

A COMPARISON OF ORAL AND TOPICAL STEROID THERAPY FOR RECURRENT APTHOUS STOMATITIS

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ABSTRACT

This study was carried out to compare the efficacy of oral and topical Steroids in the treatment of Recurrent Aphthous Stomatitis (RAS).

It was a quasi-experimental interventional study conducted on 60 patients of Recurrent Oral Ulcers seen in ENT Department of the Combined Military Hospital, Peshawar and Quetta, and was carried out in these hospitals from 01 August 2008 to 31 May 2010.

Sixty patients, age ranging from 20 to 40 years; both genders were selected for the study purpose. The patients were included on the basis, having experienced oral ulcers at least thrice during the last one year severe enough to cause significant discomfort leading to absence from work place and remained afebrile during the ailment. Patients suffering from Hypertension, Bronchial Asthma, Glaucoma or Acid Peptic Disease were excluded. People taking medicines of any kind were not included in the study. Children, lactating mothers and pregnant females were excluded. Patients fulfilling the criteria were divided into two groups. Group I were given tablet Prednisolone (45mg) in daily divided doses for three days. Group II were prescribed topical application of Steroid (Triamcinolone acetonide) for the same duration. The day on which the treatment was started was counted as Day 1, the patients were re-examined on Day 2, 4 and 7.

91% of the patients of group I were symptom free on Day 4. Rest of the patients though not fully recovered were able to resume normal pattern of life. Only 47% of the patients of group II had comparable outcome on Day 4. On Day 7 all the patients of group I were normal while 18% of group II had some residual symptoms.

Short term therapy of oral steroids brings an early and significant improvement in clinical picture of patients with RAS.

Key words: RAS, Steroids, Prednisolone, Triamcinolone.

INTRODUCTION

Oral ulcers are fairly common. About 30 to 40% of the patients with recurrent aphthous ulcers have a positive family history.¹ The exact etiology is unknown. They are thought to be due to immune system reactions.² Dietary deficiency of vitamin B12, folic acid or iron is also proposed to be a probable cause.³ They are common in people with Crohn disease.⁴ Celiac disease has been thought as a cause of aphthous ulcers; studies reveal that 33% patients with Celiac disease did have a conclusive link between the disease and apht-

hous ulcers vs control group (23%).^{5,6} Seventy-five per cent of patients with Recurrent Aphthous Stomatitis have high level of circulating antibodies to oral mucosa. There is a possibility of a cell-mediated immunity to oral mucosa antigen. The activation of the cell-mediated immune system is considered to be the primary disorder. Increased numbers of cytotoxic CD8⁺ cells and decreased numbers of helper CD4⁺ cells in peripheral blood have been noted in patients with recurrent aphthous ulcers.⁷ They cause intense pain but they resolve spontaneously. Recurrent Aphthous

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Stomatitis can be differentiated from other oral ulcers of viral etiology, by their multiplicity, recurrence and absence of fever.

A number of different treatments exist for aphthous ulcers including: analgesics, anesthetic agents, antiseptics, anti-inflammatory agents, steroids, sucralfate, tetracycline suspension, and silver nitrate.⁸ The application of silver nitrate will cauterize the sore; a single treatment reduces pain but does not affect healing time.⁹ Topically, Corticosteroid preparations containing hydrocortisone hemisuccinate or triamcinolone acetonide to control symptoms are effective in reducing inflammation¹⁰ and treating severe aphthous ulcers.^{11,12} Triamcinolone acetonide 0.1% is used as topical application 2 to 3 times a day for the treatment. Regarding systemic steroids use, treatment duration less than one month is considered short term. Corticosteroids for a few days or weeks are considered relatively safe. No tapering is required if the course of the steroid is less than 01 week. The side effects of the corticosteroids are dose related.

METHODOLOGY

Sixty patients of Recurrent Aphthous Ulcers, both genders having age ranging from 20 years to 40 years reporting to ENT Department Combined Military Hospital, Peshawar and Quetta from 1st August 2008 to 31st May 2010 were recruited in this study after formal approval of hospital ethical committee. Informed consent was obtained on a consent form. The patients were included on the basis, having experienced oral ulcers at least once during the last one year severe enough to cause significant discomfort leading to absence from work place and; remained afebrile during the ailment. This age group was selected, since there is less likelihood of co-morbidities. More males were included considering better follow up on social

grounds. The body weight range was from 59 to 71 kg. Patients suffering from Immune Deficiency, Hypertension, Diabetes Mellitus, Glaucoma or Acid Peptic Disease were excluded. People taking medicines of any kind were not included in the study. Lactating mothers and pregnant females were excluded. Patients fulfilling the criteria were divided into two groups. Group I was prescribed tablet Prednisolone(45mg) in daily divided doses for three days, while group II were given topical application of Triamcinolone acetonide three times a day for the same duration. The start of the treatment was counted as Day 1. The patients were subsequently re-examined on Day 2, 4 and 7. Patients were advised to report early if there is appearance of any side effect, about which they were briefed before starting the treatment.

