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Treatment of Oral Lichen Planus with Intra-lesional Steroid Injection: Comprehensive Overview

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Abstract

Background:Oral lichen planus is a T-cell-mediated chronic inflammatory oral mucosal disease of unknown etiology. These lesions contain few B-cells or plasma cells and minimal deposits of immunoglobulin or complement. There are no consistent serological changes associated with OLP.It predominantly occurs in adults older than 40 years, although younger adults and children can be affected. It affects women more than men in a ratio of 1.4:1. The disease affects 1-2% of the population and there is no racial predilection.It presents as white striations, white papules, white plaques, erythema, erosions, or blisters affecting predominantly the buccal mucosa, tongue, and gingivae and it is the most common non-infectious oral mucosal disease in patients referred to oral medicine and oral pathology clinics.Lesions are usually bilateral, and atrophic and erosive lesions are often sensitive or painful. There may be co-incident skin lesions that present typically as flat-topped violaceous papules affecting the wrists, ankles, and genitalia. There is ongoing concern that OLP may be premalignant. In patients who do not use tobacco products, squamous cell carcinoma may arise at the site of a pre-existing OLP lesion in less than five percent of cases, most frequently in atrophic, erosive, and plaque lesions. Hence, OLP patients are at slightly increased risk of oral cancer, although it is unlikely that OLP is inherently pre-malignant.The most commonly used group of drugs for the treatment of OLP, they have the ability to modulate inflammation and immune response. They act by reducing the lymphocytic exudate and stabilizing the lysosomal membrane. Topical mid-potency corticosteroids such as triamcinolone acetonide (TA), high-potent fluorinated corticosteroids such as fluocinonide acetonide, disodium betamethasone phosphate, and more potent halogenated corticosteroids such as clobetasol are used based on the severity of the lesion. The greatest disadvantage in using topical corticosteroids is their lack of adherence to the mucosa for a sufficient length of time

Keywords:Oral Lichen Planus (OLP), Intra-lesional Steroid Injection.

1. Introduction:

Oral lichen planus is a T-cell-mediated chronic inflammatory oral mucosal disease of unknown etiology. These lesions contain few B-cells or plasma cells and minimal deposits of immunoglobulin or complement. There are no consistent serological changes associated with OLP **(1)**

1.1. Incidence and Prevalence:

It predominantly occurs in adults older than 40 years, although younger adults and children can be affected. It affects women more than men in a ratio of 1.4:1. The disease affects 1-2% of the population and there is no racial predilection (**2).**

1.2. Clinical Features of OLP

It presents as white striations, white papules, white plaques, erythema, erosions, or blisters affecting predominantly the buccal mucosa, tongue, and gingivae and it is the most common non-infectious oral mucosal disease in patients referred to oral medicine and oral pathology clinics **(3).** Lesions are usually bilateral, and atrophic and erosive lesions are often sensitive or painful. There may be co-incident skin lesions that present typically as flat-topped violaceous papules affecting the wrists, ankles, and genitalia. There is ongoing concern that OLP may be premalignant. In patients who do not use tobacco products, squamous cell carcinoma may arise at the site of a pre-existing OLP lesion in less than five percent of cases, most frequently in atrophic, erosive, and plaque lesions. Hence, OLP patients are at slightly increased risk of oral cancer, although it is unlikely that OLP is inherently pre-malignant **(4).**

The symptoms of the disease such as burning sensation, loss of homogeneity in clinical appearance should be assessed thoroughly at each appointment and biopsy should be performed if required. Regular follow up of patients at least 3 times in a year with more frequent examinations is required for OLP with dysplasia **(1).**

Reticular form of OLP is usually asymptomatic. Atrophic/erythematous and erosive/ulcerative lesions are symptomatic. Symptoms include mucosal sensitivity, burning sensation and continuous debilitating pain. The lesions usually persist for many years and patients have periods of exacerbation and quiescence. Periods of exacerbation are generally associated with psychological stress and anxiety and during this time there is increased erythema or ulceration with increased pain and sensitivity. The lesion of OLP resulting from mechanical trauma either during dental treatments or due to cheek biting is termed as koebner phenomenon (**5).**

