

## Review: Steroids in Oral Mucosal Lesions

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**Abstract:** Glucocorticoids were first introduced in the 1940s and have become a widely prescribed class of drugs. Corticosteroids are widely used in the treatment of a large number of inflammatory and immunologically mediated diseases. The beneficial effects of systemic corticosteroids must be weighed against the probable risks associated with its use and are referred to as "double-edged sword" in the field of medicine.

**Keywords:** Corticosteroids, systemic, topical.

### I. Introduction:

Corticosteroids and their synthetic analogues are commonly used for their potent anti-inflammatory and immunosuppressive property in the management of diverse conditions associated with chronic inflammation and immune phenomenon (Kalkar *et al.*, 1982). The risks associated with corticosteroids parallel the benefits of their therapeutic power. Glucocorticoids have potent anti-inflammatory actions, including the reduction in the number and function of various immune cells, such as T and B lymphocytes, monocytes, neutrophils, and eosinophils, at sites of inflammation. Glucocorticoids decrease the production of cytokines, chemokines, and eicosanoids and enhances the production of macrophage migration inhibitory factor (Gibson 2004). This review article focuses on use of corticosteroids in oral mucosal lesions.

### II. Recurrent aphthous stomatitis

In RAU, the aim of treatment is to intercept the development of the ulcerative phase of the lesion exploiting the broad-based immunosuppressive activity of GC<sup>2</sup>. Glucocorticosteroids have no effect on the primary disease mechanisms but they are able to interfere with the inflammatory reactions as well as T & B lymphocyte functions. Therefore steroids can be used as palliatives in acute phases of the diseases or as longtime suppressors of general host defense<sup>5</sup>Topical corticosteroids: Most common topical steroids uses glucocorticoids such as hydrocortisone, triamcinolone, flucinonide, betamethasone and flumethasone.<sup>3,5</sup> Triamcinolone acetonide is used at concentrations ranging from 0.05-0.5%, applied 3-10 times a day during 3-5 minutes.<sup>11</sup> It is particularly indicated in patients with small and mild erosive lesions. Some consider the most effective concentration to be 0.1%.<sup>11</sup> 0.05% Clobetasol propionate (topical) is applied on adhesive denture paste which reduces the healing time in most patients.<sup>6</sup> Hydrocortisone hemisuccinate (pellets of 2.5 mg) and triamcinolone acetonide (adhesive paste containing 0.1% of the steroid). Gel, pellets, and pastes can be applied directly to the lesion post meals and at bedtime twice or thrice a day or mixed with an adhesive such as orabase before application.<sup>7</sup> Fluocinolone acetonide at a concentration of 0.025-0.05%, applied 5-10 times a day during 3-5 minutes, affords medium to high potency, and is widely used in patients with more aggressive lesions.<sup>11</sup> Lastly, 0.025% clobetasol propionate is the most potent topical corticosteroid, and is therefore reserved for moderate or severe disease presentations.<sup>11</sup> Ulcerations that are located in the areas which are inaccessible can be controlled by topical dexamethasone elixir, 0.5 mg/5 ml held over the area or applied with a saturated gauge pad to the ulcers, 4 times/day for 15 min or betamethasone sodium phosphate rinse by dissolving 0.5 mg in 5 ml of water and asking the patient to rinse for 2-3 min, steroid aerosol (e.g., beclometasone dipropionate), or a high-potency topical corticosteroid, such as clobetasol 0.05% in orabase or fluocinonide 0.05%, in orabase.<sup>7</sup>

Systemic corticosteroid are usually used as rescue therapy in patients with acute severe RAS outbreaks with initial dose of oral prednisone 25 mg / day and stepwise dose reduction for 2 months shows disappearance of the pain and reepithelization of the lesions in the first month of therapy.<sup>11</sup> In severe cases systemic prednisolone is used with a 2 weeks of dose starting with 60mg and has showed excellent results.<sup>3</sup>

