

Topical corticosteroids in dental practice

NW Savage,* MJ McCullough†

Abstract

Topical corticosteroids represent an important therapeutic aid in the management of a range of oral mucosal disease conditions. Like all medications, their successful use depends upon an understanding of the disease process. This includes an appropriate diagnosis, a clear view of the desirable treatment outcomes and knowledge of whether treatment is aimed at management of a chronic disease or enhanced resolution of a short-term condition. This paper reviews the use of topical corticosteroids and their possible roles in the management of oral disease.

Key words: Corticosteroids, oral ulceration.

Abbreviations and acronyms: GC = glucocorticosteroids; LP = Lichen Planus; RAU = Recurrent Aphthous Ulceration.

Aust Dent J 2005;50 Suppl 2:S40-S44

INTRODUCTION

Corticosteroids have been in regular clinical usage for a range of inflammatory and immune mediated conditions for over 50 years. Their initial recognition and subsequent development from coincidental clinical observations 80 years ago, leading to the award of the Nobel Prize in Medicine to Kendall, Reichstein and Hench in 1950, attests to the importance of these biologically active molecules both in physiological homeostasis and in clinical medicine.

The exact relationship between physiological and pathological situations continues to be elusive, even in the face of enormous advances in knowledge. A simplistic view, however, may be useful in trying to place the corticosteroids into a clinically useful context. The inflammatory response is a complex sequence of events activated following almost any noxious exposure to the body. The homeostatic objective is to limit damage and enhance healing with minimal resultant structural and functional morbidity. When the process runs successfully resolution of, for example, a traumatic ulcer of the oral mucosa, occurs within a short time span with minimal local tissue involvement and functional restriction. Most superficial traumatic ulcers heal uneventfully within two or three days.

When this process is disrupted disease ensues. In the mouth these are well represented by mucosal diseases including Recurrent Aphthous Ulceration (RAU) and

Lichen Planus (LP). RAU patients who develop a traumatic ulcer will very often not progress through a rapid healing phase. The process is frequently interrupted, leading to the development of a typical aphthous lesion. This lesion then goes on to resolve within the usual seven to ten days as the patient progresses through the defined clinical stages of an aphthous lesion, including the associated morbidity.

Similarly with LP, where trauma can solicit an exaggerated response due to the tissue atrophy and fragility inherent in the lichenoid tissue reaction. In the case of LP, there may be longer term sequelae, with the intrinsic reluctance of tissues affected by lichen to return to their pre-morbid status following resolution of a particular event.

Anti-inflammatory agents such as the glucocorticosteroids (GC) play a front-line role in the management of such conditions. Hydrocortisone is an endogenous agent which causes blood levels to spike during periods of stress. It plays a role in the modulation of the inflammatory reaction. It achieves this by inhibitory activity affecting almost all areas of inflammation by modulating production of mRNA and, thus, protein synthesis. There is an element of non-selectivity in this response, one reason why steroid usage is associated with a large group of unsolicited adverse reactions.

Glucocorticosteroids have both anti-inflammatory and immunosuppressive effects, although this separation is somewhat artificial. Both are seen most clearly with the systemic use of the agents, but there is potent activity in both areas with topical use. Importantly, there is a dramatic difference in the incidence of adverse reactions with topical use compared with systemic use, provided the GC are used with caution.

In conditions such as RAU and LP, the effects of GC both as anti-inflammatory agents and immunosuppressives can be exploited. In other situations such as trauma, both surgical and accidental, their use may also be beneficial. In the former, clinicians have the opportunity to pre-empt iatrogenic inflammation by the use of GC and so intercept some of the inflammatory sequelae of trauma. This translates readily to a reduction in patient morbidity and enhanced healing time.

General principles of use

The general principles of use of GC differ little from those of other medications and include the following considerations: (1) define the specific clinical problem; (2) arrive at a diagnosis if possible; (3) identify specific

*Associate Professor, Oral Pathology, Dental School, The University of Queensland.

†Associate Professor, Oral Medicine, School of Dental Science, The University of Melbourne.



