International Journal of Medical and Clinical Research
ISSN: 0976-5530 & E-ISSN: 0976-5549, Volume 4, Issue 2, 2013, pp.-263-268.
Available online at http://www.bioinfopublication.org/jouarchive.php?opt=&jouid=BPJ0000232

WHITE SPOTS ON TEETH OR BLACK MARKS ON TREATMENT RESULTS! A CONTEMPORARY REVIEW OF ENAMEL DEMINERALIZATION DURING FIXED ORTHODONTIC TREATMENT

SINGH R.A.*, BICHU Y.M. AND NARKHEDE S.P.
Dr D.Y. Patil Dental College and Hospital, Nerul, Navi Mumbai- 400706, MS, India.
*Corresponding Author: Email- dr.rakesh22@gmail.com

Received: June 28, 2013; Accepted: August 29, 2013

Abstract- The demineralization of enamel surfaces adjacent to orthodontic attachments is a disturbingly prevalent and clinically significant iatrogenic effect of multi bracket appliance therapy. The diagnosis, prevention and treatment of white spot lesions are crucial to prevent dental caries as well as to minimize tooth discoloration that can compromise the aesthetics of a smile. This article reviews contemporary relevant literature on enamel demineralization during orthodontic therapy with an emphasis on different modalities- both established and experimental, for its prevention and treatment.

Keywords- Enamel demineralization, orthodontic treatment, prevention, review, treatment

Citation: Singh R.A., Bichu Y.M. and Narkhede S.P. (2013) White Spots on Teeth or Black Marks on Treatment Results! A Contemporary Review of Enamel Demineralization during Fixed Orthodontic Treatment. International Journal of Medical and Clinical Research, ISSN: 0976-5530 & E-ISSN: 0976-5549, Volume 4, Issue 2, pp.-263-268.

Introduction

The demineralization of enamel surfaces adjacent to fixed orthodontic appliances is the most prevalent and significant iatrogenic effect associated with orthodontic therapy [1]. The prevalence and severity of decalcification in orthodontic patients has been reported to be greater than untreated controls; varying between 2 and 96% across studies [2]. This increased prevalence is attributable to the irregular surfaces of orthodontic attachments that create stagnation areas for plaque, render oral cleanliness difficult and predispose to an increased bacterial colonization. These events eventually culminate in the demineralization of enamel [3].

Since the translucency of enamel is directly related to it's degree of demineralization, initial enamel demineralization manifests clinically as a White Spot Lesion (WSL) [4] [Fig-1]. Such lesions have been clinically induced within a span of four weeks, the typical time period between two orthodontic appointments [5]. In the highly cariogenic environment adjacent to orthodontic appliances, these lesions can progress rapidly. If left untreated, they may eventually produce frank cavitations that may warrant restorative intervention. Although some of these WSLs might later remineralize and return to normal or a visually acceptable appearance after the completion of active orthodontic treatment, many of them persist, resulting in an aesthetically unacceptable result apart from being the forerunners of cavitation [6]. Thus the diagnosis, prevention & treatment of WSLs is crucial to prevent tooth decay as well as minimize tooth discoloration that can compromise the aesthetics of a smile.

Broad based management of WSLs includes methods for preventing demineralization as well as encouraging remineralization of existing lesions. The onus is on preventive measures due to difficulties involved in the treatment of established, multiple lesions [7]. This article reviews contemporary relevant literature regarding enamel demineralization during orthodontic treatment with an emphasis on different modalities- both verified and experimental, for its prevention and treatment.

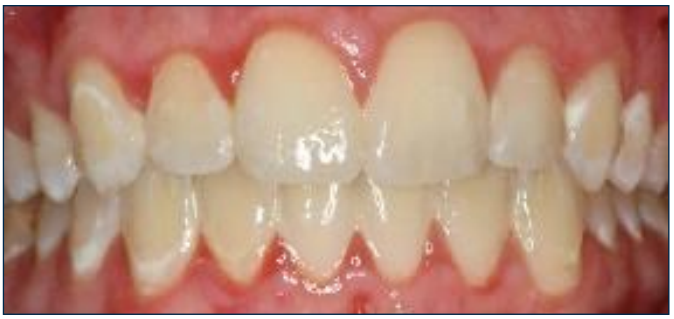

Fig. 1- White spot lesions following orthodontic treatment.