Glucocorticoid injection

Triamcinolone diacetate - 25 mg/ml

Betamethasone sodium phosphate - 6 mg/ml.<sup>10</sup>

### III. Oral Submucous Fibrosis:

Steroids inhibit the proliferation of fibroblasts and this cause reduction in the number of collagen fibres. They also act to release cellular proteases in the connective tissue extracellular compartment which in turn activate the collagens and zymogen that ingest the insoluble collagen stimulating the rate of collagen breakdown. They also act by inhibiting the inflammatory response.<sup>13</sup> Local injections consisting of a combination of Dexamethasone, Hyaluronidase and Chymotrypsin biweekly for 2-3 weeks is used depending on the severity of the condition. Usually the combination are: Biweekly submucosal injections of a combination of dexamethasone (4mg/ml) and two parts of hyaluronidase diluted in 1.0 ml of 2% xylocaine by means of a 27 gauge needle, not more than 0.2ml solution per site, for a period of 20 weeks or Injections of triamcinolone 10mg/ml diluted in 1 ml of 2% lidocaine with hyaluronidase 1500 IU, biweekly for 4 weeks (Gupta & Sharma, 1988).<sup>6</sup> Systemic Prednisone is administered systemically as 30 -40mg/day for 2-4 weeks and gradually tapered. Significant relief of burning sensation and improvement of trismus is seen in most patients.<sup>6</sup> A Therapy with hydrocortisone 25 mg tablet, in doses of 100mg/day is useful in relieving burning sensation. This is supplemented with local injection of hydrocortisone 25mg at biweekly intervals at the affected site. Increased vascularity of the site is observed, which is due to fibrinolytic, anti-allergic and anti-inflammatory action of corticosteroid.<sup>12</sup>

### IV. Oral lichen planus

The benefit of steroids to some extent can be explained by the anti-immunologic properties with suppressed T cell functions and decreased IgG synthesis.<sup>5</sup> With the suppressed inflammation, tissue destruction is lowered and a minimum of antigen released.<sup>5</sup> Steroids thereby, interrupt a vicious cycle.<sup>5</sup> Topical corticosteroids are the main stay in treating mild to moderately symptomatic Lesions.<sup>9</sup> Options (in order of decreasing potency) include 0.05% clobetasol propionate gel, 0.1-0.05% betamethasone valerate gel, 0.05% fluocinonide gel, 0.05% clobetasol ointment or cream, and 0.1% triamcinolone acetonide ointment.<sup>7,9</sup> Clobetasol propionate in the form of orabase oraqueous solution can be used at a concentration of 0.025-0.05% for 2-3 times a day applied for 3-5 minutes.<sup>8</sup> A gingival tray can also be used to deliver 0.05% clobetasol propionate with 1,00,000 IU/ml of Nystatin in orabase<sup>1</sup>. Around 3 to 5 minute application of this mixture daily appears to be effective in controlling erosive lichen planus<sup>1</sup>. Flucinonide is corticosteroid used at concentration of 0.025-0.05% for 5-10 times a day for 3-5 minutes erosive, bullous or ulcerative lesions of lichen planus.<sup>8,1</sup> Triamcinolone acetonide, is one among most commonly used topical corticosteroids which is used at concentration between 0.05%-0.5% for 3-10 times a day applied for 3-5 minutes.<sup>8</sup> High-potency steroid mouthwashes such as disodium betamethasone phosphate or clobetasol propionate, can be used in widespread oral LP but these may cause a significant systemic absorption leading to a pituitary- adrenal axis suppression.<sup>9</sup>

Systemic corticosteroid: The atrophic erosive type of oral lichen planus can be treated systematically with prednisone (50 mg/day), in combination with clobetasol ointment in an adhesive form along with antimycotics.<sup>3</sup> Systemic corticosteroids are used for recalcitrant erosive or erythematous lichen planus where topical therapy has not been effective.<sup>7</sup> Systemic prednisolone is the drug of choice, but should be employed at the lowest possible dose for the least duration (40-80 mg for 5-7 days).<sup>7,9</sup> It can be used to control the erythema and ulcers in OLP.<sup>7</sup> The oral dose of prednisone is in the range of 10-20 mg/day for moderately severe cases to as high as 35 mg/day (0.5 mg/kg daily) for extreme cases.<sup>7,9</sup> Intralesional corticosteroids injection for recalcitrant or extensive lesions involves the subcutaneous injection of 0.2-0.4 ml of a 10 mg/ml solution of triamcinolone acetonide via a 1.0 ml 23- or a 25-gauge tuberculin syringe.<sup>7,9</sup> Intralesional triamcinolone acetonide in doses of 0.5-1 ml of a 1 mg/ml suspension in the form of bi-weekly injections, or even 3-4 times a week in more severe cases can be used for the treatment of erosions.<sup>7</sup> Intralesional injection of triamcinolone acetonide (10-20 mg) or short-term regimens of 40 mg of prednisone daily for 5 days, followed by 10 to 20 mg daily for an additional 2 weeks, have also been used in most severe cases.<sup>1</sup>

