

THE ROLE OF FLUORIDE VARNISHES IN PREVENTING WHITE SPOT LESIONS IN FIXED ORTHODONTIC TREATMENT: A SYSTEMATIC REVIEW

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SUMMARY

Objective. This study examines the effect of fluoride varnish in early preventing enamel demineralization that occurs around the brackets in patients with fixed orthodontic treatment. It tries to shed light on three issues: the extent of varnish usefulness in preventing White Spot Lesions, under what conditions varnish is effective in its preventive role, and what are the factors contributing to the protection degree that fluoride varnish offers against White Spot Lesions.

Material and methods. The preventive role of fluoride varnish in the fixed orthodontic treatment is deeply investigated in this systematic scientific literature analysis. The search was conducted to identify all the studies that analyzed and reported results on varnish role. Medline via PubMed and ScienceDirect were the search engines used. Only controlled in vivo clinical studies, published in English language between 2006 and 2019 were considered in the research. From 149 identified articles, according to the inclusion criteria, only 7 clinical papers were deemed appropriate.

Results. Five of the seven selected articles examined the conventional fluoride varnish while only two evaluated the light-cured fluoride ones. In all these studies contradicting findings were reported. In particular, a study demonstrated that varnish utilization dued the 90-100% reduction of WSLs. A moderate contribution in the decrease of White Spot Lesions, approximately 40%, derived by varnish avail, was instead asserted in three otherwise articles. Finally, three papers reported a degree of varnish protection against White Spot Lesions not statistically significant when the patient is able to maintain a good standard of oral hygiene.

Conclusions. Fluoride varnishes could be a reasonable alternative to reduce the percentage of White Spot Lesions on the tooth surface around the orthodontic bracket, especially in noncompliant or patients considered to be high risk of enamel demineralization. However, Literature is agreeing to affirm that varnish exclusive use is not able to totally prevent the development of White Spot Lesions. In addition, the fews data available in literature does not allow to recommend which of the clinical protocols at present described (every 6 weeks, every 3 or 6 months, 1 single application) really help and empower fluoride varnishes in providing the greatest effect as possible.

Key words: white spot lesions, fluoride varnish, light-cured fluoride varnish, fixed orthodontic treatment.

Introduction

Enamel decalcification in the form of White Spot Lesion (WSL) is the first sign of dental caries; it usually appears as chalky white areas on tooth surface. In literature WSLs are described as frequently related to fixed orthodon-

tic treatment (1, 2). According to Mitchell (3), the incidence of WSLs adjacent to the brackets is 15-85% and their prevalence varies from 50% to 97% (4, 5). The lesions appear mainly in the labiogingival area of maxillary lateral incisors, mandibular canines and first premolars (4). While orthodontic patients have, in general, a propensity to develop dental caries, the risk of

WSLs development is increased and promoted by some conditions.

An initial condition reflects models and levels of patient oral hygiene. Dental crowding often causes difficulties in maintaining proper hygiene that if it is insufficient or not appropriate it would provide a favorable condition for the development of WSLs. The presence of orthodontic bracket, bonded to the enamel surface, represents one more condition for WSLs evolution. During the orthodontic treatment, near the bracket, sites of plaque retention can often appear; the bracket morphology is in fact able to increase the available surfaces for adhesion promoting bacterial retention and proliferation. Consequently, a third condition is related to the presence and level of plaque bacteria; they are easily removable but, at the same time, also capable to alter the oral environment causing both quantitative and qualitative changes (6).

Given the increasing concern about WSLs and the role of the above-mentioned conditions in their development, dealing with them remains an important matter to both scholars and practitioners.

From a practical point of view, clinician/orthodontist has a deep interest in knowing how to deal with WSLs because these enamel lesions can:

- quickly appear on the tooth surface, one month from the bracket placement (7);
- result hard or sometimes impossible to improve also after the debonding, and their complete resolution can rarely be achieved (8).

Theoretically, the scientific debate is focused on which factors may counter, keep under control, or contribute to the decrease of the WSLs level or to their complete restitutio ad integrum.

Topical fluorides are nowadays considered as the most specific chemical instrument able to play a protective positive role against the WSLs, resulting therapeutically very effective. They are commercially available in various typologies for the most diverse methods of application:

toothpaste or rinse (9), gel/mousse (10), solutions (11), and varnish (12-14). Yet, their application has shown a lot of problems.