Fig 1. A chronic traumatic ulceration caused by irritation against an adjacent tooth. Resolution of this type of ulcer will usually leave residual tissue changes.



Fig 3. Lichen Planus on the posterior buccal mucosa showing the typical reticular keratotic striae.

clinical goals and understand the tissue processes that require alteration to achieve these goals; (4) is medication likely to be helpful? How will the medication act? What is the specific target(s) of the agent?; and (5) what dosage is appropriate and how will response and compliance be monitored?

This leads directly to a second and equally important group of considerations. These are applicable generally as well as specifically to GC: (1) is treatment specific or non-specific?; (2) what is the anticipated treatment outcome – complete resolution and return to pre-morbid status, resolution but with residual tissue changes likely to persist in the medium term (Fig 1) or chronic disease management?; (3) can adverse reactions be anticipated and intercepted?; and (4) overall safety, including use in pregnancy.

Clinical use

Discussion thus far has raised two clinical scenarios, often occurring together, in which GC may be useful.

The first occurs when the condition is characterized by inflammation and the clinical progression is



Fig 2. A typical Minor Aphthous Ulcerative lesion with a regular outline, central umbilication and surface slough.

expected to be uncomplicated with full resolution. An example of this is traumatic ulceration. If the lesion is inflamed and oedematous GC may be helpful in truncating the clinical course.

The second is more complex and is characterized by mucosal disease with a visible inflammatory component but an underlying immunopathogenesis. Examples are RAU (Fig 2) and LP (Fig 3). Interestingly, these present two immunologically-driven scenarios but with very different expectations of the outcome. RAU is also very likely to have a strong genetic trait.

In RAU, the aim of treatment is to intercept the development of the ulcerative phase of the lesion by exploiting the broad-based immunosuppressive activity of GC. Patients are encouraged to apply the agent immediately the first prodromal awareness of a lesion presents, whether this is spontaneous or following local trauma. For established lesions the immunosuppressive activity of GC is also useful but the general anti-inflammatory activity is an additional bonus. The former will restrict the progression of the lesion whilst the latter will reduce the established inflammatory lesion and gradually improve patient comfort. The outcome is generally full resolution of the lesion with the development of any subsequent aphthae representing a further primary lesion. The general range of medium potency GC, for example betamethasone dipropionate, perform this function very successfully in the majority of patients.

LP presents a rather different clinical problem. It is typically defined as a chronic inflammatory skin/mucosal condition. In this case, GC may improve some components of the local tissue lesion, however the underlying and persistent immune mechanisms remain active. Therefore, treatment is not directed against the primary disease mechanisms. Nonetheless, the use of GC is generally the main strategy for management of most patients with LP. It is effective and a specific protocol can be developed for individual patients depending upon their disease category, severity, relapse rate and clinical responsiveness to GC. This may also

be extended to include the preventive use of GC in LP. In this situation, a clear understanding of the possible sequelae of long-term use is paramount and the patient should be an active participant in the development of such protocols.

It is important to remember that GC do not have an effect on the primary disease mechanisms. They are used in the minimization of both disease activity and clinical morbidity. Depending on the specific diagnosis and the incidence and severity of disease, they may also play a role in the development of preventive strategies. For example, in a patient with severe RAU, the cautious use of a steroid mouthrinse over an extended period may not only prevent exacerbations, but may provide the patient with an extended period of disease inactivity when the GC are ceased. Such usage, however, introduces a number of issues not usually encountered with short-term intermittent use. As a result, patients require careful monitoring for both local and systemic effects.

Adverse reactions

Possible adverse reactions include: secondary candidosis; nausea; oral use not tolerated; refractory response; mucosal atrophy; delayed healing; and systemic absorption.

Topical use of GC is generally very well tolerated. Given the high rate of commensal oral yeast carriage in the community it is expected that some patients will develop a secondary erythematous candidosis or pseudomembranous candidosis (thrush). Many of these patients can be identified prior to commencing GC and preventive treatment initiated coincident or immediately prior to the initial applications of the GC.

