COMPARISON OF SILVER DIAMINE FLUORIDE AND SODIUM FLUORIDE WITH FUNCTIONALISED TRICALCIUM PHOSPHATE ON CARIES ARREST / PREVENTION IN EARLY CHILDHOOD CARIES AND THEIR EFFECTS ON ORAL HEALTH RELATED QUALITY OF LIFE: RANDOMISED CONTROLLED TRIAL

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LIST OF ABBREVIATIONS

AAPD	American Academy of Paediatric Dentistry
ADA	American Dental Association
Ag	Silver
$AgNO_3$	Silver nitrate
ART	Atraumatic restorative treatment
CaF_2	Calcium fluoride
CCI	CariesCare International
Child-OIDP	Child Oral Impacts on Daily Performances
CRA	Caries risk assessment
ECC	Early childhood caries
ECOHIS	Early childhood oral health impact scale
f-TCP	Functionalised tricalcium phosphate
F	Fluoride
FBRS	Frankl's behaviour rating scale
FIS	Family Impact Scale
ICDAS	International caries detection and assessment system
KEMAS	Jabatan kemajuan masyarakat
Na	Sodium
NaF	Sodium fluoride
NaF-fTCP	Sodium fluoride varnish with functionalised tricalcium phosphate
nanoAg	Nanoparticles of silver
NSF	Nano silver fluoride chitosan
OHRQoL	Oral health related quality of life
P-CPQ	Parental-Caregivers Child Perception Questionnaire
PCT(s)	Pragmatic clinical trial(s)
RCT	Randomised controlled trial
SDF	Silver diamine fluoride
SDF-KI	Silver diamine fluoride with potassium iodide
SLS	Sodium lauryl sulphate
SOHO	Scale of Oral Health Outcomes
SPRG	Surface pre-reacted glass-ionomer

WBFS	Wong Baker Faces Scale
WHO	World Health Organization
β-TCP	β-tricalcium phosphate

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PERBANDINGAN DI ANTARA 'SILVER DIAMINE FLUORIDE' DAN 'SODIUM FLUORIDE WITH FUNCTIONALISED TRICALCIUM PHOSPHATE' TERHADAP PENGAWALAN DAN PENCEGAHAN DI DALAM KARIES AWAL KANAK- KANAK DAN KESAN TERHADAP KESIHATAN ORAL YANG MEMPENGARUHI KUALITI KEHIDUPAN: PERCUBAAN TERKAWAL SECARA RAWAK

ABSTRAK

Rawatan invasif minimum untuk karies awal kanak-kanak termasuk penggunaan 38% silver diamine fluoride (SDF) dan 5% sodium fluoride dengan functionalised tricalcium phosphate (NaF-fTCP). Kajian ini bertujuan untuk membandingkan keberkesanan SDF dan NaF-fTCP dalam menghentikan dan mencegah lesi karies pada gigi geraham susu dalam kalangan kanak-kanak prasekolah. Objektif khusus termasuk menentukan prevalens dan risiko karies, membandingkan kualiti hidup berkaitan kesihatan oral, tingkah laku, pengalaman kesakitan sebelum dan selepas rawatan, menilai perbezaan pengalaman karies, serta membandingkan pemberhentian lesi karies antara kedua-dua rawatan. Percubaan rawak terkawal dijalankan melibatkan kanak-kanak prasekolah berumur 4-6 tahun di Pakistan. Seramai 41 kanak-kanak dirawakkan kepada kumpulan SDF (n=35 gigi) dan NaF-fTCP (n=45 gigi). SDF dan NaF-fTCP diaplikasikan pada lesi karies pada garis asas, 6 bulan, dan 12 bulan. Penilaian Urdu-ECOHIS, tingkah laku, kesakitan, dan karies dijalankan, dengan analisis statistik seperti ujian t-berpasangan, ANOVA ukuran berulang, dan ujian pangkat bertanda Wilcoxon digunakan. Daripada 782 kanak-kanak, prevalens karies ialah 44.6% (95% CI, 41.1-48.1%) dengan median dfs 4.0 (IQR=9.0). Skor purata Urdu-ECOHIS meningkat daripada 6.13 (SD 5.53) pada garis

asas kepada 7.17 (SD 7.90) pada 12 bulan, tetapi perubahan ini tidak signifikan (p = 0.556). Dalam bahagian impak kanak-kanak (CIS), domain simptom menunjukkan peningkatan signifikan (p = 0.032), manakala domain CIS lain dan bahagian impak keluarga tidak signifikan (p > 0.05). Skor Penilaian Tingkah Laku Frankl tidak menunjukkan perubahan signifikan (p = 0.236) dalam kedua-dua kumpulan. Penilian skor kesakitan Wong-Baker menunjukkan peningkatan signifikan dalam kumpulan SDF (p = 0.012) tetapi tidak dalam kumpulan NaF-fTCP (p = 0.085) dengan tiada perbezaan signifikan antara kumpulan (p = 0.713). Dalam kumpulan SDF, median dfs meningkat secara signifikan dari garis asas ke 6 bulan [5.0 (IQR=9.8), p = 0.005] dan dari 6 ke 12 bulan [6.0 (IQR=9.0), p = 0.039]. Dalam kumpulan NaF-fTCP, dfs juga meningkat dari garis asas ke 6 bulan [9.0 (IQR=8.0), p = 0.003] dan dari 6 ke 12 bulan [10.0 (IQR=13.0), p = 0.026]. Dalam kumpulan SDF, 97.1% lesi dihentikan pada 6 bulan, menurun kepada 80% pada 12 bulan. Begitu juga, dalam kumpulan NaF-fTCP, 95.6% lesi dihentikan pada 6 bulan, menurun kepada 82.2% pada 12 bulan. Kedua-dua rawatan berkesan dalam menghentikan lesi karies. SDF lebih disarankan untuk keberkesanan jangka pendek, manakala NaF-fTCP memberikan hasil yang setanding untuk jangka yang lebih panjang.