Data were analyzed using Software SPSS-11. The variable in the study were pain relief, ability to join work and clinically healed ulcers. Chi-square test was used to assess the difference of results between the group that was given oral steroids and the group with topical steroids. The level of significance was $p \leq 0.05$. Mean and standard deviation of age, frequency and percentage of sex were given

RESULTS

The age of patients in this study was from 20 years to 40 years. Mean age of patients in group I which were given oral steroids was 29.63 +/- 7.27years while it was 27.50 +/- 7.34 in group II given topical steroids. There was no significant difference between two groups with respect to age as shown in Table 1. Most numbers of patients were in age group 21-25 years. Thus while assessing post treatment improvement in symptoms and signs considering different age groups no statistically significant difference was found ($p=0.263$).

TABLE 1: COMPARISON OF GROUPS WITH RESPECT TO AGE, WEIGHT AND GENDER

	Group I with Oral steroids (n = 30)	Group II with Topical steroids (n = 30)	Statistical Test	P value (n = 60)
Age (mean +/- SD)	29.63 +/- 7.27	27.50 +/- 7.34	T Test	0.263
Weight (mean +/- SD)	64.10 +/- 3.19	64.43 +/- 2.81	T Test	0.673
Sex, No, M/F	14/16	19/11	Chi-square	0.299

TABLE 2: IMPROVEMENT OF SYMPTOMS IN BOTH GROUPS (CROSSTABULATION)

VARIABLE		Oral steroids	Topical steroids	Chi-square p-value
PAIN ON DAY 2	Yes	11	21	0.01
	No	19	9	
PAIN ON DAY 4	Yes	2	16	0
	No	28	14	
PAIN ON DAY 7	Yes	0	7	0.005
	No	30	23	
RESUMED WORK DAY 2	Yes	11	5	0.08
	No	19	25	
RESUMED WORK DAY 4	Yes	29	19	0.001
	No	1	11	
RESUMED WORK DAY 7	Yes	30	29	0.313
	No	0	1	
CLINICALLY HEALED DAY 2	Yes	0	0	—
	No	30	30	
CLINICALLY HEALED DAY 4	Yes	24	8	0
	No	6	22	
CLINICALLY HEALED DAY 7	Yes	28	24	0.129
	No	2	6	

TABLE 3: TREATMENT RESPONSE

VARIABLE	MEDICINE	DAY 2	DAY 4	DAY 7
PAIN RELIEF	DELTACORTIL	19(63.33%)	27(90%)	30(100%)
	TRIAMCINOLONE	10(33.33%)	14(46.67%)	23(76.66%)
ABILITY TO JOIN WORK	DELTACORTIL	11(36.67%)	29(96.67%)	30(100%)
	TRIAMCINOLONE	5(16.67%)	19(63.33%)	30(100%)
CLINICALLY HEALED ULCERS	DELTACORTIL	0	24(80%)	28(93.33%)
	TRIAMCINOLONE	0	8(26.67%)	24(80%)

Mean weight of patients in group I which were given oral steroids was 64.10 +/- 3.19 years while it was 64.43 +/- 2.81 in group II given topical steroids. There was also no significant difference between two groups with respect to weight as shown in Table 1 (p=0.673).

Out of these 60 patients 55% were males and 45% were females. Out of those 30 cases that were given oral steroids (Group I) 46.66% were males and 53.33% were females. Out of those which were given topical steroids (Group II) 63.33% were males and 36.66% were females as shown in pie charts in Fig 1.

After 24 hours, pain relief was experienced in 63.33% and 33.33% in group I and II respectively. Ability to join work was 36.67% in group I and 16.67% in group II. No healing of ulcers was noticed in either group (Table 2).

On second review i.e Day 4, ninety percent (90%) of group I patients became symptom free as regards the pain as compared to 46.67% of the other group. All except one i.e 96.67% of the patients taking oral steroids were finding themselves fit to join work. Only 63.3% of the other group were able to join work. Ulcers were found to be clinically healed 80% and 26.67% in group I and II respectively (Table 2).

On day 7, group I had 100% result as regards the pain relief and joining work with 93.33% clinically healed ulcers. On the other hand, group II had pain relief, ability to join work and clinically healed ulcers were 76.66%, 100% and 80% respectively (Table 2).

The categorical data of the two groups regarding improvement of symptoms and clinical signs were

