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Evaluating the Relative Effectiveness of Methotrexate and Acitretin in Chronic Plaque Psoriasis Treatment

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ABSTRACT

Background: Chronic plaque psoriasis is a prevalent autoimmune skin disorder characterized by persistent red, scaly plaques. Methotrexate and acitretin are established systemic therapies, but their comparative efficacy in treating chronic plaque psoriasis needs further research. **Objective:** To compare the efficacy of methotrexate and acitretin in chronic plaque psoriasis treatment. **Study Design:** Randomized Controlled Trial. **Settings:** This study was conducted at DHQ Hospital, Muzaffargarh Pakistan. **Duration:** December 2022 to May 2023. **Methods:** Total 155 patients diagnosed with Chronic Plaque Psoriasis, aged 18 to 55 years, are recruited from the OPD of hospital. Inclusion criteria comprise a confirmed diagnosis of chronic plaque psoriasis and no prior exposure to methotrexate or acitretin within the last six months. Patients with previous intolerance or allergic reactions to methotrexate or acitretin, presence of severe hepatic impairment or chronic liver disease and known pregnancy or lactating mothers were excluded. Participants were randomized into two groups using computer-generated random numbers. Group A receives methotrexate at a dose once a week for 12 weeks as a tablet at a dosage of 0.3-0.5 mg/kg and Group B is treated with Acitretin in which patients were given a capsule at a dosage of 0.4 mg/kg daily for duration of 12 weeks. Statistical analysis is performed using SPSS version 23. **Results:** The study involved 150 patients with a mean age of 52.33± 16.55. Gender distribution indicated that 47(31.33%) were male, and 103(68.66%) were female. The baseline PASI scores for the methotrexate and acitretin groups were 14.12±3.21 and 14.79±1.08, respectively. At the 3-month, the PASI scores were 7.92±2.07 for methotrexate and 8.14±1.03 for acitretin. The mean reduction in PASI scores was 54.12±9.22 for methotrexate and 47.31 ± 11.31 for Acitretin, with a significant difference favoring Methotrexate (p =0.031*). Of the total participants, 68.66% demonstrated efficacy, with 78.66% in the methotrexate group and 58.66% in the acitretin group, indicating a significant difference (p < 0.005*). Conversely, 31.33% showed no efficacy, with 21.33% in the methotrexate group and 41.33% in the acitretin group. **Conclusion:** In conclusion, the frequency of effectiveness was significantly higher with methotrexate (78.66% vs. 58.66%) p=<0.005) as compared to acitretin in treating chronic plaque psoriasis.

Keywords: Acitretin, Adverse effects, Dermatology, Efficacy comparison, Methotrexate, Psoriasis treatment, Treatment complications.

INTRODUCTION

Chronic Plaque Psoriasis (CPP) stands as a prevalent and multifaceted dermatological condition that affects millions of individuals worldwide. Characterized by distinctive erythematous plaques with silvery scales, this chronic inflammatory disorder significantly impacts the quality of life of those afflicted. As a globally recognized skin disorder, CPP transcends geographical boundaries, affecting people across diverse demographics.[1,2] Globally, Chronic Plaque Psoriasis represents a substantial burden on public health, with estimates suggesting that approximately 2-3% of the world's population grapples with this chronic condition.[3]

In Pakistan, the prevalence of Chronic Plaque Psoriasis has been steadily increasing, mirroring global trends. Although precise epidemiological data is limited, clinical observations and research studies indicate a prevalence ranging from 1.5% to 2.5% in various regions of the country. The variability in prevalence can be attributed to genetic, environmental, and lifestyle factors that contribute to the heterogeneity of the population.[4,5] The etiology of Chronic Plaque Psoriasis is complex and multifactorial.[6]

Understanding the pathogenesis of Chronic Plaque Psoriasis is crucial for the development of targeted therapies. The dysregulation of the immune system, specifically involving T-helper cells and cytokines, leads to the characteristic inflammatory cascade and abnormal keratinocyte proliferation. Advances in molecular and genetic research have unraveled intricate signaling pathways, paving the way for innovative therapeutic interventions.[8] Methotrexate and Acitretin are two commonly employed systemic therapies for Chronic Plaque Psoriasis, each with distinct mechanisms of action. Methotrexate, an immunosuppressant, inhibits DNA synthesis and cellular proliferation, addressing the rapid turnover of skin cells in psoriatic lesions. In contrast, Acitretin, a retinoid, regulates skin cell growth and differentiation. The choice between these medications depends on factors such as patient characteristics, comorbidities, and treatment goals.[9,10]

This comparative study aims to contribute valuable insights to the existing literature on Chronic Plaque Psoriasis by systematically evaluating the efficacy of Methotrexate versus Acitretin. By rigorously analyzing patient outcomes, this research seeks to provide a nuanced understanding of the relative effectiveness, safety profiles, and patient tolerability of these two widely used systemic treatments.

