EFFECT OF FLUORIDE VARNISH APPLICATION ON PRIMARY DENTITION AMONG PRESCHOOL CHILDREN IN DHARAN: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Dental caries is a multifactorial disease which starts with microbiological shift within the complex biofilm and is affected by salivary flow and its composition, exposure to fluoride, consumption of dietary sugars, and by preventive behaviors (cleaning teeth). Topical application of fluoride varnish on the tooth surface prevent the dissolution rates of tooth materials and increase the re-precipitation of lost minerals. The objective of the present study was to assess the effectiveness of fluoride varnish application in primary dentition among preschool children at high risk of dental caries. Methods: A randomized controlled trial was conducted with two parallel group, comprising 3-5 year old children, 100 in each group (Fluoride varnish/FV or Placebo varnish/PV). Oral examination of children was performed using mouth mirror and WHO probe. Dental caries was recorded at baseline, three and six months using Caries Assessment and Treatment Instrument (CAST) scoring system. Analysis was done using chi-square test for categorical data, Mann-Whitney U test, independent t test and Wilcoxon Signed Ranks test for quantitative data. The level of significance was set at $p<0.05$. Results: Overall, dental caries progression from baseline to 3 month and 6 month was more in PV group children than FV (38.98% and 31.3% respectively). At the end of the study, the overall caries incidence was 28.24%. The proportion of children with new caries lesions was more in PV group than that in the FV group at every three months interval. The difference between the groups were statistically significant ($p<0.05$). FV treatment once in six months had better treatment effect with preventive fraction of 62.1% in comparison to three months (59.0%). Conclusion: Dental caries can be prevented effectively by use of 5% sodium fluoride varnish. It is efficacious when applied twice a year in children at high risk of dental caries. Trial Registration: CTRI/2016/02/006659 (Reg. date: 18/02/2016) Trial Registered Retrospectively Key Words: Dental caries, Fluoride varnish, Primary dentition, Randomized controlled trial

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Results: Overall, dental caries progression from baseline to 3 month and 6 month was more in PV group children than FV (38.98% and 31.3% respectively). At the end of the study, the overall caries incidence was 28.24%. The proportion of children with new caries lesions was more in PV group than that in the FV group at every three months interval. The difference between the groups were statistically significant ($p<0.05$). FV treatment once in six months had better treatment effect with preventive fraction of 62.1% in comparison to three months (59.0%).

Conclusion: Dental caries can be prevented effectively by use of 5% sodium fluoride varnish. Fluoride Varnish is efficacious when applied twice a year in children at high risk of dental caries.

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Background

Dental caries is the most prevalent chronic disease worldwide [1] and it has an uneven distribution in the population [2]. A number of epidemiological studies done on dental caries worldwide revealed that the prevalence and severity of carious lesions are concentrated in few, often disadvantaged social groups [3]. Dental caries prevalence is very high in eastern Nepal, that is 60.3% in primary dentition and is the most common chronic infectious disease of oral hard tissues in the developed as well as in developing countries [4]. According to the World Health Organization (WHO) report (2003), dental caries remains a major public health problem in most industrialized countries, affecting 60–90% of school children and the vast majority of adults [5].

Dental caries in primary dentition and in children of low income family group is an important public health problem in many countries thus experiencing negative effects on their oral health-related quality of life [6]. It is believed that carious primary tooth not only increases the risk of further tooth decay in childhood but also increases the chance of carious lesion later in life [7, 8]. The innovative and effective interventions in the school setting have the potential to reduce caries and the resultant impact of the disease [9]. But, for caries reduction, joint effort of communities, professionals and individuals are required to reduce the impact of sugar consumption and emphasize the beneficial impact of fluorides [10].

Fluoride is the ionic form of the element fluorine, the 13th most abundant element in the earth‘s crust. Fluoride has several caries-protective mechanisms such as enamel re-mineralization and alteration of bacterial metabolism [11]. Professional application of fluoride varnish has a strong tradition in many European countries and the therapy is often advocated as a supplement for caries risk individuals [12].

