important and effective than late treatment. In recent years, the researches on the pathogenesis and influencing factors of dental caries have also made some progress. This review focuses on the causes, treatment and prevention of dental caries in children, in order to promote the updating of research trends on dental caries in children and to help develop an individualized oral health plan for children.

Keywords: Dental caries, Cariogenic bacteria, Causes, Treatment, Prevention

1. Introduction

Dental caries in children under the age of 6 is referred to as Early Childhood Caries (ECC), which constitutes a global health issue, affecting approximately 50% of preschool-aged children [1]. The prevalence of ECC varies significantly between different countries. It has been reported that the caries prevalence among 12-year-old children in India ranges from 27% to 64%; in Sweden, it is 11.4%; and in the United States, it ranges from 3% to 6% [2, 3]. Dental caries causes progressive pathological damage of the hard tissues of teeth, resulting from the influence of multiple factors, characterized by the decomposition of organic matter and demineralization of inorganic matter. When free sugars are present in the oral cavity, bacteria adhering to the tooth surfaces can metabolize them into acid, causing a significant decrease in local pH. When the pH drops below 5.5, it can lead to the loss of phosphorus and calcium from hydroxyapatite, resulting in crystal dissolution. As the disease progresses, it is divided into three stages, from the color change of the tooth appearance to the substantial damage of the tooth. In the early stages, caries invades from the enamel, and chalky areas appear on the tooth surface. When caries continues to invade beyond the enamel into the dentin, it will be accompanied by pain, marking the intermediate stage of the disease. The advanced stage develops into pulp involvement, and the bacteria infecting the pulp resulting in pulpitis. And in more severe cases, it can lead to periapical inflammation, alveolar bone inflammation, cellulitis, lymph node enlargement, and even systemic diseases. In addition, if left untreated, it not only affects chewing function of children, the development of permanent tooth,

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and jawbone growth but also has a significant detrimental effect on children's speech abilities, psychological well-being, and overall quality of life.

Dental caries is caused by multiple factors together, with the occurrence closely related to the four interconnected factors of bacteria-host-diet-time. Besides, its occurrence is influenced by external factors such as poor oral hygiene habits, family education level, family economic status and malnutrition. The choice of interventions of dental caries is closely related to the progression of caries, and based on clinical conditions. For early-stage caries, medication treatment, fissure sealing, and infiltration techniques can all yield good treatment outcomes. Filling in root canal therapy is the primary traditional treatment method for caries in the intermediate stage. However, in recent years, some consider filling in root canal therapy to be over-treatment in certain cases, while atraumatic restorative treatment (ART), which is less invasive and less painful, is recommended by world health organizations (WHO) as a suitable filling treatment for children. When caries progresses to involve the pulp, treatment options may include vital pulp therapy (VPT) and root canal treatment (RCT). Generally, VPT is chosen when it is possible to preserve the pulp. Furthermore, in recent years, some new treatments have been increasingly researched and applied to make up for the shortcomings of traditional therapies, including the hall technique, laser therapy, and chemical-mechanical caries removal (CMCR). For dental caries, early prevention is more important and effective than later treatment, like fissure sealing, immunization against dental caries, fluoride, and probiotics. Additionally, the interplay between individuals, families, and society is essential for the prevention of caries.

This article aims to summarize the studies on caries in recent years, focusing on the causes, treatment methods and preventive measures of caries, in order to further promote the clinical study on caries.

2. Causes of Caries

Currently, it is generally believed that four factors are essential for the formation of dental caries, including bacteria, food, host and time.