Kata kunci: Kanak-kanak prasekolah, SDF, NaF-fTCP, Karies gigi, Kualiti hidup

COMPARISON OF SILVER DIAMINE FLUORIDE AND SODIUM FLUORIDE WITH FUNCTIONALISED TRICALCIUM PHOSPHATE ON CARIES ARREST / PREVENTION IN EARLY CHILDHOOD CARIES AND THEIR EFFECTS ON ORAL HEALTH-RELATED QUALITY OF LIFE: RANDOMISED CONTROLLED TRIAL

ABSTRACT

Minimally invasive treatment for early childhood caries includes the application of 38% silver diamine fluoride (SDF) and 5% sodium fluoride with functionalised tricalcium phosphate (NaF-fTCP). This study aimed to compare the effectiveness of SDF and NaF-fTCP in arresting and preventing carious lesions in primary molars among preschool children. Specific objectives include determining caries prevalence and risk, comparing oral health-related quality of life, behaviour, and pain experience before and after treatment, assessing differences in caries experience, and comparing carious lesion arrest between the treatments. A randomised controlled trial was conducted among 4-6-year-old preschool children in Pakistan. A total of 41 children were randomised into SDF (n= 35 teeth) and NaF-fTCP (n= 45 teeth) groups. SDF and NaF-fTCP were applied to carious lesions at baseline and 6- and 12-months. Urdu-ECOHIS, behaviour, pain and caries assessments were performed, and statistical analyses (paired t-test, repeated measures ANOVA, Wilcoxon signed-rank test) were used to evaluate outcomes. Of the 782 children, caries prevalence was 44.6% (95% CI, 41.1- 48.1), with a median dfs 4.0 (IQR=9.0). The mean Urdu-ECOHIS scores increased from 6.13 (SD 5.53) at baseline to 7.17 (SD 7.90) at 12 months, but the changes were not significant ($p = 0.556$). In the child impact section (CIS), the symptom domain showed a significant increase ($p = 0.032$), while other CIS domains

and family impact sections were not significant ($p>0.05$). The changes in Frankl Behaviour Rating score were not significant ($p=0.236$) in both groups. The Wong-Baker Pain Rating score showed a significant increase over time for the SDF group ($p = 0.012$) but not for the NaF-fTCP group ($p = 0.085$) and was not significant between groups ($p = 0.713$). In the SDF group, median dfs significantly increased from baseline to 6 months, [5.0 (IQR=9.8), $p = 0.005$], and 6 to 12 months [6.0 (IQR=9.0), $p = 0.039$]. Similarly, in the NaF-fTCP group, dfs increased from baseline to 6 months [9.0 (IQR=8.0), $p = 0.003$] and 6 to 12 months [10.0 (IQR=13.0), $p = 0.026$]. In the SDF group, 34 (97.1%) of lesions were arrested at 6 months ($p = 0.317$), decreasing to 27 (80%) at 12 months ($p = 0.034$). Similarly, in the NaF-fTCP group, 43 (95.6%) of lesions were arrested at 6 months ($p = 0.157$), decreasing to 36 (82.2%) at 12 months ($p = 0.020$). Both treatments effectively arrested caries lesions. SDF is preferable for short-term effectiveness, while NaF-fTCP provides comparable longer-term results.

Keywords: Preschool children, SDF, NaF-fTCP, Dental caries, Quality of life

CHAPTER 1

INTRODUCTION

1.1 Background of the study

Early childhood caries (ECC) can be defined as the existence of decayed lesions (whether cavitated or not), missing teeth (caused by caries), or filled surfaces on any primary tooth in a child younger than six years old (American Academy of Pediatric Dentistry, 2016). The consequences of ECC include increased susceptibility to developing new carious lesions in both primary and permanent teeth (Zou et al., 2022), hospitalisations and emergency room visits (Schmoeckel et al., 2020), high treatment costs (Griffin et al., 2000, Wolf and Campus, 2023), loss of school days (Blumenshine et al., 2008), compromised ability to learn, and lowered oral health-related quality of life (Filstrup et al., 2003a). The ethos of caries management mandates a comprehensive approach to ensure certainty of disease arrest and prevention (Schmoeckel et al., 2020). To effectively tackle ECC, the American Academy of Pediatric Dentistry (AAPD) recommends home-based and clinical personnel to incorporate dietary modification, oral hygiene guidance as soon as the eruption of first primary tooth, topically applying fluoride varnishes on regular visits in locally established dental clinics by 1st year of age (American Academy of Pediatric Dentistry, 2021).

Carious lesions occur due to the frequent production of acids in the biofilm, resulting from the breakdown of dietary carbohydrates. This process leads to the proliferation of acid-producing and acid-resistant organisms within the biofilm above the gingiva, causing a drop in pH levels with a disruption in the balance between demineralisation and remineralisation, and subsequently the loss of minerals from the teeth surfaces. When there exists a harmony between protective elements (such as

fluoride, calcium, phosphate, sufficient saliva flow and composition) and harmful factors (such as cavity-causing bacteria, fermentable carbohydrates and hypoplastic tooth surfaces), the demineralisation and remineralisation of the enamel remain relatively balanced, preserving the dental health (Slayton et al., 2018, Featherstone and Chaffee, 2018, Slayton, 2015, Featherstone, 2000).

Approximal carious lesions in the enamel progress rapidly in the primary dentition as compared to permanent dentition (Shwartz et al., 1984). Primary molars are of particular importance, as they exfoliate considerably later than incisors and provide a space-maintaining function for permanent dentition (Splieth et al., 2020). Proximal surfaces have been identified as the most susceptible sites to carious lesion development in primary dentition (Ekstrand et al., 2010, Martignon et al., 2010). Thinner enamel and dentine in primary dentition compared to the permanent teeth and proportionally larger pulp chambers, shorten the time for the caries process to reach the pulp and may cause pain and pulpal complications (Schmoeckel et al., 2020). Martignon et al. (2010) and Gröndahl et al. (1984) have radiographically studied the carious lesions and reported that caries progression takes around 2.5 to three years to reach dentine, respectively. Untreated lesions lead to a gradual deterioration of the clinical tooth surfaces, frequently causing significant pain and discomfort, especially in young pre-cooperative children, and often requiring sedation or general anaesthesia for adequate treatment (Splieth et al., 2020). Restoration of these teeth is not only time-consuming but also comes with substantial costs, creating a significant financial strain on healthcare systems (Marinho et al., 2013).