1.3. Etiology and pathogenesis

The etiology of this condition is unknown. Current literature suggests that T cell mediated immune mechanism is mainly implicated in the pathogenesis of OLP.Periods of psychological stress and anxiety are associated with aggravation of the disease and genetic predisposition also plays a role in its pathogenesis. Koebner phenomenon is a characteristic feature of cutaneous LP and is also observed in oral cavity. The erosive lesions are most commonly seen in areas of trauma such as buccal mucosa and lateral surfaces of the tongue. These lesions may decrease in severity with the elimination of trauma. Smoking and tobacco chewing, has been associated with the development of OLP (**6).**

Pathogenesis may be antigen-specific and non-specific. Antigen-specific mechanisms include antigen presentation by basal keratinocytes and non-specific mechanisms include mast cell degranulation and MMP activation. Both these mechanisms may combine which results in CD8+

cytotoxic T-cell accumulation in the superficial lamina propria followed bybasement membrane disruption, intra-epithelial T-cell migration, and keratinocyte apoptosis. Chronicity of the condition may be due to deficient antigen-specific transforming growth factor beta (TGF-β1) mediated immunosuppression **(5).**

Both endogenous and exogenous factors may cause cell-mediated immunity in a genetically susceptible patient. The nature of the antigen implicated is uncertain; however numerous predisposing factors are identified. These are systemic medications, dental materials, chronic liver disease and hepatitis C virus, stress, genetics, tobacco chewing and graft versus host disease, Systemic medications such as antimalarial drugs, non-steroidal anti-inflammatory drugs, antihypertensive agents, diuretics, oral hypoglycemic agents, beta blockers, penicillin, sulfonamides, tetracyclines, heavy metals, thyroid preparations and antiretroviral medication have been reported to cause OLP **(2).**

Initially keratinocyte antigen expression or unmasking of an antigen may occur followed by migration of T cells (mostly CD8+ and some CD4+ cells) into the epithelium. These migrated T cells are activated directly by antigen binding to major histocompatibility complex (MHC)-1 on keratinocyte or through activated CD4+ lymphocytes. There is up regulation of MHC-II expression along with increased number of Langerhans cells facilitating the antigen presentation to CD4+ cells, which activate CD8+ T cells through receptor interaction, INF γ and IL-2 **(7).**

The activated CD8+ T cells trigger the apoptosis of basal keratinocytes by releasing tumor necrosis factor-α (TNFα), granzyme B and by Fas and Fas Ligand (Fas–Fas L) mediated apoptosis. This results in loss of integrity of basement membrane. The MMP are principally involved in connective tissue matrix protein degradation **(8).**

The CD4+ T helper subsets are the major lymphocytes in subepithelial and lamina propria, which are clustered deeper down to form the typical lymphocyte rich band. However, the distribution and function of CD4+ Th subsets in OLP pathogenesis was not entirely clear **(9).**

A number of studies explored the following questions :(i) presence and function of distinct CD4+ Th subsets and their specific cytokines in OLP local lesions, peripheral blood, and oral saliva. (ii) The role of Th1/Th2 imbalance in OLP pathogenesis, the interaction with Th17, T regulatory (Treg) and other subsets. (iii) Whether suppression of T lymphocytes subsets would help on the OLP treatment and are there other new effective oral medicine to treat OLP patients in clinical trials **(9).**

Distinct CD4+ Th subsets with effective cytokines

Of note, CD4+ T h cells can differentiate into distinct subsets, including Th1, Th2, Treg, Th17, Th9, and T follicular helper (Tfh), accompanied with specific effective cytokines production. Helper T 1 subset, characterized mainly by producing INF γ, IL-2, and TNF- α, can promote the activation and cytokine production of macrophage and cytotoxic T lymphocytes. Th2 subset, which can secrete cytokines IL-4, IL-5, and IL-10, is crucial for antibody production of B lymphocyte cells. Interferon gamma is the signature cytokine of Th1 subset, playing a crucial role in maintaining the differentiation and proliferation of Th1.With regard to the specific cytokine of Th2, IL-4 is also responsible for Th2 cell clonal expansion **(9).**

2. Interleukin 9

Interleukin 9 belongs to a family of cytokines that use the common IL-2Rγc for signal transduction, and similar to other family members (i.e., IL-2, IL-4, IL-7, IL-15 and IL-21), IL-9 was believed to be a T-cell growth factor and its chief function was to drive T-cell proliferation. However other studies showed that IL-9 has a weak effect in proliferation of primary T cells **(10).**