Etiopathogenesis of Decalcification

Enamel demineralization during orthodontic therapy is attributable to a multiplicity of factors. The co-existence of bacterial plaque, fermentable carbohydrates, a susceptible tooth surface and a sufficient period of time are considered to be necessary for a white spot lesion to develop [8]. Fixed appliances predispose to the accumulation of plaque around the attachments as well as between the attachment and the gingival margin [9]. They may also hinder the ability of tongue to cleanse food particles from the mouth and inhibit the movement of saliva and oral musculature [3]. Concomitant presence of fermentable carbohydrates accelerates the rate of plaque formation, maturation and facilitates a reduction in the plaque pH.

Such changes are conducive for the colonization of acidogenic and aciduric bacteria such as streptococcus mutans and lactobacilli. Significantly elevated plaque and salivary levels of these organisms have been reported in orthodontic patients [3,10,11].

The white spot lesion itself occurs through a series of repeated episodes of mineral loss, with mineral from the surface being lost into the plaque fluid and saliva; and mineral from the subsurface reconstituting the surface. This is not a continuous process, but an interrupted one as the dynamics of repair and destruction alter according to the oral environment [12]. Salivary parameters such as pH, flow rate and buffering capacity can influence the degree of mineral loss, its rate of progression and the likelihood of repair [8]. Assessment of these parameters is therefore recognized as an important consideration for the diagnosis and management of severe demineralization and acute caries [12].

Measures for Prevention and Treatment

Patient Education and Oral Hygiene Practices

Reduction in patient compliance of oral cleanliness is a common phenomenon with the progression of treatment [2]. Remotivation and patient education regarding the importance of diet and oral hygiene can be the most crucial factor in minimizing decalcification. Verbal praise of patient's oral hygiene compliance has been found to be an effective method of improving patient cooperation [13]. Professional oral plaque removal on a weekly basis has shown to prevent progression of incipient lesions; the approach however cost ineffective. Mechanical plaque control supplemented by chemical aids represents the frontline defence against decalcification during treatment.

- **Mechanical Plaque Control**

Tooth brushing is the most common form of mechanical plaque removal and there exists a plethora of commercially available manual and electronic tooth cleaning aids. Both of these have been found to be efficient for plaque removal. Williams [14] found little evidence to support the contention that any particular type or design of toothbrush is superior to another; pertinent factors being their proper usage and frequency of brushing. Tooth brushing twice daily should be supplemented with an interdental cleaning aid such as a single tufted brush for effective cleaning around fixed appliances. Patients must be informed that it takes longer to clean effectively around fixed appliances than usual [2].

- **Chemical Plaque Control**

Chlorhexidene has been found to be most effective anti-plaque agent due to its absorption onto the plaque pellicle that prolongs its presence and effect in the plaque [15]. Chlorhexidene can cause brown stains on the teeth, however, these are readily removable. Anti-microbial varnishes (Cervitec: 1% chlorhexidene and 1% thymol, Ivoclar Vivadent, Leichtenstein) have been used to inhibit demineralization, but have not been found superior to conventional fluoride varnishes [16].

Minimizing Plaque Retention by the Appliance

Selection of small brackets, careful bonding technique and proper removal of adhesive flash, judicious use of complex wire designs, auxiliaries, or elastic threads as well as periodic checking of cement lute under the bands help to reduce plaque accumulation by the appliance and consequent decalcification [2].

Administration of Fluoride

The scientific cornerstone for the use of fluoride in caries prevention emanates from its ability to be incorporated into the hydroxyapatite structure of enamel by replacement of hydroxy groups or re deposition of dissolved hydroxyapatite as fluorapatite or fluor hydroxyapatite, that are more resistant to dissolution by bacterial plaque generated organic acids [17]. Patients undergoing orthodontic treatment can be exposed to fluoride in a variety of ways. These will be reviewed as follows [7]:

- **Water Fluoridation and Other Community based Distribution Programmes**

It has been reported that during early years of water fluoridation, caries levels in fluoridated communities were approximately 50% lesser than non-fluoridated ones [18]. A study demonstrated a 30-50% reduction in the caries increment of children within 2 to 3 years of initial introduction of fluoride into the water supply [19]. This significant reduction in caries prevalence has been attributed to the continuous exposure of dentition to fluoride in saliva and plaque fluid. Other forms of community distribution like salt and milk fluoridation have achieved indifferent success due to potential difficulties in their manufacture and supply and limitations in their intake.

