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

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Abstract
Hyaluronan forms the basis of the extracellular matrix in which the cell growth takes place. A commercial preparation of hyaluronan acid called Hyaluronan (Genigel) has recently been developed for intraoral use to promote healing in inflamed sites and sites aerated by periodontal disease. Patients with moderate to severe periodontal disease who were moderately or severely edentulous were selected to receive a single application of Hyaluronan 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.

The aim of the study was to determine if any beneficial treatment effects were derived from a single application of Hyaluronan after nonsurgical therapy.

Materials and Methods 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 had BPE scores of 3 or greater in at least 2 quadrants. On selection for the study patients received a full mouth assessment of bleeding on probing and pocket depth measurements recorded in millimetres, using a six point charting. Patients were excluded from the study if their medical status or prescribed medication compromised their immune system, if they only had moderate periodontal disease requiring non surgical treatment only, or if they had too few remaining teeth to allow a comparative analysis of test and control sites.

Clinical results have shown that topical application of Hyaluronan promotes healing of both leg ulcers (Ortonne 1996), and the naso orobuccal fistula surgery (Soldati et al 1999). It has also been shown to reduce the incidence of high-grade radio-epithelitis in patients who have undergone radiotherapy for head and neck cancer (Liguori et al 1997). Hyaluronan is a hygroscopic macromolecule and in solution forms a gel-like gel. These properties are likely to be relevant in controlling tissue hydration during changes to the tissue such as the inflammatory process or response to tissue injury. chlorhexidine has also been shown to have a role in controlling tissue hydration, which is important during cell proliferation and migration. These local factors of tissue hydration weaken cell attachment to the local foci of tissue hydration, which is important during cell proliferation and migration (Tamura et al 1994). As a result of this study patients were selected to receive the Hyaluronan gel, which the cell growth takes place. The aim of the study was to determine if any beneficial effects were derived from a single application of Hyaluronan after nonsurgical therapy.
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.

Root 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 52.59%. 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 within tissues and is a key component in the series of stages associated with the wound healing process in both mineralised and non-mineralised tissues (i.e. inflammation, granulation tissue formation, epithelium formation and tissue remodelling) (Culp et al 1979).

As a consequence of its non-toxicity, biocompatibility and numerous biochemical 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 concentration, 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 Hyaluronan gel in producing significant improvements in the measurement variables of inflammation in gingivitis.

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 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.

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Figure 1: To demonstrate the additional benefit in terms of reduced bleeding achieved by application of the Hyaluronan gel after non-surgical debridement

Figure 2: To demonstrate the additional benefit in terms of reduced pocket depths achieved by application of the Hyaluronan gel after non-surgical debridement