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Original Article

Efficacy of Intra-lesion Injection of Corticosteroid for Treating Patients with Oral Lichen Planus Lesions

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ABSTRACT

This study carried out to determine efficacy and safety of intra-lesion corticosteroid injection as a management of Oral Lichen Planus lesions. Twenty patients were randomly divided into two equal groups: Group I: treated with 1.4 mg intra-lesion betamethasone, and Group II: treated with (8 mg intra-lesion triamcinolone acetonide TA). Patients in the two groups were received injections once a week for 3 weeks. Clinical examination of the lesion was performed, and associated pain was recorded applying visual analogue at weekly intervals up to three weeks. The lesions were followed up after three months later to determine; the lesion disappearance and any recurrence within the following 3 months. All the included patients in the two groups completed the designed treatment protocol without complications or side effects. Healed percentage was higher with Betamethasone (80%) than with Triamcinolone (60%), and final reduction in lesion area was greater in the Group I (18.66 ± 16.32 mm2) than in the Group II (10.73 ± 9.62 mm2). Reduction in pain level was noted in the two treated groups, however did not differ significantly ($p < 0.05$). The change in VAS for pain from baseline to week 1 in Group I was significantly higher than in the Group II. It can be concluded that, intra-lesional of betamethasone may add beneficially as topical treatment of oral lichen planus lesions that avoid hazards of systemic administration of corticosteroids.

***Keywords**: Intra-lesion, Injection, Corticosteroid, Lichen Planus, Lesions.*

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INTRODUCTION

Lichen Planus (LP) is a unique inflammatory disorder that affects the skin, mucous membranes, nails and hair was first described and named by Erasmus Wilson in 1869. The pathogenesis of LP is not completely understood [1]. However, LP has been considered as a disorder of altered cell mediated immunity with exogenous antigens targeting the epidermis [2]. LP has been considered as a dermatological condition that affects the skin and/or mucous membranes, frequently encountered in middle age women, but also in males. It affects all ethnicities; no ethnic group has been identified as being of particular risk [3]. It most commonly affects the oral mucosa and skin; the genital, eye and esophageal mucosa, the nails and scalp may also be involved [4]. The frequency in general population has been reported between 0.5 and 2.6% [5]. Oral lichen planus (OLP) is a chronic inflammatory disease, associated with altered cell mediated immunological function [6]. It has long term evolution, repeated exacerbations, sometimes painful and resistant to treatment, even all of these, OLP significantly affect patient's life quality [7]. and OLP is accompanied by an increased risk of malignant transformation [8].

A wide spectrum of therapeutic options is available, but none are curative; current OLP therapy aims at eliminating all mucosal related lesions reduce symptomatology and decrease the risk of oral cancer and include corticosteroids, immunomodulatory agents, retinoids, ultraviolet irradiation and/or laser therapy [9-14]. Various medical therapies are used for the treatment of Phototherapy has been used in the treatment of LP for many years [15]. The therapeutic properties of corticosteroids were first demonstrated by Edward Kendall and Philip Hench in 1948 [16]. Corticosteroids may be applied topically as ointments, pastes, lozenges or mouthwashes or through an inhaler with a special adapter [9]. The best treatment for OLP includes the use of high-potency topical corticosteroids [17]. It has been reported that topical corticosteroids, which have fewer side effects, are equally or even more effective than systemic corticosteroids [18]. Topical corticosteroids are the main stay in treating mild to moderately symptomatic lesions, and they are widely used in the treatment of OLP to reduce pain and inflammation [19]. Options (presented in terms of decreasing potency) include: 05% clobetasol proprionate gel, 1-0. 05% betamethasone valerate gel, 05% fluocinonide gel, 05% clobetasol ointment or cream and 1% triamcinolone acetonide ointment [20-23]. Triamcinolone acetonide is commonly used either in orabase or lozenge, and there is a number of investigations have determined the efficacy of triamcinolone acetonide 0.1% suspension in treatment of OLP [24]. This drug is available over the counter and is useful in the treatment of OLP. An aqueous suspension of triamcinolone acetonide 0.1% was used as an oral rinse in the treatment of 46 patients with symptomatic oral lichen planus [25].