- **Fluoridated Toothpastes, Mouth-rinses and Gels**

Fluoridated dentrifices and mouth rinses constitute the most common form of fluoride delivery for the orthodontic patient. Geiger, et al demonstrated significant reduction in decalcification by the consistent use of 0.05% sodium fluoride rinse during orthodontic treatment [20]. It has been recommended that orthodontic patients should brush twice daily with a dentrifice containing 5000 ppm of sodium fluoride which was said to provide greater protection than the use of dentrifice containing 1000 ppm of fluoride along with a mouth-rinse containing 500 ppm of sodium fluoride [21]. A systematic review evaluating fluorides for the prevention of WSL, cited that daily use of sodium fluoride rinse can reduce the severity of demineralization adjacent to orthodontic appliances [22]. Although the use of fluoride rinses and gels has been shown to reduce enamel decalcification during orthodontic therapy, the dependence of these programs on patient compliance has been shown to reduce their effectiveness.

- **Fluoridated Cements and Orthodontic Bonding Agents**

Glass ionomer cements may provide several advantages such as chemical retention that eliminates the need for etching of enamel with phosphoric acid, compliance free fluoride release for several months and the possible development of modified, less cariogenic flora [23]. However, significantly reduced tensile and shear bond strengths as compared to composite resins, have limited their use in clinical practice [24,25]. Resin modified glass ionomer cements (RMGIC) were introduced with the dual objective of fluoride release and clinically acceptable bond strength. Their clinical handling properties are however less than ideal, deterring many practitioners from their use [26].

- **Enamel Sealants**

Enamel sealants were introduced in orthodontics with the aim of compliance free enamel protection and to allow the orthodontist to benefit from proven bond strength of traditional composite resins. Resin sealants, both chemical and light cured ones have been used to protect the enamel surface. Significant reduction in enamel demineralization using highly filled, light-cured fluoride sealant (Pro

Seal, Reliance Orthodontic Products, Itasca) has been reported in-vitro [26-28]. An in-vivo pilot study on Ultraseal XT plus (Ultradent products, South Jordan)- a highly filled (58%) clear sealant, reduced the number of white spot lesions by 3.8 times as compared to the untreated teeth [29].

Placement of sealant in vivo is very technique sensitive. Further, sealants are susceptible to oxygen inhibition while curing, resulting in incomplete polymerization. This can produce breaks in the continuity of the sealant layer and predispose the area to the development of decalcification. Mechanical and chemical wear of the sealant in-vivo is another point of clinical consideration [26,30].

- **Fluoride Varnishes**

In vitro studies on fluoride varnishes have reported significantly reduced enamel demineralization (35 to 50%) in treated teeth when subjected to artificial caries challenge [30,31]. Clinical evaluations have also affirmed these results [32,33]. The frequency of application needed to make a varnish effective in controlling white spots is an important clinical issue. A systematic review of fluoride varnishes concluded that Duraphat (DPT) and Fluor Protector (FP) should be applied at intervals of 3 to 6 months, particularly in high risk groups [34]. Some have recommended repeated applications of varnish throughout treatment, even at each appointment for the high-risk patient [35].

FP has not been tested clinically as extensively as DPT, but has demonstrated superior results in vitro [35]. Juhlin [36] compared DPT and FP and found that the demineralization depths in FP group were significantly lesser than the DPT group. Being a silane lacquer, FP has a very low viscosity and good wetting action. Further, FP forms a thin, transparent film on hardening where as DPT sets as a yellow brown coating on the tooth. This provides FP a major esthetic advantage over DPT [34]. No serious side effects have been reported with the use of varnishes. However, fluoride varnishes should not be applied to bleeding gingival tissues due to the risk of contact allergy that can result from the colophonium base present in DPT and polyurethane base of FP [34].

- **Fluoridated Elastomers and Ligature Ties**

Fluorides were incorporated in elastomeric modules for providing a continuous delivery of fluoride to the susceptible area adjacent to orthodontic brackets. Banks, et al reported a 49% reduction in the demineralization score, per tooth, in all except enamel occlusal zones with the use of such elastomers [37]. Others however have questioned their utility due to compromised force delivery and inconsistent fluoride release [38,39]. These studies indicate an initial burst of fluoride release in first 24-48 hrs. followed by an almost complete leach out in two weeks. The advent of self ligation brackets has further limited the utility of elastic ties.