The first one pertains the relationship between fluorides and patient oral hygiene. The effect of the fluoride forms depends to a large extent on patient hygiene and cooperation: somebody shows a greater dependency on patient hygiene and cooperation than others. Less than 15% of the orthodontic patients rinse daily with recommended fluorine solution (15).

The second problem pertains the effectiveness of fluoride forms. In studies comparing the level of effectiveness of various fluoride forms is shown how some fluoride forms are more effective than others. However, there is no agreement among scholars and practitioners on what fluoride form is most effective.

A third problem pertains the relationship between fluoride effectiveness and application methods. Various studies link the degree of fluoride effectiveness to the method of application. Some combinations of fluoride form with a specific application method are viewed to be more effective than other combinations. However, there is no agreement among scholars on which combination is the most effective. The lack of agreement reflects not only the multiplicity of combinations studies but also the diversity of published data (6).

Recently several studies have shown that the use of topical fluoride regresses the WSLs progression (16-18). So many Authors focused their studies on the protective role of varnish in orthodontic treatment. Fluoride varnish is distinguished from other topical formulations and is a preferred form for clinical application because:

- 1) it is safe and versatile;
- 2) its effect, unlike others, does not depend on patient's hygiene and compliance (7, 19);
- 3) it is effective, dissimilar to other topical fluorides, even in patients with a moderate and high-risk levels.

Precisely for the category of patient characterized by a moderate to high level of risk, the ADA recommends the use of fluoride varnish as the only professionally applied fluoride (20). However, the debate in literature remains unsettled and open-ended on the three following issues:

- 1) the relationship between the varnish effectiveness and the oral hygiene;
- 2) the therapeutic degree of varnish success;
- 3) the relationship between the varnish efficacy and the application method employed.

The aim of this systematic review of the scientific literature is to look on the studies conducted during the period between 2006 to 2019, to analyze the effectiveness of fluoride varnish, either in conventional or light-cured form, in preventing early enamel demineralization that occurs around the brackets in patients with fixed orthodontic treatment.

The systematic review of scientific literature conducted in the present study seeks an objective response to the following questions:

What do the results of studies show about the application and role of varnish in diminishing or eliminating WSLs?

Do their results bring something new to the debate about the role of varnish?

The aim is to identify what is currently the recognized role of varnishes in the field of prevention of WLSs in all patients undergoing fixed orthodontic multibrackets.

Materials and methods

The search in literature enclosed Medline via PubMed and ScienceDirect database for the purpose of find all studies, published between 2006 to 2019, examining the role of varnish in the orthodontic treatment. All the keywords used for getting the proper articles included the word “varnish”. The search was conducted in English and the obtained papers were in English as well. Finally, a total of 149 papers were retrieved. Based on the titles and abstracts, two researchers reviewed and compiled a list of potentially relevant clinical studies according the inclusion and exclusion criteria described in Table 1.

The papers resulting from search went through two screening selection process.

In the first one considered overall 149 studies, 89 of which were immediately excluded, after reading titles and abstracts, because of case reports, review papers, not related to use of topical fluoride or multibracket therapy, articles not in English, nonhuman studies.

In the second screening from the 60 full text remaining studies, 53 of them were excepted because of the study planning, they did not meet the all inclusion criteria above-mentioned, they did contain data for remineralization and not demineralization, or they measured only the controlling effect of fluoride varnish on active

Table 1 - The inclusion and exclusion criteria description

INCLUSION CRITERIA	EXCLUSION CRITERIA
Patients aged between 8 to 21 years old	Younger than 8 and older than 21 years old patients
Healthy subjects, neither drinkers nor smokers	Unhealthy or drinkers or smokers subjects
Multibrackets orthodontic treatment without dental extractions in act	No multibrackets orthodontic treatment in act or fixed one with dental extraction
Varnish applied throughout the orthodontic therapy according an established in advance prevention protocol	Orthodontic fixed therapy that not considered a varnish application protocol
Controlled <i>in vivo</i> clinical studies	Laboratory-based or <i>in vitro</i> studies

WSLs or their progression.