Cariogenic bacteria in the oral cavity metabolize sugars in food to produce acid, which leads to demineralization of the tooth hard tissues and the occurrence of dental caries. Among these cariogenic bacteria, Streptococcus mutans, Lactobacillus, and Actinomyces have the closest relationship with the development of dental caries. Streptococcus mutans has a strong affinity for tooth surfaces, making it prone to causing enamel caries. Zou et al. reported that the colonization of Streptococcus mutans in the oral cavity depends on tooth eruption [4]. Mothers with high levels of Streptococcus mutans increase the risk of infection in their children through vertical transmission [5]. Lactobacilli has a weak affinity to dental surfaces and cannot cause caries independently, but it contributes to the development of caries along with Streptococcus mutans. Besides, actinomyces strongly adheres to cementum and is the main pathogen of root caries.

According to the WHO's (2017) note on sugar and dental caries, free sugars are essential dietary factors in the development of dental caries, with sucrose being the most cariogenic. Free sugars provide energy for bacterial growth and activity, and the acids are produced by bacterial metabolism of free sugars, resulting in demineralization and the formation of dental caries. In many countries, sugar-sweetened beverages and 100% fruit juices are the main sources of free sugars. Due to the strong adhesion of these liquid foods, and the poor oral self-cleaning ability of children, it is more likely to cause bacterial reproduction. A systematic review conducted by Mahboobi et al. indicated a strong positive correlation between free sugars and dental caries, especially before bedtime intake [6]. WHO (2015) stated that despite the use of fluoride in drinking water and toothpaste, a 10% sugar intake can still lead to a high prevalence of dental caries. Additionally, consuming food before bedtime can also increase the risk of dental caries due to decreased flow and mobility of saliva in children at night, causing the accumulation of food debris and the adhesion of bacteria.

The teeth and saliva of the host are also the factors that affect the occurrence of dental caries. The morphology of deciduous teeth increases the susceptibility to caries in children. The neck of the deciduous teeth is significantly narrowed, and the crown is raised at 1/3 of the neck. The contact between adjacent teeth is primarily surface-to-surface, and there are physiological gaps in the dentition that easily

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trap plaque and food debris, which are difficult to clean. Deciduous teeth have lower mineralization and weaker acid resistance, making them prone to demineralization. Meanwhile, saliva can flush away plaque and food debris, and its phosphate ions can neutralize acidic substances on the teeth, reducing the risk of dental caries. In addition, saliva contains abundant immunoglobulins that inhibit the formation of dental caries, making them effective anti-caries factors. Therefore, insufficient salivary flow rate, flow volume, buffering capacity, and bacteriostatic effects can also lead to an increased incidence of dental caries.

It is noteworthy that a continuous dynamic process of demineralization and remineralization occurs at the saliva-plaque-enamel interface. Only when net demineralization occurs continuously over a sufficient period of time does enamel dissolution and demineralization occur.

Additionally, external factors also influence the formation of dental caries. Poor oral hygiene habits are significant factors in the development of early childhood caries (ECC). Incorrect brushing techniques, low brushing frequency and low use of fluoride toothpaste result in the inability effectively and timely remove dental plaque, soft deposits, and food debris, leading to bacterial growth in the oral cavity and prolonged exposure of teeth to free sugars, which finally induces dental caries. Meanwhile, Malnutrition can affect the tooth mineralization process, which depends on quantities of vitamin elements. WHO believes that vitamin D deficiency is related to dental hypoplasia, and calcium and phosphate salts also play important roles in tooth mineralization. Moreover, Chawłowska et al. found that the parents' education level and the family's economic status both significantly impact the prevalence of dental caries in children [7]. Parents with lower education levels generally lack knowledge of oral health and awareness of the hazards of dental caries and pay less attention to children's oral hygiene and dietary habits. High-income families have better conditions for early prevention and timely treatment of children's dental caries, resulting in higher rates of dental caries treatment compared to low-income families.

3. Treatment of Caries

3.1. Treatment of Superficial Caries

Non-invasive and micro-invasive treatments can be employed to intervene the progression of active carious lesions before cavitation of the enamel surface occurs.