Despite the fact that proliferation of certain T-cell clones can be strongly stimulated by IL-9, instead, IL-9 exhibits other functions, most noticeably in proliferation of mast cells, goblet cells and airway mucin-producing cells. Thus, in many ways, it is different from other IL-2Rγc cytokines as a T-cell growth factor. Interleukin 9 signals through the JAK/STAT system **(11).**

Specifically, upon binding to its cell surface receptor, which consists of a private IL-9Rα chain and the common IL-2Rγc, IL-9 induces recruitment of JAK1 and JAK3 to the IL-9Rα chain and the common IL-2Rγc, respectively, followed by cross-phosphorylation and activation of JAK1 and JAK3. This leads to the activation of STAT1, STAT3 and STAT5. Consequently, STAT1 and STAT5 form homodimers, while STAT1 and STAT3 form heterodimers, and such dimeric complexes translocate to the nucleus to drive transcription of IL-9-inducible genes **(10).**

These gene products are involved in cell survival, proliferation and secretion of inflammatory mediators. Interleukin 9 is often seen in the context of Th 2 cells in vitro or Th 2 associated inflammatory conditions in vivo, especially in allergic inflammation **(12)**.

Thus, for a long time, IL-9 was considered just another Th2 cytokine and thought to be redundant among other Th2 cytokines (i.e., IL-4, IL-5 and IL-13). Furthermore, IL-9 is not confined to Th2 cells, and other cell types including mast cells, NKT cells, Th17 cells or even T reg cells can become IL-9 producers **(13).**

The discovery that IL-9-producing cells are a unique subset of CD4+ helper T cells that is different from other subsets, with distinct features and transcriptional controls, generates renewed interest in the field **(9).**

The Th9 cells are a recently described new helper T-cell subset; the signature cytokine for Th9 cells is IL-9 (without IL-4). Together with other Th subsets, the Th9 cells form a complex array of effector mechanisms in the immune system. The frequency of Th9 cells is very low (~5%), even under optimal polarizing conditions in vitro **(11).**

This often casts considerable concerns over whether Th9 cells are truly a distinct Th cell subset. They are closely associated with Th2 cells, which co-express both IL-4 and IL-9 in the early phase of differentiation, and the Th2 cytokine IL-4 provides one of the key signals for Th9 induction. Furthermore, some of the transcription factors in Th2 development are also involved in Th9 induction. A clear example is that STAT6 knockout CD4+ T cells fail to develop to Th2 cells; they also fail to become Th9 cells **(14,15).**

In some Th2 cultures, CD4+ T cells that express IL-4 and IL-9 (Th2 cells) are completely segregated in that only those that lose the ability to express IL-4 will become IL-9 producers (Th9). Interestingly, only a small fraction of Th2 cells acquire the ability to continually express IL-9. Importantly, the transcriptional regulation mechanisms of Th9 and Th2 cells are strikingly different from each other, thus clearly setting Th9 and TH2 cells apart **(10,11).**

In most reports showing low levels of Th9 cells under TGF-β and IL-4 culture conditions, that they co-express IL-10, which is another Th2 cytokine. It is likely that such Th9 cells are derivatives of Th2 cells as a consequence of induction of additional transcription factors such as purine-rich box 1 (PU.1) and interferon regulatory factor 4 (IRF4) which shut off IL-4 and turn on IL-9 . However, other studies suggested another pathway of Th9 induction in which T0 cells can be directly converted to Th9 cells at high levels (up to 80% of the CD4+ T cells) by TGF-β and IL-4 when CD134 co stimulation is engaged **(16).**

2.1. Sources of IL9

Th2 Cells:

One of the first cells studied in association with IL9 are Th2. They were studied in murine models infected in vivo with Leishmania major and these cells were found to co-express other cytokines as well including IL-4, IL-5, and IL-13. Initially believed to be the main producers of IL-9, a correlation was found between Th2 cell expansion and IL-9 levels (**16).**

NKT Cells:

It has been demonstrated that under certain conditions NKT cells can produce IL-9. Studies using NKT cells from naive mice have shown that after stimulation with IL-2, these cells can produce IL-9. Stimulation with IL2 also triggers the expression of IL-4, IL-5, and IL-13 in NKT cells, but not IFN-γ, suggesting that these cells assist in the humoral immune response. Naïve NKT cells in the presence of TGF-β and IL-4 polarize and secrete IL-9 in murine and human thymic invariant natural killer cell (iNKT)cells .It has been observed that in the absence of CD1d, pulmonary NKT cells decrease IL-9 expression accompanied by decrease in mast cell recruitment to the lungs in allergic airway inflammation **(17,18).**

