Anti-gingivitis effect of a dentifrice containing bioactive glass particulate: A clinical and microbiological study

Eshita Dasharathbhai Patel, Sharmila Verma, Raghu T. N.

Abstract

Background: Microbiological tests along with clinical parameters provide a good support to assess the efficacy of oral hygiene regimen. Aims and Objectives: To compare the anti-gingivitis and anti-plaque effects of a dentifrice containing bioactive glass with a positive control triclosan and fluoride and negative control i.e., dentifrice with fluoride in a 6 weeks clinical study. Methods: The study sample consists of one hundred and fifty subjects with an age of 19-33 years. Plaque Index, Gingival Index, Calculus Index and saliva samples for Porphyromonas gingivalis (P. gingivalis) count were taken at baseline and after six weeks. All subjects received a supragingival prophylaxis and were asked to brush with the provided toothpaste for six weeks. Polymerase Chain Reaction was carried out for P. gingivalis quantification. Results: Changes in plaque index, gingival index and calculus index was noticed in all the three groups. Paste B showed greater anti-gingivitis effect compared to Paste A and Paste C when clinically evaluated with indices at 6 weeks from baseline. Reduction of P. gingivalis was statistically significant in Paste B (p<0.001), Paste C (p<0.001) and paste A (p<0.001) at 6 weeks compared to baseline. Conclusion: This study demonstrated that a dentifrice containing triclosan and fluoride significantly improves oral health by a reduction in plaque, gingivitis and calculus along with reduction in P. gingivalis over the 6 weeks.

Keywords: Plaque Index; Gingival Index; Calculus Index; P. gingivalis

Introduction

Dental plaque is the main etiologic factor of periodontal disease.12 Plaque-induced gingivitis is the most common form of the periodontal diseases, affecting a significant portion of the population in susceptible individuals.1-4 It is believed that the best approach to manage periodontal disease is prevention followed by early detection and treatment.5 Owing to the established relationship between bacteria, plaque and gingivitis; a major focus in the treatment is placed on the chemotherapeutic approach.6 Most individuals are unable to consistently maintain adequate levels of plaque control using routine mechanical methods alone, hence the incorporation of antimicrobials with anti-gingivitis activities as adjuncts to patient’s daily oral hygiene regimen is taken into consideration.7 Presently various dentifrices containing chemical agents are known for the anti-gingivitis effects but little information is available about anti-gingivitis effect of dentifrice containing bioactive glass.8 It was the first bioactive glass, invented by Dr. L. Hench in 1969 demonstrating the initial evidence of a direct bond between the product and bone.8,9 While the exact mechanisms of the anti-microbial activity have not yet been fully established, it is likely that the high rate of ionic release and local changes in oral pH seem to play a major role. The rapidity of a series of surface reactions results in the formation of a hydroxy-carbonate apatite layer which develops within hours of implantation in vivo. Bioactive glasses have been used in bone and tissue regeneration for over 15 years.11 Bioactive glass is effective as an adjunct to conventional surgery in treatment of intrabony defects.12 Recently, anti-microbial properties inherent in these materials have been described.13-15 One of these compositions has recently been formulated into a dentifrice and has demonstrated strong anti-microbial behaviour in-vitro.16 A study carried out by Eberhard et al showed that the topical application of 45S5 bioactive glass in humans with experimental gingivitis attenuated the clinical signs of inflammation.17 Rectenwald JE et al observed that peritoneal cavity of a mice produced instant anti-inflammatory response by early induction of IL-6 when exposed to Bioglass9 and thus support the fact that it could be used as an anti-gingivitis ingredient.18 Thus by considering the advantages of bioactive glass particulate in periodontal therapy and its anti-inflammatory effects, this clinical study was carried out to evaluate the ‘antigingivitis effect of dentifrice containing bioactive glass particulate’ in patients with gingivitis over 6 weeks period following a professional oral hygiene session.

Materials and Method

A total of 150 subjects comprising of both the genders diagnosed as suffering from chronic gingivitis were considered for this randomized double blinded controlled clinical study. The study protocol was approved by the Institutional Research Cell Committee. Sample size calculations were based on detecting a difference of 0.5 in plaque score between the test group and the control group using a significance level of 5% with a 90% power.

Inclusion criteria includes patients should be above 18 years with a minimum of 20 scorable teeth, moderate gingivitis with pocket depth less than 4mm without any systemic disease. Exclusion criteria included patients who received antibiotics or anti-inflammatory therapy within 2 weeks days of the baseline examination or were on long-term antibiotic or anti-inflammatory therapy. Teeth that are grossly carious, fully crowned, extensively restored, orthodontically banded and with periodontal pockets in excess of 4mm were excluded. Abutments and third molars were not included. Pregnant or lactating women were also excluded.
A Performa was prepared for the study. A signed consent was taken from all subjects. Clinical examination was carried out under standard conditions of light, using mirror and graduated UNC-15 Periodontal probe. A single examiner performed all clinical measurements for the study. Complete medical and dental history was reviewed. Examination of oral mucosa, teeth and periodontium was performed. Patients were asked not to perform any oral hygiene aids (including chewing gum) for 8 hours prior to the baseline. Saliva samples were collected and then sent to the Research Institute for P. Gingivalis quantification using Polymerase Chain Reaction. Assessments for Plaque index (Silness and Loe 1964), gingival index (Loe and Silness 1963), calculus index –simplified (Green and Vermilion 1964) and P. Gingivalis quantification were carried out for all subjects.

