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# Evaluation of the Effectiveness of Ursodeoxycholic Acid on PASI Score in Chronic Plaque Psoriasis

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***Abstract:***
***Background****: Increased cure from psoriasis could be achieved by remedying a possible deficiency of bile acids.*
***Objective****: To evaluate the effectiveness of T.UDCA with clobetasol propionate 0.05% and compare its effect with clobetasol 0.05% in patients suffering from chronic plaque psoriasis.*
***Methods****: Single centre, prospective, open control, comparative study in which two groups of adult patients with chronic plaque psoriasis were randomised. One group received T.UDCA and topical clobetasol while another received topic clobetasol. Primary end point was the percentage change from baseline in PASI score at the first and sixteenth week between the two groups.*
***Result****: At week sixteen, of the sixty patients, the reduction in PASI score was found to be much higher in the group that was administered UDCA and topical clobetasol and also had a significant P value(0.001). No adverse reactions were reported.*
***Conclusion****: T.UDCA along with topical clobetasol is more effective in a shorter duration with reduced incidence of relapse.*
***Keywords****: Chronic plaque psoriasis, Clobetasol propionate, PASI,Ursodeoxycholic acid*

## I. Introduction

Psoriasis is a chronic inflammatory, proliferative skin disorder characterized by thickened, erythematous and rounded plaque [1]covered by silvery micaceous scales which undergoes recurrent exacerbations and remissions [2].Psoriasis is a disorder affecting 1% of the world's population. The highest incidence of psoriasis is in Denmark. The incidence of Psoriasis in Asians is 0.4% [3].A WHO resolution [4] recognizes psoriasis as a painful debilitating disease associated with an elevated risk of serious comorbidities including cardio vascular disease, diabetes and psoriatic arthritis.The clinical appearance of psoriasis is a cosmetic concern for the patient and the disease is emotionally debilitating and can cause physical debilitation for patients with severe disease. Psoriasis is a disease of multiple etiologies; many drugs are being used in the treatment of Psoriasis.Topical therapy forms the mainstay of its treatment [5]. Current guidelines for the first line treatment of psoriasis recommend topical corticosteroids or topical Vitamin D analogues either separately or in combination [6, 7]. Since it is globally present, search for drugs having potential therapeutic effect with least adverse effects and rapid action is justified.

The basic pathophysiology of psoriasis is epidermal hyperproliferation, enhanced antigen presentation, TH1cytokine production, cell expansion and angiogenesis [8].Psoriasis is an immunologically mediated disease, the activated T-lymphocytes elaborate various cytokines, IL, TNF-α and the cascade of reactions are responsible for induction and maintenance of the pathological changes in the psoriatic skin lesion [9].Previous studies have shown that an abnormality in arachidonic acid metabolism has a causative role in psoriasis. The arachidonic cascade leads to the synthesis of eicosanoids including prostaglandins, thrombaxanes, leukotrienes and lipoxins [10]. The pathological picture of psoriatic lesions can be explained by the action of eicosanoids which affect both blood vessels and inflammatory cells and are involved in the regulation of epidermal growth and differentiation. The enzyme responsible for release of arachidonic acid in various tissues, including the skin, is considered to be phospholipase A2 (PLA2) [11]. The amount of free arachidonic acid and cPLA2d (a new member of the type IV cytosolic phospholipase A2 family) activity is dramatically increased in psoriatic skin. The release of arachidonic acid in the epidermis has been suggested to be an important event in the onset of psoriasis [12].Studies have proven that bacterial endotoxins might have a role in the pathogenesis of psoriasis. Bacterial endotoxins are important initiators of cytokine release .Under normal circumstances bile acids act as detergents and split the enteric endotoxins into nontoxic fragments. In the presence of bile acid deficiency, varying amounts of endotoxin enters the blood stream and could induce cytokine release in the skin [13].Studies prove that the administration of Ursodeoxycholic acid lowers the raised PLA2IIA (group IIA PLA2). It also

lowers the protein mass in the gallbladder and gallbladder bile of patients with cholesterol stones [14]. Expression of PLA2IIA in HepG2 cells (a human hepatoblastoma-derived cell line) is inhibited by UDCA in a dose-dependent fashion [15].Another study has proved the inhibitory effect of tauroursodeoxycholic acid on the growth of cultured human keratinocytes [16].