Fluoride compounds are widely utilized in the clinical treatment of non-cavitated carious lesions. Under acidic conditions, fluoride ions are taken up along with calcium and phosphate ions by enamel, thereby enhancing remineralization. And fluoride inhibits the formation of sugar-degrading enzymes, interrupting the metabolism of free sugars and reducing acid-induced enamel demineralization. Studies have reported that silver ions have antibacterial activity against Streptococcus mutans. Mabangkhru et al. showed that 38% diamine silver fluoride (SDF) applied semiannually can effectively intervene in dentin caries of deciduous teeth [8]. SDF application is easy to operate, effective, inexpensive. Although the side effect of stain the arrested lesion black caused by silver compounds is not widely accepted, it remains an economical treatment. Nano-silver-diamine-fluoride and Nano-silver-fluoride have promising prospects in the clinical application for treating dental caries of primary teeth due to their advantages of small particle size and better penetration, and the latter does not stain tooth tissue [9].

Additionally, Beresescu et al. demonstrated that sealants can effectively impede the progression of non-cavitated carious lesions [10]. Resin-based sealants bonded by micromechanical means and glass ionomer-based fluoride-releasing sealants bonded by chemical means are currently the predominant types used. The number and activity of cariogenic bacteria are reduced and the caries process is arrested by placing sealants on the non-cavitated carious lesion, so that the cariogenic bacteria are captured and isolated from the free sugars, thus blocking the access of other microorganisms. Besides, the infiltration technology of using resin has also been applied in the clinical treatment of non-cavitated proximal carious lesions [11]. Unlike sealants that externally seal the lesion, infiltrating materials penetrate into the lesion and block the pores of demineralized enamel, establishing a barrier that inhibits the diffusion of acids.

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3.2. Treatment of Medium Caries and Deep Caries

As the degree of dental caries cavitation increases, the possibility of solely using non-invasive methods to treat the progression of the lesion decreases. Drilling and filling are traditional clinical treatments when substantial defects of dental tissue occur. The technique is need to completely remove all infected tissue and prepare a specific-shaped cavity. After cleaning and disinfection, appropriate materials are selected to fill the resulting defect, restoring the form and function of the tooth. However, compared with the radical caries excavation, progressive or selective removal of diseased tissue can reduce the risk of pulp exposure, which is conducive to formation of tertiary dentin and prevention of pulp complications. The recent consensus no longer considers complete caries removal as the preferred treatment for deep caries lesions, but rather as overtreatment in some cases.

It is worth mentioning that the simple and painless atraumatic restorative treatment (ART) has been recommended by WHO as an early caries treatment method, especially suitable for filler treatment in children with dental caries (Table 1). This technique involves the use of manual instruments to remove decayed tooth tissue and fill it with a durable and compressive ion-based material. The fluoride ions in the material provide long-term release and promote tooth remineralization. De Amorim et al. revealed that ART has a high efficacy in the treatment of single-surface caries in primary teeth [12]. Additionally, the success rate of Hall technique in the treatment of multi-surface caries of deciduous teeth is higher than that of traditional filling repair [13]. This minimally invasive treatment intervenes the development of caries by using preformed metal crowns to seal the caries and change the microenvironment of cariogenic biofilms, which shows better retaining and sealing effect.

When the caries lesion progresses to the pulp of the tooth, vital pulp therapy (VPT) and pulpectomy need to be selected according to the severity of the inflammation. VPT is a less invasive and less adverse reaction technique with the main purpose of preserving pulp vitality, including pulp capping and pulpotomy. Pulp capping promotes tertiary dentin formation and pulp repair by directly or indirectly sealing exposed dentin and pulp to eliminate microbial stimulation, while pulpotomy requires partial removal of exposed pulp. Stratigaki et al. proposed that the success rate of VPT intervention is very high, and it could be recommended as an effective treatment for deep caries in specific conditions [14]. Generally, pulp preservation is recommended only in pulp exposure when reversible pulpitis occurs in carious teeth [15]. Otherwise, RCT is advocated, where the pulp tissue is completely debrided and the root canal is sealed, followed by restoration of the remaining crown and root to maintain the tooth's morphology and interfere further spread and worsening of the pathology. Xie et al. confirmed that the overall two-year success rate of pulpectomy in primary molars with irreversible pulpitis and periapical inflammation is 66.1%, and the treatment effect for primary molars with irreversible pulpitis is more ideal [16]. If periapical inflammation of deciduous teeth is widespread and permanent tooth embryo is affected, deciduous teeth should be removed according to the situation and subsequent treatment should be carried out to facilitate normal eruption of inherited permanent teeth.