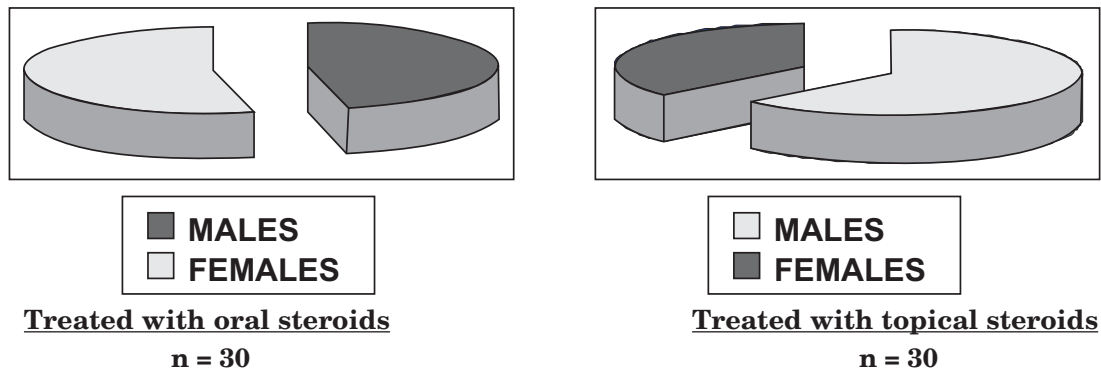


Fig 1: Gender Distribution

analyzed and crosstabulation is shown in Table 2. The Chi-Square test was applied to compare improvement of symptoms signs in two groups and it proved the hypothesis to be correct. Hence the difference of results between Group I and the Group II was statistically significant especially at the end of the treatment i.e. day 4 as shown in Table 2.

DISCUSSION

Although Recurrent Aphthous Stomatitis is a benign, self limiting condition but it causes significant pain; which at times is enough to disturb normal life routine. The use of topical steroids has been a primary therapeutic approach for this clinical condition. Topically, hydrocortisone hemisuccinate or triamcinolone acetonide are used to control symptoms¹⁰ and treating severe aphthous ulcers.^{11,12} The relief in majority of the patients is slow.

The response to other treatment modalities is also not encouraging. Other treatment options tried to treat aphthous ulcers are analgesics, anesthetic agents, antiseptics, anti-inflammatory agents, sucralfate, tetracycline suspension, and silver nitrate.⁸ Silver nitrate topical application reduces symptoms but does not affect healing.⁹ Use of local antimicrobials has been also attempted. Topically applied Milk of magnesia is considered useful against aphthous ulcers. Immunomodulatory drugs like Levamisole, Colchicine¹⁵, Dapsone, Azathioprine¹⁶ have also been tried. Thalidomide in a dosage of 200 mg once to twice daily for three to eight weeks has been used in HIV infected patients with aphthous stomatitis and found to have faster healing than placebo.^{13,14} Thalidomide is contraindicated in non-HIV -infected patients with mouth ulcers, because of its known side effects and teratogenicity.

There is paucity in literature regarding studies on administration of oral steroids as a treatment modality for oral ulcers; instead, information is mainly from case reports.¹⁷ Recommended dose for oral prednisone is 40-60 mg/day for four to seven days and then tapering the dosage over two weeks.¹⁷ In our study an effort was made to find some treatment which should bring a notable difference as compared to various treatment modalities in vogue. In this study 45 mg of Prednisolone in 3 daily divided doses for 3 days was prescribed, and was named as "**Regimen of 3**", i.e 3 tablets 3 times a day for 3 days. The dose was scheduled as 03 tablets of 5mg each with every meal i.e breakfast, lunch and dinner. This resulted in better compliance. Since the body weight range of the sample was narrow, it was preferred to have a standard dose for simplicity.

Group I claimed a dramatic relief from the symptoms on Day 2. Regarding pain, 63.33% patients of group I and 33.33% of group II were symptom free. Joining work was possible in 36.67% and 16.67% in group I and II respectively. There were no clinically healed ulcers in either group. On second review visit i.e day 4, pain relief was experienced by 90% of patients in group I as compared to 46.67% of group II. The ability to join work was seen in 96.67% and 63.33% in group I and II respectively. Group I had 80% clinically healed ulcers in contrast to only 26.67% in group II. On the final review visit i.e Day 7, all the patients of group I were pain free. Whereas, 76.66% patients of group II had complete pain relief. All the patients (100%) of both the groups were able to join work. Significant healing of ulcers was also noted clinically viz 93.33% in group I and 80% in group II. Ulcer healing was at a remarkably faster pace in group I during early days. In the

other group the response to the treatment was lagging far behind. These findings are also suggestive of possible immune etiology.

Woo s, Sonis sb conducted a study with oral prednisolone in the dose of 0.5mg/kg body weight for seven days. There was 95% healing of ulcers at the end of one week.¹⁸ In the present study similar results were achieved with less than half duration of therapy.

There can be a possible disagreement to this study about the side effects of oral steroids. The dose of steroid chosen for the trial was too small to cause any side effects. Routinely, Prednisolone is prescribed from 70 to 80mg in daily divided doses for about one week and more as indicated under different clinical scenarios. The total dose used in the present study was 135mg, which is less than two days therapy dose otherwise. Before starting the recommended treatment, it is important that all the possible contra-indications be kept in mind, for example; Diabetes Mellitus, Hypertension, Peptic ulcer, pregnancy, lactation.

In this study the response to the oral steroids was excellent in comparison to the topical use. There is a need for comparison between different oral steroids and different doses of the same drug. This would help in achieving optimal results with minimum possible dosage to minimize the risk of side effects.

CONCLUSION

There is significant supremacy of oral steroid (Deltacortil) over topical use of Triamcinolone Acetonide in the treatment of severe Recurrent Aphthous ulcers. If there is no contraindication for the use of oral steroids, then they should be preferred over topical application for dramatic symptomatic relief and early return to work.

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