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EVALUATION OF HPA-SUPPRESSIVE EFFECTS OF CLOBETASOL PROPIONATE OINTMENT IN THE TREATMENT OF ORAL LICHEN PLANUS

Dental Science

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ABSTRACT

Aims & Objectives: To evaluate the effect of topical 0.05% clobetasol propionate ointment on HPA axis function during treatment for Oral Lichen Planus in a series of 35 patients.

Material and methods: Biopsy proven and symptomatic 35 patients of Oral lichen planus were included. Patient's baseline serum cortisol levels were recorded before starting treatment with topical 0.05% Clobetasol propionate ointment. After three months serum cortisol were again evaluated to see any effect on HPA axis function.

Result: The Baseline serum cortisol levels were normal (4.30-22.40ug/dl) in 33(94.3%) patients and 2(5.7%) patients showed reduced levels of serum cortisol levels. Post treatment serum cortisol levels were normal in 33 patients (94%) and only 2 (5.7%) patients reported decreased serum cortisol levels. Both these patients showed normal baseline serum cortisol levels. No statistically significant relation was noted between the pre-treatment and post-treatment values of Serum cortisol levels (p-value = 0 .451).

Conclusion: Oral lichen planus can be treated with topical 0.05% Clobetasol propionate ointment without any systemic adverse effects when applied in tapering dose with total dose not exceeding 15gm/week.

KEYWORDS

Oral Lichen Planus, Clobetasol propionate, Serum cortisol level

INTRODUCTION

Oral lichen planus (OLP) is a chronic mucocutaneous disorder of multifactorial origin. It affects stratified squamous epithelium of oral and genital mucosa, skin, nails, and scalp[1].

Various treatment modalities have been attempted for the treatment of OLP, but a complete cure has not yet been accomplished with any treatment regimen because of its recalcitrant nature[2]. Topical steroids form the first line of treatment and offer symptomatic treatment without providing complete cure. Sometimes severe lesions don't respond to low potency steroids and hence, high-potency topical corticosteroids are required to be used for prolonged periods. No definitive guidelines have been established for the appropriate use and possible side effects of topical corticosteroids (TCTs) in oral mucosal lesions[3].

Study has shown various adverse effects of TCTs when absorbed systemically such as moon face or hirsutism[4]. Systemic absorption of steroids leads to suppression of hypothalamus–pituitary–adrenal (HPA) axis leading to adrenal insufficiency[5]. The symptoms range from minor non-specific asymptomatic symptoms (e.g. anorexia, abdominal pain, nausea, vomiting, constipation or diarrhoea, or muscle pain, etc.), to development of acute adrenal insufficiency[6]. Other symptoms include bad taste, dry mouth, sore throat, swollen mouth, candidiasis, mucosal atrophy[7], weight gain, osteoporosis, capillary fragility, striae, hypertension, sleep disorders, diabetes and propensity to infection among others.

However, studies have also shown that adrenal suppression is not seen in topical corticosteroids such as fluocinonide 0.05%; fluocinolone acetonide 0.1% and clobetasol 0.05% when used for long term management of OLP[8,9]. Side effects such as moon face and hirsutism are seen with clobetasol propionate 0.05% mouthwash when used for the treatment of OLP[10].

The objective of this study was to evaluate the effect of topical clobetasol propionate 0.05% ointment on HPA axis function during treatment for OLP in a series of 35 patients. Serum cortisol levels were used to determine percutaneous absorption of topical 0.05% Clobetasol propionate ointment.

MATERIALS AND METHODS

This prospective study was approved by the Institutional Ethical Committee of Maulana Azad institute of Dental sciences. Informed consent was obtained from all the p patients. This study consisted of 35 patients who reported to the Out Patient Department of Oral Medicine and Radiology with clinical signs and symptoms of oral lichen planus. Only biopsy proven and symptomatic cases of OLP were included in the study.

Baseline measurement of the serum cortisol levels were performed on day 1 and the sample was collected prior to the first application of 0.05% Clobetasol propionate ointment. The sample was collected between 8 am and 9 am.

The second measurement of serum cortisol was done after 3 months of topical application of 0.05% clobetasol propionate ointment.

For the first 15 days (2 weeks) patients were asked to apply the ointment throughout the affected mucosa thrice daily. After that the dose was reduced to twice daily for the next 15 days (2 weeks). Further the application was reduced to once daily for next 15 days (2weeks) followed by application of ointment alternatively until there is no need to apply.

The patients were advised to apply the minimum amount of ointment on all over the affected mucosa and to keep it for 15 minutes followed by thorough rinsing with water. The total dose that we prescribed did not exceed 15gm/week. Patients were also prescribed clotrimazole mouth paint once daily as a preventive measure for development of candidiasis.