Finally, only 7 studies were selected as eligible in the research that employed a qualitative analysis of the findings examined. Although many studies were inclined to use a meta-analysis, those selected instead have engaged different methodologies.

Results

Table 2 contains the results of the 7 *in vivo* clinical studies chosen and of each describe how it looks at the effectiveness of varnish, either in conventional or light-cured form, in preventing WSLs.

Table 3 provides a summary of all the application methods clinically applied and described in Literature.

Discussion

The efficiency of varnishes in WSLs prevention

At the question: «How effective is varnish in diminishing and preventing WSLs development?», despite several studies were conducted about fluoride varnish effectiveness which reporting varying standard of clinical success, no

Table 2 - Results of the 7 *in vivo* clinical studies chosen.

The Study	Conclusions About Varnish Effectiveness
1. Vivaldi-Rodrigues, Demito, Bowman, Ramos 2006 (7)	About the extent of varnish effectiveness: Periodic application of fluoride varnish may be eventually accepted as a contemporary standard of care for limiting enamel scars. <i>Varnish application shows 44.3% less demineralization.</i>
2. Stecsen-Blicks, Renfors, Oscarson, Bergstrand, Twetman 2007 (6)	About the extent of varnish effectiveness: Regular topical fluoride <i>varnish application during treatment with fixed appliances may reduce the development of WSL adjacent to the bracket.</i> Application of fluoride varnish should be advocated as a routine measure in orthodontic practice.
3. Farhadian, Miresmaili, Behnam, Mehrabi 2008 (8)	About the extent of varnish effectiveness: Fluoride varnish can be beneficial as a preventive adjunct in reducing demineralization adjacent to brackets. <i>Varnish application shows 40% reduction of lesion depth.</i>
4. Mehta, Paramshivam, Chugh, Singh, Halkaj,Kumar 2015 (11)	About the relationship between varnish and hygiene: Clinpro XT light-curable fluoride <i>varnish may be a reasonable alternative</i> in the reduction of enamel demineralization around orthodontic brackets, <i>especially in noncompliant and high-risk patients.</i>
5. Kumar Jena, Pal Singh, Kumar Utreja 2015 (12)	About the extent of varnish effectiveness: The use of resin-modified glass ionomer cement varnish (ClinproXT varnish) during the comprehensive orthodontic treatment <i>had modest beneficial effect in the prevention of WSL</i>
6. Perrini, Lombardo,Arreghini, Medori, Siciliani 2016 (15)	About the relationship between varnish and hygiene: Periodic application of fluoride varnish can <i>offer some protection against WSL, but not a statistically significant degree if the patients have excellent oral hygiene.</i>
7. Kirchneck, Christl, Reicheneder, Proff 2016 (16)	About the relationship between varnish, hygiene, and application method: A one-time application of fluoride varnish at the start of orthodontic treatment <i>did not provide any additional preventive advantage over sufficient dental hygiene</i> with fluoride toothpaste with regard to formation of WSL and gingivitis in patients <i>with a low to moderate caries risk.</i>

Table 3 - A summary of the varnish application methods describes in literature.

The Study	Application Method	Conclusions about Application Method
1. Vivaldi-Rodrigues, Demito, Bowman, Ramos 2006 (7)	every 3 months during 1 year treatment	<i>Periodic application of fluoride varnish may be eventually accepted as a contemporary standard of care</i> for limiting enamel scars.
2. Stecsen-Blicks, Renfors, Oscarson, Bergstrand, Twetman 2007 (6)	every 6th week during the treatment	<i>Regular topical fluoride varnish application during treatment with fixed appliances may reduce the development of WSL</i> adjacent to the bracket.
3. Farhadian, Miresmaili, Behnam, Mehrabi 2008 (8)	one single application of high concentrated varnish after 1 week of bonding.	Fluoride varnish can be beneficial as a preventive adjunct in reducing demineralization adjacent to brackets. <i>Varnish application shows 40% reduction of lesion depth.</i>
4. Mehta, Paramshivam, Chugh, Singh, Halkaj, Kumar 2015 (11)	one single application after bonding	Clinpro XT light-curable fluoride varnish may be a reasonable alternative in the reduction of enamel demineralization around orthodontic brackets, <i>especially in noncompliant and high-risk patients.</i>
5. Kumar Jena, Pal Singh, Kumar Utreja 2015 (12)	one single application after bonding	The use of resin-modified glass ionomer cement varnish (ClinproXT varnish) during the comprehensive orthodontic treatment <i>had modest beneficial effect in the prevention of WSL.</i>
6. Perrini, Lombardo, Arreghini, Medori, Siciliani 2016 (15)	every 3 months during treatment every 6 months during treatment	<i>Periodic application of fluoride varnish can offer some protection against WSL, but not a statistically significant degree if the patients have excellent oral hygiene.</i>
7. Kirchneck, Christl, Reicheneder, Proff 2016 (16)	one-time application during treatment	<i>A one-time application</i> of fluoride varnish at the start of orthodontic treatment <i>did not provide any additional preventive advantage over sufficient dental hygiene</i> with fluoride toothpaste with regard to formation of WSL and gingivitis in patients with a low to moderate caries risk.