Different methods of prevention and treatment of initial carious lesions of the occlusal and proximal surfaces of teeth have been identified, studied, and documented. Recent advances in dental materials have provided several options for the control and

prevention of caries activity. Fluoride is a well-known element that prevents dental caries when administered in appropriate concentration and frequency. For example, dental professionals can apply concentrated fluoride varnishes (22,600 ppm F) approximately four times a year to ensure adequate fluoride exposure to maximise caries protection. Marinho et al. (2013), in a Cochrane review of 13 clinical trials on 5 to 16-year-olds with permanent teeth, found that those treated with fluoride varnish saw an average decrease of 43% in surfaces affected by decay, missing teeth, or fillings. On the other hand, in 10 clinical trials studying the impact of fluoride varnish on primary teeth, the evidence pointed to a 37% reduction in affected surfaces due to decay, missing teeth, or fillings.

The application of fluoride has an effect directly at the plaque-tooth interface; it encourages the remineralisation of the initial carious process and decreases the susceptibility of enamel to dissolve (Featherstone and Ten Cate, 1988). If fluoride is present when bacterial acid affects the enamel, it significantly slows down the demineralisation process. Saliva is a primary source of protective ions, along with dissolved tooth structure and gingival crevicular fluid (Shen et al., 2011). If the pH returns to 5.5 or above, saliva saturated with calcium and phosphate ions encourages mineral reabsorption into the enamel (Goldstep, 2012). Fluoride adsorbs to partially demineralised enamel crystals and attracts calcium ions, forming fluorapatite. This process creates an acid-resistant surface (Duffin et al., 2022).

Fluoride travels with the acid from plaque into the enamel and incorporates it on the crystal surface to minimise mineral loss by altering the saturation levels related to tooth minerals. As the pH levels increase after demineralisation, fluoride has the potential to bind with dissolved calcium and phosphate ions, resulting in the formation or growth of a crystalline material similar to fluorapatite within the tooth once

saturation is attained. Fluoride amplifies this mineral gain, creating a substance that effectively withstands future acid attacks (Ten Cate, 1999).

For more than thirty years, topically applied fluoride varnish (FV) 5% sodium fluoride (NaF) has been extensively employed as a preventive measure against cavities by dental professionals. However, recent research indicates that annual application of silver diamine fluoride (SDF) solution was more effective in strengthening or halting cavities in dentin compared to the application of 5% NaF varnish at three-month intervals or a placebo (Lo et al., 2001, Chu et al., 2002). Silver diamine fluoride (SDF) has been used in Japan for the last 50 years, however, it was only published in the native language and did not receive significant attention until around 20 years later (Lo et al., 2001). Since then, multiple studies have been conducted on the use of SDF as an alternative to 5% NaF varnish for the treatment of carious lesions involving the occlusal surfaces of primary molars (Chu et al., 2002, Duangthip et al., 2018b) and the buccal and approximal surfaces of incisors (Fung et al., 2018). A meta-analysis by Gao et al. (2016a) revealed, the rate of caries arrest in primary teeth, treated using various application schedules (1 application, annually, and biannually) and monitored for 6 to 30 months, reached 81%. Chibinski et al. (2017) found that the caries arrest after 12 months due to SDF was 66% greater than with other active substances, and notably, 154% higher than the absence of any treatment.

More recently, tricalcium phosphate, modified for functionality (fTCP), has been integrated into NaF varnish to heighten the remineralisation process. Identified as a novel calcium phosphate system (Karlinsey and Pfarrer, 2012), fTCP plays a crucial role in the remineralisation process since calcium and phosphate constitute the primary mineral ions in tooth composition. An appropriate presence of both ions in sufficient quantities and balanced proportions supports mineral deposition within a

medium during the remineralisation process (Cochrane et al., 2010). The functionalised tricalcium phosphate (fTCP) operates in synergy with fluoride, regulating the delivery of calcium and phosphate ions to the tooth surface. The application of NaF-fTCP causes a shift in the pH levels of saliva to make it alkaline. The fluoride ions bind to apatite crystals and facilitate the calcium and phosphate ions to promote remineralisation. According to Abou Neel et al. (2016), for every 2 fluoride ions, 10 calcium ions and 6 phosphate ions are needed to form one unit cell of fluorapatite (Abou Neel et al., 2016). Numerous laboratory investigations focusing on fluoride in combination with fTCP have exhibited encouraging outcomes, amplifying the efficacy of fluoride and improving the remineralisation of decayed lesions (Karlinsey et al., 2010a, Karlinsey et al., 2010b). Therefore, NaF-fTCP seems to be a promising carious arresting agent.

Applying fluoride varnish involves expenses for dental staff and materials. Although these costs per application are minimal and spread across various teeth, continuous and repeated application over time has been shown to be financially burdensome for both individuals and populations (Schwendicke et al., 2018). Determining the cost-effectiveness of fluoride varnish application relies not just on delivery expenses but also on potential savings resulting from preventing additional cavities that might otherwise require restorative treatment. It is crucial to explore the capabilities of newly accessible products that prove highly efficient, as the savings they offer could potentially balance out the initial application costs in the long run. (Blackburn et al., 2017).

Additionally, numerous factors impact how a child behaves in a dental clinic. The developmental stages of children, including their cognitive and emotional growth, significantly influence their behaviour in the clinical setting. (Wilson, 2013). The

determination and completion of any form of caries management is crucially dependent on the child's behaviour (Santamaria et al., 2015). Positive non-verbal behaviour typically involves interest, delight, and cooperation, whereas negative non-verbal behaviour manifests as anxiety, tears, and refusal. Children displaying negative and non-compliant non-verbal behaviour before treatment are more inclined to reject any offered form of treatment (Santamaria et al., 2015).

