

## Topical fluoride gel application: When and to whom starts therapy?

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### ABSTRACT

This study aims at investigating the scope of topical acidulated phosphate fluoride (APF) gel effect on initial carious lesions, evaluating the effect of the gel on newly erupted teeth, as well as on the low-, moderate-, and high- risk school children.

A sample of (340) school children [177 (52.06%) males and 163 (47.94%) females] initially in the fourth grade (aged 9-11 years) were collected from (4) primary schools in Mosul city center. The children were allocated randomly to one experimental group (received topical APF gel) and one control group (did not receive any fluoride therapy).

The dental examinations were done using DMFT index: one before fluoride application and the other after one year.

It can be observed from this study that the topical APF gel is effective on initial lesions. Moreover, the efficacy of the gel on the newly erupted teeth, including those teeth erupted during the study, is found to be greater than on the previously erupted ones.

The results also reveal that the high-risk groups are the most benefitted from the fluoride treatment than the moderate- and low-risk groups. The percentages of caries reduction were (96.700%), (74.880%), and (36.071%) for the three groups, respectively.

So, the use of such a fluoride therapy as a school-based programme is advised for all children with evidence of dental caries, and is recommended to be planned to match the pattern of eruption of teeth.

**Key Words:** Topical fluoride gel, risk groups, initial lesions, newly erupted teeth, previously erupted teeth.

### الخلاصة

تهدف هذه الدراسة إلى بحث مدى تأثير هلام فوسفات الفلورايد المُحمَّض على التسوس الابتدائي، تقييم تأثير الهلام على الأسنان حديثة الظهور، بالإضافة إلى تأثيره على المجاميع ذوات الاستعداد العالي، المتوسط، والقليل للإصابة بتسوس الأسنان.

تم جمع عينة (٣٤٠) تلميذ من أربع مدارس ابتدائية في مركز مدينة الموصل [١٧٧ (٥٢,٠٦%) ذكور و ١٦٣ (٤٧,٩٤%) إناث] في المرحلة الرابعة والذين تتراوح أعمارهم عند بدء البحث بين (٩-١١) سنة. وزعت هذه العينة عشوائياً على مجموعة واحدة تجريبية (تم إعطاؤها فوسفات الفلورايد المُحمَّض موضعياً) ومجموعة واحدة ضابطة (لم تُعط أي علاج بالفلورايد).

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أجريت الفحوصات على أسنان الأطفال باستخدام المؤشر (DMFT) مرة قبل وضع الفلورايد على الأسنان والأخرى بعد مرور عام واحد. من الملاحظ في هذه الدراسة تأثير الفلورايد الموضعي على التسوس الابتدائي بالإضافة إلى أن فاعلية الفلورايد كانت أكبر على الأسنان حديثة الظهور (من ضمنها الأسنان التي ظهرت خلال الدراسة) من تلك التي ظهرت مسبقاً. كما كشفت الدراسة أن المجموعة ذات الاستعداد العالي للإصابة بتسوس الأسنان كانت مستفيدة أكثر من المجموع ذات الاستعداد المتوسط والقليل. حيث كانت نسب الانخفاض في تسوس الأسنان (٩٦,٧٠٠%)، (٧٤,٨٨٠%)، و (٣٦,٠٧١%) للمجموع الثلاثة على التوالي. ولهذا ينصح باستخدام مثل هذا العلاج بالفلورايد كبرنامج يطبق على تلاميذ المدارس كافة والذين يعانون من تسوس الأسنان مع الأخذ بنظر الاعتبار ملائمة البرنامج لأوقات ظهور الأسنان.

## INTRODUCTION

The use of concentrated fluoride solutions and gels applied topically to the dentition for the prevention of dental caries has been studied extensively during the past (50) years, although few studies have been conducted since the 1970s<sup>(1,2)</sup>. The procedure resulted in a significant increase in the resistance of the exposed tooth surfaces to the development of dental caries and, as a result, has become a standard procedure in most dental offices<sup>(2,3)</sup>.

