ABSTRACT

Aims: This study was designed to evaluate the efficacy of Dapsone for treating erosive lichen planus and to observe side effects occurring for the drug during the treatment.

Materials and methods: Twenty-two patients who were resistant to treatment with systemic antioxidants and topical vitamin were treated with systemic Dapsone 100 mg per day for 3 months. Improvement of signs and symptoms of the disease and the side effects of the drug were evaluated every 15 days and posttreatment recurrence of the disease was assessed after 6 months of treatment.

Results: A significant improvement in the burning sensation and reduction in size of the erosive areas were noticed with a 3 months course of Dapsone therapy. Systemic side effects were minimal. A reduction in hemoglobin percentage of 0.92 gm from the baseline values was the only observed side effect.

Conclusion: Results of this study show that Dapsone is an effective drug in erosive lichen planus. Dapsone can be used as a steroid sparing agent when steroids are contraindicated. There are minimal side effects for Dapsone when used in the dose of 100 mg per day for 3 months.

Keywords: Erosive lichen planus, Dapsone, Adverse effects, Vitamin A therapy.

INTRODUCTION

Lichen planus is a relatively common mucocutaneous disease. Among the mucosal surfaces affected oral mucous membrane is most frequently involved. Lichen planus has a female predilection and affects the middle-aged people. Andreasen divided oral lichen planus into six clinical forms: Reticular, papular, plaque, like, atrophic, erosive and bullous.\(^1\) First three are usually asymptomatic and later three are symptomatic. Erosive form of lichen planus is a chronic painful lesion which is difficult to treat. It is considered as a premalignant lesion with malignancy transformation rate being 0.5 to 2.5% but the malignant potential is still controversial.\(^2,3\)

Recent clinical and experimental evidence suggests that the disease have an immunological pathogenesis.\(^4-7\) Based on this theory various immunomodulatory drugs are used in the treatment of lichen planus.\(^8,9\) The standard treatment for erosive lichen planus is topical steroids like clobetasol propionate, triamcinolone acetonide, betamethasone valerate, fluocinonide, etc. Steroids are contraindicated in a wide array of common diseases like hypertension, diabetes mellitus, gastrointestinal tract disorders, osteoporosis, etc. This necessitates the search of a steroid-sparing drug for the treatment of lichen planus. A variety of immunosuppressive and immunomodulatory drugs were tried in the treatment of lichen planus that includes cyclosporine, azathioprine, cyclophosphamide, thalidomide, levamisole, mycophenolate mofetil and tacrolimus. Dapsone, an antimicrobial drug is also proved to have immunomodulatory properties.\(^10-12\) Dapsone is a widely used and economic drug which is used to treat leprosy. Dapsone is successfully used in the treatment of lichen planus in few studies.\(^13-15\) This clinical study was undertaken with the objective to evaluate the efficacy of Dapsone in the management of resistant cases of oral erosive lichen planus.

MATERIALS AND METHODS

The study was conducted in the Department of Oral Medicine and Radiology, Govt. Dental College, Thiruvananthapuram, Kerala over a period of 15 months. All patients who attended oral medicine OP clinic were screened for evidence of erosive lichen planus for a period of 4 months. From a total of 13620 patients screened, 107 patients were clinically identified as having oral lichen planus of which 36 patients were having erosive lichen planus. After histopathologic confirmation, all these patients were given vitamin A topically and antioxidants systemically for a period of 3 months. Twenty-two patients who did not show any improvement and agreed to participate were selected for the study. Informed consent was obtained in all the cases. Clearance to conduct the study was obtained from the ethical committee. All the patients were maintained on a drug-free period of 15 days to avoid residual effects of the earlier treatment overlapping the Dapsone treatment. One of the relative contraindication for Dapsone therapy is G6PD deficiency. It is an X-linked disorder affecting males. Hemolytic anemia is precipitated in affected people when exposed to oxidative stress, such as infections and drugs like NSAIDs, sulpha drugs, antimalarials and Dapsone. Detailed medical history and examination was done to rule out history of hemolytic anemia in the study group before prescribing Dapsone.
All the 22 patients were given Dapsone systemically for a period of 3 months. The Dapsone therapy regime was prescribed in accordance with protocol modified from Beck and Brandrup. An initial dose of 50 mg/day is given for first 15 days and then increased to 100 mg/day for rest of the period. Subjective and objective assessment of the lesion and hemoglobin levels were estimated every 15 days. Post-treatment recall examinations were done on 6th month. Data were recorded in a proforma specially prepared for the study.

Scoring: Subjective response was assessed by estimating severity of burning sensation which was rated on a scale of 0 to 4 by the patient. The following grades were made: 0-nil, 1-mild (occasional), 2-moderate (while eating spicy food), 3-severe (while eating any food), 4-intolerable (present always). Objective evaluation included assessing the size of the lesion and the transformation of erosive form to other forms. Size of the lesion is assessed by monitoring the extent of the erosion in millimeter, by modifying the criteria scale of Thongparson et al. Comparisons were made with pre- and posttreatment results and the data were statistically evaluated using student t-test. Adverse effects of Dapsone during the treatment were also recorded.