Reducing patient discomfort stands as a key principle in minimally invasive treatment, particularly when addressing dental anxiety and fear in paediatric patients (Milsom et al., 2003). There is limited research on the discomfort experienced by children following minimally invasive interventions for early cavities, as existing studies primarily concentrate on intricate treatments and do not explore comparisons between various treatment options (Mattos-Silveira et al., 2015). On the other hand, the Early Childhood Oral Health Impact Scale (ECOHIS) is a tool designed specifically for preschoolers to evaluate how oral health issues and their treatment may affect their oral health-related quality of life (OHRQoL). Studies have shown that children with ECC tend to exhibit notably lower OHRQoL scores compared to children without carious lesions (Filstrup et al., 2003b). The objective of treating ECC is to enhance the OHRQoL (Hashim, 2017).

1.2 Problem statement

Caries experience in the primary dentition has been estimated to be high among many countries (Martignon et al., 2010). In Pakistan, approximately 60% of the Pakistani population is affected by dental caries, necessitating nationwide attention to oral health (Siddiqui et al., 2021). The caries prevalence among children in Pakistan is reported to range from 40 to 71% with a high prevalence of unmet dental treatment

needs. In a cross-sectional study involving one thousand preschool children in Saddar Town, Karachi, the caries prevalence was 51%, with a mean decayed, missing, filled teeth (dmft) score of 2.08. The mean dmft increased with age was observed; i.e. the mean dmft of 3, 4, 5 and 6-year-olds was 1.65, 2.11, 2.16 and 3.11, respectively (Dawani et al., 2012).

Many clinical studies have been conducted to evaluate the effectiveness of sodium fluoride (NaF) and silver diamine fluoride (SDF), with and without placebos and in different concentrations, formulations and frequencies (Gao et al, 2006a). However, the effectiveness of NaF-fTCP as a caries preventive material has not been studied widely. Additionally, the off-label use of NaF-fTCP as a caries arresting agent has not been studied on primary dentition. There is a dearth of evidence regarding the effectiveness of NaF-fTCP towards caries arrest and prevention. Moreover, to the best of our knowledge, there have been no studies on the comparison between the effectiveness of SDF and NaF-fTCP application on the cavitated carious primary molars and their effect on the oral health-related quality of life of the children. Additionally, the children's behaviour and pain experience before and after the application of NaF-fTCP in comparison to SDF has not been extensively studied.

ECOHIS has been used to assess children's oral health-related quality of life of preschool children receiving SDF therapy (Duangthip et al., 2019); however, the effects of currently available treatment options have not been assessed using this OHRQoL assessment tool.

The high caries prevalence among preschool children in Pakistan indicates that the detrimental consequences of untreated caries may persist and potentially escalate in the absence of effective preventive measures and oral health interventions. Considering the multifactorial nature of dental caries, factors such as age, gender, oral

hygiene practices, dietary habits, socioeconomic status, as well as caries-risk status are important in developing effective targeted public health strategies in a population and have not been fully studied.

1.3 Justification of the study

The evidence-based clinical practice guideline on non-restorative treatments for cavitated carious lesions advocates the preventive use of silver diamine fluoride (SDF) biannually for high caries-risk patients. Further, the biannual application of 38% solution SDF for advanced cavitated lesions may be relevant if access to care is limited, for uncooperative patients, or for patients when general anaesthetic is not considered safe (Slayton et al., 2018). Although SDF has been proven to be highly effective for its off-label use in carious lesion arrest, the staining effect, metallic taste due to silver content and minimal mucosal irritation have been noted as the primary cause of disinterest among clinicians in the use of this material (Nelson et al., 2016). Therefore, there is a need for the assessment of the effectiveness of different minimal intervention strategies and treatments focusing on the prevention and arrest of carious lesions of primary teeth (Gomez et al., 2005, Lo et al., 2001) that are less technique-sensitive, commercially available, and cost-effective (Lo et al., 2001, Mattos-Silveira et al., 2014).

While four or more fluoride varnish applications per year are required to achieve maximum caries prevention benefits, multiple applications of NaF varnish may not be feasible for low-income communities and rural children (Ensor and Cooper, 2004). Additionally, Slayton et al. (2018) recommended the need for multiple randomised controlled trials (RCT) to identify an appropriate alternative to NaF as a treatment of choice in different stages of carious lesions of the primary and permanent

dentitions (Slayton et al., 2018). In a review paper by Pakdaman et al. (2018) on the effectiveness of carious lesion arrest of different materials on the approximal carious lesions, the authors concluded that the most effective treatment was one involving a combination of silver fluoride and stannous fluoride, however, this has not been substantiated. Further, the authors recommended clinical trials focusing on the effectiveness of different materials on carious lesion arrest.

With the introduction of a calcium phosphate-based delivery system, many commercial products have been formulated to achieve preventive control over dental caries by releasing calcium and phosphate ions in the saliva. Tiny amounts of calcium and phosphate ions naturally exist in salivary composition. The available amount of these ions is directly related to the salivary flow rate (Mohd Said et al., 2017). The efficacy of NaF-fTCP in relation to the occurrence of cavities over a 2-year duration has been investigated and revealed that the intervention group displayed a significantly lower count of non-cavitated lesions compared to the negative control Pitchika et al. (2013). This study emphasised the multifaceted nature of carious development and highlighted that the efficacy of biannual fluoride varnish application was apparent specifically in addressing non-cavitated lesions. However, limited evidence exists regarding the impact of fTCP on primary teeth (Karlinsey and Pfarrer (2012).

Hence, this study was carried out to compare the effectiveness of the application of SDF and NaF-fTCP in arresting and preventing carious lesions in the primary molars of preschool children in Lahore city of the Punjab province, Pakistan at baseline, 6 and 12 months. Data on the caries prevalence at the selected preschool and their caries risk status provided baseline information in formulating effective caries prevention and arrest methods for the high-risk groups. A broader understanding of the risk factors, oral health-related quality of life, patient behaviour and the

participant pain experience during treatment would be useful in developing more effective preventive strategies leading to improving the oral health status of preschool children.