Use of Casein Phosphopeptide- Amorphous Calcium Phosphate (Recaldent™)

Apart from fluorides, recently Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP: Recaldent™) has been reported to have topical anticariogenic effects. Reynolds proposed that CPP-ACP substantially increases the levels of calcium phosphate in plaque that decreases enamel demineralization and enhances remineralization [40]. In the presence of acid, CPP breaks down to release amorphous calcium phosphate (ACP) particles that buffer plaque pH and dissociate into calcium and phosphate ions which inhibit enamel demineralization [41]. An in vitro study using Topacal C-5 (a CPP-ACP preparation) demonstrated a partial reduction in demineralization in treated teeth as opposed to untreated specimens [42]. Sudjalim, et al investigated the effects of Sodium fluoride and CPP-ACP on enamel demineralization adjacent to orthodontic appliances in vitro using quantitative light fluorescence and found that the use of Sodium fluoride, CPP-ACP as well as their combination brought about a significant reduction in enamel demineralization [7].

CPP appears to have an inhibitory effect on the adherence of cariogenic streptococci. Use of CPP was shown to significantly reduce the adherence of streptococcus sabrinus and mutans in vitro [43]. Studies performed on interaction, equivalence and potential synergism of CPP-ACP and fluoride suggest that 0.5 to 1.0% w/v of CPP-ACP is equivalent to 500 ppm of fluoride in reducing caries activity [44]. Combination of CPP-ACP and fluoride forms amorphous calcium fluoride phosphate (ACFP) that localizes calcium, phosphate and fluoride ions on the tooth surface and results in an additive anticariogenic effect. CPP-ACP being relatively inert does not result in enamel fluorosis, as fluoride can. Thus the use of CPP-ACP alone or in combination with fluoride may reduce the amount of fluoride needed to inhibit demineralization with consequently lesser possibility of fluorosis [40,41]. CPP-ACP has also been used and tested as part of several restorative and bonding materials [45,46].

CPP-ACP is currently marketed under the trade name Recaldent™ (Recaldent Pty Ltd., Melbourne, Australia). It is manufactured and marketed by GC Corporation, as GC tooth mousse (CPP-ACP only) and GC tooth mousse plus (CPP-ACP with 0.2% W/W of Sodium fluoride- 900 ppm). Other products containing CPP-ACP are Recaldent Pellets, Recaldent Kids and Recaldent Mints. Being a milk-casein derivative; its use is contraindicated in patients with milk protein allergy [47]. Also, the mousse contains hydroxybenzoate as a preservative and its use in patients with an allergy of this preservative is contraindicated [47]. The facts that CPP-ACP is highly soluble, does not have adverse effects on taste and rapidly hydrolyses to form apatite under oral conditions make it a potential candidate for enamel remineralization therapy.

Use of Calcium Sodium Phosphosilicate Products (NovaMin®)

Calcium sodium phosphosilicate is a bio-active glass (BAC) in the class of highly biocompatible materials that were originally developed for bone regeneration. Bioactive glass (Bioglass)® first discovered by Hench in 1969, is a multi-component inorganic compound made of elements (silicon, calcium, sodium and phosphorous) naturally found in the body. Novamin®, a trade name for bioactive glass, is manufactured by Novamin Technologies Inc. (Alachua, FL). It was proposed that these materials are reactive when exposed to body fluids and deposit hydroxy carbonate apatite (HCA), a mineral that is chemically similar to the minerals in enamel and dentin [48]. When incorporated into a dentrifice, a combination of residual NovaMin particles and the HCA layer that forms from its particles is expected to physically occlude dentinal tubules. This formed the basis of the use of calcium sodium phosphosilicate for the reduction of dentinal hypersensitivity. Stoor, et al demonstrated that bioactive glass appears to possess a broad antimicrobial effect on micro-organisms of both supra and sub-gingival plaque [49]. Allan, et al also affirmed a reduction in the viability of streptococcus sanguis, streptococcus mutans and actinomyces viscous with NovaMin and attributed this to the alkaline nature of its surface reactions. They proposed that this mechanism may reduce bacterial colonization in vivo [50]. A study by Alauddin [51] demonstrated that a combination

of NovaMin and fluoride produced significantly greater degree of remineralization of subsurface carious lesions in human enamel than the use of a fluoridated dentrifice alone and concluded that the incorporation of NovaMin into fluoridated dentrifices could arrest tooth decay process earlier than currently available fluoridated dentrifices.