In recent years, laser technology has been introduced in dental caries treatment as an alternative to traditional drilling and filling methods. Laser treatment can effectively melt carious tissue and significantly reduce the risks of infection, swelling, inflammation, and bleeding, thereby promoting better healing of soft tissues. The technique is minimally invasive and has low levels of noise, allowing patients to experience mild discomfort and vomiting reflex [17]. Consequently, children typically do not exhibit fearful emotions and are more cooperative with medical staff during laser treatment. Additionally, chemomechanical caries removal (CMCR) also has been widely accepted as a more comfortable and effective minimally invasive treatment option. CMCR utilizes a medicated gel to chemically soften decayed tooth structure, followed by gentle removal using hand instruments. Unlike traditional surgical methods, CMCR's selective caries removal feature maximizes the preservation of dentin tissue with the potential for remineralization, promoting regeneration and repair processes. With CMCR, patients can undergo treatment with reduced discomfort, particularly for pediatric patients who find it easier to cooperate due to its painless and low-noise characteristics [18].

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4. Prevention of Caries

For dental caries, early prevention through the provision of protective factors is more effective than treating after the occurrence of lesions. Protective factors of dental caries that intervene pathological progression and promote remineralization, are able to prevent the breakdown of the dynamic balance between demineralization and remineralization caused by pathological factors.

4.1. Pit and Fissure Sealant

Pit and fissure caries account for approximately 44% of deciduous teeth caries. The pits and fissures of permanent molars are prone to food debris and bacterial accumulation, making them difficult to clean and leading to the development of cavities. In clinical practice, pit and fissure sealants are used to prevent pit and fissure caries. Without removing dental tissue, sealant material is applied to the pits and fissures to isolate bacteria and their metabolic byproducts from damaging the enamel. There is evidence to suggest that the use of sealants on sound occlusal surfaces reduces the incidence of cavities by 76% compared to that without sealants [19]. Once the sealant hardens, it adheres tightly to the pit walls and can withstand chewing pressure, typically providing long-term protection. This method is safe, highly effective in cavity prevention, painless, and minimally invasive, making it easily accepted by children. However, over time, sealants may wear off, reducing their caries-preventing effectiveness, so regular dental check-ups are necessary to monitor the condition of the sealants.

4.2. Immunization against Dental Caries

The immune anti-caries technique can be categorized into two different approaches including active immunity and passive immunity (Table 2). The former involves generating specific antigens within the body to activate immune responses and produce corresponding specific antibodies. The latter involves directly introducing specific antibodies into the body. Adhesin, glucosyltransferase (GTF), and glucan-binding protein (GBP) of Streptococcus mutans have been studied as rational targets for anti-caries vaccines. Dinis et al. used recombinant enolase of Streptococcus mutans as a target antigen and found that oral administration of this therapeutic vaccine could inhibit experimental caries formation in rats [20]. Chen et al. indicated that nanomaterials provide a potential platform for packaging and delivering DNA vaccines for caries prevention, enabling more effective mucosal immunity [21]. Oli et al. illustrated that multiple monoclonal antibodies against the adhesin P1 of Streptococcus mutans possess immunomodulatory activity. Enolase of S.sobrinus has been identified as an immunomodulatory protein [22]. Robinette et al. emphasized using specific polyclonal IgG or IgY antibody reagents against GTF and GBP, as well as monoclonal or transgenic reagents against other surface antigens (Ag I/II) of Streptococcus mutans, can both reduce the occurrence of dental caries in experimental animals during Streptococcus mutans infection [23].

