DOI: 10.14260/jemds/2015/914

ORIGINAL ARTICLE

AN OPEN LABEL PROSPECTIVE RANDOMIZED TRIAL TO COMPARE THE EFFICACY OF SALICYLIC ACID OINTMENT 3% VERSUS BETAMETHASONE DIPROPIONATE OINTMENT IN THE TREATMENT OF LIMITED CHRONIC PLAQUE PSORIASIS

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HOW TO CITE THIS ARTICLE:
K. Santha Bai, P. Sreenivas Naik. "An open Label Prospective Randomized Trial to Compare the Efficacy of Salicylic Acid Ointment 3% Versus Betamethasone Dipropionate Ointment in the Treatment of Limited Chronic Plaque Psoriasis". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 36, May 04; Page: 6296-6302, DOI: 10.14260/jemds/2015/914

ABSTRACT: AIMS AND OBJECTIVES: There is no study comparing Salicylic acid vs. betamethasone dipropionate ointment in limited chronic plaque psoriasis. The aim of this study is to compare the efficacy and safety of topical application of salicylic acid ointment with betamethasone dipropionate ointment applied once at night for 12 weeks for the treatment of limited chronic plaque psoriasis. **MATERIALS AND METHODS:** A total of 62 patients of limited chronic plaque psoriasis (body surface area <10%) were randomized into two treatment groups: Group A received topical application with 3% salicylic acid ointment and Group B received betamethasone dipropionate, once at night for 12 weeks. Results were assessed based on psoriasis area severity index (PASI) scores and patient global assessment (PGA) at each visit. **RESULTS:** Mean PASI was significantly lower at week 2(P=0.01) and week 4 follow-up (P=0.05) and the mean reduction in PASI was significantly higher at week 2(P=0.02) with betamethasone than salicylic acid, but this difference was not sustained at subsequent follow-up visits. Similarly, PGA scores at weeks 2 and 4 were significantly lower with betamethasone dipropionate ointment (P=0.003 and P=0.007 respectively). There was no significant difference in any parameter during subsequent follow-up visits or at the end of the treatment phase (12 weeks). **CONCLUSION:** Topical nightly application of betamethasone dipropionate ointment leads to an initial, more rapid reduction in disease severity, but the overall outcome parameters are comparable in the two treatment groups.

KEYWORDS: betamethasone, psoriasis, Salicylic acid.

What was known?

Both salicylic acid ointment and betamethasone ointment are topical agents for the treatment of limited chronic plaque psoriasis. Salicylic acid is conventional and inexpensive agent while betamethasone is a new and relatively expensive topical modality.

INTRODUCTION: Psoriasis is a common papulosquamous skin disorder affecting 1–2% of the world's population. In the majority of cases, the disease is mild, affecting limited body surface. Several topical modalities have been found effective in limited chronic plaque psoriasis. Salicylic acid is one of the oldest topical preparations for psoriasis. It has been found to have high efficacy and good safety profile. In a study by Kumar et al., 5% crude coal tar ointment was shown to induce 75% reduction in erythema severity index (ESI) in 59% of patients at 12 weeks.[1] Betamethasone dipropionate is a relatively new topical agent and there are numerous studies to document its efficacy in psoriasis.[2,3,4] It has been shown to produce significantly greater reduction in psoriasis area severity index (PASI) of 68.6% at week 4 compared with placebo (26.6%).

To the best of our knowledge there is no study comparing the efficacy and safety of conventional salicylic acid application with betamethasone dipropionate ointment in limited chronic plaque psoriasis.

MATERIALS AND METHODS: A prospective open label randomized trial was conducted in out-patients attending Department of DVL, Government General Hospital, Anantapuramu during the period Nov 2013 to May 2014. Patients of limited chronic plaque psoriasis (i.e., involving body surface area <10%) were included, who were off all topical medications in last 15 days and oral medications in last 1 month. A written informed consent was taken from all patients. Sample size calculation done by power analysis method. A total of 62 patients were randomized into two groups. Group A received topical application of 3% salicylic acid ointment, every night and Group B received betamethasone dipropionate ointment, every night for 12 weeks. No sun-exposure was advised in both groups. Use of emollients was allowed during the day in both groups. The endpoint was 12 weeks of treatment or attainment of PASI score 0, whichever was earlier. Patients were withdrawn from the study if there was <25% reduction in PASI at week 8, deterioration or serious side-effects warranting withdrawal.

Patients were followed-up at weeks 2, 4, 8 and 12 and assessed for disease severity by PASI score, patient's perception of disease severity (patient global assessment (PGA) on a scale of 0-10 with "10" being baseline disease and "0" being no disease and adverse effects. The following definitions were used for assessing treatment outcome.

