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A REVIEW ON INTRALESIONAL CORTICOSTEROID INJECTION AS AN EFFECTIVE TREATMENT METHOD FOR ORAL LESIONS

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ABSTRACT
Many lesions of the oral region are treated with surgical methods such as curettage and resection. Chemotherapy and radiation therapy with or without surgical intervention can be used as an adjunct in some cases. Corticosteroids are one of the most widely used drugs due to their anti-inflammatory, anti-allergic and immunosuppressive effects. Today they are used as systemic, topical, intra-articular and intralesional in the clinic. Intralesional steroid injection is a conservative procedure which is already used in various part of body and oral lesions. It is one of the main methods used for treating a wide range of lesions. It also results in a high concentration of drugs at lesion sites, with minimal systemic absorption. The intralesional corticosteroid injection could be one of the effective therapeutic methods with no significant problems in many oral lesions such as inflammatory, immunologic, and vascular ones due to its higher therapeutic effects than other topical forms of steroids and fewer side effects than systemic corticosteroid.

KEYWORDS: Intralesional corticosteroid injections, oral lesions.

INTRODUCTION
Corticosteroids are one of the most widely used drugs due to their anti-inflammatory, anti-allergic and immunosuppressive effects. Today they are used as systemic, topical, intra-articular and intralesional in the clinic. They were first used systemically in a patient with severe rheumatoid arthritis in 1948 by Hench et al.[1] Intralesional corticosteroid injection (ICSI), introduced as a medical treatment in 1951, has become one of the main methods used alone or in combination with other procedures for treating a wide range of diseases as well as benign and malignant proliferations in the head and the neck.

Beneficial effects of intra-articular corticosteroid (hydrocortisone acetate) injection was first published in 1951.[2] In 1956, prednisolone was introduced by Rothermich and Phillips,[3] as a satisfactory and more potent alternative for intra-articular injections. Boland and Liddle,[4] compared methylprednisolone with prednisolone and found them equally effective. Triamcinolone acetonide was applied in the treatment of dermatoses by Robinson,[5] in 1958. Later, triamcinolone hexacetonide was reported to be a potent synthetic corticosteroid for intra-articular usage.[6] In the 1970s, corticosteroids were administered in intra-osseous lesions such as bone cysts.[7,8]

Intralesional steroid injection (ISI) has been performed in both of bone and mucosal lesions of oral and maxillofacial region since 1980. Currently, this method is widely accepted as an alternative or aid to surgical treatment especially in large reactive lesions. The ICSI leads to a high concentration of drugs at lesion sites, with minimal systemic absorption; therefore, it has no common side effects of systemic form or even reduces them. The ICSI is preferable to the topical corticosteroids such as creams, ointments, mouthwashes, gels, and foams due to bypassing of mucous membranes, reduced risk of mucosal atrophy, higher drug concentrations, and longer durability in lesion sites.[9]

ORAL LESIONS TREATED WITH INTRALESIONAL INJECTIONS

Haemangioma
Haemangiomas, also known as haemangiomas of infancy or infantile haemangiomas (IH), are the most common benign tumour of infancy.[10] They are often called "strawberry marks" due to their clinical appearance. Infantile haemangiomas (IHs), the most common benign tumour of infancy, occur in about 10% of infants. Although they occur in 8%–12% of new-borns, this prevalence rate can reach 22% in premature babies. There is marked predominance of female cases.

Classically, IHs appear shortly after birth as a light pink telangiectatic macule. They have a natural history of rapid growth during the first year of life, followed by a slow spontaneous regression phase after 12–18 months. Approximately 70% of haemangiomas regress completely by the age of 7. IHS that do not regress by the sixth year of life will develop residual abnormalities, the most common of which are telangiectasia, atrophic wrinkling, yellowish discoloration, redundant skin, scarring, and alopecia.[11] Most infantile haemangiomas do not require treatment because they resolve on their own, although complicated infantile haemangiomas require treatment and recently, beta blockers such as oral propranolol (2mg/kg/day) have been shown to be effective as first line therapy. However, the side effect profile of propanolol includes bradycardia, hypotension, bronchospasm, and hypoglycemia. Oral prednisone (2-4mg/kg/day) is an alternative therapy that can be used.[11] The high dose of prednisone would have to be slowly tapered over weeks to months. Prednisone's adverse reactions would include irritability, sleep disturbance, hypertension, bone demineralization, cardiomyopathy, and growth retardation.

