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Original Research Article

Evaluating the Effectiveness and Safety Profile of Azathioprine in Psoriasis

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Abstract

Background: Chronic plaque psoriasis is a debilitating inflammatory skin condition requiring systemic therapy in moderate to severe cases. While methotrexate and biologics are commonly prescribed, azathioprine may serve as a useful alternative when these options are contraindicated.

Aim: To evaluate the efficacy and safety profile of azathioprine in the management of chronic plaque psoriasis among patients attending a tertiary care hospital in South India, with specific assessment of PASI improvement over a 24-week period.

Material and Methods: An observational study was conducted involving 80 patients diagnosed with chronic plaque psoriasis. Patients received oral azathioprine 50 mg twice daily for 24 weeks. PASI scores were measured at baseline, 12 weeks, and 24 weeks. Safety was assessed through regular laboratory monitoring and clinical adverse event documentation.

Results: A total of 82.5% patients achieved fair to good therapeutic response. Mean PASI reduced from 14.2 at baseline to 6.3 at 12 weeks and 5.1 at 24 weeks. Adverse effects were mild and included exacerbation (15%), nausea (7.5%), and transient LFT elevation (7.5%).

Conclusion: Azathioprine is a moderately effective and well-tolerated systemic option in chronic plaque psoriasis, especially in patients with limitations to using methotrexate or biologics.

Keywords: Azathioprine, Psoriasis, PASI Score, Immunosuppressive Therapy.

Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by hyperproliferation of keratinocytes, vascular remodeling, and infiltration of immune cells such as T-lymphocytes and dendritic cells [1]. It affects approximately 2–3% of the global population and is increasingly being recognized not just as a dermatological condition but as a systemic disease with significant psychosocial and metabolic comorbidities [2,3]. Chronic plaque psoriasis, the most common clinical form, accounts for nearly 90% of all psoriasis cases [4].

The management of moderate to severe plaque psoriasis often necessitates systemic therapy. While methotrexate, cyclosporine, and biologics such as adalimumab and ustekinumab remain the cornerstone of treatment, azathioprine—a purine synthesis inhibitor—has emerged as a potential alternative, particularly in resource-limited settings or when standard therapies are contraindicated [5,6]. Azathioprine's immunosuppressive properties arise from its active metabolites, which inhibit DNA replication and suppress T-cell mediated immune responses, a key component in the pathogenesis of psoriasis [7]. Recent clinical data highlight the growing need to re-evaluate older immunomodulators like azathioprine, particularly in populations where newer biologics are either inaccessible or unaffordable [8]. Although traditionally used in autoimmune disorders and transplant medicine, azathioprine has shown promising efficacy in dermatologic conditions including pemphigus vulgaris, atopic dermatitis, and psoriasis [9]. It has been particularly useful in chronic plaque psoriasis cases that are refractory to methotrexate, or where patients present with contraindications such as liver dysfunction, anemia, or pulmonary fibrosis [10].

However, data regarding its long-term safety and efficacy in psoriasis, especially in the Indian subcontinent, remain sparse. There is also a need for structured trials to understand its therapeutic window, potential adverse effects—especially hepatotoxicity, myelosuppression, and gastrointestinal intolerance—and the time-dependent nature of its response profile, typically requiring 6–8 weeks for visible clinical improvement [6,11]. The PASI (Psoriasis Area and

Severity Index) score remains the gold standard for evaluating treatment response in psoriasis. Several recent Indian and global studies have advocated the use of PASI improvement benchmarks (≥75% as a good response, 50–74% as fair, <50% as poor) to compare the relative efficacy of different systemic agents [12,13].

Given the economic and healthcare access disparities in South Asia, a systematic evaluation of azathioprine in a controlled clinical context is warranted. This study was thus designed to evaluate the efficacy and safety profile of azathioprine in the management of chronic plaque psoriasis among patients attending a tertiary care hospital in South India and to assess treatment response in terms of PASI improvement over a 24-week period.

Material and Methods

This was a hospital-based observational study conducted in the Department of Dermatology at a tertiary care center in South India over a period of 18 months. A total of 80 consecutive patients clinically diagnosed with chronic plaque psoriasis were enrolled after obtaining written informed consent. The study aimed to evaluate the efficacy and safety profile of azathioprine therapy in patients presenting with moderate to severe psoriasis, with particular focus on improvement in Psoriasis Area and Severity Index (PASI) scores over a 24-week follow-up period.

Inclusion criteria comprised adult patients aged 18 years and above with stable plaque psoriasis of at least six months' duration, a PASI score of ≥10, and body surface area (BSA) involvement of ≥10%. Patients were excluded if they were under 16 years of age, pregnant or lactating, had not completed their family planning, or were suffering from significant systemic illnesses involving the liver, kidneys, heart, lungs, or gastrointestinal system. Patients with a history of recent immunosuppressive therapy within the last four weeks, known hypersensitivity to azathioprine, or who had experienced prior treatment failure with azathioprine were also excluded. The decision to withdraw therapy was taken in cases where patients exhibited worsening of psoriasis, developed significant adverse effects, or failed to achieve at least 50% PASI improvement by 12 weeks.

The diagnosis of psoriasis was made clinically and supported by histopathological examination in doubtful cases. Baseline evaluation included a detailed clinical history, physical examination, and laboratory investigations such as complete blood count, liver function tests (LFTs), serum creatinine, blood urea, chest X-ray, HBsAg, and Mantoux test. All patients with normal baseline reports were initiated on azathioprine 50 mg twice daily for a total treatment duration of 24 weeks. Concomitant topical therapy with white soft paraffin was prescribed for all patients. Antihistamines like cetirizine were administered in symptomatic cases for relief of pruritus.