After the data was collected, subjects received supragingival prophylaxis and polishing to remove plaque, calculus and extrinsic stains. Patients were instructed for proper oral hygiene and were given any one of the three dentifrice using lottery method.

Paste A (Negative Control): A commercially available dentifrice with 1,100 PPM fluoride (NaF)
Paste B (Test Group): A dentifrice formulation with 5.0 wt% NovalMin® plus 1,000 PPM fluoride (MFP)
Paste C (Positive Control): A commercially available dentifrice with 1,000 PPM fluoride (NaF) and triclosan.

Patients were advised to brush for 1 minute twice a day with soft brush using Modified Stillmans method. All toothpastes had similar taste, texture and colour. The pastes were packed in plain white tubes labeled only with lot numbers to insure proper blinding. Subjects were asked to refrain from all other unassigned forms of oral hygiene, including non-study toothpaste, dental floss, chewing gum or oral rinse during the study. The patients were asked to strictly use only the given oral hygiene aids for 6 weeks. Patients were recalled after 6 weeks for recording all the clinical parameters including saliva sample for microbiological examination of P. Gingivalis.

Results
The present study results pertain to 150 patients between the age range of 19-33 years (Table 1) suffering from chronic gingivitis. The data was analyzed using Paired t test, oneway ANOVA test and Wilcoxon's signed ranked test. None of the patient treated with this method showed any untoward side effect.

Comparison of reduction in P. Gingivalis count (cells/ml) by three pastes using PCR at baseline and after 6 weeks gives p<0.001 (S) for paste A, p<0.001(S) for paste B and p<0.001(S) for paste C. The Wilcoxon signed-rank test was applied and all the pastes showed statistically significant reduction in P. Gingivalis count after 6 weeks..

Table 1: Demographic Data of Study Population

<table>
<thead>
<tr>
<th></th>
<th>A (N=50)</th>
<th>B (N=50)</th>
<th>C (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Range (years)</td>
<td>19-33 years</td>
<td>19-33 years</td>
<td>19-33 years</td>
</tr>
<tr>
<td>Gender</td>
<td>M 14 F 36</td>
<td>M 11 F 39</td>
<td>M 18 F 32</td>
</tr>
</tbody>
</table>

Table 2: Comparison Of Plaque Index Among Different Pastes At Baseline And After 6 Weeks

<table>
<thead>
<tr>
<th>Paste</th>
<th>Pre Mean ± S.D</th>
<th>Post Mean ± S.D</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.46±0.38</td>
<td>0.93±0.52</td>
<td>5.81</td>
<td>&lt;0</td>
</tr>
<tr>
<td>B</td>
<td>1.65±0.34</td>
<td>0.43±0.23</td>
<td>21.01</td>
<td>&lt;0</td>
</tr>
<tr>
<td>C</td>
<td>1.73±0.3</td>
<td>1.08±0.49</td>
<td>7.99</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 3: Comparison Of Gingival Index Among Different Pastes At Baseline And After 6 Weeks

<table>
<thead>
<tr>
<th>Paste</th>
<th>Pre Mean ± S.D</th>
<th>Post Mean ± S.D</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.96±0.27</td>
<td>0.56±0.24</td>
<td>7.82</td>
<td>0.00</td>
</tr>
<tr>
<td>B</td>
<td>0.99±0.29</td>
<td>0.39±0.15</td>
<td>12.9</td>
<td>0.00</td>
</tr>
<tr>
<td>C</td>
<td>1.04±0.17</td>
<td>0.53±0.21</td>
<td>13.34</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 4: Comparison Of Calculus Index Among Different Pastes At Baseline And After 6 Weeks

<table>
<thead>
<tr>
<th>Paste</th>
<th>Pre Mean ± S.D</th>
<th>Post Mean ± S.D</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.025±0.4</td>
<td>0.35±0.24</td>
<td>10.15</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>B</td>
<td>1.22±0.39</td>
<td>0.29±0.24</td>
<td>14.3</td>
<td>&lt;0</td>
</tr>
<tr>
<td>C</td>
<td>1.47±0.50</td>
<td>0.53±0.43</td>
<td>10.4</td>
<td>0.00</td>
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</table>
A study was conducted to determine the anti-inflammatory and anti-gingivitis effect of a dentifrice containing bioactive glass particulate. The study evaluated the efficacy of various combinations of bioactive glass particulate and fluoride in reducing supragingival plaque and gingival bleeding over a 6-week period. The study used a randomized, double-blind, controlled clinical trial with 50 participants in each group (A, B, and C). The results showed statistically significant differences between the groups, with paste B (p<0.001) and paste C (p=0.0) demonstrating the greatest reduction in plaque index compared to paste A (p=0).