Factors that may affect improvement or recurrence of OLP lesions after intralesional steroid injection were investigated in a sample of 62 patients diagnosed as OLP treated with intralesional corticosteroid injection. Total severity score of OLP was assessed, and to identify factors affecting the therapeutic effect of intralesional steroid injection, factors were compared between symptom-improved group and symptom-not improved group. In a comparison between both groups, OLP with lip involvement was only variable which showed significant difference. This study suggested that patients suffering from lip OLP lesion might not be effective to treatment by intralesional corticosteroid injection. Intralesional injections of hydrocortisone, dexamethasone, triamcinolone acetonide and methylprednisolone have been used in treatment of OLP [26]. However, the injections can be painful, are not invariably effective, and have a localized effect such as mucosal atrophy. Intralesional triamcinolone acetonide in doses of 5–1 ml of a 1-mg/ml suspension seems to be a practical supplement for the treatment of erosions. Furthermore, in most cases, a remission of several months was noted; recurrences were milder than the original disease state and were managed with topical agents alone. It is unclear why the response to topical corticosteroid therapy is so variable [27].

Systemic prednisolone is the drug of choice, but should be used at the lowest possible dosage for the shortest duration (40-80 mg for 5-7 days) [28]. Systemic prednisone can be used to control the ulcers and erythema in OLP, and may be indicated in patients whose condition is unresponsive to topical steroids, but adverse effects are possible even with short courses. The oral dose of prednisone for a 70-kg adult ranges from 10–20 mg/day for moderately severe cases to as high as 35 mg/day (0. 5 mg/kg daily) for severe cases, and should be taken as a single morning dose to reduce the potential for insomnia and should be taken with food to avoid nausea and peptic ulceration [23]. When systemic corticosteroids are prescribed for periods of longer than 2 weeks, the dosage of steroid must be gradually tapered to avoid precipitating an adrenal crisis. Studies compared the efficacy of corticosteroids with some other drugs, thus a double-blind randomized controlled study, compared the efficacy of topical zinc sulfate in combination with 05% fluocinolone ointment in the treatment of OLP after 2 weeks of treatment, reported that topical zinc sulfate in combination with 0. 05%

fluocinolone ointment reduced the severity erosive OLP better than 05% fluocinolone separately [29-32]. Thus, this study carried out to determine efficacy and safety of intra-lesion corticosteroid injection as a management of Oral Lichen Planus lesions.

METHODS

Patients and Grouping

A total sample of 20 patients who had been diagnosed with OLP by means of clinical and histopathologic examination was included in this study. Subjects were excluded if they were under 18 years old; had a history of topical or systemic corticosteroid usage for treating OLP in the past 4 weeks; had a history of using medications capable of inducing lichenoid reactions; had a history of taking the immunosuppressive medication; had a history of corticosteroid allergy; had oral cavity malignancy; were experiencing pregnancy and lactation; or were unwilling to attend the study. The included patients in Group I: treated with 1.4 mg intra-lesion betamethasone, and Group II: treated with (8 mg intra-lesion triamcinolone acetonide TA). Patients in the two groups were received injections once a week for 3 weeks. The injection was placed directly into subepithelial tissue just underlying the lesion adjacent to the normal mucosa. The study nature was explained to all patients at time of evaluation and upon their agreement to participate into the study, each patient was asked to sign a written informed consent.

Pain Measurement

To assess the pain of the OLP patients, patients filled out a 10-cm visual analogue scale (VAS) at each time they visited the clinic either for injection or follow up. The VAS was divided into oral pain and burning mouth sensation; then the sum of VAS subcategories was measured (range, 0 to 20 points). Quality of life of patients with OLP was evaluated with Oral Health Impact Profile-14 (OHIP-14) at every visit. This OHIP-14 is a self-administered questionnaire that evaluates quality of life using 14 items to measure seven dimensions: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. Each dimension is measured by two questions; subjects were asked how often they had had negative impacts in these dimensions [4].