### V. Mucous membrane pemphigoid:

Mucous membrane pemphigoid is a rare chronic blistering condition of the mouth, eyes and genitals and, rarely, the skin<sup>1</sup>. Topical steroids: Mild oral lesions should be managed with topical and intralesional steroids. Desquamative gingivitis can often be managed with topical steroids in soft dental splint covering the gingiva.<sup>7</sup> Fluocinonide (0.05%) and clobetasol propionate (0.05%) in an adhesive vehicle can be used three times a day for up to 6 months. In patients with lesions confined to oral mucosa, triamcinolone acetonide 0.1%, flucinolone acetonide 0.05%, clobetasol propionate 0.05% orabase for 3-4 times a day applied for 9-24 weeks to resolve the lesion.<sup>8</sup> Systemic corticosteroid: Systemic therapy of mucous membrane pemphigoid prednisone is usually given at a dose of 1 to 1.5 mg/kg/day, with appropriate monitoring for side effects.<sup>14</sup> To stop new bullae formation, Prednisolone is given as 30-80 mg /day for 2-3 weeks and tapered by 20% every 2-3 weeks until the

dose of 10 mg is reached and then dose maintained on alternate days and reduced by 5 mg every 2 weeks, then stopped.<sup>6</sup>

## VI. Pemphigus:

The initial aim of treatment is to induce disease remission. This should be followed by a period of maintenance treatment using the minimum drug doses required for disease control in order to minimize their side-effects.<sup>21</sup> Topical corticosteroids can be given to maintain remission, allowing reduction in systemic dose.<sup>4</sup> In patients with no progressing oral lesions, moderate to high potency topical corticosteroids are recommended, applied 2-3 times a day, such as 0.05% fluocinolone acetonide or 0.05% clobetasol propionate.<sup>9</sup> Systemic administration of corticosteroids at doses of 1-2 mg/kg/day is effective for principal treatment of pemphigus vulgaris.<sup>4</sup> Injectable corticosteroids: Isolated lesions can be treated with injectable corticosteroids.<sup>4</sup> Intralesional corticosteroid therapy accelerates the scarring process of a lesion or is used to treat persistent lesions.<sup>9</sup> Sublesional injections given every 7 to 15 days; treatment is stopped after 3 injections if there is no improvement.<sup>9</sup> To minimize iatrogenic effects, Lever and Schaumburg recommended a treatment called the "high Lever scheme" with very high loading doses (100–175 mg taken twice daily for 5–10 weeks), followed by the "low Lever scheme," which includes a rapid reduction in dosage over a few weeks, with a maintenance dose of 40 mg every 2 days accompanied by local adjuvant treatment (Lever 1984).<sup>9</sup> A tailored dosing schedule has been advocated according to disease severity and a modified regimen is suggested here.<sup>22</sup> Patients with mild disease are treated with initial prednisolone doses of 40–60 mg/day and in more severe cases, 60–100 mg/day.<sup>22</sup> If there is no response within 5–7 days, the dose should be increased in 50–100% increments until there is disease control, i.e. no new lesions and healing of existing ones.<sup>22</sup> If doses above 100 mg/day are required, pulsed intravenous CS could be considered.<sup>22</sup> This refers to the intermittent administration of high doses of intravenous CS, usually methylprednisolone (250–1000 mg) or equivalent doses of dexamethasone given on one to five consecutive days.<sup>22</sup> The theoretical aims of pulsing are to achieve more rapid and effective disease control compared with conventional oral dosing, thus allowing a reduction in long-term maintenance CS doses and CS side-effects.<sup>22</sup> Pulsed CS could be considered in severe or recalcitrant PV to induce remission, particularly if there has been no response to high oral doses.<sup>22</sup> Once remission is induced and maintained with healing of the majority of lesions, the dose of CS can be cautiously tapered.<sup>22</sup> A 50% reduction every 2 weeks has been suggested.<sup>22</sup> Pulsed intravenous corticosteroids has yet to be demonstrated conclusively.<sup>22</sup> Triamcinolone acetonide, diluted to 5–10 mg/mL, may be used for intralesional injections of cutaneous lesions. A higher concentration, 10–20 mg/mL, is recommended for intraoral lesions. Multiple injections may be necessary for large lesions. The injections should be administered at weekly or biweekly intervals until complete resolution of the lesions is achieved.<sup>5</sup>

**Bullous pemphigoid:** Potent topical corticosteroids should be the treatment of choice in patients with limited or moderate disease.<sup>3</sup> Systemic corticosteroids: Patients with severe diseases require use of systemic corticosteroids alone or combined with immunosuppressive drugs.<sup>5</sup> Recommended initial doses of prednisolone are 20 mg/day or 0.3 mg/kg/day in localised or mild disease, 40 mg/day or 0.6 mg/kg/day in moderate disease, and 50–70 mg or 0.75–1 mg/kg/day in severe disease.<sup>9</sup> Intralesional corticosteroids: Intralesional triamcinolone acetonide 3–10 mg per ml can be administered to resistant lesions.<sup>9</sup> Experience in injecting correctly is necessary to maximise efficacy and minimise atrophy.<sup>9</sup>