Mast Cells:

It has also been discovered that activated mast cells can secrete IL-9. Several cytokines were found to stimulate IL-9 production by mast cells, while IL-9 acts as a growth factor and promotes mast cell expansion. Mast cells are stimulated in an autocrine manner in response to IL-9-induced signals and the cross-linking of Ig E molecules on the surface of mast cells triggers release of numerous other cytokines. Histamine and IL-1β, two cytokines released after mast cell degranulation, have been found to further induce IL-9 production, and along with IL-9 itself, seem to behave in a positive feedback loop inducing IL-9 production **(19).**

Th 9 Cells:

A distinct CD4+ T subpopulation based on the cultivating CD4+ murine lymphocytes under different groups of inductor cytokines which polarized the differentiation toward Th1, Th2, Th17, Treg, and CD4+IL-9+ cells. There was evidence that these cells, which acquired the IL-9 phenotype lost expression of other characteristic cytokine of T effector lymphocytes including IL-4, IL-5, IL-13 (Th2), IL-17-α (Th17), or IFN-γ (Th1) **(20).**

Th17 Cells:

Studies have demonstrated that polarized mouse Th17 cells can produce IL-9 while co-expressing IL-17 as well. However, IL-23 was observed to suppress IL-9 production and given its importance in the maintenance of Th17 cells it remains unclear whether this IL-9 production by Th17 cells is transient. In vitro studies have shown that human Th17 cells also produce IL-9. Differentiated T0 need repeated stimulation by Th17 inducing conditions to co-express IL-17 and IL-9. Memory CD4+ T cells subjected to Th17 inducing cytokines such as IL-1β and IL-21 result in the co-expression of IL-9 and IL-17 **(19).**

Treg Cells:

Few studies have suggested the production of IL-9 by Treg cells. Although a couple of studies have confirmed that IL-9 is produced by Treg cells, there are conflicting reports under the circumstances which this occurs. One study reported co-expression of Foxp3 and IL-9 in Treg cells in tolerant murine allografts. This has not been reported in other studies, which studied the function of Treg cells in vitro. Additionally, in human donors the co-expression of Foxp3 and IL-9 has not been reported either **(21).**

Innate lymphoid cells:

It was discovered as a subset of innate lymphoid cells (ILC) that release type 2 cytokines named group 2 ILC cells. Studies with IL-9 reporter mice in vivo have demonstrated that in certain inflammatory milieu, ILC2 cells have been found to express IL-9 cells to variety of stimuli. In a papain-induced lung inflammation model in mice. Interleukin 9 was discovered to be largely produced by ILC2 cells. This production was demonstrated to be dependent on IL-2, but rapidly diminished as other the production of other cytokines, such as IL-13 and IL-5 increased. When IL-9 production was neutralized in ILC2 cells, a lower expression in IL-13 and IL-5 was observed, suggesting that the production of IL-9 by ILC2 cells may play a role in regulation of Th2 cells **(22).**

