Evaluation of recombinant human platelet derived growth factor-bb, beta-tricalcium phosphate with collagen membrane in the treatment of gingival recession
Preetinder Singh, Suresh.D.K, Sumit Kaushal, Sarita Dabra, Alka Kaushik

Abstract
Background: Use of latest periodontal regenerative therapies is a boon in periodontal plastic surgery field. Aims: To evaluate the clinical outcome of rhPDGF-BB with beta tricalcium phosphate (GEM 21S®) and a collagen membrane in the treatment of recession defects using coronally advanced flap. Materials and Methods: A total of fourteen sites from seven subjects were selected and divided into two groups and postoperatively and healing was evaluated at 1st, 3rd and 6th months, with recession depth as the primary outcome measure. Results: This study revealed a favorable tissue response to GEM 21S® and collagen membrane. Conclusion: In conclusion on clinical and aesthetic point of view recombinant human platelet derived growth factor-bb, beta-tricalcium phosphate with collagen membrane showed an excellent plastic surgery results for gingiva.

Key Words: PDGF; gingival recession; beta tricalcium phosphate; periodontal plastic surgery

Introduction
Periodontal regeneration has become one of the primary objectives of periodontal therapy including root coverage procedures. The resulting scientific endeavors have elucidated modes of periodontal wound healing, the growth of periodontal cells and their association with the surrounding matrix, and growth-promoting factors. Growth factors such as platelet-derived growth factor (PDGF) and transforming growth factor-(TGF), contained in the granules of blood platelets and released at sites of injury, have been shown to be important in the normal healing of bone, gingiva and skin. This study was carried out a) to evaluate the clinical efficacy of GEM 21S® (rhPDGF-BB and Beta Tricalcium Phosphate) along with a collagen membrane in root coverage using coronally advanced flap and b) to compare GEM 21S® and collagen membrane with collagen membrane in root coverage using coronally advanced flap.

Materials and Methods
The subjects for the present study were selected from the outpatient department, Department of Periodontology, M.M.College of Dental Sciences, Mullana, India. The subjects were clearly explained the study protocol and procedure and a duly signed written consent were taken from them. A total of fourteen sites from seven subjects were selected and divided into two groups. Group A and Group B based on the treatment modalities by using split mouth design technique. Group A: Seven sites were treated with GEM 21S® (rhPDGF-BB plus Beta Tricalcium Phosphate) and collagen membrane with coronally advanced flap. Group B: Seven sites were treated with coronally advanced flap with only collagen membrane.

Group A: After evaluation of pre-clinical records and obtaining adequate local anesthesia, a trapezoidal-shaped flap was elevated with a split-full-split approach from the coronal to apical direction. The surgical papillae comprised between the horizontal incisions. The probable sulcular area apical to the root exposure was elevated by split thickness keeping the blade almost parallel to the root. The soft tissue apical to the root exposure was elevated full thickness inserting a small periosteal elevator in to the probable sulcus and proceeding in the apical direction to expose 3-4 mm of bone apical to the bone dehiscence.

In order to permit the coronal advancement of the flap, all muscle insertions present in the thickness of the flap were eliminated. Coronal mobilization of the flap was considered “adequate” when the marginal portion of the flap was able to passively reach a level coronal to the CEJ of the tooth with the recession defect. The exposed root surface, after thorough root planning, was conditioned with ethylene-di-amine-tetra-acetic acid (EDTA-24%) for 2 minutes to remove the smear layer and thoroughly rinsed with sterile saline.

Any remaining PDL tissue coronal to the alveolar bone was preserved. The rhPDGF-BB solution was then applied to the exposed root surface and to the coronal ligament fibers. A small amount of β-TCP saturated with the rhPDGF-BB solution and placed below the CEJ,
over the denuded root surface and extending approximately 2 to 3 mm onto the adjacent bone. The collagen membrane was also saturated with the PDGF solution prior to membrane placement. Once saturated, the membrane was placed over the beta TCP according to standard GTR surgical procedure and sutured bilaterally to the de-epithelialized papilla region. Subsequently, the membrane was covered with the coronally advanced flap. The tissue flap was then secured at the level of the CEJ by suturing the flap to the de-epithelialized papilla regions with 5-0 gut sutures. The vertical incisions were closed with 5-0 gut sutures. Any remaining rhPDGF-BB solution was dispensed onto the coronally advanced flap, followed by placement of tin foil and periodontal dressing. Post-operative instructions were given with medications and mouthwash was prescribed.