- Complete clearance-attainment of PASI score 0 at any point of time during the treatment period.
- Responders-attainment of PASI > 50 at the end point of treatment ('complete clearance' cases + cases achieving 50 < PASI < 100).
- Poor responders-attainment of PASI > 50 at the end point of treatment.
- Deterioration-increase in PASI from baseline any time during 12 weeks of treatment.
- Relapse-appearance of disease in the treatment phase after attaining PASI score 0 and stopping treatment.
- Loss to follow-up: Any patient who did not return for the follow-up visits after initiation of treatment.

The primary efficacy parameter was a comparison of reduction in PASI from baseline to endpoint of treatment or week 12. secondary efficacy parameters were mean reduction in PASI at each follow-up visit, proportion of patients achieving PASI 75 and PASI 50 at week 12 or end point of treatment whichever, earlier and PGA score. Other treatment outcomes such as complete clearance, responders, poor responders, deterioration and relapse were also compared between the two groups.

Statistical Analysis: Two-sample Wilcoxon rank-sum (Mann-Whitney) test was used to assess statistical significance of difference in PASI, PGA, mean reduction and mean percentage reduction in PASI at each visit between two groups. Chi-square test was used to assess statistical significance of achievement of PASI 75 and PASI 50 in two groups. A $P < 0.05$ was considered significant.

RESULTS: A total of 62 patients were randomized into two groups: 33 patients in Group A (Salicylic acid group) and 29 patients in Group B (betamethasone dipropionate group). Among 62 study population 12 were female patients and 50 were male patients. Of these 13 patients in Group A and 8

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in Group B were lost to follow-up. Hence 20 cases in Group A and 21 in Group B completed the study period of 6 months (Figure 1). The two groups were comparable with respect to demographic and clinical profile. Mean PASI score at baseline in Group A (mean psoriasis area and severity index [mPASI] = 52) was comparable with Group B (mPASI=4.4).