Local steroid injection for treatment of haemangiomas was first described by Kushner in 1982 and has been used because of fewer side effects compared with systemic corticosteroids.[12] Several authors reported successful treatment of haemangiomas with intralesional steroid therapy. Gangopadhyay et al. reported that response rate was 88.6% with administration of intralesional triamcinolone and no side effects occurred.[13]

Pyogenic Granuloma

Pyogenic granuloma is a relatively common benign mucocutaneous lesion. The term is a misnomer as the lesion neither contains pus nor it is granulomatous. It was originally described in 1897 by two French surgeons, Poncet and Dor,[14] The most common intraoral site is marginal gingiva, but lesions have been reported on palate, buccal mucosa, tongue, and lips. Extraoral sites commonly involve the skin of face, neck, upper and lower extremities, and mucous membrane of nose and eyelids.[15] Oral pyogenic granulomas show a striking predilection for the gingiva, which accounts for 75% of all cases. Gingival irritation and inflammation that result from poor oral hygiene may be a precipitating factor in many patients. The lip, tongue, and buccal mucosa are the next most common sites.[16] It has been reported in the literature that intralesional injection of triamcinolone acetonide 15mg/ml mixed with adrenaline, once every 3 weeks for 4 times, the lesion gradually decreased in size and after 4th visit the lesion was cured up to 90%.

Central Giant Cell Granuloma

The central giant cell granuloma (CGCG) was first described by Jaffe in 1953. CGCG occurs almost solely within the jaws and it is a benign proliferation of fibroblasts and multinucleated giant cells. It typically presents as a solitary radiolucent lesion of the mandible or maxilla. The lesions occur twice as often in the mandible than in the maxilla and is predominantly found in young adults before the age 30 with a female preponderance.[17] Based on its clinical behaviour, CGCG has been classified as non-aggressive and aggressive lesion, where non-aggressive lesions tend to grow slowly and do not perforate the cortical bone. Aggressive lesions are characterized by rapid growth, pain, expansion or perforation of the cortical bone, root resorption, and a high recurrence tendency.[18]

The treatment of CGCG with corticosteroids was first reported by Jacoway et al in 1988. They suggested is a 50/50 mixture of 2% lidocaine with 1:100000 epinephrine and triamcinolone acetonide (TA) to inject 2 mL/1 cm of lesion and to repeat this six times at weekly intervals. Later, Terry and Jacoway presented four patients treated with steroids in 1994. A weekly done intralesional injections during six weeks resulted in a complete resolution in three patients, while one patient needed additional surgery. Nogueira et al,[19] contributed to literature with 21 new cases in 2010 using ISI with triamcinolone hex acetonide. Two patients did not respond to the treatment and surgical resection was needed; a moderate improvement noted in four patients (curettage in two patients) and 15 of the cases showed good response.

Oral Submucous Fibrosis

Oral submucous fibrosis (OSF) is a chronic disease of the oral mucosa. It affects the pharynx, oral cavity, upper third of the oesophagus and it is characterized by inflammation and a progressive fibrosis of sub-epithelial tissues. Connective tissue fibres of the lamina propria and deeper parts change, which in turn lead to mucosal stiffness and limitation in mouth opening.[20] OSF is considered as high-risk precancerous disease,[20,21] Several factors contributing to OSF include general nutritional or vitamin deficiencies and hypersensitivity to various dietary constituents. The primary factor appears to be chewing of the areca (betel) nut. Genetic factors are thought to be involved in the aetiology. The potential morbidities of OSF are restriction of mouth opening, difficulty with swallowing, mastication, speech, and a burning sensation as well. It has a mortality potential because of the possibility of transformation into squamous cell carcinoma.[21] Nonsurgical options are Intralesional steroid injections, hyaluronidase and interferon gamma. Surgery primarily targets to improve the mouth opening and comprises the excision of the fibrous bands, skin grafts and splitting of the temporalis tendon. A study conducted in 2015 concluded that administration of intralesional injection of dexamethasone1.5 ml, hyaluronidase 1500 IU with 0.5 ml lignocaine HCL injected intra lesionally twice weekly for 4 weeks. Improvement in the patient's mouth opening with a net gain of 6 ± 2 mm (92%), the range being 4-8 mm. Definite reduction in burning sensation, painful

ulceration and blanching of oral mucosa and patient followed up for an average of 9 months.[20]

Oral Lichen Planus

Oral lichen planus (OLP) is a chronic mucocutaneous disease of unknown cause, with oral lesions occurring most commonly in women over 30 years of age. The most common type is the reticular form which is characterized by numerous interlacing white keratotic lines or striae that produce an annular or lacy pattern.[17,22] Patients complain of pain, burning, sensitivity and generalized discomfort in particularly erosive and atrophic types. Patients with reticular and other asymptomatic OLP lesions usually require no active treatment but symptomatic lesions may also need treatment. Nonsurgical treatments are systemic drug therapy, topical corticosteroids-calcineurin inhibitors - retinoids, injection of steroids and ultraviolet irradiation. The other methods are surgery, laser therapy and cryosurgery.[22]