Although topical fluoride applications have been in wide spread use by dental practitioners for the past fifty years, questions continue to be raised regarding the most appropriate use of these treatments for the prevention and control of dental caries. In recent years, the need for professional fluoride treatments has been questioned by scientists on the basis of the relatively low prevalence of dental caries in many patients and the fact that very few studies of these systems have been conducted in such populations<sup>(4)</sup>. Although a recent review questions the merits of professional fluoride treatments on a cost-benefit basis<sup>(5)</sup>, other reviews have supported their use in patients with evidence of at least modest caries activity or caries risk<sup>(2,6)</sup>.

The Workshop on Changing Pattern of Fluoride Intake (WCPFI) held at the University of North Carolina in Chapel Hill in 1991 recommended that dental patients be evaluated for their risk of decay and that only children and adults with caries activity or with a moderate to high risk of developing caries be given routine professionally applied fluoride treatments using "clinically proven products in the correct way"<sup>(7)</sup>. A moderate-risk group was defined as patients with some caries activity and/or that moderate risk of developing caries. A high-risk group involves patients with high caries activity and/or at high risk of developing caries<sup>(1)</sup>. The degree of caries risk is determined by considering several factors. Since fluoride is most effective on smooth- and root- surface caries, patients with orthodontic appliances, individuals undergoing head and neck irradiation and patients with a decreased salivary flow –usually due to systemic conditions or side effects from medications- will greatly benefit from these fluoride treatments<sup>(8,9)</sup>.

Another frequent question concerns whether professional fluoride applications are appropriate for children in the absence of significant caries activity. Although there is no consensus on this matter, Stookey states that such applications are

appropriate for all children having significant caries risk between the ages of (6) and (14) years as a preventive measure. This opinion is based upon several important factors, the first of which is the long-recognized fact that the time when teeth are the most susceptible to caries formation is during the first two years after eruption. An examination of the tooth formation and eruption patterns for the permanent dentition indicates that, throughout the period between ages (6) and (14), at least one permanent tooth type is undergoing post-eruptive enamel maturation and is in the period of greatest risk of developing caries<sup>(4)</sup>.

Finally, the results of numerous clinical trials have consistently demonstrated that the benefits of professionally applied topical fluoride treatments are always of a greater magnitude upon newly erupted teeth than upon teeth that are more completely matured; with the teeth erupting during the course of the study receive the most benefit<sup>(10, 11, 12)</sup>. Special effort should be made by the dentist to schedule topical fluoride applications so as to provide the treatment to newly erupted teeth within at most (12) months after eruption, and preferably as close to eruption as possible<sup>(2)</sup>. Generally, professionally applied topical fluoride treatments are *not* recommended for children under age six and adolescents at low risk for developing caries who live in fluoridated communities and use a fluoridated toothpaste<sup>(9, 13)</sup>.

So, the purpose of the present study was to investigate the scope of topical acidulated phosphate fluoride (APF) gel effect on initial carious lesions, evaluate the effect of the gel on newly erupted teeth, as well as on the low-, moderate-, and high-risk school children.

## MATERIALS AND METHODS

The study was conducted during the period between March 2000 to March 2001 in four primary schools from different areas in Mosul City center/ Ninevah province.

A sample of (467) school children initially in the fourth grade (initial age ranges from 9-11 years) were collected from four primary schools. The selection of the schools was based mainly on the co-operation of the school authorities. Two of these schools contained (2) fourth grade classes for each, while the other two contained (1) fourth grade class for each. Therefore, a total of (6) classes out of (4) primary schools were included in the study.

The parents of each child were sent detailed explanatory letters concerning the aims and benefits of the study and including their approval about the research.

Instruments and supplies that had been used include: - 1) plane mouth mirrors; 2) sharp sickle-shaped caries explorers; 3) tweezers; 4) kidney dishes; 5) fluoride trays (stock trays) with different sizes; 6) drum for placing the sterilised instruments; 7) pan for sterilising the instruments with concentrated sterilising solution (4% Septicin) for 15 minutes then washed with water; 8) cotton for removing debris from around the teeth; and 9) fluoride gels [0.4% APF thixotropic gel (Dentaclean: UK made)].

All the students were clinically examined 2 times during the study: (1) at the beginning of the study (before application of fluoride gel) in March 2000, and (2) after one year of APF treatment in March 2001. The two examinations were carried out by the same examiner in good natural daylight, using plane mirrors and probes with the student sitting in a chair in front of the examiner. After drying the teeth with cotton, they were examined carefully.