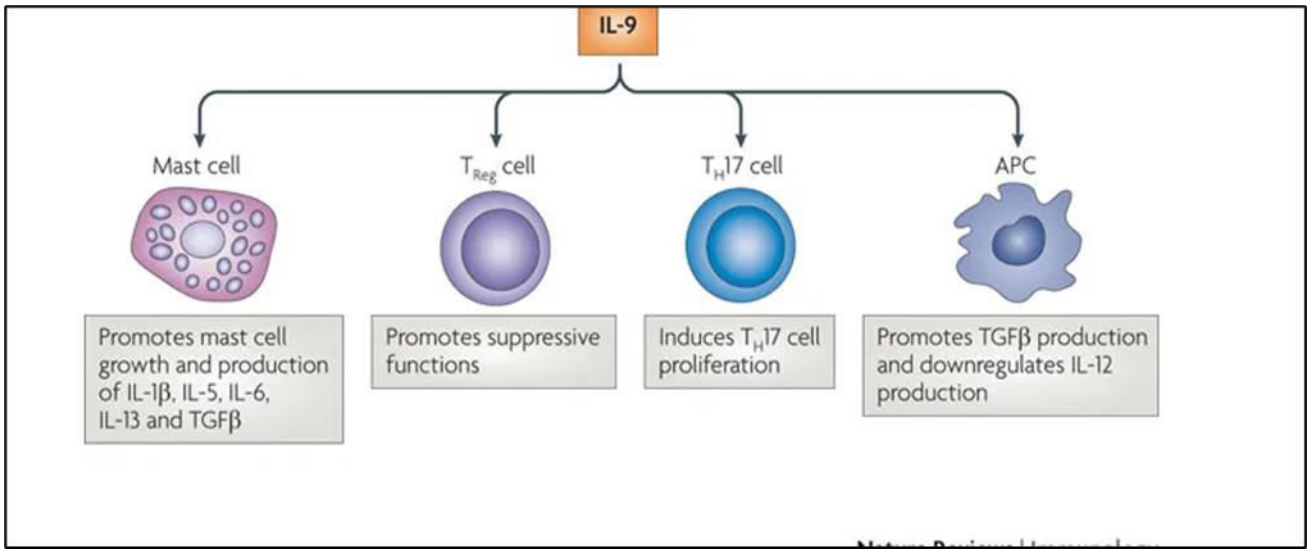

Figure 1: Targets of IL-9 function **(23,24)**

2.2. Immune cell target of IL 9

The effects of IL-9 have been primarily associated with mast cells; however, this does not preclude IL-9 from exerting effects on other cell types. The observed effects of IL-9 on mast cells and other cell types were summarized in figure (1). However, as there is currently no way to confirm the expression of IL-9Rα on specific, rather than heterogenous, cell populations, it may

be difficult to determine the relative importance of each individual cell type **(23,24).**

Mast cells

One of the main targets of IL-9 is the mast cell and initial studies described a role for IL-9 in promoting the expansion of mast cell populations. Subsequent work in mice that were deficient for both IL-9 and IL-9Rα showed that IL-9 is not required for the generation of mast cell precursors, as the basal numbers of mast cells in these mice were normal. However, mice that were deficient for IL-9 or IL-9Rα showed defective expansion and recruitment of mast cell populations in response to intestinal nematode infection or following the induction of experimental autoimmune encephalomyelitis. Interleukin 9 was reported to induce mast cell production of TGFβ, which can have pro-inflammatory downstream effects on neurons and epithelial cells during intestinal inflammation **(24).**

T cell subsets

There are some indications that IL-9 can target certain T cell subsets, specifically, Th17 cells and Treg cells. In the case of Th17 cells, IL-9 seems to function as an autocrine growth factor that facilitates the expansion of Th17 cell populations in vitro. This is also supported by the decreased accumulation of Th17 cells seen in IL-9Rα-deficient mice during autoimmune encephalomyelitis **(23,24).**

Antigen-presenting cells

A careful analysis of the specific antigen-presenting cell (APC) subsets that express the IL-9 receptor has not yet been carried out. However, there are indications that professional APCs are also targets of IL-9. During lipopolysaccharide-induced activation of a heterogenous population of macrophages and monocytes, IL-9 can promote the expression of TGFβ; this results in a decrease in the oxidative burst of these cells, as well as in decreased expression of TNF **(24).**

2.3. Functions of IL9

Interleukin 9 exerts its effect on multiple types of cells and different tissues and initially was considered as a growth factor of activated T cells. Later, its potent proliferative effects were demonstrated in other cell types mainly mast cells hematopoietic erythroid precursors and on myeloid leukemia cell lines **(25).**

Allergic Inflammatory Processes

Interleukin 9 plays an important role in the regulation of airway inflammation and airway hyperresponsiveness. It has been demonstrated that IL-9 exerts proliferative effects on goblet cells and cells that produce mucin in the airways, which is reflected with an increased production of mucus, favoring allergic inflammation in the respiratory tracts. Increased Th9 cell numbers in peripheral blood of allergic patients correlated with IgE titers. In B lymphocytes, IL-9 in the presence of IL-4 increases secretion of IgG1 and IgE and it also promotes an isotype switch contributing to the pathogenesis of allergic diseases of the respiratory tract, specifically in asthma and bronchial hyperreactivity **(26).**

