Summary of: Treatment of early caries lesions using biomimetic self-assembling peptides – a clinical safety trial

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VERIFIABLE CPD PAPER

FULL PAPER DETAILS

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Online article number E6
Refereed Paper – accepted 2 July 2013
DOI: 10.1038/sj.bdj.2013.741

Objective We previously reported that a rationally designed biomimetic self-assembling peptide, P_{11}-4, nucleated hydroxyapatite *de novo* and was apparently capable of *in situ* enamel regeneration following infiltration into caries-like lesions. Our present aim was to determine the safety and potential clinical efficacy of a single application of P_{11}-4 on early enamel lesions. **Materials and methods** Fifteen healthy adults with Class V 'white spot' lesions received a single application of P_{11}-4. Adverse events and lesion appearances were recorded over 180 days. **Results** Patients treated with P_{11}-4 experienced a total of 11 adverse events during the study, of which two were possibly related to the protocol. Efficacy evaluation suggested that treatment with P_{11}-4 significantly decreased lesion size ($p = 0.02$) after 30 days and shifted the apparent progression of the lesions from 'arrested/progressing' to 'remineralising' ($p < 0.001$). A highly significant improvement in the global impression of change was recorded at day 30 compared with baseline ($p < 0.001$). **Conclusions** The results suggest that treatment of early caries lesions with P_{11}-4 is safe, and that a single application is associated with significant enamel regeneration, presumably by promoting mineral deposition within the subsurface tissue.

EDITOR'S SUMMARY

As practitioners we are more usually concerned with the physical ravages of caries than the chemical processes behind its insidious progress. Indeed, it is the social as well as the treatment consequences that engage us most in explaining to our patients the diagnosis and treatment planning options, as well as the aesthetic implications, functional limitations and financial considerations.

Looking at what is after all a biological process from another view, it is the chemical reactions of acids and mineralised tissues which provide the analytical answers as to how caries progresses, and why. What though if we look at the equation the other way around and ask if it possible to reconstruct the crystalline scaffolding that has been destroyed? In times past this has perhaps seemed like a tall order. Rather like trying to stir the jam dropped into a rice pudding the other way and expecting it to reform in its original blob.

Not so it seems. This interdisciplinary team of biochemists, chemists and clinicians has been investigating enamel biomineralisation and the role of enamel matrix proteins in the control of crystal growth. As a result they have been developing a common goal towards the identification of a new, minimally invasive treatment for patients using peptide self-assembly.

In some ways this seems like, if not science fiction, then certainly just plain fiction or perhaps wishful thinking. Can we really reconstruct that which nature has first created and then subsequently deconstructed? Once again we are in the realms of future-gazing but as with the current research in the regenerative power of stem cells, the possibilities are both exciting and inspiring. We quite correctly debate the possible evolution of dental materials without the use of amalgam but what if the 'material' that we use is not an artificial placement but a regenerated replacement?

Much work is still to be done and we are not likely to be displaced in our daily tasks just yet by the likes of designer peptides in the form of bespoke therapeutic applications but a future line of investigation lies here somewhere. It is my guess that a '50 years ago' reflective column in the *BDJ* of 2063 may well mark this, and papers like it, as the beginnings of a very new dawn.

The full paper can be accessed from the *BDJ* website (www.bdj.co.uk), under 'Research' in the table of contents for Volume 215 issue 4.

Stephen Hancocks
Editor-in-Chief

DOI: 10.1038/sj.bdj.2013.811

IN BRIEF

- Describes a rationally-designed peptide-based biomaterial capable of infiltrating early caries lesions where it is thought to form scaffold-like structures via a process of self-directed assembly.
- Suggests that peptide scaffolds promote enamel regeneration *in situ* within the lesion, potentially providing a new therapeutic option that is minimally invasive and highly acceptable to patients.

COMMENTARY

This paper details the first steps in translating original basic-science caries research on a technology for promoting new mineralisation within initial 'white spot' caries lesions from the laboratory to the clinic. The full article sets out the specific aim of the present study: 'to conduct a first-in-man clinical safety study applying a single treatment of P_{11}-4 (a self-assembling peptide) to class V enamel lesions in healthy human volunteers'. This aim was addressed fully for the 15 volunteers studied. A total of 12 lesions were monitored within separate patients after a single peptide application for 4, 8, 30 and 180 days. Only one patient involved experienced any adverse event (transient dental hypersensitivity), which could potentially be attributed to the treatment. The overall patient reaction to this treatment modality was positive. The authors also quite properly declare competing interests for those who have developed the technology and have a stake commercially.

There is also considerable detail in the paper about the basic science underpinning this preliminary, small trial and also on the attempts to monitor the behavior of the 11 clinical lesions that were assessed in a variety of ways for a total of 180 days after the application of the new agent. However, the authors themselves caution that 'this is not an efficacy trial and as such we cannot compare the data obtained here with a 'do nothing' control or any other intervention, such as the application of topical fluoride'.

The authors are to be congratulated for their diligence and endurance in pursuing this line of enquiry for such a long period of time and for trying to address such an important 'gap' in our current clinical armamentarium. There are a number of issues where the approach may fall short of an ideal non-invasive preventive strategy (as it still requires a destructive acid-etch to open up the surface of initial lesions and may replicate the very structure which has succumbed to caries). It is to be hoped that the subsequent work the authors outline in the paper can lead to meaningful clinical outcomes for controlling initial caries and preventing surgical intervention.

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AUTHOR QUESTIONS AND ANSWERS

1. Why did you undertake this research?
Our work is inspired by Nature and, in this case, how we might translate our understanding of enamel biomineralisation and the role of enamel matrix proteins in the control of crystal growth. Our motivation was to use this knowledge to design biomimetic materials that can be used to repair the mineralised tissues, including the teeth. Our understanding of enamel biomineralisation resulted from our parallel studies of enamel development and the dysplasias associated with inherited enamel disorders in amelogenesis imperfecta (from genotype to phenotype). Our interdisciplinary team of biochemists, chemists and clinicians shared a common goal towards identification of a new, minimally invasive treatment for patients.

2. What would you like to do next in this area to follow on from this work?
We are seeking to validate the findings of the first in-man study in wider randomised, placebo-controlled clinical trials. We are also using the same family of peptides to determine their utility in regeneration and repair of bone, including maxillo-facial applications. Our interdisciplinary team is working on the design of 'second generation' peptides optimised for particular therapeutic applications in tissue regeneration. This includes a potential role for such peptides in autologous mesenchymal stem cell-based therapies, including cells derived from the dental pulp. Finally, we are continuing to further our understanding of the kinetics and physico-chemical properties of these materials.