NovaMin is not available as an over the counter product by itself but is a component of several oral health-care formulations worldwide such as SootheRx™ (3m/Omnii) and Oravive™ (Oravive Co.) in the US; Nanosensitive (Miradent products by Hager and Werken) and SensiShield™ (PeriProduct, UK) in Europe and SHY-NM™ (Group Pharmaceuticals, India) and Vantej (Dr. Reddy's Laboratories, India) in Asia among others.

Performing Microabrasion and Vital Tooth Bleaching

Croll and co-workers described microabrasion as the application of acidic and abrasive compounds to the enamel surface and this technique has been widely used for removal of superficial non-carious enamel [52]. When enamel remineralizes; calcium, fluoride and phosphate ions precipitate on the sound enamel at the margins of the subsurface, demineralized areas, resulting in a highly dense compaction of minerals that appears whiter than natural enamel. Such whitened enamel that is very apparent can be a potential candidate for microabrasion [53]. Use of 18% hydrochloric acid and pumice constitutes the standard microabrasion protocol [54]. Usually 5 to 10 applications of the compounds suffice with each application of around 1 minute and usually followed by a four minute application of 2% sodium fluoride [53]. A prospective clinical trial demonstrated 61 to 92% reduction in white spot lesions and recommended enamel microabrasion as an effective approach for cosmetic improvement of long standing post-orthodontic demineralized lesions [55]. If the microabrasion is unable to attain optimal esthetics and whitened enamel still persists, then vital tooth bleaching can be considered. Mild whitening can be attempted to be camouflaged by conventional tray based tooth whitening systems used overnight or with hydrogen peroxide-impregnated polyethylene strips. If a two to four week bleaching regime is ineffective then microabrasion followed by peroxide bleaching is recommended [53].

Use of Argon Laser for Enamel Surface Attenuation

Recent studies focusing on the use of argon laser for preventing enamel demineralization suggest that laser treatment may alter the crystalline structure of the enamel [56]. A prospective clinical study proposes that enamel exposure to argon laser results in the creation of micro spaces that stabilize ions during an acid attack and prevent them from being lost from the enamel. Available calcium, phosphate and fluoride ions may then precipitate into these micro spaces and increase enamel resistance to demineralization [57]. Further studies- both in vitro and in vivo, are required to establish the optimal fluence (energy density) for simultaneous curing of the orthodontic bonding agents and prevention of enamel decalcification using argon laser [56,57].

Utilization of Ozone Therapy

Ozone (O_3) is considered to be one of the most powerful natural oxidants and currently finds application in the management of conditions such as ulcerative colitis, chronic bacterial diarrhoea and cancer amongst others [58]. Ozone acts as a disinfectant and possesses a unique feature of decomposing into a non-toxic and environmentally safe molecule (oxygen). Baysan and Lynch found a significant reduction in the total micro-organism count in root caries treated with ozone as compared to untreated controls [59]. Subsequent studies on ozone have demonstrated specific reduction in caries causing organisms such as streptococcus mutans and streptococcus sobrinus [58,59]. The HealOzone system (KaVo Dental) consists of a corona discharge type generator and delivery system for principally intra oral application. This device is intended to kill bacteria with a flow of ozone delivered to the tooth surface for 10 to 40 seconds depending on the depth of the lesion [58,60]. Ozone treatment should be followed by the use of remineralizing solutions or fluoride rinses. Periodic reapplication has also been suggested [60]. Kronenberg, et al in possibly the first clinical evaluation of ozone for the prevention and treatment of white spot lesions found that the effect of Cervitec and Fluor Protector therapy was superior to ozone in the prevention of development of white spots [61].

A review of medical use of ozone recommends its application when conventional treatment modalities are ineffective but cautions against its use in too high a concentration. Recent reviews of ozone treatment of caries suggest that it may be efficacious, but further clinical evidence is needed to establish usefulness. Further research is required to investigate the efficacy and cost benefit of this treatment modality [58-61].

