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ORIGINAL ARTICLE

A STUDY OF COMPARATIVE EFFEICIENCY OF ORAL MINI PULSE THERAPY VERSUS ORAL ACITRETIN IN GENARALISED LICHEN PLANUS

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ABSTRACT: BACKGROUND: Lichen planus is a chronic inflammatory disease that effects skin, mucous membranes, hair and nails. There are several drugs both topical and systemic for the treatment of lichen planus. **AIMS AND OBJECTIVES:** Present study was done to compare the efficacy between oral mini pulse therapy with betamethasone and with acetretin in the management of generalised lichen planus. **MATERIALS AND METHODS:** The study was carried out on patients who were clinically diagnosed as generalised lichen planus, attending the outpatient department of dermatology, venereology and leprosy, King George hospital, affiliated to Andhra medical college, Vishakhapatnam from November 2011 to December 2012. A total of 60 patients were included in study and divided into two equal groups. Group1 patients were treated with 0.1mg/kg of oral betamethasone given on 2 consecutive days in a week till 8 weeks and tapered. Group 2 patients were treated with 0.5mg/kg of acetretin for 8 weeks and tapered. **INCLUSION CRITERIA:** All patients of age group in between 11-60 years, of either sex, suffering from lichen planus of duration >3 months, and women in group 2 who were in reproductive age group on two methods of contraception were included. **EXCLUSION CRITERIA:** Pregnant and lactating women, in Group 1: patients suffering from diabetes, hypertension, peptic ulcer disease, renal, hepatic, heart disease or tuberculosis, in Group 2: patients with abnormal lipid profile, diabetes, hypertension, renal, liver or heart disease were excluded. **RESULTS:** out of 60 patients enrolled in study, 2 patients from group 1 and 5 patients from group 2 were dropped from study and results were concluded. Majority of patients were in age group of 31-60 (78.3%) with male to female ratio of 2.1:1.Group 1 patients at the end of 8 weeks response was seen in 92.8%, with relapse rate of 15.38% after 6 months of follow up. Group 2 patients at end of 8 weeks response was seen in 72 % with relapse rate of 5.5%. **CONCLUSION:** In our study oral mini pulse therapy with betamethasone has early onset of action and with a complete response in majority of patients with slightly more relapse rate when compared to oral acetretin. Oral acetretin has less relapse rate due to prolonged half-life.

KEYWORDS: Lichen planus, Mini pulse therapy, Betamethasone, Acetretin.

INTRODUCTION: Lichen planus (LP) is an immunologically mediated inflammatory disorder of skin, hair, nails and mucous membranes characterised by well-defined purple pruritic papular lesions mainly distributed in flexor aspects of extremities.[1] The main pathogenic mechanism underlying lichen planus lesions is keratinocyte apoptosis induced by cytotoxic T cells and NK cells initiated by specific self-antigens in genetically predisposed individuals with several predisposing, triggering or exacerbating factors treatment of lichen planus is aimed at suppression or modification of inflammatory response. Generalised lichen planus is treated more commonly used systemic agents like corticosteroids, acitretin, sulfasalazine, dapsone, cyclosporine, azathioprine and topical PUVA

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and NBUVB. The present study was done to compare the efficacy between oral betamethasone mini pulse therapy and oral acitretin and to know the relapse rate.[2,3,4,5,6,7,8,9,10]

MATERIALS AND METHODS: The study was carried out on patients who were clinically diagnosed as generalised lichen planus, attending the outpatient department of dermatology, venereology and leprosy, King George hospital, affiliated to Andhra medical college, Visakhapatnam from November 2011 to December 2012. A total of 60 patients were included in study and divided into two equal groups. Informed consent was taken. Details of patient like age, sex, occupation, patients with generalised lichen planus of >3months duration, symptoms, past history was taken. Routine blood investigations like hemogram, total leucocyte count, platelet count, random blood glucose levels, renal function tests, liver function tests, lipid profile, 2D-ECHO, chest X ray P-A view and skin biopsy were done to rule out systemic disease and to confirm LP. After confirming diagnosis and ruling out the systemic diseases, the patients were randomly divided into 2 groups. Group1 patients were treated with 0.1mg/kg of oral betamethasone given on 2 consecutive days in a week till 8 weeks and tapered. Group 2 patients were treated with 0.5mg/kg of acitretin for 8 weeks and tapered. Both the groups were followed up for 6months.