After complete withdrawal of the TCTs treatment, patients were kept under regular follow up for 6 months. They were informed about the possibility of recurrence of the lesions and to report back whenever needed

STATISTICAL ANALYSIS

Statistical analysis was performed using the program SPSS for Windows.The comparison of two related samples was done by non-parametric Wilcoxon Signed Ranks Test.

RESULTS

35 patients (29 females, 6 males; aged 20–65 years) with OLP were studied. Out of the total patients included in study 21(60%) patients had never applied any form of topical corticosteroids,7(20%) patients

were using 0.1% triamcinolone acetonide in the past and had discontinued since 1-2 months and 7(20%) patients were actively applying 0.1% triamcinolone acetonide (since 7-15 days). The patients who were applying topical steroids were asked to stop applying any kind of steroidal preparation for a period of 2 weeks before obtaining the blood sample for estimation of serum cortisol levels. None of the patients had used clobetasol propionate ointment prior to enrollment in this study.

Baseline serum cortisol levels

Baseline serum cortisol levels before the start of clobetasol ointment therapy were measured in all the patients and cortisol levels were normal (4.30-22.40ug/dl) in 33(94.3%) patients and 2(5.7%) patients showed reduced levels of serum cortisol levels 2.05ug/dl and 3.75ug/dl respectively.

Serum cortisol levels after 3 months

19(54%) patients reported after 3 months, 3(8.5%)patients reported after 3.5 months and the rest of 13(37%) patients reported after 4 month with post treatment serum cortisol levels.Out of a total 35 patients included, 33 patients(94%) reported with normal levels of post treatment serum cortisol levels and only 2 (5.7%) patients reported decreased serum cortisol levels <1.0ug/dl and <0.04ug/dl respectively. Both these patients showed normal baseline serum cortisol levels.

All the patients showed excellent resolution of symptoms during treatment with uneventful healing. 4(11%) patients reported candidiasis which was treated with topical application of clotrimazole mouth paint.

One(2.8%) of the patients whose post treatment serum cortisol levels were low reported gastritis and altered taste. Temporarily alteration in taste was reported by a total of 3(8.5%) patients. No other side effects were seen in any of the patients during their regular follow ups. There was no statistically significant relation between the pre-treatment and post-treatment values of Serum cortisol levels (p-value = 0 .451). Hence, topical application of 0.05% Clobetasol propionate ointment for 3-4 months in tapering dose can be given without suppressing hypothalamus–pituitary–adrenal (HPA) axis.

DISCUSSION

For the diseases of oral mucosa local drug delivery system provided by topical corticosteroids provides more targeted drug delivery for the management of oral lichen planus when compared to systemic delivery. The main advantages of the local drug delivery system are less side effects, more efficient and targeted delivery. Adrenal gland suppression is the most common side effect of systemic steroids. However, when applied in higher doses (20-30 grams per day) even topical corticosteroids such as Clobetasol propionate can also decrease the serum cortisol levels[11].

In our study 33 patients(94%) reported normal levels of post treatment serum cortisol levels and only 2 (5.7%) patients reported decreased serum cortisol levels. The possible explanation includes the total weekly dose that we prescribed did not exceed 15gm/week even when patients were applying the ointment thrice daily due to the strict instructions given. They were asked to apply only on the affected part that too the minimum quantity. Also the ointment was allowed to remain in mouth only for a period of 15 minutes followed by thorough rinsing with water.

Out of 2 (5.7%) patients who reported decreased serum cortisol levels, one patient was totally asymptomatic but the other one complained of gastric irritation with altered taste and both these symptoms subsided after stoppage of the ointment.

Studies have shown that it is safer to use an Clobetasol propionate with an adherent vehicle in the oral cavity when compared to an aqueous solution. Due to the fact that adherent vehicle is applied to the localised affected mucosa when compared to aqueous solution. Hence, aqueous solution should be reserved for lesions with extensive involvement of oral cavity and where retention of medications in an adhesive base is difficult such as tongue and gingiva[3,12].

In our study some patients did find it difficult to retain the ointment in the oral cavity, especially the gingiva and tongue which is one of the drawbacks of this study.

CONCLUSION

In our study 70-80% of improvement was seen in first 2-3 weeks time and hence, based on our findings an optimal approach to the management of patients oral lichen planus treated with Clobetasol propionate 0.05% ointment would be to use it three times daily for a initial period of 2 weeks and then reduce the dose and frequency depending upon the severity of the lesions until symptoms abate. Total weekly dose should not exceed 15 gm /week so as to decrease the systemic side effects to minimum with maximum treatment benefits.

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