Several studies including clinical trials have shown the effect of fluoride varnish on carious deciduous and permanent dentition [13]. A Cochrane review estimated the preventive fraction of Fluoride Varnish to be 33% for the primary teeth [6]. A recent review by Petersson, et al., (2004) found an average preventive

fraction of fluoride varnish in children as 30% and in range of 0-69% [10]. Increasing emphasis on the need for evidence-based health interventions requires the evaluation of the efficacy of fluoride varnish in primary dentition by a carefully designed randomized controlled trial that use placebo and may generate sound data in our part of the world.

Methods

METHODS

The aim, design and setting of the study

The aim of the study was to assess the effect of fluoride varnish on caries progression and reduction in incidence of dental caries in primary dentition. Null Hypothesis: There is no significant difference in progression of dental caries on application of fluoride varnish and placebo. A randomized controlled clinical trial with parallel groups study was implemented from October 2015 to September 2016, among primary school children of Government schools in Dharan, Nepal. Ethical approval for the study was obtained from the Institutional Review Committee, BPKIHS, Dharan (Ref. No. 448 /071/072). The study was registered retrospectively as a clinical trial (www.ctri.nic.in) by the National Institute of medical Statistics (India Council of Medical Research); the Clinical Trial Registry India identifier no. CTRI/2016/02/006659 (Reg. date: 18/02/2016) (http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=13701)

Participants: Out of 38 Government schools of Dharan, initially 8 schools (20% of total) were randomly chosen from the list using lottery method. Being unable to achieve the required number of subjects from previous schools, additional 6 schools were selected. A total of fourteen Government schools of Dharan were approached and the principals of all the schools gave consent for conducting the research. Written informed consent was obtained from parents/guardian and proxy consent was obtained from school principals, where parents' consent was not acquired. A total of 290 children of age 3-5 years were examined from all the selected schools at baseline and those who had ≥1 decayed/missing/filled tooth were enrolled in the study. Finally a total of two hundred children were recruited for intervention. However, children who had a history of allergic reaction that required hospitalization, un-cooperative and those who were not willing to take part in study were excluded.

Sample size: Sample size was calculated based on two previous study two studies[4, 14]. Taking 1:1 ratio of sample unit, alpha=0.05, power of the study 80% and CI at 95%. Putting all these values into EPI-info 2007 software (CDC, Atlanta, USA, WHO), sample size was determined to be 87. Adding 15% to compensate for dropout rate, the required sample was 100 in each group.

Randomization and Masking: Each child was assigned to a group (Group A or Group B) by biostatistician using computer generated random numbers. An assistant, not participating in the field study, prepared the intervention tubes according to the allocation lists, placing a tag for each treatment group. Group A consisted of Fluoride varnish and Group B consisted of Placebo varnish. Patients, researcher, and

outcome assessor were kept unaware of the type of the treatment they received during and after randomization and not unveiled until the analysis of data.

Oral examinations: The baseline and follow-up study visits at 3 and 6 months involved a full mouth oral examination of all the teeth using the Caries Assessment and Treatment Instrument (CAST) scoring system. CAST is the most recent index developed in 2011 by joint effort of Radboud University Nijmegen Medical Centre, The Netherlands (Jo E. Frencken, Rodrigo G. de Amorim) and from the University of Brasília, Brazil (Jorge Faber and Soraya C. Leal). This diagnostic tool contains the feature of the three indices; ICDAS, PUFA and the DMF Index. It can evaluate complete spectrum of dental caries [15]. The codes used in this system are as follows. (see Chart 1 in the Supplementary Materials)

All the examination throughout the study was done by the same investigator. The examiner was trained and calibrated prior to initiation of the study and during the study. Intra-examiner reliability was assessed at baseline and in-between the study duration by re- examining 25 randomly selected participants. All the subjects were examined in the supine position under natural light. Oral examination was carried out by using sterilized instruments including mouth mirror for indirect vision and a probe for removing excess plaque. A pro forma (record form) was used to collect and record the data. The record form included the details of demographic characteristics (name, age and gender, school, class) and a dental chart for coding 20 primary teeth.