RESULTS AND DISCUSSION

Patients who were diagnosed as having erosive lichen planus and those who were willing for the study were evaluated for their signs and symptoms. 68.18% of patients had severe burning sensation and 31.81% had moderate burning sensation while having spicy food. They were initially treated with topical vitamin A and systemic antioxidants (combination of vitamin A, C and E). After 3 months of treatment 81.86% had their symptoms reduced to moderate burning sensation. Remaining 18.18% continued to have severe burning sensation. Areas of erosion were persistent in all the patients. This finding is in accordance with the observations of Giustina et al. They found that after 2 months of topical vitamin therapy only reticular lesions improved whereas erosive lesions persisted. 50% of patients showed increased pigmentation in the site of erosion.

A drug-free period of 15 days was maintained before starting dapsone therapy for the patients. During this period 36.36% of patients had relapse. 54.54% had severe burning sensation and rest 45.45% had moderate burning sensation. Immediate relapse following the stoppage of topical vitamin therapy was observed by Eisen.

After 3 months of dapsone therapy, clinical improvements were evaluated. 54.54% were totally relieved from burning sensation, 45.45% had mild burning sensation while having spicy food and rest 4.62% had moderate burning sensation (Graph 1). Erosive areas were completely cured in 83.36% patients. 13.64% had minimal or no change in the size of the erosion (Graph 2). This indicates that there is a significant improvement in signs and symptoms of erosive lichen planus following Dapsone treatment. Statistical comparison of results with Dapsone therapy and vitamin therapy using Student t-test shows that the observations are highly significant. These results are comparable with the findings of Falk et al, Beck and Brandrup, Camisa et al and Mathews et al. In this study, three patients were found to be resistant for the Dapsone therapy. Probably this may be due to the shorter duration of treatment.

Mechanism of action of Dapsone in erosive lichen planus is not well-understood. It is thought that anti-inflammatory activity of Dapsone is due to the inhibition of migration of polymorphonuclear leukocytes as a result of interference with leukocyte cytotoxic system and prevention of the leukocytes from responding to chemotactic stimuli by inhibiting the calcium-dependent tissue damaging oxidants could be the possible mechanism of action. Due to its
immunomodulatory action, Dapsone is used in various immunologic diseases like dermatitis herpetiformis, linear IgA bullous dermatoses, pemphigus, Behcet’s syndrome, etc.22,23

During the follow-up visit after 6 months, 59.09% of patients were free of burning sensation, 31.81% had mild burning sensation and rest 13.6% had moderate burning sensation. None of the patients had severe burning sensation. 18.18% of patients found to have recurrence of erosive lesions (an increase of 4.44%). This shows that the remission of signs and symptoms of erosive lichen planus achieved with Dapsone therapy is long-lasting.

Pigmentary changes: During the initial visit, it is observed that all the patients had some amount of pigmentation associated with the erosive areas of which 36.36% had severe pigmentation. After 3 months of Dapsone therapy 41% developed marked pigmentation and 31.8% had mild pigmentation in the lesional site. After 6 months pigmentation decreased in intensity in most of the patients, but 9% had persistent pigmentary changes. Hyperpigmentation was not reported with any of the previous studies during the treatment of oral lichen planus except with Grenz ray therapy.24

Change in hemoglobin percentage: Mean value of hemoglobin before the Dapsone treatment was 12 gm% ranging from 10.5 to 14 gm%. During the course of the therapy, 82% showed a slight drop in their hemoglobin percentage. After 3 months of Dapsone treatment mean hemoglobin percentage was 11.08 gm% ranging from 9.5 to 14 gm%. A mean reduction of 0.92 gm% of hemoglobin from the baseline pretreatment level was observed. Piette et al in their study observed a decrease in hemoglobin concentration of 0.32 gm/dl from the baseline after 2 weeks of Dapsone gel treatment.25 In G6PD-deficiency patients Dapsone may precipitate hemolytic anemia. Since only the older population of RBCs is destroyed, hemolytic crisis is usually self-limiting even if the exposure to oxidant continues. In India, the incidence rate of G6PD deficiency is 0.5 to 0.8%.26 According to De Gowin, 50 mg of Dapsone can be safely administered in G6PD-deficiency patients without many side effects.27 Cimetadine and vitamin E supplements can be effectively used in reducing the hematologic effects of Dapsone therapy.28,29 No adverse effects were observed in our study during the course of the treatment.

CONCLUSION

It can be concluded from the results of this study that Dapsone is an effective drug of choice in erosive lichen planus. Dapsone can be used as a steroid-sparing agent when steroids are contraindicated. Dapsone is a widely used drug with minimal toxicity for the treatment of leprosy. With proper administration and monitoring this drug can be considered as a useful and safe agent for many immunologic diseases. In this group of patients with erosive lichen planus Dapsone therapy resulted in 86.36% improvement. Relative contraindication for Dapsone includes G6PD deficiency and anemia, since Dapsone can cause hemolysis and methemoglobinemia in such patients and it reduces the hemoglobin level. Prospective controlled studies are required to compare the effect of Dapsone with other forms of therapy in the treatment of erosive lichen planus and to know the exact mechanism of action of Dapsone in immunologic disorders.

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Dapsone in the Treatment of Resistant Oral Erosive Lichen Planus: A Clinical Study


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