IN BRIEF

- Sjögren's syndrome may lead to dental caries, periodontal disease, denture intolerance, candidosis and dysphagia.
- This study evaluated the use of a hydrogel polymer buccal insert as a controlled release delivery vehicle for pilocarpine.
- The insert delivered in excess of 85% of a 5 mg dose of pilocarpine hydrochloride with minimal side-effects; oral and eye comfort scores generally improved on therapy.

VERIFIABLE CPD PAPER ONLINE

A controlled release buccal insert

A controlled release pilocarpine buccal insert in the treatment of Sjögren's syndrome **J. Gibson,[1] J. A. Halliday,[2] K. Ewert[3] and S. Robertson[4]**

ABSTRACT

Objectives
To assess the efficacy of a novel hydrogel polymer buccal insert containing 5 mg pilocarpine in releasing the pilocarpine in a controlled fashion over a three hour period, and to assess the effects of this on quantitative tear and saliva production and the acceptability of the insert to the patient.

Design
This was an open, uncontrolled pilot study for which Ethics Committee approval was obtained prior to starting. Hydrogel buccal inserts containing 5 mg pilocarpine were used three times a day for seven days.

Setting
The Department of Oral Medicine, Glasgow Dental Hospital & School.

Subjects
Eight patients with Sjögren's syndrome.

Main outcome measures
Changes over baseline in (1) Schirmer test, (2) whole saliva flow rate, (3) oral comfort score (VAS), (4) ocular comfort score (VAS), (5) patient acceptability.

Results
The buccal inserts successfully released in excess of 85% of their 5 mg pilocarpine load over three hours. There was a general improvement in oral and ocular comfort scores assessed by visual linear analogue scale, and saliva and tear production generally increased. The inserts were well tolerated by all patients except one (who wore dentures). Adverse events were few and none was serious.

Conclusion
This novel form of buccal pilocarpine delivery demonstrated potential for use in treating patients with Sjögren's syndrome.

EDITOR'S SUMMARY

The xerostomia experienced by patients with Sjögren's syndrome may lead to severe oral effects, and while treatments such as pilocarpine are available, many patients resort only to palliative care due to the unpleasant side effects that these drugs may cause. Any method of treatment that can limit these side effects while effectively stimulating tears and saliva has the potential to be a useful tool in treating patients with Sjögren's syndrome, and could significantly improve their quality of life.

The hydrogel buccal insert tested by Gibson *et al.* in this study may prove to be useful in this regard. The insert was designed to be placed in the buccal sulcus, where it swells and sticks to the mucous membrane. By releasing pilocarpine in a controlled manner over a period of three hours, the insert had a significant beneficial effect on the tear and salivary flow rates of patients, who generally experienced improved oral and eye comfort. There were few adverse side effects, none of which were serious.

As the authors themselves point out, the design of this study was limited and further controlled trials are needed to more clearly determine the benefits and effectiveness of this treatment method. However, the early signs are promising and it is to be hoped that further research will help improve the therapies available to Sjögren's syndrome sufferers and lead to more acceptable treatment for this debilitating condition.

The full paper can be accessed from the *BDJ* website (www.bdj.co.uk), under 'Research' in the table of contents for Volume 202 issue 7.

Rowena Milan,
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FULL PAPER DETAILS

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AUTHOR QUESTIONS AND ANSWERS

Why did you undertake this research?
This research was undertaken in response to the request from many patients over the years with Sjogren's syndrome to 'make a difference to their quality of life'. Although patients with Sjogren's syndrome, whether primary or secondary, may have a multitude of other symptoms, it is often dryness of the mouth which makes life so difficult, causing problems with taste, swallowing, denture retention and oral mucosal discomfort.

Pilocarpine is a useful drug to use in patients with salivary hypofunction but its side-effect profile often precludes long-term use. The research focussed on developing a way of delivering the drug which would maximise the beneficial effects and minimise the adverse effects.

What would you like to do next in this area to follow on from this work?
This pilot study has given encouraging results for further work in assessing the hydrogel polymer buccal insert's controlled release of pilocarpine in patients with Sjogren's syndrome.

It is always encouraging in research to witness an advance that may impact positively on the management of patients, particularly when such patients have a debilitating disease like Sjogren's syndrome. A number of the pilot study patients requested to be issued with the inserts for long-tem use at the close of the study, such was the improvement in symptoms they sensed.

Further work would involve the use of placebo inserts and also a comparison with active inserts and oral pilocarpine treatment and no active treatment at all. Drug release in this pilot study was excellent but further work would also allow the establishment of the insert thickness which would give the optimally sustained release of pilocarpine over hours.

COMMENT

Sjögren's syndrome is a chronic autoimmune condition affecting exocrine glands and results in reduction of secretion. The disease affects between 1–2% of the population and most noticeably produces dry eyes and dry mouth. The oral consequences may be severe, resulting in widespread dental decay, mucosal problems and reduction in oro-pharyngeal function. Current palliative oral care is limited – muscarinic agonists (cevimeline hydrochloride and pilocarpine hydrochloride) will stimulate exocrine gland function, but when taken systemically may cause a number of side effects that prevent patient acceptability.

This study used a hydrogel polymer buccal insert carrying 5 mg of pilocarpine to provide controlled release of the drug over a three hour period. Efficacy was assessed by increase of tear and saliva production and by patient tolerability. Hydrogel polymers have been shown to be tolerated on mucosal surfaces such as eye and genital mucosa and in the latter site have a known ability for controlled drug release. Orally, this study has shown that they are generally well tolerated and effective in releasing a drug into the systemic circulation with few undue side effects. What was interesting was that these hydrogel inserts were able to be retained even in extremely dry mouths and that absorption of moisture into the gel occurred. It also seemed that for seven of the eight patients trialled, the insert was tolerated without discomfort. The potential efficacy of pilocarpine is variable, as actively increasing exocrine gland secretion is dependant on the degree of functional loss in the glands due to the autoimmune disease process. It was encouraging that even in patients with a zero Schirmer-I test result at the start of the trial, an increase in lacrimation was obtained, albeit small.

The study needs to be taken forward as a randomised controlled trial with sufficient numbers of patients to assess the efficacy of such a drug delivery system in patients with Sjögren's syndrome. The hydrogel buccal insert system could also be used to carry other drugs to be released in a similar controlled manner, a potential which surely needs investigation.

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