Group B: A procedure identical to that used in sites of Group-A subjects was performed. However, instead of PDGF and beta TCP (GEM21S®), sites of Group-B subjects received a collagen membrane only over the denuded root surface followed by coronally advanced flap. Patients were called after 24 hours for check up to evaluate any discomfort, swelling, pain, any bleeding or displacement of periodontal pack. One week following surgery, periodontal pack was removed and area irrigated with saline, repeat periodontal pack was placed in case of uneventful healing. Patients were recalled every 2 weeks following surgery for 1 month and subsequently every month for the next 6 months for examination of the treated surgical site. Clinical measurements recorded pre-operatively, were repeated at 1st month, 3rd month and 6th month post-operatively and subjected to statistical analysis.

**Results**

Gingival recession depth: Group A there was a statistically significant (p<0.05) reduction in mean difference of gingival recession depth scores from baseline to 1st month, 3rd month and 6th months with the p value of 0.016, 0.016, 0.016 respectively(Table 1 and Graph 1). In group B (Table 1 and Graph 1) there was a statistically significant (p<0.05) decrease in mean difference of gingival recession depth scores from baseline to 1st month, 3rd month and 6th months with the p value of 0.016, 0.024, 0.024 respectively.

Clinical attachment level: Group A there was a statistically significant (p<0.05) increase in mean difference of clinical attachment level scores from baseline to 3rd month and 6th months for p value 0.016 and 0.017 respectively (Table 1 and Graph 1). The percentage gain in clinical attachment levels at 3rd month was 52.86 % and increased to 58.10 % at 6th month. Group B (Table 1 and Graph 1) there was a statistically significant (p<0.05) increase in mean difference of clinical attachment level scores from baseline to 3rd month and 6th month with the p value of 0.015 and 0.026 respectively. Comparison between Group A and Group B: On comparison, there was a statistically not significant (p>0.05) difference in clinical attachment level scores between the groups at baseline and 3rd month with the p value of 0.833 and 0.075 respectively but at 6th month, there was a statistically

<table>
<thead>
<tr>
<th>Baseline Time Intervals in month</th>
<th>Gingival Recession Depth</th>
<th>Clinical Attachment Level</th>
<th>Width of Keratinized Tissue</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Z Value</td>
<td>p Value</td>
</tr>
<tr>
<td>A</td>
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<tr>
<td>1st</td>
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<td>2.41</td>
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<td>2.29±0.75</td>
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<td>0.016*</td>
</tr>
<tr>
<td>6th</td>
<td>2.29±0.75</td>
<td>2.40</td>
<td>0.016*</td>
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<tr>
<td>B</td>
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<tr>
<td>1st</td>
<td>1.71±0.75</td>
<td>2.40</td>
<td>0.016*</td>
</tr>
<tr>
<td>3rd</td>
<td>1.29±0.75</td>
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<tr>
<td>6th</td>
<td>1.86±0.69</td>
<td>2.41</td>
<td>0.016*</td>
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</tbody>
</table>

Table 1: Mean Differences in Gingival Recession, Clinical Attachment Level & Width of Keratinized Tissue between Group A & Group B

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Gingival Recession Depth</th>
<th>Clinical Attachment Level</th>
<th>Width of Keratinized Tissue</th>
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</thead>
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<td>Mean ± SD</td>
<td>Z Value</td>
<td>p Value</td>
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<td>0.352 (NS)</td>
</tr>
<tr>
<td>3rd</td>
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<td>1.910</td>
<td>0.056 (NS)</td>
</tr>
<tr>
<td>6th</td>
<td>1.43±1.662</td>
<td>1.910</td>
<td>0.056 (NS)</td>
</tr>
</tbody>
</table>

Table 2: Mean Differences in Gingival Recession, Clinical Attachment Level, Probing Depth & Width of Keratinized Tissue between Group A & Group B at different intervals

* S - Significant ; NS - Not Significant
significant (p<0.05) difference with the p value of 0.049 which showed higher gain in clinical attachment level of Group A (Table 3 and Graph 1).

Probing depth: Group A: In this study, there was a statistically significant (p<0.05) reduction in mean difference of probing depth scores from baseline to 3\textsuperscript{rd} month and 6\textsuperscript{th} month with the p value of 0.025 and 0.020 respectively. The percentage reduction in probing depth at 3\textsuperscript{rd} month was 30.95% and increased to 42.86% at 6\textsuperscript{th} month (Table 2 and Graph 2).

Width of keratinized tissue: Group A (Table 1 and Graph 1) In this study, there was a statistically significant (p<0.05) decrease in mean difference of width of keratinized scores from baseline to 1\textsuperscript{st} month, 3\textsuperscript{rd} month and 6\textsuperscript{th} months with the p value of 0.016, 0.016, 0.016 respectively, which is suggestive of increase in width of keratinized tissue at the site. The percentage gain in width of keratinized tissue at 1\textsuperscript{st} month was 46.19%, increased to 58.10% at 3\textsuperscript{rd} month and remained same (58.10%) at 6\textsuperscript{th} months.

