Clinical Article

A comparison in postoperative healing of sites receiving non-surgical debridement augmented with and without a Hyaluronan 0.8% gel

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Abstract

Hyaluronic acid forms the basis of the extracellular matrix in which the cell growth takes place. A commercial preparation of hyaluronic acid called Hyaluronan (Gengigel) has recently been developed for intraoral use to promote healing in inflamed sites and sites aerated due to periodontal disease. 52 patients with moderate to severe periodontal disease were measured for their ability to receive a single application of Haluronan gel immediately after thorough root surface debridement. Sites to receive the Hyaluronan gel or a placebo gel were selected on a randomised basis for each patient.

Aim: The aim of the study was to determine if any beneficial treatment outcomes derived from a single application of Hyaluronal after nonsurgical therapy.

Materials and Methods 52 patients were randomly selected from those aged greater than 45 years who attended for treatment for chronic periodontal disease. For inclusion in the study all patients had been previously treated with periodontal therapy. A total of 104 treated quadrants were divided into two groups. One group of 52 subjects received a single application of Hyaluronan gel immediately after root surface debridement and the treated quadrants. At baseline and at 3 and 6 months postoperatively, a subjective analysis of test and control sites was performed.

Results have demonstrated highly significant improvements in the clinical variables of bleeding on probing and root pocket depth were completed. Individual and group mean values were subjected to Student’s t-test and linear ANOVA using the SAS statistical software package.

Conclusion: The results of this study suggest that topical application of Hyaluronan gel is effective in promoting healing after periodontal surgery. The use of this agent in the prevention and treatment of periodontal disease is a promising approach in the field of oral health care.

Introduction

Chronic Adult Periodontitis affects over 2/5 of all patients in the aged greater than 45 years (Agerholm D 2001), and is also the second most common cause of tooth loss in the U.K. (McCaul LK et al 2001). Treatment of these patients has characteristically involved manual scaling and root-planing to provide a smooth root surface for reattachment, supplemented with intensive oral hygiene instruction, to prevent contamination of the healing sites by the oral flora. More recently, this approach to treatment has been reappraised, so that instead of aiming for smooth root surface treatment, treatment now aims to disinfect and decontaminate the root surface cementum of aerated sites. Topical agents are increasingly being used as adjuncts to manual root surface debridement in an attempt to promote healing.

Although Chlorhexidine irrigation is almost ubiquitous in general dental practice for the suppression of oral microorganism, a recent review has concluded that there is no beneficial effect of this over scaling and root planing alone (Hanes P et al 2005). Locally delivered chlorhexidine in the form of a control released resorbable “chips” has been shown to have a significant adjunctive effect (Kil wor Y 1996), but control released re-lease Doxycycline was shown in a comparative study of topical antibacterials with chlorhexi-dine (Salvi E et al 2002), to be the preparation of choice. These devices are only effective at the site of placement and are relatively costly. However, increasing evidence indicates that, while plaque is the primary aetiologi-cal agent in establishing periodontal disease, the host reaction to the bacterial challenge is crucial to the initiation and progression of periodontal diseases.

More recent work has therefore focused on the management of the host response, rather than the microbial challenge from bacterial plaque biofilm.

“Periostat” (Alliance Pharma UK) is a sub antimicrobial dose Doxycycline preparation. It derives its benefit from the well-documented anti-inflammatory properties of the tetracycline group of antibiotics and several studies have concluded that this product achieves significant attachment gains and prob-ing depth reductions over and above those achieved by scaling and root planning alone (Abdel et al 2005). However, it has the major disadvantage of being a systemic preparation, with long treatment times, and may need to be re-peated at intervals. More recently a topically applied anti-inflammatory product based on Hyaluronan (Gengigel: Oraldent UK) has been launched. Hyaluronan (HA) is a linear polymer derived from two repeating disaccharide subunits (D-Glucuronic acid and N-acetylglucosamine), and is a natural constituent of the body’s glycosaminoglycan (GAG) population. Its synthetic form is referred to as Hyaluronan (Gengigel). It has many properties that make it a potential ideal molecule for assisting wound healing by inducing early beneficial granulation tissue forma-tion, inhibiting destructive inflammation during the healing phase, promoting epithelial turnover and also con-nective tissue angiogenesis. (Ichikawa et al 2002, Moseley et al 2003). Local delivery of HA has been shown to have a moderate effect on treating root pockets resistant to mechanical debridement. More recently being used as adjuncts to non-surgical periodontal therapy.

Aim

The aim of this study was to determine the clinical benefits of a Hyaluronan-based gel (Gengigel Prof) used as an adjunct to non-surgical periodontal therapy.

Methods and materials

52 patients were randomly selected from patients aged 18-65 who attended for treatment for chronic periodontal disease. For inclusion in the study all patients wereFree of adverse patient reactions or drug interactions. As Hyaluronan is presented in gel form, it can be cheaply and easily delivered to all areas under- going therapy. When used in combination with non-surgical periodontal therapy, a more effective outcome is achieved.