Table 1. Active and passive immunization to prevent caries

Approaches of Immunization	Principle	Target Points	Example	Reference
Active Immunity	Generate specific antigens within the body to activate immune responses and produce corresponding specific antibodies	Adhesin, GTF, and GBP of Streptococcus mutans	Oral vaccine with Streptococcus mutans recombinant enolase as a target antigen can inhibit experimental caries formation in rats. Nanomaterials provide a potential platform for packaging and delivering DNA vaccines for caries prevention.	[20,21]

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Table 1. (continued)

Passive Immunity	directly introduce specific antibodies into the body	Adhesin, GTF, and GBP of Streptococcus mutans	Multiple monoclonal antibodies against the adhesin P1 of Streptococcus mutans possess immunomodulatory activity. Using specific polyclonal IgG or IgY antibody reagents against GTF and GBP, as well as monoclonal or transgenic reagents against other surface antigens (Ag I/II) of Streptococcus mutans, can both reduce the occurrence of dental caries in experimental animals during Streptococcus mutans infection.	[22,23]

4.3. Fluoride

Fluoride functions by inhibiting demineralization of tooth enamel and promoting remineralization, thereby serving as a key element in caries prevention. At present, fluoride applications mainly consist of topical and systemic approaches. Topical fluorine application involves direct application of fluoride to the tooth's surface to enhance its resistance to decay, and includes fluoride toothpaste, fluoride mouthwash, fluoride gel, fluoride foam and fluoride varnish. Systemic fluorine application involves the absorption and transport of fluoride to the teeth or saliva and other tissues by the body, which is ingested through sources like drinking water fluoridation, dietary fluoride, fluoridated milk, fluoride tablets and fluoride drops, to achieve the goal of caries prevention. Casein phosphopeptide–amorphous calcium phosphate (CPP-ACP) stabilizes calcium and phosphate ions in an amorphous or soluble state, preventing demineralization, promoting remineralization, and enhancing the activity of fluoride. Tao et al. suggested that the combined use of CPP-ACP and fluoride appears to achieve better caries prevention results [24].

4.4. Probiotics

In the past decade, probiotics have been continuously explored as a potential method of oral therapy. It is generally believed that probiotics can inhibit dental caries in several ways. Firstly, probiotics can inhibit the adhesion of cariogenic bacteria by aggregating and competing for attachment sites with cariogenic bacteria. Secondly, probiotics can compete for nutrients and produce antibacterial compounds to inhibit the growth and metabolism of cariogenic bacteria. Thirdly, the intake of probiotics can enhance the host's immune response to reduce inflammation and tissue damage. Wasfi et al. demonstrated that probiotic Lactobacillus can co-aggregate with streptococcus mutans and inhibit their growth [25]. Staszczyk et al. indicated that 3-6-year-old children who regularly consumed probiotics had significantly lower levels of cariogenic bacteria in their mouths compared to the control group [26]. Nadelman et al. reported a significant increase in children's oral pH and significant cariostatic effects on oral biofilm acidogenicity after short-term consumption of probiotic beverages [27]. Therefore, products containing probiotics may offer an effective new approach to combat childhood caries.

4.5. Other interventions

The prevention of children's dental caries should start with prenatal education for expectant parents. During pregnancy, education of oral hygiene for expectant parents and adequate dental treatment for expectant mothers can reduce or delay infant ECC. After birth, soft and clean clothes should be used to wipe baby's upper gum pads, lower gum pads and tongue. During the six-month-old period when babies generally erupt their first deciduous teeth, parents are supported to be instructed to use a finger brush to clean their babies' mouths. At about 2 to 3 years old, parents should ask their children to brush their teeth independently and guild them on the correct brushing method. In addition, reducing the amount and frequency of free sugar intake and increasing the intake of fiber foods can contribute to oral health.