Group B: In this study, there was a statistically significant (p<0.05) decrease in mean difference of width of keratinized scores from baseline to 1\textsuperscript{st} month, 3\textsuperscript{rd} month and 6\textsuperscript{th} month with the p value of 0.016, 0.024 and 0.024 respectively which is suggestive of increase in width of keratinized tissue at the site. The percentage gain in width of keratinized tissue at 1\textsuperscript{st} month was 45.48%, decreased to 35.00% at 3\textsuperscript{rd} month and remained same (35.00%) at 6\textsuperscript{th} month (Table 1 and Graph 1).

Comparison between Group A & Group B (Table 3 and Graph 1): On comparison, there was a statistically not significant (p>0.05) increase in mean difference of width of keratinized tissue scores from baseline, 1\textsuperscript{st} month, 3\textsuperscript{rd} month and 6 months with the p value of 1.000, 0.731, 0.061 and 0.061 respectively.

Discussion

Gingival recession depth: The percentage gain in root coverage from baseline to 1\textsuperscript{st} month was 57.14%, increased to 70.24% at 3\textsuperscript{rd} month and remained same (70.24%) at 6\textsuperscript{th} months. These results are in accordance with the clinical pilot study done by Michael K. Mc. Guire et al. Myrons Nevins did the largest, prospective, randomized, triple blinded clinical trial to date assessing a putative regenerative and wound healing therapy using rhPDGF-BB and B-TCP and giving similar results such as reduced gingival recession (5). Studies done by various authors used rhPDGF-BB and allograft (demineralised freeze-dried bone allograft) in various periodontal defects has reported root coverage (6-8).

The percentage gain in root coverage from baseline to 1\textsuperscript{st} month was 45.95%, decreased to 34.76% at 3\textsuperscript{rd} month and remained same (34.76%) at 6\textsuperscript{th} months. The results are in accordance with the study done by Kenneth M. Kimble et al who reported 68.4% root coverage at 6 months using only collagen (9). These results also harmonize with earlier bio-absorbable barrier studies as done in the literature(10-12) which showed root coverage ranging from 55% to 75%.

Comparison between Group A & Group B (Table 2 and Graph 1) On comparison of Group A versus Group B, there was a statistically not significant (p>0.05) decrease in mean difference of gingival recession depth scores from baseline, 1\textsuperscript{st} month, 3\textsuperscript{rd} month and at 6 months with the p value of 0.362, 0.352, 0.056 and 0.056 respectively.

Clinical attachment level: The percentage gain in clinical attachment levels at 3\textsuperscript{rd} months was 31.97% and decreased to 29.59% at 6 months. The results are in accordance with the study done by Kenneth M. Kimble (9) which reported gain in clinical attachment levels from baseline to six months.

Probing depth: In this study, there was a statistically significant (p<0.05) reduction in mean difference of probing depth scores from baseline to 3\textsuperscript{rd} month p value 0.046 and statistically not significant (p>0.05) decrease from baseline to 6\textsuperscript{th} month with the p value of 0.083. The percentage reduction in probing depth
at 3rd month was 28.57% and decreased to 21.43 % at 6th month.

Comparison between Group A & Group B (Table 3 and Graph 2): On comparison of Group A versus Group B, there was a statistically not significant (p>0.05) difference of probing depth scores at baseline, 3rd month and 6th month for p value of 0.141, 0.606 and 0.298 respectively. However, there was a more reduction in probing depth observed for the group A sites.

Conclusion

On observing the clinical parameters, the present study showed better results in both the groups of GEM 21S® and collagen and only collagen treated sites with a statistical significant difference in clinical parameters at various intervals. On comparison, there was not statistically significant difference observed; these suggestive of, that both GEM 21S® along with collagen and only collagen can be used effectively in root coverage procedures. However, Group A sites showed better results in root coverage than Group B sites, suggesting a great use of the above mentioned products in periodontal plastic procedures. The present study was short term clinical study with small sample size and no histological evaluation. Studies should be designed with large sample sizes and histological evaluation to further compare the predictability of above said procedures, as there is paucity of literature regarding the same.

Affiliations of Authors: 1. Dr. Preetinder Singh, MDS, Senior Lecturer, Department of Periodontology & Oral Implantology, Swami Devi Dyal Hospital & Dental College, Barwala, Distt, Panchkula 2. Dr. Suresh. D.K., MDS, Prof. and Head, Department of Periodontology & Oral Implantology, MMCDSR, Mullana, Ambala, 3.Dr.Sumit Kaushal, MDS, 4. Dr. Sarita Dabra, MDS, 5. Dr. Alka Kaushik, MDS, Swami Devi Dyal Hospital & Dental College, Barwala, Distt.Panchkula, Haryana, India.

References


Address for correspondence
Dr. Preetinder Singh, MDS, H.no 28, Sangam Enclave, Sector 48-A, Chandigarh-160047, India. Ph : 0091.9915652946 Email: preetinder.perio@yahoo.com

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