Table II shows the comparison of mean plaque index at baseline and after 6 weeks for the three respective pastes. Paste A (p=0), paste B (p<0) and paste C (p=0) show statistically significant results after 6 weeks (Fig 1).

Table III shows comparison of mean Gingival Index at Baseline and after 6 weeks for the three respective pastes. Paste A (p<0.001), paste B (p<0) and paste C (p=0) show highly significant reduction in calculus index after 6 weeks. (Fig 3)

Discussion
Periodontal diseases are complex processes with strong cause and effect relationships proven between the accumulation of supragingival plaque and the development of gingivitis. Various chemotherapeutic agents have been incorporated into dentifrice formulations to prevent and reduce gingivitis. The present study randomized, double-blinded, controlled clinical trial was conducted to determine the anti-inflammatory and anti-gingivitis effect of a dentifrice containing bioactive glass particulate.

Various chemotherapeutic agents have been incorporated into dentifrice formulations to prevent and reduce gingivitis and for the prevention of caries. Toothpastes are ideal carriers for antibacterial substances, if only because tooth brushing represents the most common oral hygiene method. Among the various agents available, triclosan and fluoride are most common ingredients in the dentifrices.

Even though fluoride has antimicrobial effect it also can lead to tooth staining. Triclosan has good anti-tartar effect it can cause adverse effects too. Tetra sodium pyrophosphate used as an anti tartar agent forms highly alkaline solution upon use in oral cavity and hence can irritate oral membranes. The high concentration flavoring agents added to mask the bitter taste of pyrophosphates can act a sensitizers. Increased concentration of detergents added to toothpastes for allowing the dissolution of pyrophosphates can lead to hypersensitivity reaction. Taking into consideration the drawbacks of triclosan and fluoride over the added advantages of bioactive glass, the present randomized, double-blinded, controlled clinical trial was carried out with the objective of comparing experimental dentifrice containing bioactive glass and fluoride, dentifrice containing triclosan and fluoride (positive control) and dentifrice containing only fluoride. This study protocol was chosen in order to avoid the potential biases in the data. The results of this study were in accordance with that carried out by Tai BJ et al which demonstrated that a dentifrice containing Novamin® significantly improves oral health as measured by a reduction in gingival bleeding and reduction in supragingival plaque compared with a negative dentifrice over the 6 weeks study period.

A study was conducted to determine the anti-inflammatory and anti-gingivitis effect of a dentifrice containing bioactive glass particulate. The evaluation of the anti-inflammatory effects of bioactive glass placed in periodontal defects by Han et al found that crevicular elastase production in crevicular fluid was significantly lower in bioactive glass grafted sites compared with root planing and debridement sites indicating less tissue destruction and lower inflammation at the sites. Triclosan has the ability to inhibit both cyclo-oxygenase and lipooxygenase pathways of arachidonic acid metabolism with similar efficacy. In cell culture, Modeer et al demonstrated that triclosan inhibited interleukin-1 β-induced prostaglandins E2 production by human gingival fibroblasts.

In the present study Paste A (p<0.001); paste B (p<0.001) and paste C (p<0.001) showed statistically significant reduction in P. gingivalis count after 6 weeks. PCR is the most sensitive and rapid test, offers a faster detection time, increased accuracy compared to traditional culture, is easy to use, relatively low cost in terms of laboratory manpower, rapid turnaround time, and potential to be fully automated. It can amplify small amounts of bacterial nuleic acid and can detect as few as 10 organisms in a plaque sample.

Stoor et al first published results of exposure of planktonic organisms known to be involved in the progression of gingivitis and periodontitis to particulate bioactive glass compositions. In these studies, it was found that exposure of a 40% solution of bioactive glass to the cultures for 10 min resulted in a 3 log reduction in Actinobacillus Actinomycetem Comitans and Porphyromonas Gingivalis and total loss of viability of the organism with a 60 minute exposure.13 Allan et al, using particulates of bioactive glass with a size range from 300 to 500 mm, showed an antibacterial effect against S. Mutans, S. Sanguis, P. Gingivalis, Fusobacterium Nucleatum, A. Actinomycetem Comitans and Prevotella Intermedia with a one hour exposure to the particulates. Allan ascribed much of the effect of the bacterial kill to an increase in pH of the bioactive glass in solution, although it appears that the release of large quantities of calcium from the bioactive glass might also play a role in the observed behavior towards the microbes. The present study very well supported the above findings.

Conclusion
All three combinations demonstrated a significant reduction in gingivitis in a relatively short period of time with paste B showing greatest reduction. There were no adverse events reported in the study. This is the first clinical study evaluating the efficacy of dentifrice containing bioactive glass using PCR as an aid for microbiological parameters. Further clinical studies are required to determine the long-term effectiveness of this new compound. Additional studies should also be undertaken to determine if there will be any build-up of microbial resistance.
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