An aqueous TA suspension is suitable for intralesional injection, which aims to achieve a sufficiently high steroid concentration locally and remains at the injection site for a longer period of time.[22] The beneficial effect of a local steroid injection on OLP has been suggested in the recent literature. Approximately 2 to 20 mg of TA at slightly different concentrations (20 to 40 mg/mL) has been shown to be effective.[23]

Temporomandibular Disorder (TMD)

Temporomandibular disorders (TMD) are a wide group of pathologies that affect the temporomandibular joint (TMJ) and its adjoining structures. They are characterised mainly by pain, decreased range of motion and joint noise.[24] Disorders of the TMJ include extra and intracapsular disorders. Extracapsular disorders affect the structures surrounding the TMJ, while intracapsular or internal disorders of the TMJ affect the structures inside it. Internal TMJ disorders are present in approximately 80% of patients with symptomatic TMD, where inflammatory and nociceptive mediators are present in the synovial fluid of these joints.

The treatment of internal TMJ disorders can range from conservative, minimally invasive and invasive therapies. Among the minimally invasive therapies, we find the intra-articular infiltration of substances, such as corticosteroids, hyaluronic acid (HA) and platelet- rich plasma, accompanied or not by an arthrocentesis.[25] 0.5–1 mL of intra- articular corticosteroids with lidocaine in the treatment of internal TMJ disorders, such as triamcinolone, betamethasone, dexamethasone, hydrocortisone, methylprednisolone. results suggest that there is a significant improvement in active mouth opening after TMJ injection plus manual mobilization and that TMJ injection with corticosteroid and local anaesthetic.[26]

Mucoceles

Mucoceles are most common benign lesions of the oral cavity developing as a result of retention or extravasation of mucus material from the minor salivary glands. Mucoceles are broadly classified into two types: extravasation and retention type. Extravasation mucocele results from a traumatized salivary gland duct with consequent spillage into the soft tissues around the gland whereas retention type appears due to a decrease or absence of glandular secretion produced by blockage of the salivary gland ducts.[27] They are benign soft tissue masses clinically characterized by single, painless, soft, smooth, spherical, and translucent and fluctuant nodule, which is usually asymptomatic.

There are various treatment modalities which include surgery, laser ablation, cryosurgery, sclerotherapy, micro-marsupialization, laser surgery, and intralesional injection of sclerosing agent or corticosteroid.[28] 1 mL of betamethasone (4 mg/1 mL) was slowly injected by insulin syringe. Mortazavi et al. (2014) reported a large labial mucocele treated with combined intralesional dexamethasone and micro-marsupialization which led to complete healing.[29]

Mucous Membrane Pemphigoid

Mucous membrane pemphigoid (MMP) is a heterogeneous group of chronic, autoimmune subepithelial blistering diseases which predominantly involves the mucous membranes and occasionally the skin. In vivo, it is characterized by linear deposition of IgG, IgA, or C3 along the epithelial basement membrane zone.[30] Oral lesions usually involve the palate and gingival areas, and also on labial, tongue, and buccal mucosa. The lesions manifest as erythema, erosions, pseudomembrane, and sometimes intact blisters. The common ocular lesions are conjunctival inflammation and erosions, fornices shortening, corneal neovascularization and scarring.

Management includes topical, intralesional and systemic. High-potency topical corticosteroids remain the mainstay of treatment. Typically, prescribed agents include fluocinonide, clobetasol propionate and betamethasone dipropionate. Desquamative gingival lesions may be managed effectively with the application of gel based topical corticosteroids to the lesion. Intralesional corticosteroids are useful for treating recalcitrant lesions or as an adjunct to topical steroid delivery. Intralesional injections usually result in accelerated healing. Multiple site injection should be performed to distribute the steroid throughout the lesion. For the oral cavity 0.1 cc/cm2 triamcinalone 10mg/ml may be used with improved results.[30]

When topical or intralesional therapies prove ineffective, or if there is involvement of the eyes, throat, or esophagus (“high-risk” patients), systemic medications are mandatory. Tetracycline (1500–2000 mg/day) or minocycline (50–100 mg/day) Dapsone: Initial dose of

50mg/day, increase by 25 mg every 7 days to 100–200 mg/day as needed and tolerated. Corticosteroids: Prednisone 0.5–1.0 mg/kg/day.[30]