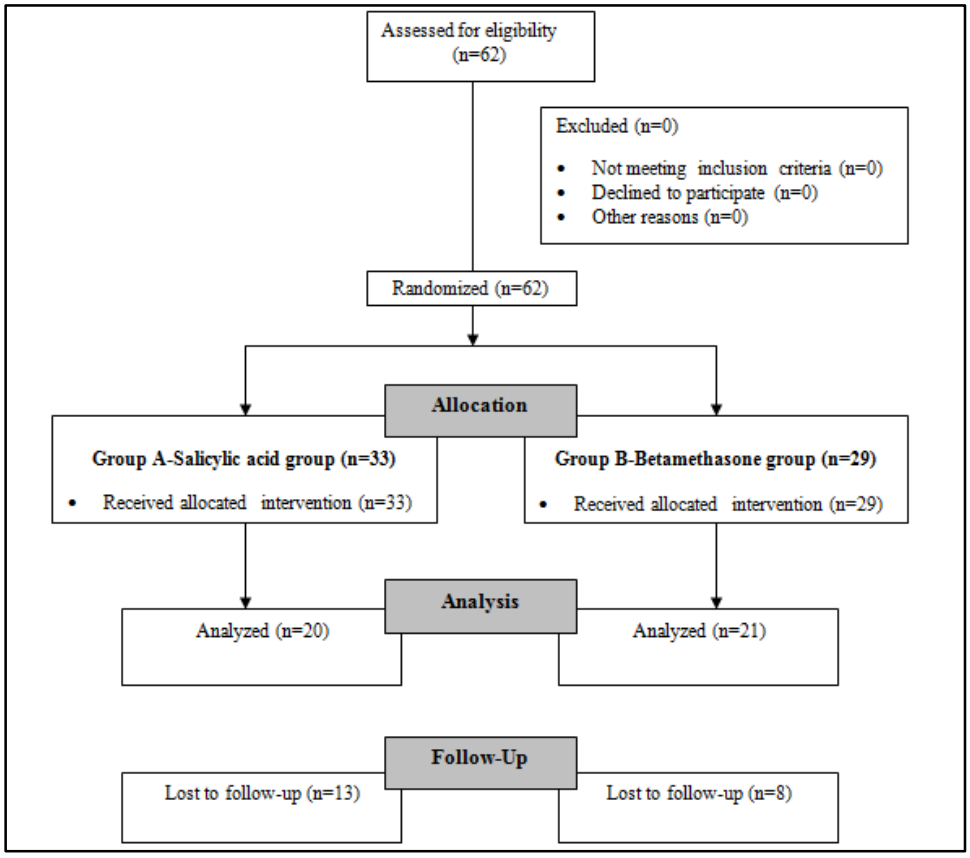

Fig. 1: Enrolment of cases in the study

After treatment, mean PASI at week 2 was significantly lower in Group B (2.7) compared with Group A (4.4) and the results were statistically significant (P=0.01; z= 2.55). Mean PASI at week 4 was also significantly lower in Group B (2.3) compared with Group A (3.5) (P=0.05; z=1.96) but there was no significant difference in mean PASI at week 8 (mPASI A = 2.9 and mPASI B = 2.6; P = 0.39; z=86) and week 12 (mPASI A=2 and mPASI B = 2.59; P = 0.17; z = -1.36) [Figure. 2]. Mean percentage reduction in PASI was significantly higher in Group B compared with Group A at week 2(15.4% in Group A vs. 38.6% in Group B) (P=0.02; z=-2.36), but not at subsequent follow-up visits. Mean percentage reduction in PASI at week 12 was 61.5% in Group A versus 40.7% in Group B (P = 0.18; z = 1.34). Hence at treatment completion, there was no statistically significant difference in PASI score or PASI reduction between the two groups. Follow-up visits conveniently done for a period of 6 months.

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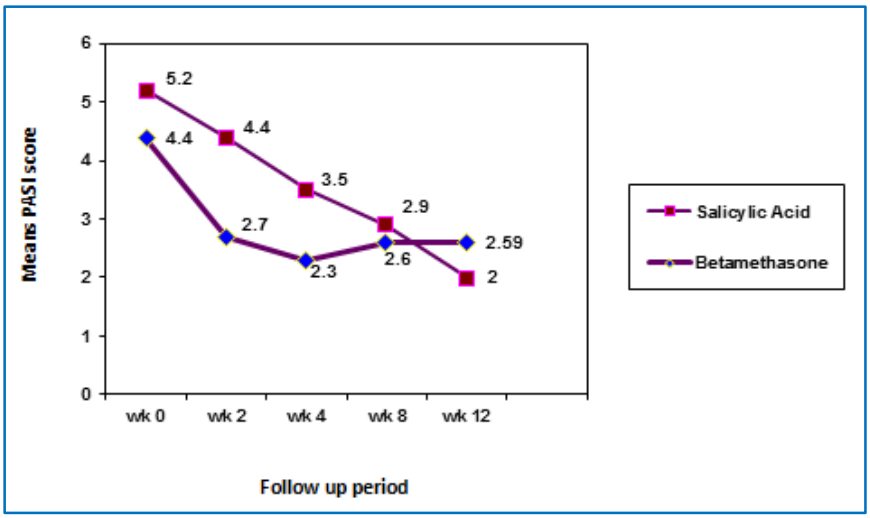

Fig. 2: Mean psoriasis area severity index score in two treatment groups at each follow-up visit

PASI 50 was attained by 8 of 20 cases (40%) patients in Group A compared to 9 of 21(42.8%) patients in Group B (P=0.36; χ^2 = 1.48; d. f. =1) at the end of treatment. PASI > 75 was achieved by 2 of 20 (10%) patients in Group A compared to 6 out of 21 (28.5%) patients in Group B (P=0.92; χ^2 = 0.33; d. f. = 1) [Table 1].

Treatment outcome	Group A Salicylic Acid ointment N = 20 (%)	Group B Betamethasone ointment N = 21 (%)
Complete clearance	1 (5)	4 (19)
Responders ('complete clearance' cases + cases achieving 50 < PASI < 100)	1+7=8 (40)	4+5=9 (42.8)
Poor responders	7 (35	6 (28.5)
Deterioration	5 (25)	6 (28.5)
Relapse*	0/1	¾ (75%)
Loss to follow-up	13/33 (39%)	8/29 (28%)

Table: 1: Comparison of treatment outcomes in the two groups

- One case in Group A and 4 cases in Group B achieved complete clearance. P = 0. 303; PASI: Psoriasis area severity index.

The difference in disease outcome at the end of treatment between the two groups was not statistically significant (P= 0.303; χ^2 = 5.07; d. f. = 4) [Table 1]. One case (5%) in salicylic acid group and 4 cases (19%) in betamethasone group had complete clearance of the disease during the treatment phase. Of the four cases in Group B who achieved complete clearance, 3(75%) cases relapsed on stopping treatment. The only case who cleared completely in Group A, did not relapse during 12 weeks

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of the study. PGA scores were significantly lower in Group B compared to Group A at week 2(6.75 and 8.24 respectively) and week 4(5.41 and 7.92 respectively); (P = 0.003; z = 2.95 and P = 0.007; z = 2.70 respectively). In subsequent follow-up visits, PGA scores were comparable and not statistically significant in the two groups [Figure 3].