Clinical criteria for the diagnosis of dental caries followed the WHO guidelines<sup>(14)</sup> using DMFT index for permanent teeth with the exception that a score for the initial caries (white or chalky spots) was included in the scoring of decayed teeth<sup>(15)</sup>. Radiographs were not taken because of practical limitations, which make radiography for each child very difficult.

The (6) classes from the (4) primary schools were allocated randomly to (1) group of treatment (experimental group), and (1) control group. Five classes were allocated randomly to the experimental group, while the sixth class was allocated to the control group.

All the children in the experimental group received no prior prophylaxis. Five children at a time were treated according to the following procedure: each child was asked to rinse thoroughly with water in order to dislodge loose debris, then the children were seated in upright position and a suitable tray for each child was carefully selected. The teeth of each child were then wiped with cotton to remove any remaining debris and dry the teeth. The selected trays, each containing a ribbon of APF gel, were inserted over the maxillary arch for each child. Individual timer was used for each child to ensure that all children had the appropriate time contact with the fluoride gel (4 minutes). After that, the trays were removed and the children were allowed to expectorate thoroughly. Then, the same procedure was repeated for the mandibular arch and the children were asked to expectorate thoroughly once again to remove any excess fluoride, but instructed not to eat, drink, or rinse for at least 30 minutes following the treatment.

The percentage of dental caries reduction compared to the control group was calculated according to the following equation:

$$\frac{\left( \begin{array}{c} \text{Mean of caries increment} \\ \text{of the control group} \end{array} \right) - \left( \begin{array}{c} \text{Mean of caries increment of} \\ \text{the experimental group} \end{array} \right)}{\text{Mean of caries increment of the control group}} \times 100$$

The percentage of caries increment of each group was calculated with the following equation:

$$\frac{\left( \begin{array}{c} \text{Mean of caries at the} \\ \text{second examination} \end{array} \right) - \left( \begin{array}{c} \text{Mean of caries at the} \\ \text{first examination} \end{array} \right)}{\text{Mean of caries at the first examination}} \times 100$$

The term "*newly erupted teeth*" used in this text refers to those teeth that erupted shortly before the beginning of the study as well as those teeth erupted during the study. It includes canines, first and second premolars, and second molars. Whereas the term "*previously erupted teeth*" refers to those teeth erupted a long period before starting the study. It comprises centrals, laterals, and first molars.

Throughout the study, the children with a mean DMFT of "1" and "2" at the first examination were considered as "*low risk*", those with "3" and "4" were considered as "*moderate risk*", and those with "5 and more" DMFT were recorded as "*high risk*" groups. Regarding the so-called "*caries free*" children (those with a mean DMFT of "0" at the first examination): since they were only (8) and of little significance, therefore neglected from these results.

The statistical analysis of the data, which was conducted using SPSS (for Windows version 9.0), include the followings:

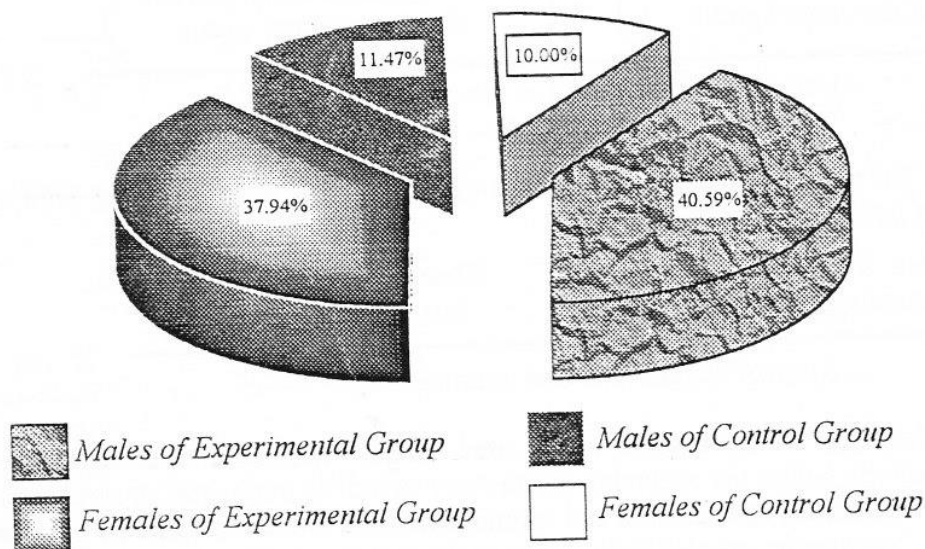
1. Classification of data and calculation of frequencies.
2. Calculation of statistical parameters: the mean and standard deviation.
3. F-test was used for determining the differences among previously erupted, newly erupted, and all teeth; and within the low-, moderate-, and high-risk groups.