agreement is revealed in literature on the topic. The 7 selected studies show that varnish in vivo efficacy is extremely variable, thus it can outcome in a high, moderate, or low response (Table 2). Mehta et al. reported a high level (90%-100%) of fluoride varnish efficacy in orthodontic patients: no significant demineralized lesions appeared on the enamel around the brackets during the investigation period, except in 2-3 teeth at 90 days from the treatment beginning and, in 1 tooth after 120 (21). A moderate effectiveness of varnishes in enamel demineralizations prevention and in decreasing of WSLs manifestation are well described in three studies. According to Stecsen-Blicks et al. the WSLs incidence is ranging at 34%, Farhadian et al. described it at 40%, instead Vivaldi-Rodrigues et al. at 44% (12-14).

Stecsen-Blicks et al. noticed that in the orthodontic patient sample treated with varnishes the WSLs incidence was about one third respect to it is observed in the placebo group, specifically 7.4% vs. 25.7%. On the other side, Kumar Jena et al. reported a very low or insignificant level of varnish clinical effectiveness (22). Apparently, it does not help in providing a clear-cut answer, thus although all the seven studies selected focus on clarifying the issue of varnish effectiveness, the issue continues to remain open to further research works and experiments. Following the diversity in conclusions reached, this situation can only generate other questions. What may explain the disparity in issues with regard to varnish effectiveness as supported by

each study? Why the results by Authors are so different? Why some studies end up reporting high level of varnish effectiveness, whereas other studies report moderate or even modest levels of varnish effectiveness? Three are the hypotheses that could be formulated to give an objective explanation of this situation. The first one, is only attributable to the insufficient number of documents produced by the scientific literature on this argue. The need for a greater number of studies is essential to finally clarify the actual role of fluoride varnishes in WLSs prevention and treatment. The second hypothesis pertain the no repetibility of methods of varnishes analysys followed by the different studies. Conducting more studies, however, would not suffice if it will not use similar conditions of analysis and so thecnically comparable. Doing so would help compare study reports and make a better sense of them. So far, the studies described have not tried to replicate other studies and see what results they would get, they have instead explored varnish effectiveness though individual venues. The last hypothesis would concern the scarce scientific knowledge of the relationship between the varnish application, oral health conditions and other factors that influence the effectiveness of the varnish.

Given that the studies conducted during 2016-2018 period conclude that varnish effectiveness could be high, moderate, and low, this paper points to two issues that it considers to be important to and need to be addressed by the community of researchers studying varnish effectiveness.

One issue derives from the variation in results about varnish effectiveness among studies. In order to have valid results and findings, each study should be conducted in such a way to be comparable to other studies and replicable. In other words, each study should enable that other subsequent studies be conducted in similar conditions and be able to confirm or not the findings of a previous study.

The other issue reflects the findings about of the degree of varnish effectiveness. Given that so far studies have identified high, moderate, and low levels of varnish effectiveness, this situation may suggest that the studies conducted about varnish effectiveness instead of focusing on the degree of effectiveness should explore the condition and factors linked to and influencing the degree of varnish effect.