Conclusion

Prevention is better than cure' goes the adage and the significance of prevention cannot be overemphasized with regards to white spot development during multi-bracket appliance therapy that is associated with a disturbingly high prevalence of enamel decalcification. Proper bonding technique with removal of adhesive flash, judicious use of complex wire designs and elastomeric products marks the first line of defence for minimizing iatrogenic demineralization resulting from creation of plaque retentive areas. Systemic fluoride delivery systems such as community water fluoridation ensure a daily fluoride exposure and build up of fluoride reservoir; however community water fluoridation may not be accessible to everyone. Patient education and remotivation regarding the importance of diet and oral hygiene practices throughout the treatment could be the most important factor in minimizing enamel demineralization. Verbally praising the patient on compliance of instructions can help to effectively sustain patient cooperation. Periodic professional oral prophylaxis and the daily use of fluoridated dentrifices and mouth rinses would constitute the next logical step in the prevention of decalcification. The choice of additional topical delivery systems would depend upon individual patient assessment and the clinician's perspective. Fluoridated cements, adhesives, sealants and varnishes allow the orthodontist to ensure a totally compliance free, constant exposure to fluoride. These products have demonstrated significant success in preventing enamel decalcification both in vitro and in vivo and may be recommended in the non-compliant patient. The utility of these delivery systems however is questionable in situations after decalcification has already occurred such as post-treatment lesions. CPP-ACP and calcium sodium phosphosilicate present the clinician with non fluoride topical delivery systems and may be indicated as a supplement to fluoride during treatment or as an alternative in situations where the chances of fluorosis are deemed to be significant. They may also be recommended in cases where white spot lesions have already occurred such as post-treatment lesions. Microabrasion and vital tooth bleaching may help in the treatment and camouflage of long standing post orthodontic white spots. Restorative intervention and laminates may be the only option where esthetics and form have been severely compromised.

Modalities such as argon laser and ozone are in various stages of experimental refinements and may be expected to provide alternatives when traditional treatment modalities fail. A schematic illustration of management strategies for prevention and treatment of enamel demineralization during orthodontic treatment is provided [Fig-2].

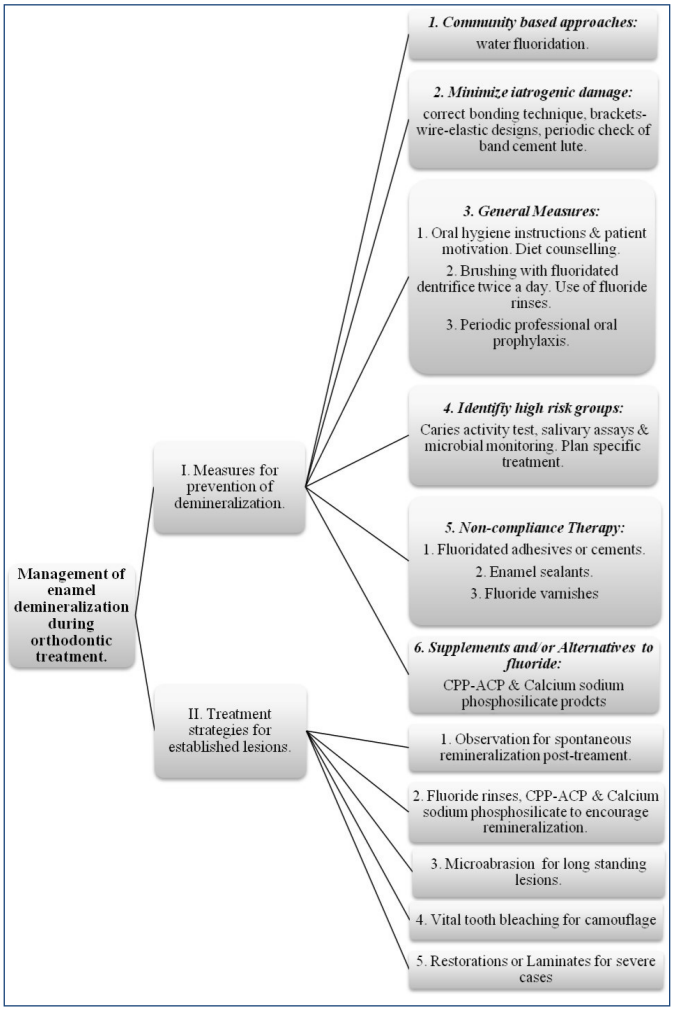

Fig. 2- Management strategies for prevention and treatment of enamel demineralization during orthodontic treatment.