The differences were considered significant when the probability ( $p$ ) level was equal to, or less than, 0.05 ( $p < 0.05$ ). When the ( $p$ ) level was more than 0.05 ( $p > 0.05$ ), it was regarded as non-significant (N.S); those values less than 0.01 ( $p < 0.01$ ) were regarded as highly significant (H.S); while values less than 0.001 ( $p < 0.001$ ) were regarded as very highly significant (V.H.S).

## RESULTS

Among (467) school children involved initially at outset, (340) completed the study, representing a (27%) loss. Most subjects failed mainly in moving from one school to another or being absent from the school on the day of fluoride application or the second examination. The distribution of the sample by sex in the experimental and control groups was given in figure (1). The sample consisted of [177 (52.06%)] males, and [163 (47.94%)] females. It was distributed to the two groups in such away that the experimental group contained [267 (78.53%)] children, whereas the control group consisted of [73 (21.47%)] children.

Figure (1): Distribution of the sample according to sex



The comparison in caries increment was done between both males and females and between the experimental groups and the control group regarding the previously erupted, newly erupted, and all teeth; with respect to the DMFT (DFT) index (table 1). The differences between males and females clearly revealed to be non-significant; while those differences between the experimental and control groups were highly significant in the three parameters. Similarly, the differences were highly significant

between the total teeth, which were previously erupted, and those newly erupted for both experimental and control groups.

Table (1): A comparison of caries increment among previously erupted, newly erupted, and all teeth regarding (DFT) index

Situation of Teeth		Mean ± SD			F-Test Between Males and Females
		Male	Female	Total	
Experimental Group	Previously Erupted Teeth	0.304 ± 1.438	0.287 ± 1.193	0.296 ± 1.323	N.S
	Newly Erupted Teeth	0.065 ± 0.248	0.077 ± 0.268	0.071 ± 0.257 <sup>***</sup>	N.S
	All Teeth	0.369 ± 1.414	0.364 ± 1.152	0.367 ± 1.292	N.S
Control Group	Previously <sup>***</sup> Erupted Teeth	1.410 ± 1.859	1.088 ± 1.505	1.260 ± 1.700	N.S
	Newly <sup>***</sup> Erupted Teeth	0.333 ± 0.477	0.206 ± 0.410	0.724 ± 0.449 <sup>***</sup>	N.S
	All Teeth <sup>***</sup>	1.743 ± 1.996	1.294 ± 1.467	1.534 ± 1.772	N.S

<sup>\*\*\*</sup> Highly significant difference between experimental and control groups (males, females, and total).

<sup>\*\*\*</sup> Highly significant difference between previously erupted, and newly erupted teeth.

The changes in the initial lesion within the two groups were expressed as a number and percentage of teeth (table 2). Regarding those lesions that have been remineralised; i.e, became regressed, the percentage for the experimental group was found to be (24.63%), with no any lesion regression found in the control group.

The initial lesions that remained so during the study recorded the percentage in the experimental group to be (19.56%), whereas the control group represented the percentage (7.69%).

Analysing those lesions that have progressed (demineralised) revealed that the experimental group comprised the percentage (55.80%), while the control group represented the higher percentage (92.31%). This means that the lesions, which progressed in the control group, were nearly twice as those in the experimental group.

Table (2): The number and percentage of teeth with initial lesions and their changes throughout the study

Groups	Initial Lesious					
	Remineralised		Remained So		Demineralised	
	No.	%	No.	%	No.	%
Experimental	62	24.63	50	19.56	137	55.80
Control	0	-	3	7.69	36	92.31

Table (3) showed a comparison of low-, moderate-, and high- risk groups between the first and second examinations as follows:

#### Low - Risk Group

The results of this group denoted a non-significant difference between experimental and control groups for both the first and second examinations. The differences were statistically highly significant in the experimental groups between the first and second examinations; whereas the control group revealed significant differences between the two examinations. The percentage of caries reduction in comparison with the control group was (36.07%) and the percentages of caries increments of experimental and control groups were (53.15%) and (87.50%), respectively.