The relationship between varnish effectiveness and oral hygiene

Given the patient hygiene role and influence, at the question: “To what extent does varnish diminish or eliminate WSLs when patient displays patterns of hygiene ranging from low to medium to high?”. Although many scholars argue that fluoride varnish differs from other forms of topical fluoride because its effectiveness is independent of the patient’s oral hygiene level, some of the results reported in the 7 studies selected for this systematic review are so contradictory that two of them even seem to deny this argument, question the effectiveness of varnish during the orthodontic treatment (23, 24). Mehta et al. asserted that varnishes show a great ability in WSLs preventing, especially in non-compliant patient that are classified by inadequate requirements of oral hygiene as high-risk patients in caries developing. Perrini et al. (23), and Kirchneck et al. (24) observed that in those patients with excellent or otherwise sufficient oral hygiene, fluoride varnishes does not show a statistically significant preventing effect in WSLs development.

What do we make of such results? How do such results help clarify the issue of varnish effectiveness in the context of patient hygiene? It seems the results reported from the three above studies help to better specifying the “condi-

tions” upon which varnish can be expected to show effectiveness. Varnish application does not show any impact and becomes unnecessary when patient maintains a “good” oral hygiene, in that case varnish and WSLs appear at low level (22-24). Varnish application becomes useful when patient does not maintain oral hygiene and displays a risk level of WSLs development ranging from medium to high level. For higher-risk patients, varnish, chewing sticks or casein derivatives would be required (25). Do these results bring something new about varnish effectiveness in the context of patient hygiene? The above findings, if true and replicable by other studies, may put into question the widely accepted notion that varnish effectiveness does not depend on patient hygiene. Linking varnish effectiveness to the presence or absence of oral hygiene and to the degree of the risk for developing caries is a hypothesis that needs to be tested by further studies. So far, for ethical reasons, there are no studies where the control group does not follow the routine oral hygiene (24). Thus, while varnish may be effective to a statistically significant degree in patients with poor oral hygiene it does not totally prevent the formation of WSLs and it is impossible to have a direct confirmation of the extent of the protection generated by varnish against WSLs.

The correlation between clinical application protocols and varnishes efficacy

Does varnish effectiveness depend on the method of application? In what way the seven studies contribute to the open-ended debate about varnish effectiveness?

From Table 3 it is possible to take note of two elements. First of all, there is a wide diversity in the varnish application methods. The varnish effectiveness is analyzed related to three proce-

dures: 1) the number of application, i.e. how many times is varnish applied during the treatment, one single time or multiple times 2) the frequency of application, i.e. how much time elapses from one application to the other, is it measured in weeks or months, and 3) the level of dose concentration, i.e. whether it is high, medium, or low. The second element is the contradicting results studies report: the importance of application method to effectiveness of varnish in terms of number of applications, periodicity of application, and dose concentration arises from limitations that characterize varnish by itself. Shah et al. found that the duration of conventional varnish effect is only 45 days whereas light-cured varnish protection can last up to 120 days (26).

What do studies tell us in terms of number and periodicity of applications? How many times during the orthodontic treatment should one apply varnish? Is it enough a single application? Or, should there be 2 or more applications? Does the periodicity of varnish application matter to varnish effectiveness? If periodicity matters, how much time should lapse from one application to the other? Is there any specific frequency that makes varnish be most effective? If yes, which frequency is best for getting the maximum level of effectiveness out of varnish? The American Dental Association (ADA) suggests repeating varnish application at an interval of 3 months or 6 months, especially for moderate or high-risk patients (20). Cochrane review, however, suggests repeating varnish application every 6 weeks (27). Despite the fact that Cochrane review did not include studies with split-mouth design, its suggestion differs in a significant way from ADA's. Thus, looking at both, the number and frequency of varnish application, remains open to further studies.

The studies analyzed in this paper offer their suggestion in terms of number and frequency of varnish application, yet their results too are very heterogeneous.

In terms of the number of varnish application, four studies, Mehta et al. in 2015 (21), Farhadian et al. in 2008 (14), Kumar Jena et al. in 2015 (22), and Kirchneck et al. in 2016 (24), opt for one single varnish application. The three other studies, Vivaldi-Rodrigues in 2006 (13), Stecsen-Blicks in 2006 (12), and Perrini et al. in 2016 (23), decide on 2 or more varnish applications.