Recurrent Apthous Stomatitis

Recurrent aphthous stomatitis (RAS) is characterized by the appearance of initially necrotic ulcers, with well-defined limits surrounded by an erythematous halo. The lesions are located on the oral mucosa, but are infrequent on the gums.[31] RAS is the most frequent chronic disease of the oral cavity, affecting 5-25% of the population.[32] It is more common in patients between 10-40 years of age, and predominantly affects women and individuals of higher socioeconomic levels. The underlying aetiology is not clear, though a series of factors are known to predispose to the appearance of oral aphthae, including genetic factors, food allergens, local trauma, endocrine alterations (menstrual cycle), stress and anxiety, smoking cessation, certain chemical products and microbial agents.[31]

As regards the clinical manifestations, the basic lesion is a recurrent, painful, rounded or oval ulcer with a necrotic base. Treatment used is multifocal and varies according to the predisposing factors. In all cases management is symptomatic, and seeks to reduce inflammation of the aphthae and afford pain relief by administering topical or systemic treatments.[31,32] Antiseptics, anti-inflammatory and analgesic. Antibiotics (doxycycline gel), topical corticosteroids (triamcinolone acetonide 0.05-0.5% 3-10 v/day), Hyaluronic acid, topical anaesthetic. Intralesional steroid injection reduces the symptoms, the course of the disease, and the period of normal mucus repair; but it does not affect the rate and the frequency of its recurrence.

Pemphigus

Pemphigus diseases are a group of rare autoimmune bullous diseases that affects the skin and mucous membranes. They originate from the production of pathogenic autoantibodies (usually of the IgG class) directed against different proteins of desmosomes (desmogleins).[33] The union of these autoantibodies to the components of the desmosomes compromises intraepidermal adhesion, leading to acantholysis and formation of vesicles, blisters, and erosions on the skin and/or mucous membranes. The main forms are pemphigus vulgaris (PV) and pemphigus foliaceus (PF). The clinical manifestation of PV may present mucosal or mucocutaneous involvement. Oral lesions are characterized by painful erosions; blisters are rarely intact, probably because they are fragile and break easily. The most affected areas are the buccal and palatine mucosa, lips, and gingivae. The erosions are multiple and present in different sizes and irregular shapes; they extend peripherally and there is usually a delay in re-epithelization. Cutaneous lesions have flaccid blisters of clear content on normal or erythematous skin. The blisters break easily, resulting in painful erosions that bleed easily.[34]

The primary treatment of these lesions is using the systemic corticosteroid, which can be employed in combination with immunosuppressive drugs. The intralesional steroid injections in these lesions is not recommended during relapse/flare periods due to inadequate effects. It seems that the given method is the most effective one in the maintenance phase; as more than 70% of the lesions are improved and the systemic corticosteroid is getting tapered.[35] In this respect, a study in 2018 demonstrated that the ICSI in combination with immunosuppressive drugs could lead to reduced dose of corticosteroids and shortened time of clinical improvements.[36]

Trigeminal Neuralgia

Trigeminal neuralgia (TN) is defined as sudden, severe, brief, stabbing, and recurrent pain within the distribution of one or more branches of the trigeminal nerve.[37] TN is characterized by episodes of spontaneous pain or a triggered intense facial pain that last for short duration. Pain may be like stabbing, electric shocks, burning, pressing, crushing, exploding, shooting, boring, shock‑like sensations, migraine like, piercing, prickling, or a combination.

Carbamazepine (CBZ) is drug of choice in TN; baclofen, lamotrigine, clonazepam, oxcarbazepine, topiramate, phenytoin, gabapentin, pregabalin, and sodium valproate can be used. Intravenous infusion of a combination of magnesium and lidocaine can be very effective in some patients.[37] Five percent lidocaine plaster,[38] and 8% capsaicin patch can be useful in some TN. Tetracaine nerve block as an additional treatment after CBZ, acupuncture and peripheral nerve stimulation can be used. The intralesional corticosteroids is one of the proposed therapies in this painful disorder particularly in the trigger point of pain or involved neural branch blocks.[39]

OTHER USES

In addition to the above-mentioned applications of the intralesional steroid injections for the treatment of intraoral lesions, corticosteroid injection is further employed in other dental conditions; e.g., controlling postoperative pain and swelling, increasing teeth movements in orthodontic treatments, and preventing oesophageal stenosis after endoscopic dissection and joint stiffness after trauma.[40]

CONCLUSION

Intralesional corticosteroid injections is one of the most preferable non-surgical methods for the treatment of many oral lesions such as inflammatory, immunologic, and vascular disorders. It can also have higher therapeutic effects than other topical forms of steroids and fewer side effects than systemic corticosteroids. Various studies suggest that intralesional corticosteroid injection is well tolerated by patients, the probability of postoperative complications is less than those of other methods and patient complaints diminish rapidly,

especially in large lesions, it can be applied as an alternative or adjunct to surgical procedures. Intralesional corticosteroid injections are scarcely invasive and relatively inexpensive.

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