The above studies have proven that Ursodeoxycholic acid has a definite role in reducing PLA2IIA. The major enzyme responsible for the release of arachidonic acid is PLA2 and the arachidonic acid level is increased in psoriatic skin. Also by remedying a possible deficiency of bile acids, an increased cure from psoriasis could be achieved. This correlation has encouraged to take up this study in which the effectiveness of Ursodeoxycholic acid to reduce the severity of psoriasis is investigated. Ursodeoxycholicacid, is derived from 7 β epimerization of chenodeoxycholic acid in the colon & it is less than 5% of the normal bile acid pool in humans.

## II. Aim

To evaluate the effectiveness of Tablet. Ursodeoxycholic acid with Clobetasol propionate 0.05% ointment in patients suffering from chronic plaque psoriasis and to compare its effect with Clobetasol propionate 0.05 % ointment, which is used topically for psoriasis.

## III. Objectives

To compare the percentage change from baseline in PASI score at $1^{st}$, $2^{nd}$, $3^{rd}$, $4^{th}$, $5^{th}$,$6^{th}$,$7^{th}$,$8^{th}$,$12^{th}$ and 16weeks between the two groups .

## IV. Methodology

This Prospective randomized open labeled study was started after getting the approval of the institutional ethics committee of Govt. Stanley medical college. Written informed consent was obtained from the study participants after explaining the details regarding the research in their own native language.The study was conducted at the outpatient department of dermatology of Stanley medical college from July 2014 to June 2015. Each patient received drug for a period of 12 weeks, followed by post trial observation for 4 weeks.

**1.1 Inclusion Criteria:**Patients more than 18 years and less than 60 years of both sexes, patients with Chronic Plaque Psoriasis having lesions in upper limb, lower limb and trunk and patients who were not on any specific treatment for psoriasis in preceding 3 months were included in the study.

**1.2 Exclusion Criteria:**Pregnant, lactating women were excluded from the study. Patients with any other type of psoriasis and those with other systemic illness were excluded. Also patients with known history of drug allergy, patients with evidence of infection at the affected site, those taking systemic therapy for psoriasis and those already on topically applied immunosuppressants were excluded from the study.

After carefully screening the patients for inclusion and exclusion criteria, a total number of 60 patients were included in the study. These patients were subjected to the following investigations.

*Haematological investigations:* Complete hemogram, Platelet count and Peripheral smear.

*Hepatic Investigations:*Serum Transaminase levels, Alkaline Phosphatase level and Serum Proteins

*Renal Investigations:* Urine analysis, Albumin, sugar, deposits, Serum creatinine, Blood urea and Serum uric acid. Blood sugar, HIV screening, ENT examination, Dental Examination and Chest X-ray.

These investigations were done prior to the selection. Only patients who are medically fit were included in the study. These investigations were repeated at the end of each month till the completion of the study. A detailed clinical examination was also done. Site and size of the lesions were assessed.PSORIASIS AREA and SEVERITY INDEX (PASI's SCORE) was used to measure the severity and coverage of the disease and also to assess the benefits of drugs in psoriasis treatment [17].Fredriekson and Petterson first introduced PASI in 1977. This scoring was done before and after treatment with drugs.