About the frequency of varnish application, Stecsen-Blicks in 2006 (12), apply a 6-week frequency; three other studies, Vivaldi-Rodrigues in 2006 (13), Farhadian in 2008 (14), and Perrini et al. in 2016 (23), choose a 3-month frequency; Mehta et al. in 2015 (21), suggest a 4-month frequency; Kirchneck et al. in 2016 (24) propose a 5-month frequency, and two studies, Kumar Jena et al. in 2015 (22), Perrini et al. in 2016 (23), decide for a 6-month frequency.

The heterogeneity in number and frequency of varnish application makes it almost impossible to gain a sense about the most optimal number and frequency of its better manner of utilization. While each study offers its own suggestion with regard to the number and frequency of varnish application, they vary how they reached into their conclusions. Perrini et al. compared the results of varnish application every 3 months versus every 6 months and found that frequency plays no role in determining varnish effectiveness. Kirchneck et al. applied a single dose of varnish and concluded that the number of applications, even when it is a single dose, plays no role on varnish effectiveness. Given the heterogeneity among studies in terms of the number and frequency of varnish applications they applied and examined in their clinical studies it is difficult to conclude by a clear-cut answer. To clarify this issue is needed not only further studies, but also studies that are similar in terms of the number and frequency of varnish applications.

The other set of question pertain the issue of concentration. Fluoride varnish is a high-con-

centrated form of topical fluoride, from 1000 to 22600 ppm. In 1996, Basdra et al. found that fluoride agents, that initially release a high dose of fluoride, would be more effective in the resistance increasing at enamel decalcifications (28). Already in 2008, Ogaard et al. explained the mechanism underlying this phenomenon: the high dose of fluoride is able to physically block the surface layer of enamel to the penetration of calcium ions towards subsurface/underlying layers (7). In 2009, Linton et al. reported instead that, in enamel remineralization a low dose of fluoride is more effective than a higher, thus putting into question the concept than only a high-concentrated varnish may be effective in WSLs decreasing (29).

Therefore, it is required to clarify whether varnish application can be effective when only used at high (1000 to 22600 ppm) or also at medium (500 ppm to 1000 ppm) and low (100 ppm to 500 ppm) level of concentration? And, on this issue, what results derive from the selected studies? Is the concentration level important for the effectiveness of the varnish? If it is important, what level of concentration makes the varnish role more effective?

The only study, of the seven analyzed in this review, which deals precisely with this problem is that of Farhadian et al. in 2008. It confirmed the argument made by previous studies that varnish effectiveness is higher when applied as a highly concentrated dose and it affirmed that one single application of LCFV (light cured fluoride varnish) provides 90-100% protection even after 3 months (21). However, further studies need to be conducted in order to confirm these assertions.

So, the main interest for both scholars and practitioners is to know how effective the varnish can be in controlling or eliminating WSLs, especially during or after fixed orthodontic treatment.

Although in literature there are studies that examine the clinical efficacy of the varnish, the

great diversity in the methodology according to which they were conducted, did not help in what was the intent of this systematic revision and, since they fail to provide a conclusive answer, they do not definitively resolve this problem which therefore continues to remain a matter of strong debate both from the clinical and scientific point of view. It was quite difficult to find at least two studies showing similarities in terms of design, sample, WSLs measuring instrument, varnish formulation, or other factors and conditions of interest that could be useful to establish the efficacy of fluoride varnish in the ambit of a multibrackets orthodontic treatment. Overall, the seven selected studies exposed to concerns related to:

- 1) the tools used to measure WSLs and the related factors,
- 2) the protocol followed by each study and
- 3) the dimension of the sample under examination.

The first issue that makes it difficult to compare and give credibility to their results pertain the diversity in measuring instruments and methods and their accuracy. While the most popular and well-accepted instruments used to measure WSLs are, digital intraoral photographs and DIAGNodent Pen (25) the studies analyzed in this paper use different instruments either alone or in combination.

Much more in detail, the analyzes were conducted through:

- Polarized Light Microscopy (Stecken-Blicks et al.) (Farhadian et al.);
- DIAGNodent pen (Kuma-Jena et al.) (Perrini et al);
- Direct visual inspection (ICDAS and GI) (Kumar-jena et al.) (Kirshneck et al.);
- Intraoral Photographs (Vivaldi-Rodrigues et al.).