Effect on Neoplasia

Interleukin 9 has been demonstrated to play an important role immune regulation in neoplasia. One important aspect is related to hematologic neoplasms. Animal studies have demonstrated that ectopic expression of IL-9 induces the proliferation of mouse thymic lymphomas. In humans, in vitro studies have observed increase of IL-9 production in cells of Hodgkin's lymphoma by promoting the growth of these cultured cells. The effect of IL-9 in neoplasia may depend on whether the tumor is solid or not. In solid tumors, specifically in melanoma, it has been demonstrated that Th9 and IL-9 have an important antitumor effect favoring the recruitment of both innate adaptive immune cells, reducing tumor burden **(27).**

Immunity against parasites

It has also been shown that IL-9 participates in immunity against parasites, IL-9 transgenic mice overexpressing IL-9 eradicate Trichinella spiralis infections faster than wild-type mice. This nematode requires a great amount of intestinal mast cells for its elimination. Nevertheless, IL-9 −/− mice did not show alterations in the development of T cells, in the antibody-mediated response or the clearance of the infection caused by Nippostrongylusbrasiliensis, which suggests a high redundancy for IL-9 function and the intervention of other cell phenotypes, such as Th2 cells **(25).**

Anti-inflammatory Effects

Apart from inflammatory effects of IL-9, anti-inflammatory effects of the cytokine were demonstrated to depend on the cell types expressing it as well as on the microenvironment in which it is produced. Secretion of IL9 by Treg cells participates in the induction of tolerance. It has been demonstrated that IL-9 stimulates the differentiation of non-allergic mast cells with the capability of inducing local tolerance during allogeneic skin transplants on mice. In contrast, neutralization of IL-9 via monoclonal antibodies promotes an accelerated rejection to skin allotransplants on previously tolerant mice. This anti-inflammatory regulation demonstrates the important role IL-9 plays in immune tolerance (**28).**

Autoimmune Disease

Interleukin 9 has been implicated in numerous pathogenic processes of diseases, mainly allergic diseases as asthma and atopic dermatitis. IL-9 serum levels are elevated in patients with systemic lupus erythematosus, rheumatoid arthritis and systemic sclerosis but their clinical significance is still not completely understood. It has been debated if IL-9 has a role in the pathogenesis of these diseases, or if its presence is due to an epiphenomenon caused by a broad activation of inflammatory mechanisms, and this has made it difficult to define its function in the development of the disease **(20)**.

3. Intra-lesionalSteriod Management of Oral Lichen Planus

The most commonly used group of drugs for the treatment of OLP, they have the ability to modulate inflammation and immune response. They act by reducing the lymphocytic exudate and stabilizing the lysosomal membrane. Topical mid-potency corticosteroids such as triamcinolone acetonide (TA), high-potent fluorinated corticosteroids such as fluocinonide acetonide, disodium betamethasone phosphate, and more potent halogenated corticosteroids such as clobetasol are used based on the severity of the lesion. The greatest disadvantage in using topical corticosteroids is

their lack of adherence to the mucosa for a sufficient length of time **(29).**

Patients with widespread forms of OLP are prescribed high-potent and super-potent corticosteroids mouthwashes and intralesional injections. The potential tachyphylaxis and adrenal insufficiency is high when using super potent steroids like clobetasol, especially when used for a longer period of time. Systemic corticosteroids are reserved for recalcitrant erosive or erythematous LP where topical approaches have failed **(30).**

Intralesional therapy is the injection of a higher concentration of a drug directly into skin lesions without significant systemic absorption. Cortisone and hydrocortisone acetate suspensions were used from the early 1950s before introduction of preparations with lower solubility such as TA, which is now the most common agent used. Dexamethasone acetate, hydrocortisone acetate and methylprednisolone acetate are also used for keloids, alopecia areata, hidradenitis suppurativa, localized and nail psoriasis, resistant oral pemphigus, hemangiomas, etc. The number of injections depends on the disease, site of lesions, age of the patient and response to previous injections. The maximum dosage of TA should not exceed 40 mg/ml/session. Corticosteroids can be injected in full strength or diluted with normal saline or local anesthetic **(31).**

Side effects of topical and intralesional corticosteroids include secondary infection, nausea, oral dryness, sore throat, bad taste, refractoryresponse, mucosalatrophy and delayed healing. Systemic absorption has been reported and it is thought that absorption of small amounts through the oral mucosa can take place, but clinical experience and laboratory studies have shown this not to be of clinical significance in almost all cases **(32).**