Intervention and Measurements:

Fluoride Varnish Application: Fluoritop SR Varnish (ICPA Health Product LTD, India) is an alcohol based material. Fluoride varnish contains Sodium Fluoride (50mg) equivalent to 22.6mg of fluoride. Varnish was painted in a thin layer with the help of disposable applicators on all the primary teeth present in oral cavity except on root stump and tooth with pulpal involvement. An application took 4 minutes for each child. Before application, each tooth was wiped and dried with cotton wool rolls or gauze and varnish was painted onto all surfaces of the maxillary and mandibular anterior and posterior teeth. Parents/caregivers and children were asked to refrain from brushing their children‘s teeth with fluoride toothpaste on the day of varnish treatment and were instructed to avoid eating hard and hot food and drinking for 2 hours. Varnish was applied at baseline and every three months for a period of six months. A total of three applications were received by each child. Placebo: Placebo varnish (PV; Manoj Pharmaceutical (P) Ltd. Dharan, Nepal) was identical to Fluoride varnish except that it did not contain fluoride. Application procedure was similar to fluoride varnish.

Outcomes: The primary outcome was caries progression as measured by changing from the baseline enamel and dentinal caries into enamel, dentinal, pulp involvement and missing due to caries. Baseline CAST codes were subtracted from the codes recorded at 3 month and 6 month follow-up.

The secondary outcome was caries incidence as measured by the proportion of children developing any new enamel and dentinal caries during the study. Sound, pits and fissure sealant and restored tooth at baseline was subtracted from the number of sound, restored and decayed tooth at 3 and 6 months of

follow-up. A child was considered to be an incident case of dental caries if the subtraction score was more than zero.

Statistical analysis: After completion of the survey, data obtained were entered in Microsoft Excel Sheet version 2007 and analyzed using the Statistical Package for Social Sciences (SPSS version 11.5, SPSS, Inc., Chicago, IL, USA). The level of significance was set at 0.05. Intra-examiner reproducibility for coding was measured by Cohen's kappa coefficient. Descriptive analysis was performed to summarize the clinical and socio-demographic characteristics of each group at baseline in order to assess how comparable the groups were at beginning of the study. Chi- Square test was used to assess the difference in the proportion of children with caries progression and incidence in both the groups. Differences in mean dmft component between FV and placebo groups were evaluated using Mann-Whitney U test and independent t-test.

Results

Enrolment and Retention: Out of 290, only 200 subjects matched the inclusion criteria of the study and were randomized into two groups. The mean age was 4.15±0.82 years and majority of the children in both the groups were 5 years old. The first and second follow-up examinations were done at three month interval, consecutively. During the second follow-up, 177 children were examined which represented 88.5% retention rate. However 18 participants didn't received treatment at 3month and 23 children at 6 month and (reasons: absent at the time of examination and some left the school). The CONSORT flow diagram tracks subject participation for the entire study (Figure 1). There were total of 200 children allocated into two groups with a mean age of 4.15±0.82 years and majority of the children in both the groups were 5 years. Overall, 44.5% male and 55.5% female participated in the study. Baseline mean dmft in all children who took part in the test and control group (Table 1 and 2) shows that,dental caries was more among the children of control group and it was more in male than female participants in both the groups but the difference in mean dmft among the groups were found to be insignificant ($p > 0.05$).

Intra-examiner reliability: The overall kappa value for CAST code ranged from 0.86 to 0.93 at baseline and at 3 months of follow-up Kappa value was in range from 0.81 to 0.91. Kappa values suggested that the clinical intra-examiner reproducibility for detecting dental caries was very good.