References

[1] Ogaard B., Bishara S., Duschner H. (2004) *Risk Management in Orthodontics: Experts' Guide to Malpractice*, Quintessence, 19-46.

[2] Mitchell L. (1992) *Br. J. Orthod.*, 19, 199-205.

[3] Rosenbloom R.G., Tinanoff N. (1991) *Am. J. Orthod. Dentofacial Orthop.*, 100, 35-37.

[4] Bishara S., Ostby A.W. (2008) *Semin. Orthod.,* 14, 174-182.

[5] Ogaard B., Rolla G., Arends J. (1988) *Am. J. Orthod. Dentofacial Orthop.*, 94, 68-73.

[6] Sudjalim T.R., Woods M.J., Manton D.J., Reynolds E.C. (2007) *Am. J. Orthod. Dentofacial. Orthop*., 131(705), e1-e9.

[7] Sudjalim T.R., Woods M.J., Manton D.J. (2006) *Aust. Dent. J*., 51(4), 284-289.

[8] Murray J.J. (1989) *The Prevention of Dental Disease*, Oxford University Press.

[9] Gwinnett A.J., Ceen R.F. (1979) *Am. J. Orthod*., 75(6), 667-77.

[10] Scheie A.A., Arneberg P., Krogstad O. (1984) *Scand. J. Dent. Res*., 92, 211-217.

[11] Lundstrom F., Krasse B. (1987) *Eur. J. Orthod*., 9(2), 109-116.

[12] Chang H.S., Walsh L.J., Freer T.J. (1997) *Aust. Dent. J*., 42(5), 322-327.

[13] Zimmer B.W., Rottwinkel Y. (2004) *Am. J. Orthod. Dentofacial. Orthop*., 126, 318-324.

[14] Williams P., Fenwick A., Schou L., Adams W. (1987) *Eur. J. Orthod*., 9, 295-304.

[15] Hogg S.D. (1990) *Dental Update*., 17, 330-333.

[16] Øgaard B., Larsson E., Henriksson T., Birkhed D., Bishara S.E. (2001) *American Journal of Orthodontics and Dentofacial Orthopedics*, 120(1), 28-35.

[17] ten Cate J.M. (1999) *Acta Odontol. Scand*., 57, 325-329.

[18] Forss H. (1999) *Acta Odontol. Scand*., 57, 348-351.

[19] Riordan P.J. (1999) *Community Dent. Oral Epidemiol*., 27, 72-83.

[20] Geiger A.M., Gorelick L., Gwinnett A.J., Griswold P.G. (1988) *Am. J. Orthod. Dentofacial Orthop*., 93(1), 29-37.

[21] Alexander S.A., Ripa L.W. (2000) *Angle Orthod*., 70, 424-30.

[22] Derks A., Katsaros C., Frencken J.E., van't Hof M.A., Kuijpers-Jagtman A.M. (2004) *Caries Res*., 38, 413-20.

[23] Matalon S., Slutzky H., Weiss E.I. (2005) *Am. J. Orthod. Dentofacial Orthop*., 127, 56-63.

[24] Fox N.A., McCabe J.F., Gordon P.H. (1990) *Br. J. Orthod.*, 18, 125-130.

[25] Voss A., Hickel F., Holkner S. (1993) *Angle Orthod*., 63, 149-153.

[26] Buren J.L., Staley R.N., Wefel J. and Qian F. (2008) *Am. J. Orthod. Dentofacial Orthop.*, 133, S88-94.

[27] Frazier M.C., Southard T.E., Doster P.M. (1996) *Am. J. Orthod. Dentofacial Orthop*., 110(5), 459-65.

[28] Hu W., Featherstone J.D.B. (2005) *Am. J. Orthod. Dentofacial Orthop*., 128, 592-600.

[29] Benham A.W., Campbell P.M., Buschang P.H. (2009) *Angle Orthod*., 79, 337-344.