The results from this study could provide clinical evidence regarding the effectiveness of SDF and NaF-fTCP on caries prevention and arrest in the preschool environment that can be recommended to be applied bi-annually, and in turn, may significantly reduce the burden on dental treatment needs and treatment costs. The results could also aid clinicians in addressing challenges like the metallic taste and dark stains in halted cavities, the perceived pain experienced during the application of SDF and NaF-fTCP, the preschool children's behaviour and their oral health-related quality of life before and after the application of SDF and NaF-fTCP. Findings from this study could potentially drive policy shifts, advocating for the incorporation of cavity management strategies into school-based health services, caries management planning and evaluation strategies.

1.4 Objectives of the study

1.4.1 General objective

To assess the effectiveness of SDF and NaF-fTCP application on the carious primary molars and their effect on the oral health-related quality of life among the preschool children attending Crescent Montessori school in Punjab province of Pakistan.

1.4.2 Specific objectives

1.4.1(a) Baseline phase

1. To determine the prevalence of dental caries and caries experience at the baseline phase.
2. To assess the caries risk status of children participating in the intervention phase at the baseline phase.
3. To determine the oral health-related quality of life, behaviour and pain experience of children participating in the intervention phase at the baseline phase.

1.4.1(b) Post Intervention phase

1. To compare the oral health-related quality of life, behaviour and pain experience at pre- and post-intervention phases at baseline, 6 and 12 months.
2. To compare the difference in the mean caries experience between baseline and post-intervention phases at 6 and 12 months.
3. To compare the effectiveness of caries arrest using SDF or NaF-fTCP within and between each group at baseline and post-intervention phases at 6 and 12 months.

1.5 Research question

1. What is the caries prevalence among preschool children attending Crescent Montessori school in Punjab province of Pakistan?
2. What is the caries risk status among the preschool children participating in the intervention phase?

3. What are the differences in the oral health-related quality of life, behaviour, and pain experience of the children before and after the application of SDF and NaF-fTCP at 6 and 12 months?
4. What is the difference in the mean caries experience of the children before and after the use of SDF and NaF-fTCP at 6 and 12 months?
5. What is the effectiveness of carious lesion arrest on the treated carious primary molars between SDF and NaF-fTCP at 6 and 12 months?

1.6 Research hypotheses

1. There is a significant difference in the preschool children's oral health-related quality of life, behaviour, and pain experience before and after the application of SDF and NaF-fTCP.
2. There is a significant difference of total caries experience in the children before and after the use of SDF and NaF-fTCP.
3. There is a significant difference of effectiveness of carious lesion arrest on the treated carious primary molars between SDF and NaF-fTCP.

1.7 Conceptual framework

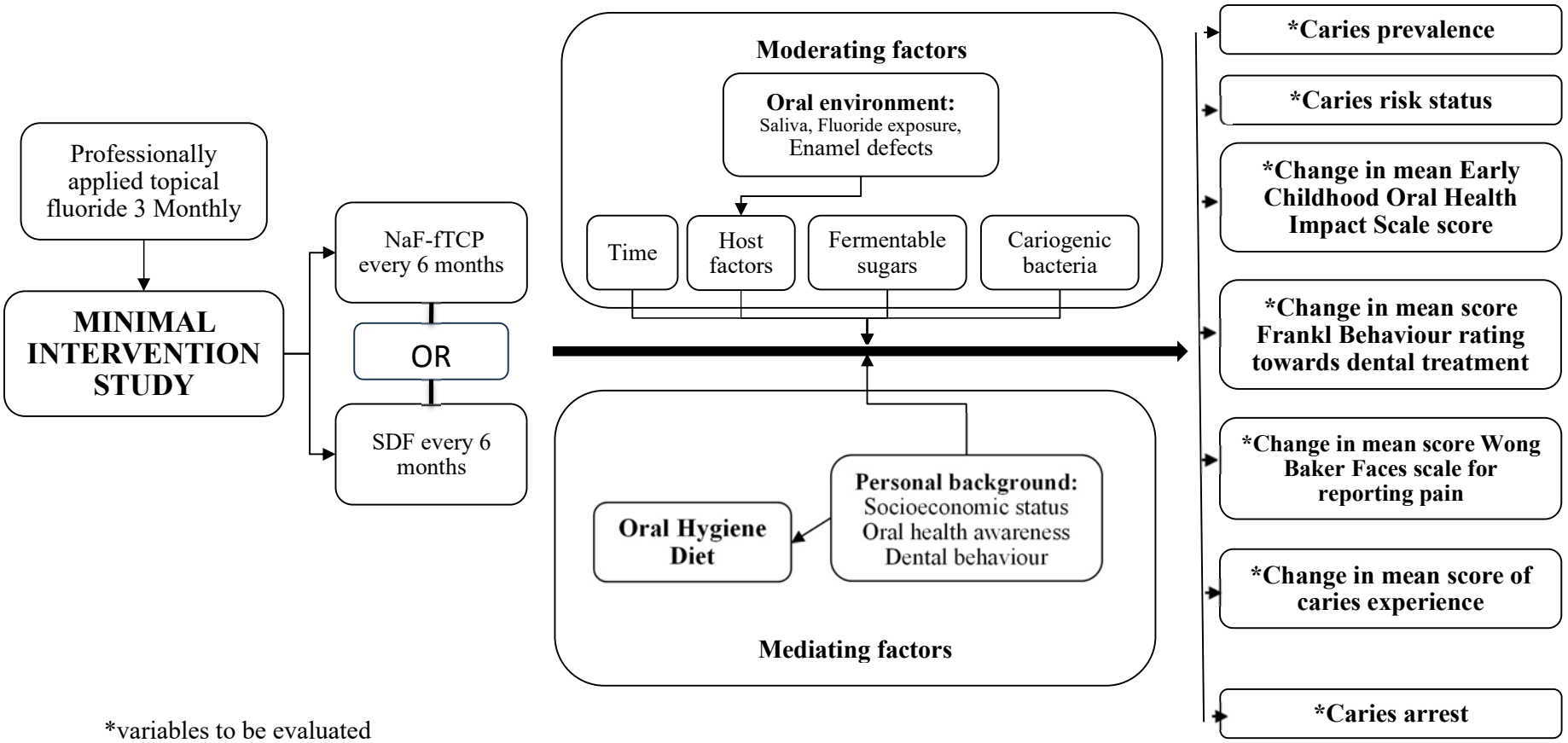
According to Schmoeckel et al. (2020), the minimal intervention of ECC may be managed successfully with non-operative operative approaches (SDF, regular fluoride application) and moderately well with operative approaches, but the decision is affected by many other variables, such as pulpal involvement, the child's cooperation or the treatment setting. Figure 1.1 depicts the study's conceptual framework by integrating the investigated core elements in the minimal intervention for ECC in a preschool setting. The multifactorial aetiological factors for ECC that highlight the importance of considering factors such as age, gender, oral hygiene

practices, dietary habits, socioeconomic status, as well as caries-risk status in developing effective public health strategies in a targeted population have been incorporated.