Auspitz's sign was elicited and presence of kobner's phenomenon was looked for. Examination of the scalp, nail and mucous membrane was also done. Only patients with characteristic lesions consisting of sharply demarcated, dull red scaly plaques in upper limb, lower limb and trunk were selected and divided into two groups of 30 each, namely Group I and II. All the patients in Group I were asked to apply topical Clobetasol propionate once a day before bedtime. All the 30 patients in Group II were treated with Clobetasol propionate once daily at bedtime and T.Ursodeoxycholic acid 300 mg, 1 tablet in the morning and 1 tablet at night after food.Drug Treatment period is 12 weeks. During the study, the drugs were stopped in patients whose PASI score showed zero and they were not asked to continue the drugs though they were followed upto 16 weeks. After the drug treatment period of 12 weeks all the patients were followed for a further period of 4 weeks which is a drug free period. Patients were requested to attend the outpatient department of dermatology once in a week on a fixed day to evaluate the treatment outcome as mentioned earlier. The parameters-Induration, erythema, and desquamation were evaluated and PASI score was calculated every week upto the $8^{th}$ week, then once at $12^{th}$ week and once at the $16^{th}$ week. Patients were also questioned and examined for adverse effects like diarrhea,

itching, burning, pigmentation and atrophy. Compliance of the patient was confirmed by asking them to return the empty tubes and the empty tablet blister pack on the next visit. Only on returning the empty tube and the blister pack,new tubes and new tablet packs were given to the patient.

**1.3 Statistical Analysis:** Data was expressed as mean ± standard deviation. Students independent ' t' test was used for comparing quantitative data between the two groups. At the end of the study the effects of topical Clobetasol alone and combination of topical Clobetasol with tablet Ursodeoxycholic acid was compared in terms of therapeutic efficacy and adverse effects.

## V. Results

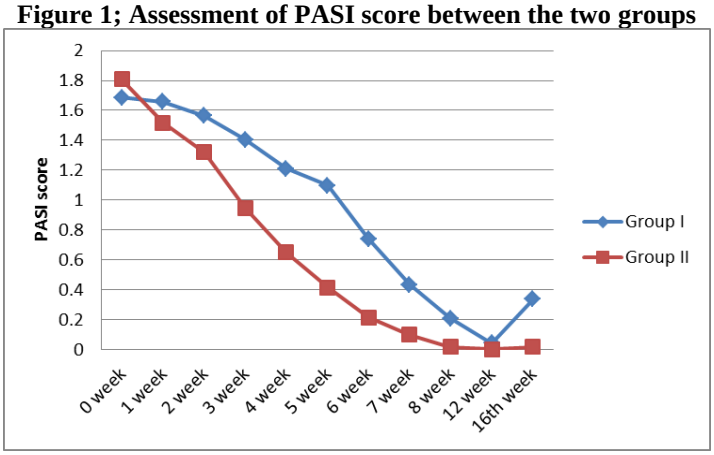
A total of 78 patients were selected and screened for the study Based on the selection criteria, 18 patients were excluded and the remaining 60 patients were randomly allocated into two groups of 30 patients each. There were no dropouts in each of the groups. Baseline characteristics of both the groups including the mean age, sex distribution, baseline induration, erythema, desquamation was assessed and tabulated. Group I consisting of 30 patients were treated with topical Clobetasol 0.05% and were compared with Group II, in which the 30 patients were treated with T. Ursodeoxycholic acid 300 mg twice daily along with topical Clobetasol 0.05%.There was no focal sepsis in any patients and none of them had any systemic diseases. Induration, erythema, desquamation were assessed and PASI score was calculated to evaluate the severity of lesion& benefits of the treatment.Both the study and control groups had comparable age distribution.There was no significant difference in the gender distribution between the two groups.There was a male preponderance in both the groups.