METHODS

This randomized controlled trial was conducted at DHQ Hospital Muzaffargarh from December 2022 to May 2023. The sample size of 150 patients was calculated to detect a clinically significant difference in PASI scores between the two groups, with a efficacy of 76.7% in methotrexate and 56.7% in acitretin group significance level was 95% and margin of error was 5%. Total 150 patients diagnosed with Chronic Plaque Psoriasis, aged 18 to 55 years were recruited from the OPD of hospital. Inclusion criteria comprise a confirmed diagnosis of chronic plaque psoriasis and no prior exposure to methotrexate or acitretin within the last six months. Patients with previous intolerance or allergic reactions to methotrexate or acitretin, presence of severe hepatic impairment or chronic liver disease and known pregnancy or lactating mothers were excluded.

Participants were randomized into two groups using computer-generated random numbers.Group A receives methotrexate at a dose once a week for 12 weeks as a tablet at a dosage of 0.3-0.5 mg/kg and Group B is treated with Acitretin in which patients were given a capsule at a dosage of 0.4 mg/kg daily for duration of 12 weeks. The primary outcome measure is the Psoriasis Area and Severity Index (PASI) score, assessed at baseline then at 3 months (12 weeks). Secondary outcome was adverse events in both groups. Data was collected at baseline and subsequent follow-up visits. Trained assessors, blinded to treatment allocation, perform clinical evaluations.

Statistical analysis is performed using SPSS version 23. Descriptive statistics was used to summarize baseline characteristics. The primary analysis involved comparing mean changes in PASI scores between the two treatment groups using independent t-tests or non-parametric equivalents.

RESULTS

The study involved 150 patients with a mean age of 33.52 years (SD ± 6.55). Age distribution showed that 95(63.33%) were in the 18-35 age range, while 55(36.66%) were between 36-55 years old. Gender distribution indicated that 47(31.33%) were male, and 103(68.66%) were female. Smoking status revealed that 25(17%) were current smokers, 90(60%) were non-smokers, and 35(23%) were former smokers as shown in table 1.

Table 1: Baseline characteristics of study sample

Parameter	Characteristics	N (%)
Age	Mean ± SD	33.52 ± 6.55
	18-35 years	95 (63.33%)
	36-55 years	55 (36.66%)
Gender	Male	47 (31.33%)
	Female	103 (68.66%)
Smoking Status	Current Smokers	25 (17%)
	Non-Smokers	90 (60%)
	Former Smokers	35 (23%)
Family History of Psoriasis	Yes	55(37%)
	No	95 (63%)
Previous Treatments	Topical	80 (53%)
	Phototherapy	30 (20%)
	Systemic	50 (33%)
	Biologics	15 (10%)

The baseline PASI scores for the methotrexate and acitretin groups were 14.12 ± 3.21 and 14.79 ± 1.08, respectively, with no statistically significant difference (p = 0.525). At the 3-month mark, the PASI scores were 7.92 ± 2.07 for Methotrexate and 8.14 ± 1.03 for Acitretin, showing no significant difference (p = 0.568). The mean

reduction in PASI scores was 54.12 ± 9.22 for Methotrexate and 47.31 ± 11.31 for Acitretin, with a significant difference favoring Methotrexate (p = 0.031*) given in table 2.

Table 2: The PASI score at baseline and 3 months, as well as the percentage reduction between the study groups

Parameters	Methotrexate	Acitretin	P-value
PASI	14.12±3.21	14.79±1.08	0.525
At 3 months	7.92±2.07	8.14±1.03	0.568
Mean Reduction	54.12±9.22	47.31±11.31	0.031*

The table 3 compares the effectiveness of adverse effects between methotrexate and acitretin treatments. Of the total participants, 68.66% demonstrated efficacy, with 78.66% in the methotrexate group and 58.66% in the acitretin group, indicating a significant difference (p < 0.005*). Conversely, 31.33% showed no efficacy, with 21.33% in the methotrexate group and 41.33% in the acitretin group.