Common conditions likely to predispose to candidal overgrowth include: xerostomia; systemic and/or topical use of antibiotics; corticosteroid asthma inhalants; prostheses; and cigarette smoking.

Development of a candidosis causes: immediate interruption to treatment; prolonged and amplified morbidity; additional treatment for the infection; delayed management of the original condition; and clouding of the baseline pathosis present. Wherever possible, anticipation and prevention are preferable to a reactive response.

Denture hygiene management and correct use of asthma medications are usually all that is required. The xerostomic patient is more complex and consideration should be given to concurrent antifungal treatment and strategies to enhance salivary function, at least in the short-term.

Nausea is uncommon but is occasionally reported even with conservative topical use. Delayed healing is a frequently quoted adverse reaction but the depth of clinical experience now available indicates it is a rare clinical occurrence.

A refractory response may result from a number of areas including: poor patient compliance; inappropriate



Fig 4. Lichen Planus with marked tissue atrophy and fragility compounded by heavy use of topical corticosteroids over several years.

instruction and patient use; inappropriate application, for example, a carrier may be helpful for the gingiva; agent of insufficient potency; incorrect diagnosis; and failure to remove any local cause, for example, a corroded amalgam restoration causing a lichenoid stomatitis.

An incorrect diagnosis is of some concern and patients not responding within a few days should be reassessed and, preferably, referred for specialist evaluation. Conditions such as chronic ulcerative stomatitis are, by definition, not steroid responsive and require alternative therapy. Neoplastic change can also present in a clinically bland manner and always needs to be excluded as a possibility in non-responsive lesions.

Systemic absorption continues to be of some concern. There is always absorption of small amounts through the oral mucosa but clinical experience and laboratory studies have shown this not to be of clinical significance in almost all cases. Exceptions arise and this is an issue that should receive consideration with particular patient groups along with the occasional idiosyncratic response. Patients and conditions of which to be particularly aware include: diabetes; hypertension; tuberculosis; steroid mouthrinses; extensive area of coverage; and excessive and unmonitored usage.

Mucosal atrophy is a very real consideration both with prolonged use (Fig 4) and for patients who have mucosal atrophy as an intrinsic component of their condition, for example in LP (Fig 5). It is an issue that should be discussed with patients requiring prolonged use of GC so that an informed decision can be made in partnership with the patient. In some cases it is an undesirable consequence but one which has been anticipated given the need for clinical management of the mucosal condition. Fortunately, the normal passage of time will provide many patients with sustained remission and so atrophy, when it occurs, is more readily coped with. An example very familiar to oral medicine specialists is the patient with LP and a



Fig 5. Atrophic Lichen Planus with a central atrophic, erythematous zone and surrounding keratotic striae.

coincident lichenoid drug reaction, for example an anti-inflammatory used to manage the symptoms of severe arthritis (Fig 6). The need for the anti-inflammatory to ensure quality of life and the resultant flare of the LP is a complex scenario that requires some ingenuity to manage.

Use in children

As a general rule, steroids should be avoided in growing children. However, the child with recurrent severe aphthae would be poorly managed without addressing the individual lesions. Controlled and intermittent use of a medium potency GC is often the treatment of choice. Compliance and application require careful monitoring.

General guidelines for topical GC

Ensure there are no medical contra-indications; ensure there is no likely infectious component; be confident about the clinical diagnosis; select a mid-range GC for the oral mucosa; do not use on the facial skin or lips; provide detailed instructions, written if possible; monitor the amount used carefully; monitor the clinical response; monitor the development of adverse reactions; ensure full resolution or the anticipated goal of treatment; taper withdrawal to ensure recurrence is minimized; encourage short-term,



Fig 6. Drug-related Lichen Planus in a patient using a long-term systemic non-steroidal anti-inflammatory drug.

intermittent use rather than prolonged use; if high potency agents are used, change to a lower potency drug as soon as possible if treatment is likely to be prolonged; and obtain a second opinion if non-responsive.