Responses to the questions were recorded using a 5-point Likert scale: 0, never; 1, hardly ever; 2, occasionally; 3, fairly often; and 4, very often. The overall score for the OHIP-14 was achieved by summing all responses (range, 0 to 56 points). Signs of OLP were quantified using a special scoring system for OLP.35 The lesion extent and disease severity at each site was measured and scored; oral cavity was divided into 17 sites, and criterion-based numerical scores for each site were given. Variables assessed were the extent of site involvement (site score: range, 0 to 2 points) and the severity of the lesion at each site (activity score: range, 0 to 3 points). The pain score was included; pain was self-evaluated by the patient on a scale of 0 to 10. Improvement of symptoms was defined as when the sum of VAS had decreased more than 50% by the last treatment as compared to the VAS of the first visit. Recurrence was defined as recurrence of symptoms and signs from 2 weeks after the end of treatment.

Statistical Analysis

The recorded data at baseline, which had been collected upon the patients' first visit to the clinic, were mainly used to examine. Differences between the symptom-improved group and not-improved group parameters were explored. For the symptom-improved group, the differences between the recurrence group and no-recurrence group parameters were also explored. Independent-sample t-test and chi-square test were performed to compare each group via univariate analysis. Statistical significance was accepted at $P<0.05$.

RESULTS

All the included patients in the two groups completed the designed treatment protocol without complications or side effects. Symptoms were

improved in 8 patients (80%) and in 6 patients (60%) after treatment with intralesional injection of Betamethasone or Triamcinolone, respectively. In a comparison between the symptom-improved and the symptom-not-improved OLP lesion, showed statistically significant difference ($p< 0.05$). Healed percentage was higher with Betamethasone (80%) than with Triamcinolone (60%), and final reduction in lesion area was greater in the Group I (18.66 ± 16.32 mm2) than in the Group II (10.73 ± 9.62 mm2).

Subjective severity of OLP such as VAS and OHIP-14 scores, and objective severity of OLP such as the total severity score of OLP at baseline, did not show significant differences between the two treated groups; there was no significantly different in VAS, OHIP-14, and the severity score of OLP, accompanying conditions, involvement site. Reduction in pain level was noted in the two treated groups, however did not differ significantly ($p < 0.05$). The change in VAS for pain from baseline to week 1 in Group I was significantly higher than in the Group II.

The comparison between the two groups regarding the lesion recurrence; it was evident that no significant difference was noted between the two treatments modalities applied in the present study ($p< 0.05$). Figure 1 illustrating the obtained results.

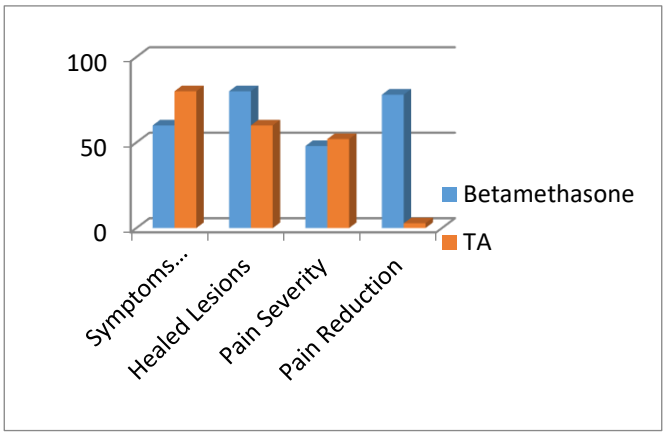

Figure 1. Hectograph illustrating the comparison between the two treated groups regarding symptoms improvements, healing of the lesions, pain severity and reduction of associated pain.