Table 3: Comparison of effectiveness of Adverse effect of both treatments methotrexate and acitretin

Parameter	Yes / No	Methotrexate	Acitretin	Total	P-value
Efficacy	Yes	59 (78.66%)	44 (58.66%)	103 (68.66%)	<0.005*
	No	16 (21.33%)	31 (41.33%)	47 (31.33%)	

Table 4 details the occurrence of adverse effects in the methotrexate and acitretin treatments. For individuals receiving methotrexate, the adverse effects and their respective percentages were as follows: nausea/vomiting in 14 (18.66%), hair loss in 7 (9.33%), pruritus in 17 (22.66%), headache/dizziness in 19 (25.33%), and loss of appetite in 6 (8.0%). In the acitretin group, the corresponding figures were 16 (21.33%) for nausea/vomiting, 13 (17.33%) for hair loss, 19 cases (25.33%) for pruritus, 22 (29.33%) for headache/dizziness, and 10 (13.33%) for loss of appetite.

Table 4: Adverse effect of both treatments methotrexate and acitretin

Complications	Methotrexate	Acitretin
Nausea/ vomiting	14 (18.66%)	16 (21.33%)
Hair loss	7 (9.33%)	13 (17.33%)
Pruritus	17 (22.66%)	19 (25.33%)
Headache/dizziness	19 (25.33%)	22 (29.33%)
Loss of appetite	6 (8.0%)	10 (13.33%)

DISCUSSION

Chronic plaque psoriasis is a persistent skin condition characterized by raised, red, and scaly patches, affecting a substantial number of individuals globally.[11] Treatment approaches often involve systemic medications, with methotrexate and acitretin being commonly prescribed.[12]

In our study involving 150 psoriasis patients, we observed a mean age of 33.52±6.55 years, with a predominant age distribution in the 18-35 range (63.33%). Gender distribution revealed 31.33% male and 68.66% female participants. Family history of psoriasis showed a positive history in 37% of cases. Previous treatments included topical therapies (53%), phototherapy (20%), systemic treatments (33%), and biologics (10%). Comparing our findings with Saadiya *et al*. (2023), we note a higher mean age in our study and a higher proportion of female participants, potentially influenced by psychosocial factors.[13] Our age distribution aligns with Mohd *et al*. (2016), demonstrating similarities with the Malaysian Psoriasis registry.[14] Additionally, our gender distribution is comparable to Gawlik *et al*. (2016), suggesting variations in psoriasis demographics across different regions.[15] Our study on chronic plaque psoriasis, we observed a different gender distribution compared to Augustin *et al*. (2010), who reported a higher prevalence among males (76%) and a lower proportion among females (24%) in Germany.[16]

The comparative analysis of our study findings with Saadiya *et al*. (2023) underscores the efficacy and differential impact of methotrexate and acitretin in chronic plaque psoriasis. In our study, Methotrexate demonstrated a significant mean reduction in PASI scores compared to Acitretin, aligning with Saadiya *et al*.'s observations of a 53.46±10.64% reduction in the methotrexate group and a 48.24±10.24% reduction in the acitretin group.[13]

The findings of our study align with those of Naldi *et al*., where methotrexate demonstrated clinical improvement in 75% of patients, mirroring our study's efficacy rate of 76.7%.[17] Haider *et al*. reported a mean baseline PASI reduction from 14.8±4.2 to 4.9±4.3 in 40% of patients, achieving partial remission (75% reduction in PASI) in 60% of cases.[18] In our study, 76.7% of methotrexate-treated patients achieved a 50% or greater reduction in PASI, surpassing the partial remission rate in Haider *et al*.(2014) Heydendael *et al*. observed partial remission in 60% of methotrexate-treated patients after 16 weeks, using a 75% reduction in PASI as an endpoint, indicating consistency with the higher reduction threshold in our study.[19]

Our study's findings on adverse effects align closely with those reported by Parsam *et al*. (2015), reinforcing the

consistency of medication profiles across different populations. For methotrexate, both studies identified nausea/vomiting (20% in Parsam *et al*. and 18.66% in our study) and hair loss (8% in Parsam *et al*. and 9.33% in our study) as primary adverse effects, showcasing a parallel pattern.[20]

CONCLUSION

In conclusion, the frequency of effectiveness was significantly higher with methotrexate (78.66% vs. 58.66%) p=<0.005) as compared to acitretin in treating chronic plaque psoriasis. However, further research and long-term assessments are warranted to comprehensively evaluate the safety and efficacy profiles of these medications in managing chronic plaque psoriasis.

LIMITATIONS

A limitation of our study is the reliance on self-reporting for adverse effects, which may introduce subjective bias and underreporting.

SUGGESTIONS / RECOMMENDATIONS

Recognizing the importance of future investigations in this field is essential.

CONFLICT OF INTEREST / DISCLOSURE

None.

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