Dental caries progression:

Overall, progression of dental caries from baseline to 3 month and 6 month follow-up was 31.3% and 38.98%, respectively in FV and control group. Dental caries progressed in children of both FV and control group at 3 month and 6 month follow-up. However, control group children showed significant progression of dental caries at different interval (Table 3).

Pair wise comparison of FV and placebo group at different time period revealed that there was gradual increase in severity of dental caries at 3^{rd} and 6^{th} month of follow-up from baseline and difference was statistically significant ($p<0.05$). However, rate of increase in dental caries from 3^{rd} to 6^{th} month was

almost static in comparison to that from baseline which was not significant (p=0.258). Likewise in children of control group, difference in dental caries progression in each interval was statistically significant (Tables 4 and 5).

Preventive fraction (PF): The treatment effect expressed as preventive fraction is the difference in caries incidence of the placebo varnish and fluoride varnish group, divided by the incidence of the placebo varnish group expressed as a percentage. FV treatment at six month had the best treatment effect with preventive fraction of 62.1% in comparison to three month (59.0%).

Caries incidence:

Overall, the caries incidence was 28.24% at the end of the study. At three months, out of ninety-two subjects in control group, twenty-two children had developed new lesion compared to FV group where only eight participants had developed new cavity. At six months, 37 children showed caries incidence in control and 13 children in FV group. The proportion of children with new caries lesions was more in control group than in the test group at every three month interval and the difference was statistically significant (Table.6).

Adverse Events: None of the children and children's caregiver reported any adverse effects associated with the interventions.

Discussion

This study was carried out to determine the effectiveness of fluoride varnish in prevention of dental caries in primary dentition compared to placebo applied every three month during the year. The results showed positive effect of fluoride varnish on dental caries. Mean dental caries in Fluoride varnish group was 3.75 and in the placebo varnish group 4.17,which was statistically not significant at baseline (p=0.54). However, dental caries progression was less in subsequent follow-up in both the groups from baseline, which was statistically significant. The magnitude of dental caries progression in fluoride varnish was 23.33% and 26.66% and 9.1% at 3 month, 6month and 3-6 months interval respectively, likewise in placebo varnish group it was 39.13%, 51.72% and 20.2%, respectively. Difference in between these groups were statistically significant at follow-up period. There was a significant difference in progression of dental caries from baseline to first (p=0.01) and second (p=0.001) applications. The progression between the 2nd and 3rd application was not significant (p=0.285) which revealed that fluoride varnish is effective at 3-6months. However, a statistically significant difference existed at every stage (p<0.05) in control group. Mohammadi, et al. (2015) also reported the reduction in dental caries at 6 month by 14% in comparison to control which is less than the present study [13]. A study done by Ekstrand, et al. (2010) also reported the progression of dental caries in semi-annual application of varnish in proximal surface of primary molars in children aged 5-8 years. Out of 42 participants, progression was observed in 28 children on fluoride varnish group and 13 in resin infiltration followed by FV (2.26% F) application after one year[16]. It is slightly more than the report of present research. American Dental Association (ADA) recently concluded that ―Fluoride varnish applied every six months is effective in preventing caries in