3.1. Mechanism of action:

They have anti-inflammatory and immunosuppressive effects by several important mechanisms. First, corticosteroids inhibit leukocyte traffic and access to the sites of inflammation. Second, corticosteroids interfere with the function of cellular components such as leukocytes, fibroblasts, and endothelial cells, as well as the function and production of humoral factors including prostaglandins, leukotrienes, and cytokines at the site of inflammation **(33).** These mechanisms are induced through the genomic and non-genomic effects of corticosteroids. The effects of corticosteroids are mediated by their genomic effects: transactivation and transrepression. In transactivation, corticosteroids, due to their lipophilic nature, pass through plasma membranes to enter the cell. They bind to cytosolic corticosteroid receptors forming a corticosteroid-corticosteroid receptor complex, which is translocated into the nucleus. The complex, within the nucleus, binds to specific DNA sites; glucocorticoid responsive elements (GRE), upregulating the synthesis of anti-inflammatory proteins. At the same time, several genes involved in the side effects of corticosteroids are activated **(34).**

Non-genomic effects of corticosteroid include nonspecific interactions with membrane-bound corticosteroid receptors, nonspecific interactions of corticosteroids with cellular membranes. These effects are mediated by cytosolic corticosteroid receptors and they contribute to the additional rapid effect of high-dose corticosteroids (prednisone >100 mg per day), because at these doses there is already complete saturation of cytosolic corticosteroid receptors **(33).**

3.2.Administration:

Intralesional steroid injection can be done without prior application of local anesthesia. Sometimes topical anesthetic cream can be applied 30 to 60 minutes before treatment to minimize pain from the injections Topical anaesthetic spray is preferred for mucosal lesions, applied 3 to 5 minutes before treatment. Prior injection of local anaesthetic is not preferred as the discomfort associated with the steroid injection is very similar to that caused by an injection of local anaesthetic**(35).**

A

B

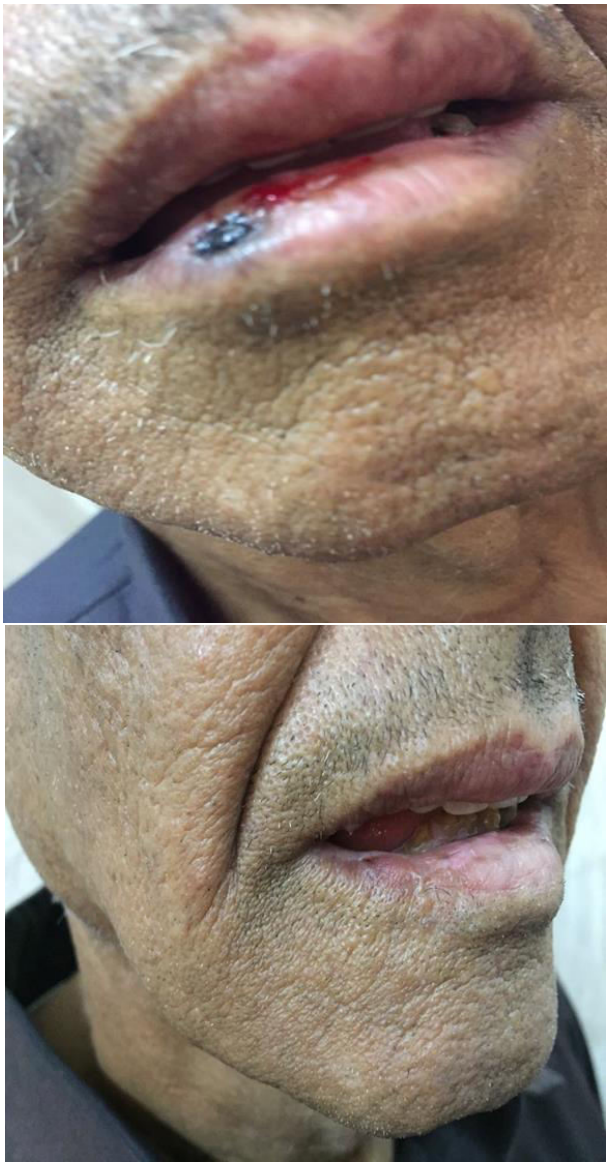

Figure (2):A male patient, 50 years old showing erosive OLP and hemorrhagic crusts at lower lip, before treatment with intralesional of TA injection.

B: The same patient showing complete healing of erosive lesions (excellent response) after 4 sessions with intralesional of TA injection.

ConflictofInterest: Noconflictofinterest.

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