Inclusion Criteria: All patients of age group in between 11-60 years, of either sex, suffering from generalised lichen planus of duration >3 months were included.in group 2 women in reproductive age group followed two methods of contraception were included.

Exclusion Criteria: Pregnant and lactating women, in Group 1: patients suffering from diabetes, hypertension, peptic ulcer disease, renal, hepatic, heart disease or tuberculosis, in Group 2: patients with abnormal lipid profile, diabetes, hypertension, renal, liver or heart disease were excluded.
Data analysis: the data is analysed using percentages, ratios and p-values.

RESULTS: Total of 60 confirmed cases of generalised lichen planus were selected after considering exclusion criteria. Other variants of lichen planus were excluded from study. Results were analysed and tabulated.

Age Distribution: (Table1) Maximum number of cases 73% were detected in age group of 31-40, least number of cases 2% were in age group of 11-20years age group. Sex distribution (Table 2): 40 out of 60 were female patients with female to male ratio of 2.1:1. Out of 60 patients severe pruritus was observed in 66.66% of cases, moderate pruritus in 21.66% and mild pruritus in 5%, no pruritus in 2% of cases. Of the clinical variants of lichen planus patients with generalised cutaneous involvement were included in study. out of 60 patients, 50% are having classical lichen planus lesions, where as 26.6% has classic LP lesions with mucosal involvement, 6% has hypertrophic lesions, 3% with classical lesions and follicular lesions and 8 % has hypertrophic lesions alone.

Among 30 patients in group 1 there are 2 drop outs, and response to treatment after 8 weeks is 92.8%. Among 30 patients in group 2 there are 5 drop outs, and the response rate is 72% slightly low when compared to group 1. The difference observed among two groups was statistically significant with a p- value <0.05. In 51-60 year age group the response rate was 66.6% in both groups. Response rate was 80-100% and 66-70% between ages of 21-50 years with oral mini pulse and oral acitretin respectively. (Table 4) Response rate was 100% with oral mini pulse therapy in

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11-20 years age group. Response rate was slightly more in females treated with oral mini pulse and males treated with acitretin. [Table 5] Side effects most commonly noted in group 1were gastritis (53%) and weight gain (35.7%) [Table 6] Side effects most commonly noted in group 2 were dry lips (80%), nausea, and vomiting and hair loss (20% each). Serum triglycerides were elevated only in 1/25 patients. [Table 7]

Among 28 patients in group 1 there is a relapse rate of 3.84%, 7.69% and 15.38% was observed at the end of 2nd, 4th and 6th months of follow up respectively. [Table 8]

DISCUSSION: Lichen planus is an immune mediate disease affecting skin, hair, nails and mucous membranes with genetic predisposition and various triggering factors.[1] There are many clinical variants of disease. The disease can be generalised where systemic therapies were given in order to treat the disease.[2,3,4,5,6,7,8,9,10] Out of all systemic modalities oral corticosteroids,[3,11,12,13] are the mainstay of therapy, in present study an attempt was made to compare the efficacy between oral mini pulse therapy with betamethasone,[12] and oral acitretin.[5]

Age Distribution: In present study, Out of 60 patients, 78.33% of lichen planus cases were in age group of 30-60years which is comparable to western study by melgren et al. Sex distribution (Table 9): In present study female patients outnumbered males in a ratio of 2.1:1, which is nearly comparable to study by vijay kumar et al, In a study done by ramesh et al,[13] male patients outnumbered females, (54.28%) patients were males and 16(45.71%) were females. Present study out of 60 patients, 40(66.66%) patients had severe pruritus with sleep disturbance affecting quality of life and itching subsided around 4-6 weeks after starting treatment and is slightly early in patients treated with mini pulse therapy. Severe pruritus was seen in 16(45.7%) patients in study done by ramesh et al.,[13] present study severe itching was present in higher percentage.

Response Rate: Group 1 patients at the end of 8 weeks, response was seen in 92.8%, with relapse rate of 15.38% after 6 months of follow up. The relapse rate was compared to study done by ramesh et al, (14%) Corticosteroids have been used as a therapeutic modality for LP topically, intralesionally or systemically. Oral mini pulse therapy was taken in order to decrease the side effects of pulse therapy and improve the efficacy.[11,12,13] Side effects are less with oral mini pulse therapy than with daily therapy. The most common side effects in this study group were gastritis, weight gain and nausea seen in around all patients (25/28).