#### Moderate - Risk Group

In this group, the difference was not significant between the experimental and control groups at the first examination. This difference was increased to be highly significant at the second examination. When comparing the differences between the two examinations for both experimental and control groups, they were highly significant. The percentage of caries reduction of the experimental in comparison with the control groups was found to be (74.88%), while the percentages of caries increments were (8.39%) for the experimental, and (32.53%) for the control groups.

#### High - Risk Group

Within this group, the differences were non-significant between experimental and control groups at the first examination, and the experimental groups at the two examinations. There were highly significant differences between the experimental and the control groups at the second examination, and the control group at the two examinations. The caries reduction was (96.70%), and the caries increment was (1.60%) and (49.21%) regarding the experimental and control groups, respectively.

From the abovementioned three sections, one can easily notice that the high risk group gained the greatest benefits from the programme, followed by the moderate risk group; with the low risk group being the least benefitted.

Table (3): A comparison of low-, moderate-, and high- risk groups between the first and second examinations

Examination	Low Risk			Moderate Risk			High Risk		
	Exp No=38	Cont No=5	F-Test	Exp No=146	Cont No=55	F-Test	Exp No=64	Cont No=11	F-Test
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
First	1.684 ± 0.471	1.600 ± 0.548	N.S	3.753 ± 0.432	3.855 ± 0.356	N.S	5.828 ± 1.316	5.727 ± 0.786	N.S
Second	2.579 ± 1.222***	3.000 ± 1.000**	N.S	4.068 ± 1.106***	5.109 ± 1.663***	N.S	5.921 ± 1.702*	8.545 ± 2.876***	H.S
% CR	36.071			74.880			96.700		
% CI	53.15	87.50		8.39	32.53		1.60	49.21	

\* Non-significant difference between the first and second examinations.

\*\* Significant difference between the first and second examinations.

\*\*\* Highly significant difference between the first and second examinations.

Exp = Experimental; Cont = Control; CR = Caries Reduction; CI = Caries Increment.

## DISCUSSION

Whilst an obvious objective of topical fluoride treatments is the prevention of new carious lesions, such therapy should also aim at retarding or arresting the development of any initial lesion already present<sup>(16)</sup>. This concept is obviously noted in the present study as shown by the percentages of those lesions which were regressed or retarded (remineralised), became arrested (remained so), and progressed (demineralised) at the end of the study. Those belonged to the remineralised lesions were (24.63%) for the experimental group, compared to no any regressed lesion found in the control group. Those lesions, which became arrested, were represented by (19.56%) for the experimental group as compared to (7.69%) for the control group. In the same way, the demineralised lesions comprised (55.80%) and (92.31%) for the experimental and control groups, respectively. This study, therefore, indicated the high effect of fluoride in the remineralisation of initial lesion and/or arrestment of the incipient lesions; i.e, retarding the progress of caries.

There is considerable evidence to support the hypothesis that the presence of fluoride during lesion *formation* is essential to its caries inhibitory action<sup>(17, 18)</sup>. It would seem that under optimal conditions, incipient lesions cannot only be arrested but also can be made more resistant than normal enamel. It follows, therefore, that such initial lesions should always be treated with fluoride and observed rather than attacked immediately with the dental drill.

The remineralisation capacity of incipient lesions under the influence of fluoride could be related to their greater affinity for fluoride uptake in the surface and



subsurface enamel in comparison with the adjacent sound enamel. Current concepts of fluoride – caries preventive mechanisms support the view that concentrated topical fluoride forms  $\text{CaF}_2$  – like deposits on the tooth surface and that the fluoride from this material within porosities and microchannels at different cariogenic sites in the enamel can gradually leach away and provide elevated fluoride levels in the local tooth environment, thereby helping to inhibit demineralisation and promote remineralisation, resulting in reversal or "healing" of the lesion. This is in agreement with other studies<sup>(19, 20)</sup>