The preschool children's caries risk status, oral health-related quality of life, behaviour towards dental treatment, pain experience, caries experience and caries arrest on the application of the SDF and NaF-fTCP on primary molars mainly depend on the moderating and mediating factors (Ribeiro Junior et al., 2022). Subsequently, these factors may contribute to the prevalence of dental caries in the selected population.

In the management of ECC, the time of deleterious effects, the host factors such as oral environment (quality and quantity of saliva, fluoride exposure in drinking water and fluoridated toothpaste, presence of enamel defects), fermentable carbohydrates and cariogenic bacteria were considered as the moderating factors. The mediating factors for ECC include the personal background consisting of the socioeconomic background, oral health awareness and dental behaviour which contributes to the oral hygiene practice and the dietary intake.

As shown in Figure 1.1, the minimal intervention of ECC through the application of NaF-fTCP or SDF approach at every 6 months is targeted for the high caries risk group, interacted with the influence of the moderating and mediating factors would result in a better outcome for the oral health-related quality of life as assessed through ECOHIS, children's behaviour towards dental treatment measured via Frankl Behaviour rating scale and the perceived pain while getting the treatment as assessed through Wong-Baker Faces scale. Subsequently, the effectiveness of NaF-fTCP or SDF will be evaluated by the mean score of caries experience and caries arrest will be evaluated for comparison between baseline and at 6 and 12 months.



*variables to be evaluated

Figure 1.1 Conceptual framework of the study

CHAPTER 2

LITERATURE REVIEW

2.1 Early childhood caries

Early childhood caries (ECC) refers to the occurrence of carious (either cavitated or non-cavitated lesions), missing teeth resulting from carious process, or filled tooth surfaces in any primary tooth younger than six years. Diverse pathological factors contribute to the occurrence of a site-specific disturbance in the mineral content of tooth structures. These sites are referred to as carious lesions. Acidogenic bacteria such as *Streptococcus mutans* and *Lactobacilli* species, salivary disturbances, and dietary factors have been identified to contribute to the caries progression (Hernández-Sierra et al., 2008).

Dental caries is a chronic health problem that has affected populations worldwide. It remains the silent epidemic of childhood that is neither self-limiting nor amendable to short-term pharmacological management (Li and Tanner, 2015). A general trend of greater levels of tooth decay has been associated with lower socio-economic groups (Marinho et al., 2013). Untreated dental caries causes progressive breakdown of tooth structure which subsequently leads to dental infection and severe pain. Unrestored carious lesions can lead from sensitivity to pain upon stimulation and subsequently spontaneous pain if left untreated; therefore, any carious lesion requires clinical intervention for the restoration of tooth function.

2.2 Epidemiology of dental caries among children in Pakistan

Caries is among the most prevalent diseases in humans and a caries prevalence of 100% in adults and 60 to 90% in children has been documented (World Health Organization, 2012). Andrian et al. (2018) estimated that caries was the most prevalent

pathology worldwide with approximately 2.4 billion people having untreated carious lesions. In Malaysia, a national survey conducted in 1995 revealed 87.1% caries prevalence among the population (Othman et al., 2009). The National Oral Health Survey for Preschool children revealed, in the span of 10 years between the Malaysian surveys, the caries prevalence showed only a small decline; i.e. from 76.2% in 2005 to 71.3% recorded in 2015 (MOH, 2016). Therefore, despite efforts to improve oral health, the epidemiologic data indicates that caries among preschool children is of concern and continues to be a major challenge for oral health practitioners. Furthermore, caries interventional treatment need in primary dentition is known to increase with age. Cross-sectional studies carried out in Denmark demonstrated an increase of 25 to 52% restorative procedures in approximal surfaces with the increase in age of 7 to 9 years, respectively (Ekstrand et al., 2010).

In Pakistan, a recent systematic review conducted by Siddiqui et al. (2021) provides a comprehensive overview of the prevalence of dental caries in Pakistan. The review encompassed 30 studies with a total of 27,878 subjects. It revealed a significant national prevalence of dental caries estimated at 56.62%. This prevalence was consistent across different provinces, with rates of 58.95% in Sindh, 55.44% in Punjab, and 51.17% in Baluchistan and Khyber Pakhtunkhwa (KPK) combined.

A cross-sectional study in Bhakkar, Punjab, Pakistan, aimed to compare dental caries status among 11-12-year-old school children using the World Health Organisation (WHO) criteria and the modified ICDAS method. The prevalence of caries was found to be 56% in the children. The study found no statistically significant difference in the prevalence of dental caries between the two methods of caries detection. However, the modified ICDAS method required more time for scoring teeth,

on the other hand intra-examiner reproducibility was higher with the WHO index (Taqi et al., 2019).

In Sargodha district, a cross-sectional study assessed the prevalence and associated factors of dental caries, gingivitis, and calculus deposits in school children aged 3 to 12 years. Among the 518 children studied, the prevalence was 45.9% for dental caries, 14.5% for gingivitis and 14.3% for calculus. The researchers also reported that older children and those living in urban areas exhibited higher dental issues (Umer et al., 2016). In another study on 6 and 12-year-old school children in Karachi revealed an overall caries prevalence of 69.6%, with a mean DMFT score of 2.98. The prevalence was higher in 6-year-olds compared to 12-year-olds, and significant differences were observed between public and private school children (Mohiuddin et al., 2015).