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A conceptual model has been established that combines the individual, family, and social determinants of ECC, demonstrating the interrelationship and mutual influence among these factors (Figure 1) [28]. Therefore, the social determinant is also important for preventing oral diseases. Society ought to improve the national awareness of oral health care and focus on oral health education for preschool children through publicity lectures, knowledge competitions and other forms.

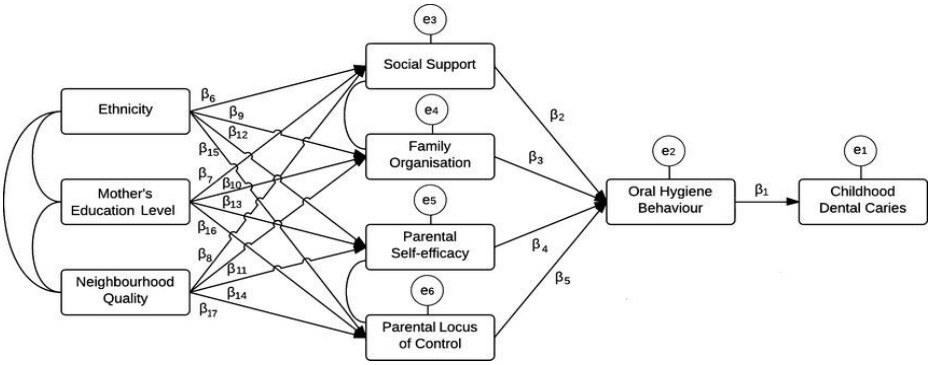

Figure 1. Schematic illustration of the theoretical model. Connecting lines imply that variables are associated. Values in circles represent unexplained variance of variables. β1 to β17 represent standardised path coefficients and e1 to e6 represent unexplained variance.

5. Conclusion

The incidence of caries is closely related to the four factors of bacteria-host-food-time and many external factors. In recent years, there have been a number of new therapies that are less invasive and more suitable for children than traditional caries treatment, such as the hall technique, laser therapy and CMCR. Prevention plays a crucial role in reducing the incidence of dental caries, emphasizing the importance of comprehensive clinical, individual, family and social management. It is very significant for individual management of caries prevention, early identification, intervention and progressive development.

References

[1] Uribe, S.E., N. Innes, and I. Maldupa, The global prevalence of early childhood caries: A systematic review with meta-analysis using the WHO diagnostic criteria. Int J Paediatr Dent, 2021. 31(6): p. 817-830.

[2] N., S., et al., Oral Health in India. A Report of Multi-centric Study. . Director General of Health Services, Ministry of Health and Family Welfare, Government of India and WHO collaborative programme., 2007.

[3] Strömberg, U., et al., Geo-mapping of time trends in childhood caries risk--a method for assessment of preventive care. BMC Oral Health, 2012. 12: p. 9.

[4] J., Z., Z. X., and L. S., One-year dynamic observation of early oral colonized flora in infants. West China Journal of Stomatology 2004. 22(2): p. 126-128.

[5] Latifi-Xhemajli, B., et al., Streptococcus Mutans Infections in Infants and Related Maternal/Child Factors. Acta Stomatol Croat, 2021. 55(3): p. 308-315.

[6] Mahboobi, Z., et al., Dietary free sugar and dental caries in children: A systematic review on longitudinal studies. Health Promot Perspect, 2021. 11(3): p. 271-280.

[7] Chawłowska, E., et al., Exploring the Relationships between Children's Oral Health and Parents' Oral Health Knowledge, Literacy, Behaviours and Adherence to Recommendations: A Cross-Sectional Survey. Int J Environ Res Public Health, 2022. 19(18).

[8] Mabangkhru, S., et al., A randomized clinical trial to arrest dentin caries in young children using silver diamine fluoride. J Dent, 2020. 99: p. 103375.

[9] Ahmadian, E., et al., Local treatment of the dental caries using nanomaterials. Biomed Pharmacother, 2018. 108: p. 443-447.