It is obvious in the present study that, although the differences in the mean DFT increments between the newly and previously erupted teeth were highly significant for both the experimental and control groups, the difference in means between the newly and previously erupted teeth for the experimental group outweighed those of the control group indicating that the newly erupted teeth, which included also those teeth that erupted during the study, benefitted more from the fluoride programme than the previously erupted ones. These findings are consistent with Grøn<sup>(21)</sup>. The main reason for these findings is the greater reactivity, permeability, and ease of formation of fluorhydroxyapatite (FOHAp) in enamel still undergoing calcification (or maturation). Crabb<sup>(22)</sup> showed very clearly porous enamel surfaces of newly erupted premolar teeth. This porosity enables the topical fluoride to penetrate readily into deeper layers of the enamel, and promote maturation and remineralisation in these teeth more than the previously erupted ones. Thus, the greatest benefit would be derived when topical fluorides are applied to the teeth shortly after eruption at approximately ages of (3), (7), (9), (10), and (12) years to coincide with the eruption of teeth. This is in agreement with Knutson<sup>(23)</sup>.

The findings of the anticaries effectiveness of APF gel on low-, moderate-, and high- risk groups showed the great benefit of fluoride on the high- risk subjects (96.7% reduction) followed by the moderate- risk children (with 74.88% reduction), and the little effect on those with a low- caries activity (36.07% reduction). These results are in agreement with other studies<sup>(24, 25)</sup> who found a lack of significant caries reduction in a group of children experienced low prevalence of dental caries; and other studies which noted a substantial protection in population experiencing high increment of caries<sup>(26, 27, 28)</sup>.

This relatively little benefit of fluoride on the group experienced low caries activity may be contributed to the fact that most children in this group have a low caries prevalence, so topical fluoride application cannot further reduce a caries increment which is already low. In the same way, children belonged to the moderate- and high- risk groups experienced a high prevalence of dental caries with probably higher percentage of initial lesions than those of the low- risk group, on which the APF may be more effective. This is in agreement with a study carried out by Øgaard *et al.*<sup>(29)</sup>

It appears that professionally applied APF gel treatments continue to be a practical caries preventive measure. The use of such treatments is considered for all patients with evidence of caries activity, regardless of age, and for all children between the ages of (6) and (15) years who appear to be at risk of developing caries. In all instances involving such treatments, the time and frequency of application should be dictated by professional judgement related to the caries risk of each child.

Taking into account the results of this study, one can imagine how such a programme carries benefits to the Iraqi school children especially if conducted for a longer period of time, and in combination with other measures as dental health education and other sources of school-based fluoride programmes (fluoridated

mouthrinses, fluoride supplements, or fluoridated toothpastes), or with a fissure sealant. This is considered as an important method, which makes it possible for our community to shift further out of the restorative dentistry, dominated era into the disease prevention and health promotion era.

## CONCLUSIONS

- ☞ The findings of this study clearly revealed that the effect of topically applied fluoride gel is greater on those newly erupted teeth including the teeth erupted during the study than on the previously erupted teeth. It is also found that from those newly erupted teeth, the second molars are the most affected teeth by fluoride programme.
- ☞ Application of APF gel has been shown by the present study to be effective on initial lesions.
- ☞ The results of the study demonstrated that the high-risk groups are the most benefitted from the fluoride programme.

## REFERENCES

1. Wei SHY, Yiu CKY. Evaluation of the use of topical fluoride gel. *Caries Res.* 1993; 27: 29-34.
2. Stookey GK, Beiswanger BB. Topical fluoride therapy. In: Harris NO, Christen AG (Eds): Primary Preventive Dentistry. 4<sup>th</sup> Edn. Appleton & Lange. Norwalk, Connecticut. 1999. Pp; 193-233.
3. Khamrco TY, Jazrawi KH. Caries – preventive effect of topical APF gel with three different frequencies of application in 9 – 11 years old school children in Ninevah. *Al-Rafidain Dent J.* 2001; 1(Sp Iss): 201-214.
4. Stookey GK. Caries prevention. *J Dent Educ.* 1998; 62: 803-811.
5. Van Rijkom HM, Truin GJ, Van't Hof MA. A meta – analysis of clinical studies on the caries – inhibiting effect of fluoride gel treatment. *Caries Res.* 1998; 32: 83-92.
6. Ripa LW. An evaluation of the use of professional (operator-applied) topical fluorides. *J Dent Res.* 1990; 69 (Sp Iss): 786-796.
7. Bawden JW. Changing patterns of fluoride intake. Workshop held at the University of North Carolina, Chapel Hill, April 23-25, 1991. *J Dent Res.* 1992; 71: 1214-1255.
8. Ripa LW. Office fluoride gel-tray treatments: current recommendations. *NY State Dent J.* 1992; 15: 47-50.
9. Cooper MD, Kracher CM. Topical fluorides. *RDH.* 1998: 28-32.
10. Averill HM, Averill JE, Ritz AG. A 2 – year comparison of three topical fluoride agents. *J Am Dent Assoc.* 1967; 74: 996-1001.
11. Szejda LF. Fluorides in community programs: a study of four years of various fluorides applied topically to the teeth of children in fluoridated communities. *J Public Health Dent.* 1972; 32: 25-33.