**Systemic lupus erythematosus:** The goals of SLE management are based on prevention, reversal of inflammation, maintaining states of remission and alleviation of symptoms. Avoidance of flare-ups of lupus and skin lesions consists of protection from ultraviolet sunlight.<sup>20</sup>

Topical steroids: are the mainstay of treatment of DLE.<sup>9</sup> Patients usually start with a potent topical steroid (e.g., betamethasone or clobetasol) applied twice a day, then switch to a lower-potency steroid as soon as possible.<sup>9</sup> Oral ulcerations of systemic lupus erythematosus are transient, occurring with acute lupus flares.<sup>9</sup> The minimal use of steroids reduces the recognized side effects like atrophy, telengiaectasiae, striae, and purpura.<sup>9</sup> Symptomatic lesions can be treated with high potency topical corticoids or intralesional steroid injections.<sup>9</sup>

Systemic corticosteroids: Systemically low dose prednisone 10–20 mg/day or an alternate day dose of 20–40 mg may be needed.<sup>9</sup> Intralesional corticosteroids: Intralesional injection of corticosteroids, triamcinolone acetonide 3 mg/mL is useful as adjunctive therapy for individual lesions.<sup>9</sup>

**Erythema multiforme:** Systemic steroids have been suggested as adjuvant therapy based on their immunosuppressant effects.<sup>18</sup> They suppress cytokine and chemokine response, as well as T cell function, and decrease adhesion of inflammatory molecules to blood vessel endothelium.<sup>18</sup> To date, their use has been limited to EM major, as EM minor is self-limited.<sup>18</sup>

Topical steroids: Adhesive paste (Orabase) form of clobetasol propionate, the most potent topical corticosteroid is a safe and efficacious alternative to systemic therapy in erosive oral lesions.<sup>9</sup> Mouthwashes of clobetasol propionate in aqueous solution provides ready access to all lesional areas, and there is excellent control over the contact time between drug and lesion.<sup>9</sup>

Systemic corticosteroid: Early therapy begins with systemic prednisone (0.5 to 1.0 mg/kg/day) or pulse methylprednisolone (1 mg/kg/day for 3 days) has shown to be very effective. Intravenous (IV) pulsed dose methylprednisolone (3 consecutive daily infusions of 20 to 30 mg/kg to a maximum of 500 mg given over 2 to 3 hours) has also been reported, with the suggestion that this approach is superior to oral prednisone because the greatest benefit is seen when treatment is administered as early as possible in the progression of the cutaneous insult.<sup>1,3,19</sup> Prednisone may be used in patients with many lesions at dosages of 40 to 80 mg per day for one to two weeks then tapered rapidly.<sup>17</sup> Dexamethasone pulse therapy (1.5 mg/kg IV over 30 to 60 minutes on 3 consecutive days) to avoid long-term use of systemic corticosteroids.<sup>9</sup>

**Mucocele:** Oral mucoceles are common lesions of the oral mucosa, very often arising from the rupture of a minor salivary gland duct with subsequent extravasations of mucus into surrounding soft tissue. Clinically they are seen as a soft, painless, translucent bluish swelling occurring most frequently on the lower labial mucosa.<sup>16</sup> Injection of dexamethasone is a simple, repeatable, cost effective and potentially curative method of treatment, and can be used as the first choice or substitute for surgery in the treatment of salivary mucocele.<sup>15</sup>

**Behcet disease:** Behcet's disease (BD) is a chronic, relapsing, and debilitating systemic vasculitis of unknown aetiology with the clinical features of mucocutaneous lesions, ocular, vascular, articular, neurologic, gastrointestinal, urogenital, and pulmonary involvement.<sup>21</sup> Topical corticosteroids suppress the inflammation associated with the formation of aphthae, and are effective when they are used in the early stage of the lesion.<sup>21</sup> Triamcinolone acetonide as cream 0.1% in Orabase or spray, prednisolone tablets in 20mL water as rinse four times daily like those of dexamethasone elixir (0.5 mg/5 mL) can be used for oral ulcers. Major oral ulcers can be treated by intralesional triamcinolone, 5–10mg/mL.<sup>21</sup>

## VII. Conclusion

Corticosteroid drugs are widely used in oral medicine. Topical corticosteroids should be considered the treatment of choice unless the disease is very extensive. Systemic therapy is reserved for those with severe, refractory disease.<sup>23</sup>

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