[30] Todd M.A., Staley R.N., Kanellis M.J., Donly K.J., Wefel J.S. (1999) *Am. J. Orthod. Dentofacial Orthop*., 116, 159-167.

[31] Demito C.F., Vivaldi-Rodrigues G., Ramos A.L., Bowman S.J. (2004) *Orthod. Craniofacial Res*., 7, 205-210.

[32] Vivaldi Rodrigues G., Demito C.F., Bowman S.J., Ramos A.L. (2006) *World J. Orthod*., 7(2), 138-144.

[33] Farhadian N., Miresmaeili A., Eslami B., Mehrabi S. (2008) *Am. J. Orthod. Dentofacial Orthop*., 133, S95-S98.

[34] Petersson L.G. (1993) *Caries Res*., 27(1), 35-42.

[35] Staley R.N. (2008) *Semin. Orthod*., 14,194-199.

[36] Juhlin T.L. (2004) *The Effect of Two Fluoride Varnishes Duraphat and Fluor Protector on the Inhibition of Enamel Demineralization Adjacent to Orthodontic Brackets*, Doctoral dissertation, University of Iowa.

[37] Banks P.A., Chadwick S.M., Asher-McDade C., Wright J.L. (2000) *Eur. J. Orthod*., 22, 401-407.

[38]Wiltshire W.A. (1999) *Am. J. Orthod. Dentofacial Orthop*., 115, 288-292.

[39]Doherty U.B., Benson P.E., Higham S.M. (2002) *Eur. J. Orthod*., 24, 371-378.

[40]Reynolds E.C., Black C.L. (1987) *Caries Res*., 21(5), 445-551.

[41]Reynolds E.C. (1997) *J. Dent. Res*., 76, 1587-1595.

[42]Nasab N.K., Kajan Z.D., Balalaie A. (2007) *Aust. Orthod. J*., 23, 46-49.

[43]Schupbach P., Neeser J.R., Golliard M., Rouvet M., Guggenheim B. (1996) *J. Dent. Res*., 75(10), 1779-1788.

[44]Reynolds E.C. (1987) *J. Dent. Res*., 66(6), 1120-1127.

[45]Mazzaoui S.A., Burrow M.F., Tyas M.J., Dashper S.G., Eakins D., Reynolds E.C. (2003) *J. Dent. Res*., 82(11), 914-918.

[46]Dunn W. (2007) *Am. J. Orthod. Dentofac. Orthop*., 131(2), 243-247.

[47]Tung M.S., Eichmiller F.C. (1999) *J. Clin. Dent*., 10(1), 1-6.

[48]Andersson O.H., Kangasneimi I. (1991) *J. Biomed. Mater. Res*., 25, 1019-1030.

[49]Stoor P., Soderling E., Salonen J.I. (1998) *Acta Odont. Scand*., 56(3), 161-165.

[50]Allan I., Newman H., Wilson M. (2001) *Biomaterials*, 22(12), 1683-1687.

[51]Alauddin S.S. (2004) *In vitro remineralization of human enamel with bioactive glass containing dentifrice using confocal microscopy and nanoindentation analysis for early caries defense* Doctoral dissertation, University of Florida.

[52]Croll T.P., Bullock G.A. (1994) *J. Clin. Orthod*., 28, 365-370.

[53]Donly K.J., Sasa I.S. (2008) *Semin. Orthod*., 14, 220-225.

[54]Welbury R.R., Carter N.E. (1993) *Br. J. Orthod*., 20, 181-185.

[55]Murphy T.C., Willmott D.R., Rodd H.D. (2007) *Am. J. Orthod. Dentofac. Orthop*., 131, 27-33.

[56]Anderson A.M., Kao E., Gladwin M., Benli O., Ngan P. (2002) *Am. J. Orthod. Dentofac. Orthop*., 122, 251-259.

[57]Elaut J., Wehrbein H. (2004) *Eur. J. Orthod*., 26, 553-560.

[58]Baysan A. (2007) *The Management of Caries*, Quintessence, 61-65.

[59]Baysan A., Lynch E. (2006) *Prim. Dent.* Care, 13, 37-40.

[60]Thopmson V.P., Kaim J.M. (2005) *Dent. Clin. N. Am*., 49, 905-921.

[61]Kronenberg O., Lussi A., Ruf S. (2009) *Angle Orthod*., 79, 64-69.