**Table No: 1**Statistical analysis for PASI score in Group I and Group II

| | Group I | | Group II | | Student Independent t test | Repeatedmeasures ANOVA |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Baseline | 1.68 | 0.70 | 1.80 | 0.92 | t=0.40,p=0.69 | Between groups: F=16.54 P=0.001(very high significance)<br><br>Within groups: F=195.88 P=0.001(very high significance) |
| Week 1 | 1.65 | 0.70 | 1.51 | 0.82 | t=0.73p=0.46 | |
| Week2 | 1.56 | 0.69 | 1.32 | 0.74 | t=1.32,p=0.19 | |
| Week 3 | 1.40 | 0.59 | 0.93 | 0.51 | t=3.01,p=0.004 | |
| Week 4 | 1.21 | 0.51 | 0.65 | 0.45 | t=4.49,p=0.001 | |
| Week 5 | 1.09 | 0.48 | 0.41 | 0.38 | t=6.05,p=0.001 | |
| Week 6 | 0.74 | 0.38 | 0.21 | 0.29 | t=7.45,p=0.001 | |
| Week 7 | 0.43 | 0.21 | 0.09 | 0.10 | t=5.48,p=0.001 | |
| Week 8 | 0.20 | 0.18 | 0.01 | 0.05 | t=5.34,p=0.001 | |
| Week 12 | 0.04 | 0.10 | 0.00 | 0.00 | t=0.00,p=0.001 | |
| Week 16 | 0.33 | 0.23 | 0.01 | 0.05 | t=6.29,p=0.001 | |

PASI score is psoriasis area severity index. The severity of psoriasis is assessed using the PASI score. The parameters considered for calculation are erythema, induration and desquamation.PASI score calculation for both the groups were done before starting therapy and at the end of every week of therapy till the 8$^{th}$ week and at twelve weeks, and also at the end of 16 weeks.On statistical analysis of the PASI scores, the mean value of the PASI score before starting therapy in group I is 1.68 and Group II is 1.80.The reduction in mean is very much greater in Group II when compared to Group I at the end of 1st week till the 12$^{th}$ week and the mean of the PASI score in Group I is 0.04 whereas in Group II is 0.00.Student T-test for PASI scoring shows that the values are very highly significant from the end of third week.At the end of 3$^{rd}$ week, P value is 0.004 & from the fourth week onwards it was 0.001which is highly significant.

**Figure 1; Assessment of PASI score between the two groups**



## VI. Discussion

The effect of oral Ursodeoxycholic acid plus topical clobetasol propionate in chronic plaque psoriasis was assessed in 30 patients in comparison with 30 patients who were treated with topical clobetasol. One more group of patients treated with Ursodeoxycholic acid alone could have been included, but for ethical reasons this was not done since the patients should not be denied of established drug treatment.The results of the study were found to be highly encouraging than the earlier studies done using Ursodeoxycholic acid .From the results, it is clear that the combination therapy with Ursodeoxycholic acid and clobetasol are having greater effects than clobetasol given alone. Clinically the rate of remission and reduction in PASI score is faster in Group II. This is also proved statistically.The analysis of the results shows that combination therapy which was used in Group II are producing faster and greater beneficial effects. Both topical Clobetasol and oral Ursodeoxycholic acid did not produce any systemic or local adverse effects during the study.UDCA also has suppressive effect on PLA2IIA activity and therefore be beneficial in psoriasis . Previous studies have shown positive effects in acute form of psoriasis, this study was attempted in chronic plaque psoriasis.[18]The current study was done in 30 patients to evaluate the efficacy of Ursodeoxycholic acid in Chronic plaque psoriasis .The sample size is small but this study can form a basis for a larger study in our set up to define the precise role of UDCA in psoriasis.The high incidence of psoriasis makes the treatment of this disease an important public health issue .Any treatment modality appearing to be better than previously used methods can rightfully command interest.The sample size of the study is small .Quality of life assessment was not done.

## VII. Conclusion

In this study which has been conducted at Stanley Medical College Out Patient Department of Dermatology,oral Ursodeoxycholic acid along with topical Clobetasol propionate has been found to be effective in the treatment of chronic plaque psoriasis in a shorter duration with reduced incidence of relapse even after the drug free period. Our study encourages further studying of the pathophysiology of psoriasis and the intestinal factors.The effectiveness,safety, simplicity of bile acid supplementation makes this treatment modality suitable for a wider use.

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