Co-prescribing

Co-prescribing covers both proprietary and prescription medications. The proprietary medications are usually well known to patients with oral mucosal disease. Antiseptic/anaesthetic preparations provide immediate symptomatic relief of established lesions and their use on an 'as required' basis can reduce morbidity levels significantly. They will not, however, address the underlying disease process and, therefore, will not truncate the disease course. Co-prescription with GC addresses the latter issue and patients should understand the rationale of treatment and the expectations following use of both groups.

Co-prescription of GC with an antifungal agent has been addressed. It is noteworthy that the preventive use of agents such as nystatin and miconazole can be at a much reduced dosage, frequency and duration of treatment compared with treating an established infection. Their use, however, must be dictated by a specific clinical indication and they should not be used as a matter of routine. The azole antifungals may cause resistance in *Candida*.

The final medication is antibiotic mouthrinses, usually a tetracycline and less commonly amoxicillin. While there are some indications for the use of antibiotic mouthrinses, they are generally over-prescribed and their use is often without any specific scientific basis. There is no bacterial component in the cause of any of the common oral mucosal diseases and so prescribing to treat either a cause or so-called bacterial super-infection is inappropriate. If ulcerative lesions carry surface slough it is difficult to obtain close application of the GC to the lesion. Here, tetracycline rinses may be used to chemically debride the lesion prior to applying the GC. Apart from this and their use in herpetic and herpetiform lesions, there is little indication for their prescription and their use should therefore be occasional only. Clinicians should be very aware of the acidity of some of these agents to the extent they are readily capable of causing chemical erosion of dental hard tissues.

Intra-lesional corticosteroids

Intra-lesional corticosteroids are generally not recommended in general practice. Notwithstanding this, there is a very real place for this route of administration and its effectiveness makes it a powerful technique in the management of many patients with severe oral mucosal lesions and disease.

Agents in aqueous suspension, such as triamcinolone acetonide and methylprednisolone acetate, can be placed as superficial injections in small volume under local anaesthetic cover. The level of inflammatory and

immune activity in most oral disease is within the lamina propria, and to a lesser extent the superficial submucosa. It is in the former area that the agent is deposited. The lips should be approached with great caution to avoid the rare occurrence of either severe dermal atrophy or sclerosis. The technique is useful for managing both severe disease as well as chronic lesions that plateau and will not progress to a healing phase.

Topical corticosteroid prescriptions

These include: triamcinolone acetonide 0.1%, Kenalog in Orabase; hydrocortisone acetate 1% ointment; and betamethasone dipropionate 0.05% ointment.

When to refer

GC are a group of anti-inflammatory agents with broad-based therapeutic activity that can be used with confidence and the reasonable expectation that they will assist most patients with correctly diagnosed oral mucosal disease. The correct diagnosis is often the stumbling block, and the clinician must make an informed decision concerning the need to watch, treat or refer. If the latter path is chosen, the general practitioner still has an active role to play in patient management, particularly ensuring compliance and that the agents chosen are providing the desired clinical result.

CONCLUSION

GC can do much to decrease patient morbidity and for the general practitioner with an interest in oral

medicine they provide a very useful tool in the management of oral mucosal disease. As with all medications, it is implicit that the agents are prescribed with a full understanding of the likely tissue responses they are to intercept and that there is a defined endpoint. Is the treatment curative or part of ongoing management? Will the pre-morbid tissue status be returned or will the patient have a changed mucosa, at least in the short to medium term?

ADDITIONAL READING

1. Greenberg MS, Glick M, eds. *Burket's Oral Medicine. Diagnosis and Treatment*. 10th edn. Hamilton: BC Decker Inc, 2003.
2. Ellepola AN, Samaranayake LP. Inhalational and topical steroids, and oral candidosis: a mini review. *Oral Dis* 2001;7:211-216.
3. Pedersen A, Klausen B. Glucocorticosteroids and oral medicine. *J Oral Pathol* 1984;13:1-15.
4. Kalmar JR. Topical corticosteroids and oral vesiculo-erosive disease: where's the beef? *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;89:395-396.

Address for correspondence/reprints:
Associate Professor NW Savage
Oral Medicine
School of Dentistry
200 Turbot Street
Brisbane, Queensland 4000
Email: n.savage@uq.edu.au