12. Downer MC, Holloway PJ, Davies TGJ. Clinical testing of a topical fluoride caries preventive program. *Br Dent J.* 1976; 141: 242-247.
13. Meskin LH. Caries diagnosis and risk assessment. *J Am Dent Assoc.* 1995; 126 (Sp Iss): 15-24.
14. WHO. Oral Health Surveys: Basic Methods. 4<sup>th</sup> Edn. World Health Organization, Geneva, Switzerland. 1997.
15. Schwarz E, Lo ECM, Wong MCM. Prevention of early childhood caries. Results of a fluoride toothpaste demonstration trial on Chinese preschool children after three years. *J Public Health Dent.* 1998; 58: 12-18.
16. Craig GG. Towards a rational approach to topical fluoride therapy at the mixed dentition stage. *Int Dent J.* 1981; 31: 121-124.
17. Houwink B, Backer Dirks O, Kwant GW. A nine – year study of topical application with stannous fluoride in identical twins and the caries experience five years after ending the applications. *Caries Res.* 1974; 8: 27-38.
18. Joyston-Bechal S, Kidd EAM. Histopathological appearance of artificially produced caries – like lesions of enamel treated with APF during lesion formation in vitro. *Caries Res.* 1980; 14: 45-49.
19. Hicks MJ, Flaitz CM, Silverstone LM. Fluoride uptake in vitro of sound enamel and caries like lesions of enamel from fluoride solutions of relatively low concentrations. *J Pedod.* 1986; 11: 47-61.
20. Wei SHY, Lau EWS, Hattab FN. Time dependence of enamel fluoride acquisition from APF gels. II. In vivo study. *Pediatr Dent.* 1988; 10: 173-177.
21. Grøn P. Chemistry of topical fluorides. *Caries Res.* 1977; 11 (suppl. 1): 172-204.
22. Crabb HSM. The porous outer enamel of unerupted human premolars. *Caries Res.* 1976; 10: 1-8.
23. Knutson JW. Sodium fluoride solutions: technic for application to the teeth. *J Am Dent Assoc.* 1948; 36: 37-39.
24. Englander HR, Sherrill LT, Miller BG, Carlos JP, Mellberg JR, Senning RS. Incremental rates of dental caries after repeated topical sodium fluoride application in children with lifelong consumption of fluoridated water. *J Am Dent Assoc.* 1971; 82: 354-358.
25. Mainwaring PJ, Naylor MN. A three- year clinical study to determine the separate and combined caries - inhibiting effects of sodium monofluorophosphate toothpaste and an acidulated phosphate – fluoride gel. *Caries Res.* 1978; 12: 202-212.
26. Englander HR, Keyes PH, Gestwicki M, Sultz HA. Clinical anticaries effect of repeated topical sodium fluoride application by mouthpieces. *J Am Dent Assoc.* 1967; 75: 638-644.
27. Ingraham RQ, Williams JE. An evaluation of the utility of application and cariostatic effectiveness of phosphate – fluoride in solutions and gel states. *J Tenn Dent Assoc.* 1970; 50: 5-12.
28. Horowitz HS, Doyle J. The effect on dental caries of topically applied acidulated phosphate – fluoride: results after three years. *J Am Dent Assoc.* 1971; 82: 359-365.
29. Øgaard B, Seppä L, Rølla G. Professional topical fluoride applications – clinical efficacy and mechanism of action. *Adv Dent Res.* 1994; 8: 190-201.