[10] Beresescu, L., et al., The Assessment of Sealants' Effectiveness in Arresting Non-Cavitated Caries Lesion-A 24-Month Follow-Up. Healthcare (Basel), 2022. 10(9).
[11] Cebula, M., et al., Resin Infiltration of Non-Cavitated Proximal Caries Lesions in Primary and Permanent Teeth: A Systematic Review and Scenario Analysis of Randomized Controlled Trials. J Clin Med, 2023. 12(2).
[12] de Amorim, R.G., et al., Survival percentages of atraumatic restorative treatment (ART) restorations and sealants in posterior teeth: an updated systematic review and meta-analysis. Clin Oral Investig, 2018. 22(8): p. 2703-2725.
[13] Splieth, C.H., et al., How to Intervene in the Caries Process in Children: A Joint ORCA and EFCD Expert Delphi Consensus Statement. Caries Res, 2020. 54(4): p. 297-305.
[14] Stratigaki, E., et al., Contemporary management of deep caries in primary teeth: a systematic review and meta-analysis. Eur Arch Paediatr Dent, 2022. 23(5): p. 695-725.
[15] Duncan, H.F., et al., European Society of Endodontology position statement: Management of deep caries and the exposed pulp. Int Endod J, 2019. 52(7): p. 923-934.
[16] Xie, Y., et al., Survival analysis of pulpectomy in primary molars performed under dental general anaesthesia: a two-year retrospective study. BMC Oral Health, 2022. 22(1): p. 597.
[17] Vaddamanu, S.K., et al., In vitro Evaluation of Laser vs. Handpiece for Tooth Preparation. J Pharm Bioallied Sci, 2022. 14(Suppl 1): p. S526-s529.
[18] Maashi, M.S., et al., Chemomechanical caries removal methods: A literature review. Saudi Dent J, 2023. 35(3): p. 233-243.
[19] Evidence-based Clinical Practice Guideline for the Use of Pit-and-Fissure Sealants. Pediatr Dent, 2016. 38(6): p. 263-279.
[20] Dinis, M., et al., Oral therapeutic vaccination with Streptococcus sobrinus recombinant enolase confers protection against dental caries in rats. J Infect Dis, 2009. 199(1): p. 116-23.
[21] Chen, L., et al., Enhanced nasal mucosal delivery and immunogenicity of anti-caries DNA vaccine through incorporation of anionic liposomes in chitosan/DNA complexes. PLoS One, 2013. 8(8): p. e71953.
[22] Oli, M.W., et al., Redirecting the humoral immune response against Streptococcus mutans antigen P1 with monoclonal antibodies. Infect Immun, 2004. 72(12): p. 6951-60.
[23] Robinette, R.A., et al., A therapeutic anti-Streptococcus mutans monoclonal antibody used in human passive protection trials influences the adaptive immune response. Vaccine, 2011. 29(37): p. 6292-300.
[24] Tao, S., et al., Efficacy of fluorides and CPP-ACP vs fluorides monotherapy on early caries lesions: A systematic review and meta-analysis. PLoS One, 2018. 13(4): p. e0196660.
[25] Wasfi, R., et al., Probiotic Lactobacillus sp. inhibit growth, biofilm formation and gene expression of caries-inducing Streptococcus mutans. J Cell Mol Med, 2018. 22(3): p. 1972-1983.
[26] Staszczyk, M., et al., Effect of a Short-Term Intervention with Lactobacillus salivarius Probiotic on Early Childhood Caries-An Open Label Randomized Controlled Trial. Int J Environ Res Public Health, 2022. 19(19).
[27] Nadelman, P., et al., Are dairy products containing probiotics beneficial for oral health? A systematic review and meta-analysis. Clin Oral Investig, 2018. 22(8): p. 2763-2785.
[28] Duijster, D., et al., Modelling community, family, and individual determinants of childhood dental caries. Eur J Oral Sci, 2014. 122(2): p. 125-33.