DISCUSSION

The present study investigated the efficacy of intra-lesion corticosteroid injection as a management of OLP patients, as it has been thought that OLP is closely related to cell-mediated immunity [4]. Cell-mediated immunity and cytokines play an important role in OLP's pathogenesis, particularly cytokines as tumor necrosis factor-α, interleukin-8, and interferon-γ which cause increased activity of lymphocytes and apoptosis of keratinocytes [16]. Due to the immunological pathogenesis of OLP, a good response to corticosteroids is expected; therefore, systemic and local corticosteroid therapies are widely used to treat OLP [10,11]. In an attempt to minimize the systemic side effects of corticosteroid treatment, injection of the drug directly to the lesion was proposed as effectively alternative method of administration [17].

Intra-lesion injection of Betamethasone and TA as a therapeutic modality were chosen in this study. TA is a synthetic corticosteroid and aqueous, remains longer in OLP lesion site owing to its insolubility [18,19]. It has been used successfully in treatment of oral submucous fibrosis, temporomandibular joint osteoarthritis, and central giant cell granuloma [20-22]. Additionally, using of TA to treat OLP lesions revealed successful results in several studies and it was reported that 80 % cure rate after 6 weeks of intralesional TA injection was noted [13,23,24]. Equally, various reports have been acknowledged that Betamethasone showed beneficial use as a potent therapeutic agent in management of several chronic inflammatory disorders [33-35].

It is worthy note that, limitation in proper assessment of any therapeutic modality for the OLP lesions is the lack of standard as well as objective assessment criteria. In this respect, an attempt was paid in the present study to obtain ensuring objectivity assessment of OLP lesion, through utilizing both the total severity score 15 and the OHIP-14, as they provide a basis tool that evaluates the subjective quality of life among the oral healthcare workers. Intralesional injections of corticosteroids represent an effective treatment for OLP, which can guarantee a

significant improvement of symptoms, and lead to the healing of lesions, but it is only reserved for the most serious cases that do not respond to topical therapy [36]. The analyzed articles show a protocol for this treatment characterized by one injection per week, which should be performed in the subepithelial connective tissue, for about 2-4 weeks [7,37]. In particular, a study compared injections with triamcinolone and injections with betamethasone and they highlighted that betamethasone is significantly more effective [38]. Moreover, a study observed that there were no statistically significant differences between the topical application and the intralesional injections of triamcinolone. The efficacy of steroid injections was found, and confirmed that triamcinolone was the most used drug [36]. It has been found that intralesional injection of steroids gave variable results; in addition, they can be painful and have localized side effects as mucosal atrophy [15]. The use of topical steroids is associated with various side effects, probably more so than those induced by many other second-line drugs, but not too serious to prevent their use [24]. Studies demonstrated two main adverse effects, namely a burning sensation and irritation of the mucous membranes, and oral candidiasis [37], the latter is easily resolvable by adding antifungal drugs to the therapy, such as rinsing with nystatin (100000 U/ml, 3 times a day) or application of miconazole gel (2%, once a day) [39,40]. The most common complaint of patients with OLP was oral pain with burning sensation in the oral cavity causes difficulty in oral intake; and this pain makes people go to the hospital to relieve the pain. For these reasons, it has been thought that using a sum of VAS scores as an index could immediately reflect the oral discomfort of patients. Hence, improvement of symptoms has been considered in the present study when the sum of VAS scores was found to be decreased more than 50% by the final treatment. It was found that vast number of patients suffering from OLP showed improved symptom, in both groups but more in the group treated with TA; however, the difference did not statistically significant. Thereby, TA or Betamethasone injected directly into OLP lesions should be considered as effective drug that can remove the disease symptoms. This may suggest that patients suffering from OLP with lesion on the lip might not be effective in treating with intralesional corticosteroid injection.

CONCLUSIONS

OLP is one of the most frequently encountered mucosal pathology in dental practice, and. no therapy currently available for OLP is completely curative; treatment aims to alleviate painful symptoms, to heal ulcerative and/or atrophic lesions, to reduce the risk of malign transformation and to prolong the symptom-free intervals. Generally, these objectives can be achieved through corticosteroids use, with or without the combination of other immune modulators.

Competing interests

Authors have declared that no competing interests exist.

Authors' Contributions

This work was carried out in collaboration between authors.

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