In a study assessing dental caries status in children aged 6 to 9 years in Islamabad, the overall mean dmft for each child was 6.33. Most decayed teeth were untreated, with lower second primary molars being the most affected. The study provides insights into the prevalence and distribution of dental caries in this age group, emphasising the need for preventive and treatment interventions (Maxood, 2008). Reports from Multan and Lahore contributed additional data on dental caries prevalence. Pervaiz reported a DMFT value of 0.8 between 12-15 years old children in Multan, and Khan observed a DMFT score of 0.9 in his study population, with 83% of all children with decay having caries in the first molars (Haleem and Khan, 2001, Muhamad Pervaiz et al., 2008).

A study investigating the prevalence of dental caries among 5 to 14 years old children in poor localities of Lahore found an overall caries prevalence of 71% (Ali et al., 2012). An additional study conducted in Lahore focused on evaluating dental caries prevalence among 3 to 5-year-old children and its association with urbanisation and

family income. Among 601 examined children, the overall caries prevalence was 40.5%, varying across age groups. The study revealed a higher caries prevalence in 4 and 5-year-olds and a significant association with low socioeconomic status and rural residence. Urban areas exhibited a higher caries prevalence (45.2%) than rural areas (31.5%). The study emphasised the need for oral health interventions, particularly in urban settings and for children from low-income families (Sufia et al., 2011). Another study focusing on preschool children in Islamabad reported a 49% prevalence rate and emphasised the importance of brushing, sugar consumption, and regular dental visits in managing dental caries. The study concluded that children who practiced regular brushing were four times more likely to have a low DMFT score (Masoud et al., 2020)

In summary, these epidemiological studies offer a comprehensive insight into the prevalence of dental caries in children throughout Pakistan. The wide range of caries prevalence among children is influenced by the diverse populations, geographic locations, and research methodologies, providing nuanced understanding into the substantial burden of dental caries in Pakistan.

2.3 Minimally invasive treatment approach for the management of carious approximal lesions in primary molars

In the management of ECC, the preventive approach requires adequate daily oral hygiene and fluoride application via toothpaste, with the supervision by caregivers and an emphasis on reducing the amount and frequency of sugar intake. Schmoeckel et al. (2020) conducted a systematic review on how to intervene the caries process in ECC. In the management of ECC, different kinds of studies with different levels of evidence were found for the different aspects in the management of ECC. The decision on the selection of caries management approach is affected by many other variables such as

pulpal involvement, the child's cooperation, or a general anaesthesia setting. In cases with persisting high caries activity, multiple lesions, and limited cooperation, caries control should consist of robust measures with high success rates, including extraction (Splieth et al. 2020).

In the non-operative caries management approach, SDF showed a high potential for arrest of ECC on a high level of evidence, while a low level of evidence for a moderate effect of fluoride varnish in arresting or remineralising, especially non-cavitated lesions, was observed. For the restorative approach in primary molars, preformed metal crowns are more successful than multisurface restorations. In proximal surfaces of primary molars without irreversible pulpal inflammation, the preformed metal crowns using the Hall's technique is significantly more successful than caries removal and restorations or the non-restorative caries control treatment (Splieth et al. 2020).

Since the early 1990s, the management of carious lesions has shifted the paradigm of drilling and restorations into the paradigm of prevention, control and minimally invasive restoration. The minimally invasive dentistry (MID) describes contemporary ultraconservative operative management of cavitated lesions requiring surgical intervention (Banerjee, 2013). Longbottom et al. (2009) described an array of treatment options for carious lesions involving approximal surfaces of primary dentition. One of the earliest developments of MID approaches is the Atraumatic Restorative Treatment (ART), and later, the concept caries inhibition using resin infiltration technique were introduced. More recently, strong evidence has emerged for arresting even cavitated dentine lesions in ECC with SDF (Schmoeckel et al., 2020). Table 2.1. lists some of the commercial dental materials products commonly for non-invasive treatment of approximal carious lesions. Most of the commercial products have

laboratory tested for effectiveness. However, in most of the products clinical trials have been recommended to warrant their potential indications.

Table 2.1 Commonly used dental materials for minimally invasive carious lesion management and their commercial brand names

Material	Commercial Products
5% Sodium Fluoride varnish (NaF)	Duraphat® (Colgate, Sao Paolo) Nupro® White Varnish, (Dentsply, York, PA, USA)
5% Sodium Fluoride varnish with Functionalised Tricalcium Phosphate (NaF-fTCP)	Clinpro® White Varnish (3M, St. Paul, Minnesota, USA) Clinpro XT® (3M ESPE, Minnesota, USA)
Silver Diamine Fluoride (SDF)	Advantage Arrest® USA Saforide® Japan
Silver Diamine Fluoride with Potassium Iodide (SDF-KI)	Riva Star® (SDI Ltd, Victoria, Australia)
Silver Nitrate ($AgNO_3$) solution	Silver nitrate®, (Gordon Labs, Carson, CA, USA)

2.3.1 Atraumatic restorative treatment (ART)

The necessity for a fresh approach to oral care in economically disadvantaged regions prompted the inception of atraumatic restorative treatment in 1994 (ART) (Phantumvanit and Pilot, 1994). The ART technique was developed to minimise cavity preparation and dimensions as the commonly used glass ionomer cement has low wear resistance and strength (Frencken et al., 1996). The benefits of ART encompass various aspects: the utilisation of readily accessible and comparatively affordable manual tools as opposed to costly electrically operated dental machinery, a biologically considerate approach that involves extracting only decayed tooth tissues, resulting in smaller cavities and preserving healthy tooth structure, reduced pain. Therefore, ART minimises the necessity for local anaesthesia, simplified and uncomplicated infection control practices without the requirement for consecutively sterilised handpieces. The chemical bonding of glass ionomers diminishes the need to remove healthy tooth structure and the fluoride release prevents the onset of secondary caries and potentially aiding in remineralising decayed dentin. Hence, ART combines the preventive and

corrective treatments into a single procedure with easy rectification of flaws in the restoration, and overall affordability. However, for multisurface cavities, ART may increase the risk of restoration failure as compared to the conventional restoration (Splieth et al., 2020). Glass ionomer cements with high fluoride release is also known to have a limited and short-duration prevention action on different types of caries (Sinha et al., 2011, Llodra et al., 2005, Liu et al., 2012).