Table 1. Demographic (Completed in gel form, it can be cheaply and easily delivered to all areas under-going therapy. When used in combination with non-surgical periodontal therapy, a more effective outcome is achieved.

<table>
<thead>
<tr>
<th>TIME</th>
<th>N</th>
<th>MEAN</th>
<th>SD</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
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<tr>
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<tr>
<td>TEST</td>
<td>5m Post-op</td>
<td>52</td>
<td>0.8137</td>
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Table 2. Demographic (Completed in gel form, it can be cheaply and easily delivered to all areas under-going therapy. When used in combination with non-surgical periodontal therapy, a more effective outcome is achieved.

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<th>TIME</th>
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<td>Baseline</td>
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<td>3.9601</td>
<td>0.9139</td>
</tr>
<tr>
<td>PLACEBO</td>
<td>5m Post-op</td>
<td>52</td>
<td>2.8584</td>
<td>0.8785</td>
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<tr>
<td>TEST</td>
<td>Baseline</td>
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<td>2.588</td>
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<tr>
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<td>5m Post-op</td>
<td>52</td>
<td>0.72</td>
<td>0.397</td>
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Table 3. Tannin yield test results of Minto showing the effect of mean and control sites during the study.

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<tr>
<th>TIME</th>
<th>MEAN</th>
<th>SD</th>
<th>P VALUE</th>
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<tbody>
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<td>18.099</td>
<td>p&lt;0.0005</td>
</tr>
<tr>
<td>TEST</td>
<td>35.844</td>
<td>135.942</td>
<td>p&lt;0.0005</td>
</tr>
<tr>
<td>DRUG</td>
<td>3.594</td>
<td>73.542</td>
<td>p&lt;0.0005</td>
</tr>
</tbody>
</table>

Table 4. Topographic (Completed in gel form, it can be cheaply and easily delivered to all areas under-going therapy. When used in combination with non-surgical periodontal therapy, a more effective outcome is achieved.

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<tr>
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All of the clinicians were calibrated against a standard predetermined protocol for the study, to ensure a high level of intra- and inter-examiner reproducibility. This was achieved by means of a preliminary pilot study in which five patients, who were not included in the study, were subjected to repeated measurements of the clinical variables used in the study by all of the clinicians. Both intra and inter-examiner reproducibility was found to be high.

Boost surface debridement was carried out in all pockets equal or greater than 4 mm and the healing of these sites was used in the statistical analysis. Debridement was undertaken in two quadrants at a time. Patients were randomly selected to receive a post debridement application of the active gel or the placebo, in the treated quadrants. Wherever possible the left and right quadrants were used as adjunctive gel/non-adjunctive gel comparisons, but where this was not possible (due to too few teeth being present), the upper and lower quadrants were compared. 0.8% Hyaluronan gel was applied into the pockets in those sites that had been randomly assigned to receive it, using a prefilled syringe after completion of the mechanical debridement. The other sites received an application of an inert placebo gel.

At both baseline and at the three months follow-up assessment appointments, bleeding on probing and pocket depths were measured and annotated for each subject. These variables were then consolidated into individual and then group mean values which were then subjected to simple (Student’s t-test) and linear ANOVA using the SAS statistical software package.

Results

It can be seen from table 1 that highly significant improvements occurred in the group bleeding scores in both placebo and test sites from baseline to the three-month review appointment. Similarly table 3 shows highly significant improvements in periodontal pocketing in both the placebo and test groups from baseline to three months after treatment.

In table 2 it can be seen that the mean improvement in bleeding scores in the placebo group was 24.6%, while in the test group it was over double at 59.05%. This is a highly significant incremental improvement (p<0.0005). Similarly table 4 illustrates the improvements in pocket depth measurements. In the placebo group pockets improved by an average of 18.45%, whereas in the test group it was nearly double that level of improvement at 32.59%. This is reflected in a highly significant p-value of p=0.0027.

While the group on the test drug (Hyaluronan) was shown to have a significant benefit over the time period of the study, the results of ANOVA illustrated in table 5 show that the individually significant results are substantiated when time/drug interactions are accounted for in the analysis.

Discussion

Hyaluronan has been identified in all periodontal tissues, being particularly concentrated in the non-mineralised tissues such as gingival and periodontal ligament. It is also present in low concentrations in mineralised tissues such as cementum and alveolar bone. Hyaluronan has many structural and physiological properties, the use of exogenous hyaluronan applied topically to inflamed periodontal sites, would appear to offer beneficial effects in modulating and accelerating the host response. Several double blind studies have demonstrated the beneficial effect of Hyaluronan 0.2% gel in the treatment of Gingivitis. Jentsch et al (2003) showed that 0.2% gel produced a significant improvement in both clinical and para-clinical variables in plaque induced gingivitis.
Demineralised white spot lesions occur frequently after orthodontic treatment. Some teeth are more prone to demineralisation, typically the maxillary lateral incisors and the mandibular canine teeth. The disto-gingival area of the labial enamel surface is the area most commonly affected (Fig. 1). In the first few weeks after removal of the fixed appliances, there is a reduction in white spot lesion size and appearance, possibly due to the action of saliva (Fig. 2).