In study by ramesh et al, side effects due to treatment were seen in 20(57.1%) patients; most commonly weight gain, insomnia and epigastric pain. Group 2 patients at end of 8 weeks complete response was seen in 72% with relapse rate of 5.5%. As acitretin has long t 1/2 when compared with oral mini pulse and due re-esterification a small amount of drug is released from fat stores so therapeutic effect is maintained even after stopping the drug. So there are few relapses in patients treated with acitretin group. The response to therapy was comparable with study done by Laurberg G et al,[14] patients treated with acitretin (30mg/day) showed reponse rate of 64%, at the end of 8th week which is slightly less when compared to present study. Regarding side effects typical retinoid side effects were seen in only 80% of patients treated with acitretin but in study done by Laurberg et al typical retionoid side effects were seen in all patients (Table 10).

CONCLUSION: The present study concluded that oral mini pulse treatment has good response rate and more symptomatic relief but with high relapse rate, acitret in treated group has less relapse rate. More comparative studies has to be done in future.

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Age	Number of Cases	Percentage %
11-20years	6	10%
21-30years	7	11.6%
31-40years	22	36.66%
41-50years	17	28.33%
51-60years	8	13.3%
Total	**60**	**100%**

Table 1: Age Distribution in Present Study

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Sex	Number of Cases	Percentage %
Males	20	31.66%
Females	40	66.66%
Total	**60**	**100%**

Table 2: Sex Distribution in Present Study

Modality of Treatment	Total Number of Patients Tried	Total Number of Patients Completed Treatment Excluding Dropouts	Resolution at the End of 4 Weeks	Resolution at the End of 6 Weeks	Resolution at the End of 8 Weeks	Total Number of Patients with Response at the End of 8 Weeks.
Oral Betamethasone Mini Pulse Therapy	30	28	5	11	10	26(92.8%)
Oral Acitretin	30	25	2	6	10	18(72%)

Table 3: Response of the Disease in Relation to Duration of Therapy and Modality of Treatment

	ORAL MINI PULSE			ORAL ACITRETIN		
Age in Years	No. of Patients Treated	No. of Patients Responded	Percentage	No. of Patients Treated	No. of Patients Responded	Percentage
11-20years	5	5	100%	0	0	0%
21-30years	4	4	100%	3	2	66.6%
31-40years	11	11	100%	9	7	77.7%
41-50years	5	4	80%	10	7	70%
51-60years	3	2	66.6%	3	2	66.66%

Table 4: Response rate in relation to age after deducing dropouts

	ORAL MINI PULSE			ORAL ACITRETIN		
Sex	No. of Patients	No of Patients Responded	Percentage	No. of Patients	No. of patients Responded	Percentage
Male	10	9	90%	8	6	75%
Female	18	17	94.4%	17	12	70.58%

Table 5: Response Rate in Relation to Sex

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Adverse Effects	No. of Patients	Percentage
Gastritis	15	53%
Weight Gain	10	35.7%
Nausea /Vomiting	2	7%
Acneiform Eruptions	2	7%
Insomnia	1	3.5%

Table 6: Adverse Effects in Group 1- Oral Mini Pulse Therapy

Adverse Effects	No. of patients	Percentage
Dry Lips	20	80%
Nausea /Vomiting	5	20%
Hair Loss	5	20%
Xerosis of Skin	4	16%
Pruritus	4	16%
Serum Triglyceride Elevation	1	4%

Table 7: Adverse Effects in Group 2- Oral Acitretin Therapy

	<2 months		3-4 months		5-6 months	
	No of Patients With Relapse	Percentage	No of Patients with Relapse	Percentage	No of Patients With Relapse	Percentage
Oral Mini Pulse	1	3.84%	2	7.69%	4	15.38%
Oral Acitretin	0	0	0	0	1	5.5%

Table 8: Relapse Rate After 6 Months of Follow up After Treatment in Both Groups

	Present Study	Ramesh et al.
Male	31.66%	54.28%
Females	66.66%	45.71%
Male: Female Ratio	1:2.1	1.18:1

Table 9: Comparison of Sex Ratio Between Present Study and Ramesh et al.

	Present Study With Acitretin	Laurberg et al.
Total Patients in Study	25	65
Response Rate	72%	64%
Side Effects Typical Retinoid Side Effects	80%	100%
Elevated Serum Triglycerides	4%	None

Table 10: Comparison between Present Study with Acitretin and Study by Laurberg et al.

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