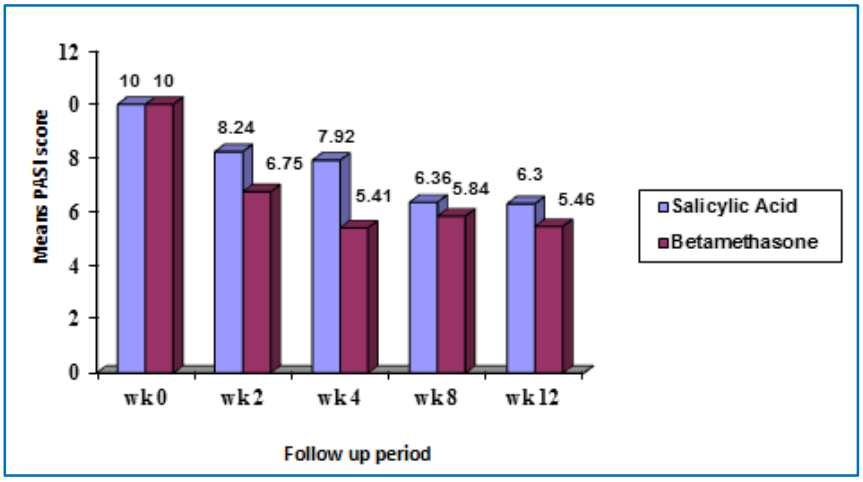

Fig. 3: Mean patient global assessment scores in two treatment groups at each follow-up visit

No side-effects were observed in the 2 groups. Unpleasant odour and staining of clothes were not reported by any patient in both groups.

DISCUSSION: Topical therapies are the mainstay of treatment for limited chronic plaque psoriasis. These include keratolytics, salicylic acid, corticosteroids, anthralin, topical PUVA, calcipotriol alone and in combination with topical steroids (betamethasone dipropionate or mometasone and tazarotene).[5,6] The antipsoriatic efficacy of salicylic acid and betamethasone has been individually reported in a number of studies.[7] Salicylic acid most commonly used, cheap, safe and effective treatment for psoriasis and its utility, either alone or in combination with phototherapy has been proved in many studies. salicylic acid present in commercially available ointments reduces the thickness and scaling of psoriatic plaques, thereby enhancing the penetration of the active medication. In the study by Kumar et al., all patients reported at least 50% reduction and 59.3% had greater than 75% reduction in ESI score with 5% crude coal tar.[1] Its clinical efficacy was found comparable with 0.1% tazarotene gel.[1] In our study, PASI 50 was achieved in 40% cases and PASI 75 in 10% cases after 12 weeks of treatment with salicylic acid ointment.

The two-compound formulation of betamethasone has been found to be superior to either component used alone in a large trial on 1605 patients, in which end point of absent-to-mild disease was achieved in 48% patients treated with a calcipotriol-betamethasone combination compared to only 16.5% patients treated with calcipotriol alone and 26.3% patients treated with betamethasone alone.[8,9] Another study found the efficacy of calcipotriol/betamethasone formulation to be better than calcipotriol alone at 2 and 4 weeks follow-up and showed a greater reduction in mean PASI in the combined formulation group (68.6% in once daily, 73.8% in twice daily group) than in the twice daily calcipotriol alone group (58.8%) and the vehicle group (26.6%).[10] PubMed search did not yield any literature on studies comparing salicylic acid with a betamethasone combination our study showed

that though a betamethasone combination resulted in an initial more rapid reduction in PASI (weeks 2 and 4), but this difference was not sustained at later follow-up visits. At the end of the treatment phase, greater mean reduction in PASI was achieved with salicylic acid combination. Greater though not significant number of cases achieved complete clearance, PASI 50 and 75 with a betamethasone combination. The other outcome parameters were also comparable at the end of the treatment phase. No side-effects were observed with both medications.

CONCLUSION: Ointment containing Betamethasone, initially produced significant faster clinical improvement and patient satisfaction than ointment containing salicylic acid applied once daily, but this effect is not sustained and the results are comparable after 12 weeks of treatment. A limitation of our study was high drop-out rate of cases in both groups. Hence further studies with larger sample size are required to compare betamethasone ointment with conventional topical agents.

ACKNOWLEDGEMENT:

- We would like to thank Dr. Penchalaiah, Associate Professor, incharge HOD, Dept. of Dermatology, GMC, GGH, Ananthapuramu.
- We would also like to thank Dr. Balarami Reddy for supporting with our study.
- We would also extend our thanks to entire staff of Dept. of Pharmacology, GMC, Anantapuramu.

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DOI: 10.14260/jemds/2015/914

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FINANCIAL OR OTHER COMPETING INTERESTS: None

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Date of Submission: 07/04/2015.
Date of Peer Review: 08/04/2015.
Date of Acceptance: 24/04/2015.
Date of Publishing: 02/05/2015.