Various treatment methods have been proposed to assist the process of remineralisation. It is important to note that fluoride should not be used in high concentrations, as it tends to prevent demineralisation and can lead to further unsightly staining. Low concentrations of fluoride, however, may assist remineralisation, such as those found in casein calcium phosphate materials. Additionally, stimulation of salivary flow by chewing sugar-free gum is helpful.

This article will describe a revolutionary new approach to the cosmetic treatment of white spot lesions (Fig. 5). With Icon, a microinvasive technology from German manufacturer DMG, demineralised enamel can be filled and reinforced without drilling or anaesthesia (Figs. 4 & 5).

One of the reasons that earlier approaches to the treatment of white spot lesions have fallen short is that fluoride therapy is not always effective in the advanced stages, and the use of restorative fillings usually sacrifices significant amounts of healthy tooth structure.

Instead of adopting a wait and see approach, Icon has been
shown to arrest the progress of early enamel lesions up to the first third of dentine in one simple procedure (Fig. 6), without unnecessary loss of healthy tooth structure.

In the procedure described here, the surface area of the white spot lesion is eroded with a 15 % HCl gel, which opens the pore system of the lesion. This is then dried with ethanol, followed by the application of Icon onto the lesion with the application aid. The extremely high penetration coefficient enables it to penetrate into the lesion pores. Excess material is then removed, and the material is light-cured. The total treatment time should be about 15 minutes (Fig. 7).

The cosmetic treatment of cariogenic white spots in one visit can be very appealing, especially to young patients and their parents (Figs. 8a & b). No drilling or anaesthesia is required and those patients who have already demonstrated poor compliance with their brushing can be treated earlier.

I would recommend that clinicians try the Icon product when attempting to remineralise white spot lesions post-orthodontic treatment. This is not just minimally invasive dentistry; it is micro-invasive dentistry.

Fig. 1 Typical white spots: C-shaped or irregular.
Fig. 2 Smooth surface caries lesion.
Fig. 3 Clinical image of an incipient caries lesion.
Fig. 4 Clinical image of an incipient caries lesion.
Fig. 5 Pore system of an incipient caries lesion.
Fig. 6 The first treatment to bridge the gap between prevention and restoration.
Fig. 7 Smooth surface procedure.
Figs. 8a & b Lesions before and after Icon treatment.

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givitis compared to placebo. Pagnacco et al (1997) and Pistorius et al (2005) in separate double blind studies demonstrated the beneficial effect of Hy- aluronan gel in producing significant improvements in the measurement variables of inflammation in gingitis.

A study by Yi Xu et al (2004) concluded that there was no clinical improvement was achieved by the adjunctive use of Hyaluronan 0.2% gel compared to mechanical debridement. However, in this study Hyaluronan 0.2% gel was applied only once a week for six weeks, a total of seven applications over a six week period, compared to the recommended application level of three times daily for at least 4-8 weeks. The absence of observed clinical improvements, contrary to other published studies, may indicate that the Hyaluronan levels used in this study were well below the optimum levels required to achieve a significant clinical improvement.

Mesa Aguado et al (2001) in a double study on patients with periodontal disease concluded that Hyaluronan gel was effective in controlling inflammation and gingival bleeding and a reduction in the depth of gingival pockets was observed along with a significant reduction in epithelial and lymphocyte cell proliferation.

This study has demonstrated that the use of Hyaluronan gel statistically improves patient outcome (reflected by highly significant improvements in bleeding indices and pocket probing depths) when used as an adjunct to non-surgical periodontal therapy.

The bleeding index improved by 24.6% in the placebo group, whereas the treatment group displayed a reduction of 59.05%. This equates to a twofold improvement in outcome in the treatment group. Pocket probing depth also demonstrated a highly significantly (P=0.0027) incremental improvement in the treatment group. The test group therefore experienced a 75.75% better treatment outcome in comparison to the baseline healing rate (placebo group). These results markedly demonstrate the additional benefits afforded by the use of Hyaluronan 0.8% gel.

Conclusions

This study confirms results, which indicate that exogenous Hyaluronan gel has a beneficial effect in the growth, development and repair of tissues in periodontal disease.

In this study it was shown that even a single subgingival application of Hyaluronan gel after non-surgical debridement results in highly significant improvements in treatment outcomes as assessed by reductions in bleeding and pocket depth measurements.

It is therefore concluded that the adjunctive use of Hyaluronan after thorough mechanical debridement potentially has major clinical benefits in terms of improved healing after non-
surgical therapy. However further work needs to be done to confirm the results of this study and to assess the long term healing of the tissues in sites in which the Hyaluronan was applied. If you wish to contact any of the authors of this article see below for contact details: Address: 28 Bandell Crescent, Hendon, London NW4 1RF, United Kingdom.

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