There are also studies that have used a combination of measuring instruments. Three studies use a combination of instruments polarized light microscopy and digital photographs, diagnodent

pen and direct visual inspection, Clinical examination and CRT bacteria test (Farhadian et al. 2008; Kumar Jena et al. 2015; Kirchneck et al. 2016). The difference in the measuring instruments they used makes it difficult to compare and make sense of the results and their credibility.

The other problem with the credibility of their results reflects the issue of measuring instruments accuracy. The issue of measuring instrument underscoring or overscoring is a known and accepted problem (30, 31). DIAGNODENT tend to be very sensitive to stains, calculus and plaque (32) and are based on bacterial metabolites (33), thus, have the tendency to produce overscored results. This problem calls for cautious interpretation of the diagnodent readings because the statistically significant differences observed might not necessarily have clinical significance. Since the DIAGNODENT readings may be affected by stains, calculus and plaque (32) and are based on bacterial metabolites (33) the results obtained may not directly related to the problems perceived by patients or doctors. The studies analyzed in this paper reported photographs that tended to both underscored and overscored when compared to clinical photographs. 2 studies analyzed in this paper used DIAGNodent to measure WSLs. They report a level of WSLs statistically insignificant, thus concluding that varnish application does not contribute to protection against WSLs (Kumar Jena, Perrini).

The method of Direct Visual inspection (Kumar Jena) has its problems too. One regard the issue of calibration and re-calibration. The examiners will require calibration and recalibration throughout the experimental period. Since the treatment period may be quite long, in order to ensure consistency of measurements calibration and re-calibration is needed. The other problem pertains the issue of bias. The examiners may not be able to eliminate the risk of bias related to allocation (27).

The second issue in making sense of the results concerns the study design and their accompanying problems. Five of the seven papers analyzed in this paper use split-mouth design (13, 14, 21-23), whereas two use two or three parallel arm design (12, 24): both of the studies show the following critical issues. In split-mouth design the subjects act under own control, thus eliminating inter-subject variability and increase the power of the study compared to the other design. However, due to carry-across effects, it may lead to biased treatment effect estimates (22). Five studies demonstrated indeed, that while varnish application did not prevent the WSLs formation, it did anyway show a positive effect on them. This is due to carry-across effect that can be related with the under-estimated effect. Because both the experimental and the control teeth belong to the same patient, confounding factors such as sex, oral hygiene, cooperation, tooth structure, fluoride uptake from other sources, composition of saliva, and so on are avoided (12). In parallel arm one, the problem remains the opposite of split mouth design, as has been observed in two different studies. They reported a respectively positive effect from topical application of varnish; however, both do not have any additional effect if varnish is used in conditions of sufficient oral hygiene.

The last problem in making sense of the results reported by studies pertain the sample size and composition. As a general rule, the larger the sample, the more credible are the results. However, while studies on fluorides and topical varnishes abound, there is a distinct diversity in terms of sample and composition based on which the study is conducted, and the results are reported.

Some studies offer results based on sample of 200 to 300 people; other studies report results obtained from samples of 30 to 50 patients. The problem of sample size is heightened even more in meta-analysis review, where the conclusions are inferred by huge samples comprised of the

samples of the studies reviewed taken together as one sample. The meta-analysis reviews increase their “sample size” under the assumption that doing so would make it easier overcome the problem generated by the diversity of measuring methods and instruments, study designs, and factors examined. Yet, doing so does not always make conclusions more credible. The studies reviewed in this paper vary in their sample as well. They use small, medium, and large size samples to make their conclusions. Three studies used small-size, others two utilized medium-size and, three used large-size samples. The diversity in sample size makes it difficult to evaluate the validity and credibility of the results reported and the suggestions than can be daily made to professional practitioners (1 study Steczen Blicks has a big sample. 273 and all the other have samples below 90).

Conclusions

The conclusion of these notes is that while fluorid varnish continues to be seen as very effective factor in controlling or diminishing WSLs, the issues of the degree of varnish effectiveness, the role that patient hygiene plays in determining varnish effectiveness, and the role that combination of varnish application with various techniques and methods plays in increasing varnish effectiveness remains open to further experiments and studies. The seven studies analyzed in this paper could contribute by confirming or not previous studies' findings, but they are not definitely sufficient to settle any of the debated issue.

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