the primary and permanent dentition of children and adolescents. Two or more applications of fluoride varnish per year is effective in reducing the caries prevalence in primary or permanent teeth for moderate to high risk children[17]. The clinical recommendations given by ADA (2006) also suggested that the application of varnish at every three-month interval among the people at highest caries risk may obtain caries prevention benefit [17]. The present study shows that there is an increment in caries with time. New caries development in children of Varnish group were 8.88%, 14.44% and 6.8% during 3 month, 6month and 3-6 months of follow-up respectively. In comparison to control group, during the respective follow-ups it was 23.91%, 42.52% and 21.4%. Incidence of dental caries was less evident within the children of varnish group who were exposed twice to fluoride varnish. Overall, the caries incidence was 28.24% at the end of the study. A study [18] revealed that children with good oral health and who had received at least one fluoride varnish treatment, 37.73% were caries free whereas, among the participants who had never received fluoride varnish treatment, only 26.80% were caries-free and the difference was statistically significant (p=0.001). This finding supports the preventive action of fluoride varnish shown by the present study. This could be because application of fluoride varnishes in a thin layer adheres to the tooth surface for longer periods (12 hours or more), and prevents the immediate loss of fluoride after application. It inhibits demineralization and stimulates the remineralization process. A study [19] also proved that incidence of caries was reduced by applying varnish twice a year with respect to single application. A Cochrane review done by Marinho, et al. [20] concluded that fluoride varnish can reduce development of dental caries by preventive fraction (PF) of 65% over a 3 year period. Present research shows that preventive fraction (PF) of fluoride varnish at three and six months was 59.0% and 62.1%, respectively. Hence, the use of fluoride varnish in the targeted population was proved to be effective in prevention of dental caries. Adverse effect of the fluoride varnish was not reported in any of the children who were followed for a year. In this study amount of varnish painted on teeth was 0.5ml and one of the study reported that this quantity of varnish delivers 3 to 11mg of fluoride ions per dose. Which is far below the probable toxic dose of 5 mg/kg body weight [21]. This result is also supported by the study [22], as varnish is painted on teeth the plasma fluoride concentrations of 3.2 to 6.3 micromolar were found post two hour of application, followed by a rapid decrease over next two hour and a slower decrease thereafter. These levels were comparable with those found after brushing with a fluoridated toothpaste (mean ± standard deviation, 3.63 ± 0.45 μmol/L) or after ingesting a 1-mg F– tablet (4.47 ± 0.47 μmol/L) and were considerably lower than those reported for APF gels (16 to 76 μmol/L). These data signify the minimal risk of varnishes. Anderson, et al. (2016) did not report any serious adverse effects of varnish which was applied in 1 year old child and followed them till 3 years [7]. A study [6] reported concerns of parents as discoloration of teeth after first application of FV, similarly some children had burning sensation on first day of placebo varnish application.

Thus, the study recommends that fluoride varnish application should be included compulsory in school oral health programmes, as it is very easy to apply and does not require sophisticated armamentarium. It is suitable and practical for use in community especially in young children and in other special need groups.

Besides these findings the study had few limitations. All the potential caries risk factors for all the groups were not assessed. Also, the confounder was not omitted as fluoridated toothpaste can reduce the dental caries progression and occurrence. Face to face parent's interview could be done to control these factors. Another limitation was that the study findings may not be generalized to all the students as this study includes high risk populations with caries.

Conclusion

The study strongly suggests that dental caries can be prevented effectively by use of 5% sodium fluoride varnish. Topical application of fluoride varnish not only prevents the occurrence but can also stop the further progression of caries. It is more efficacious when applied twice a year in children at high risk of dental caries. Moreover, the application procedure was simple and acceptable by all the children.

Abbreviations

ADA; American Dental Association; CAST; Caries Assessment and Treatment Instrument; CONSORT; Consolidated Standards of Reporting Trials; FV; Fluoride Varnish; PV; Placebo Varnish; PF; Preventive Fraction;

Declarations

Ethics approval and consent to participate: Ethical approval for the study was obtained from the Institutional Review Committee, BPKIHS, Dharan (Ref. No. 448 /071/072). All parents/Principals provided their informed consent in writing.

Consent for publication: Not applicable

Availability of data and material: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: the authors declare that there is no competing interests.

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Authors' contributions: SKA, AS and TKB conceptualized and designed the study. SKA performed clinical examination of both the groups, collection of data, analysis, prepared final report and manuscript. AS and TKB supervised all the procedure, did moderation in protocol and final editing and approval of manuscript.

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