2.3.2 Resin infiltration

A few RCTs have focused on the long-term effect of resin-based infiltration for approximal surfaces, however, resin infiltration may require multiple appointments to allow tooth separation using orthodontic elastic separators to allow infiltration. According to the protocol followed in these RCTs, the injection of local anaesthetic was administered after the placement of a rubber dam for isolation to carry out the resin infiltration procedure. Resin-based infiltration technique was found to postpone the placement of first restoration significantly. However, the paediatric patient comfort has not been evaluated for such a time consuming and technique sensitive procedure (Gomez et al., 2005, Ekstrand et al., 2010, Martignon et al., 2012, Martignon et al., 2006, Paris et al., 2010, Meyer-Lueckel et al., 2016).

Martignon et al. (2010) reported the use of resin infiltration for the first time in primary molars and found promising results despite the meticulous and tedious approach for achieving tooth separation prior to the treatment. Several randomised control trials (RCT) have used a split-mouth design to study the effectiveness of resin infiltration as compared to the NaF varnish. However, the carry-across effect associated with the fluoride release of NaF has been overlooked. Therefore, it is imperative to employ parallel designed study groups to ensure the elimination of the carry-across

effect associated with fluoride (Meyer-Lueckel et al., 2016, Paris et al., 2010, Martignon et al., 2006, Martignon et al., 2012, Ekstrand et al., 2010).

A network meta-analysis was conducted which included six studies on treatment of approximal carious lesions (Urquhart et al., 2019). The analytical study estimated that the resin infiltration and sealants applied on approximal tooth surfaces after achieving temporary access space ensured double greater chance of carious lesion arrest and prevention. They reported that a combination of resin infiltration with sodium fluoride (NaF) varnish showed five times greater chance of carious lesion arrest and prevention versus no treatment, whereas resin infiltration and sealant application after short term tooth separation showed two times greater chance of carious lesion arrest and prevention versus no treatment. The results for the application of NaF varnish alone also showed two times greater chance of carious lesion arrest and prevention versus no treatment. However, this result was not statistically significant (Urquhart et al., 2019).

2.3.3 Silver diamine fluoride (SDF)

SDF it as a colourless liquid which contains silver and fluoride ions (Gao et al. (2016a). In late 1960s the use of silver diamine fluoride was reported in Japan (Yamaga, 1969, Nishino, 1969). Chu and Lo (2008) reported several clinical uses of SDF which include arresting or stunting the caries progression (Li, 1984, Yamaga, 1969, Gotjamanos, 1996), desensitisation of sensitive teeth (Liu et al., 1995), post root canal treatment application of SDF to prevent fractures (Yokoyama et al., 2001) and re-infection (Yamashita, 1985).

More recently, SDF has gained clinical interest globally. Systematic reviews consistently support SDF's effectiveness in arresting coronal caries in primary dentition and preventing root caries in older adults (MOH, 2021). SDF is effective in the arrest

of caries progression which if left untreated can lead to pain and infection. It has an affordable cost with a simple treatment objective. The procedure is easy to carry out and requires minimal staff support to perform (Chu and Lo, 2008). However, SDF is contraindicated if the patient is allergic to silver. SDF has a metallic taste and staining of clothes and skin has been known as a potential drawback of SDF. SDF can cause gingival and mucosal irritations, which are common within 2 days of application (Galui et al., 2018).

Therefore, SDF holds promise as a therapeutic option that can benefit various patient groups. Specifically, it is valuable for patients with extreme caries risk, those who cannot tolerate conventional treatments (such as special needs patients or medically compromised individuals), and those residing in remote areas with limited access to dental care. SDF provides a safe, effective, and painless alternative to traditional cavity drilling procedures for these patients.

The effect of SDF on cariogenic bacteria, mineral content of enamel, mineral content of dentine and the dentine organic matrix has been examined in numerous studies. An extensive literature review regarding mechanism of action of SDF concluded that SDF is a bactericidal agent and reduces the growth of cariogenic bacteria. The antibacterial action of silver ions takes place by forming silver phosphate ions on the carious surface (Mei et al., 2013a). SDF inhibits demineralisation and promotes the remineralisation of demineralised enamel and dentine. SDF also inhibits the growth of cariogenic biofilms on teeth and hampers degradation of the dentine collagen (Zhao et al., 2018).

Dental caries is a dynamic process involving the demineralisation and remineralisation of dental hard tissues, including enamel and dentin. Demineralisation

occurs due to acids produced by bacterial metabolism, while remineralisation helps repair non-cavitated lesions (Featherstone, 2008). When SDF is applied, it reacts with hydroxyapatite, forming calcium fluoride, silver phosphate, and ammonium hydroxide. These compounds serve as reservoirs for fluoride and phosphate, aiding in remineralisation and enhancing the tooth's resistance to further demineralisation (Fontana and Zero, 2006). In addition to the application of SDF, regular oral hygiene and dental check-ups are crucial for preventing and managing dental caries.

Lo et al. (2001) reported a significantly higher rate of caries arrest with SDF when compared to NaF or water. Extending their research to 30 months, Chu et al. (2002) observed that SDF treatments outperformed all other groups in caries arrest. Additionally, the researchers noted that more lesions treated with SDF appeared black after arrest compared to those in other groups. However, parental satisfaction with their dental appearance of their child and health did not show significant changes. Furthermore, Chu et al. (2002) found that the removal of soft decayed tissue before applying SDF did not significantly alter the rate of cavity cessation when compared to applying SDF without excavation.

Duangthip et al. (2016) compared the efficacy of caries arrest across three treatment categories: SDF and NaF, using different application frequencies (annual and every three weeks), and evaluations conducted at 6, 12, and 18 months. The arrest was notably higher in the SDF groups (annual and every three weeks) compared to NaF (every three weeks). By the 30-month mark, Duangthip et al. (2018b) noted that the rate of arrest in Group 1 (annual SDF application) significantly surpassed both Group 2 (SDF every three weeks) and Group 3 (NaF every three weeks).