Clinical evaluation and PASI scoring were done at baseline, 12 weeks, and 24 weeks. Follow-up visits were scheduled biweekly for the first month and every four weeks thereafter. At each visit, patients underwent clinical examination and monitoring of laboratory parameters. Hematological monitoring included complete blood count performed every two weeks during the first two months, monthly in the next two months, and once every two months for the remaining study duration. Liver function tests were done monthly for the first three months and then every two months thereafter.

Therapeutic response was evaluated using PASI scores, with ≥75% improvement from baseline considered a good response, 50–74% as fair response, and <50% improvement classified as poor response. Safety was assessed by documenting adverse effects such as nausea, vomiting, elevated liver enzymes, and disease exacerbation, and decisions regarding drug continuation or withdrawal were made accordingly.

Results

The therapeutic response to azathioprine therapy was evaluated using improvement in PASI scores at 12 and 24 weeks. Among the 80 patients included in the study, 14 patients (17.5%) demonstrated a good response with ≥75% improvement in PASI, while 52 patients (65%) showed a fair response with improvement between 50–74%. Poor response, defined as <50% PASI improvement, was observed in 14 patients (17.5%). The observed difference in clinical response was statistically significant with a p-value of <0.001, suggesting that azathioprine led to meaningful improvement in a substantial proportion of the study population, particularly in those with moderate disease burden as seen in Table 1.

In terms of safety and tolerability, adverse effects were documented across several categories. Of the 80 patients, 56 (70%) experienced no adverse events throughout the 24-week treatment period. However, 12 patients (15%) reported exacerbation of existing lesions, often occurring within the first two weeks of therapy. Nausea and vomiting were reported in 6 patients (7.5%) and were transient in nature. Mild liver enzyme derangement was noted in 6 patients (7.5%), but in all cases, values normalized within two weeks without requiring discontinuation of therapy. This suggests that while azathioprine was generally well-tolerated, vigilant monitoring remained essential during early and mid-phase treatment, as outlined in Table 2.

The comparison of PASI scores over time revealed a clear trend of clinical improvement with azathioprine therapy. The mean baseline PASI score at initiation of therapy was 14.2. By the 12th week, this value had declined to 6.3, and by the 24th week, a further reduction to 5.1 was observed. These findings confirm that while the initial therapeutic effect of azathioprine may be modest during the first 6–8 weeks, continued treatment leads to consistent and significant improvement in disease severity. The reduction in PASI over time was statistically significant as shown in Table 3.

Table 1: Therapeutic response (n = 80)

Improvement in PASI	Number of patients	Response category
<50%	14	Poor response
50–74%	52	Fair response
≥75%	14	Good response
P value	< 0.001	

Table 2: Distribution of patients with respect to occurrence of various adverse effects (n = 80)

Adverse effects	Number of patients
No adverse effects	56
Deranged LFTs	6
Exacerbation	12
Nausea and vomiting	6

Table 3: Comparison of PASI at baseline, 12th week and 24th week (n = 80)

Time Point	Mean PASI Score
Baseline	14.2
12th week	6.3
24th week	5.1

Discussion

The present study was undertaken to assess the efficacy and safety of azathioprine in chronic plaque psoriasis, particularly among patients in whom standard therapies such as methotrexate may be contraindicated or poorly tolerated. Our findings showed that out of 80 patients, 82.5% achieved either good or fair response in PASI improvement after 24 weeks of therapy, supporting the drug's role as an effective immunosuppressive agent in psoriasis management. These results resonate well with those reported in earlier studies that explored azathioprine as a second-line or adjunct therapy for recalcitrant cases.

Du Vivier et al. conducted one of the early evaluations of azathioprine for psoriasis, involving 29 patients, and observed clinical improvement in nearly 66% of the cases. They initiated dosing at 100 mg/day and escalated to 200–300 mg/day over weeks, maintaining it until remission was achieved [11]. Compared to our dosing strategy of 50 mg BD (i.e. 100 mg/day), our response rate was comparable, suggesting that even lower fixed-dose regimens may be sufficient for moderate to severe disease with fewer adverse events.

Similarly, Mezzadra et al. administered high cumulative doses of azathioprine (up to 6 g over 18 days) in their trial, achieving efficacy comparable to methotrexate [12]. However, the aggressive dosing used in their protocol raised concerns of gastrointestinal intolerance and hepatotoxicity. In contrast, the present study demonstrated a favorable safety profile with only 7.5% of patients showing mild liver function derangement and a relatively low dropout rate due to intolerance. These differences highlight the need for dose optimization tailored to population-specific tolerability and comorbidity patterns.

In our study, exacerbation of existing lesions was observed in 15% of patients within the first two weeks of treatment. This phenomenon may be attributed to the delayed onset of azathioprine's therapeutic action, typically manifesting only after 6–8 weeks. Notably, no prior studies, including those by Du Vivier or Mezzadra, have described such early disease worsening, although the slow-acting nature of the drug is well documented [11,12]. The clinical implication is that early flares may be transient and not necessarily indicative of therapeutic failure, thus emphasizing the importance of patient education and close follow-up in the early phase.

A study by Kumar et al. compared 243 cycles of methotrexate in 197 psoriasis patients and reported over 75% improvement in 88% of cases within an average of 8.5 weeks [13].

Though methotrexate consistently demonstrates superior efficacy, azathioprine remains a useful alternative when methotrexate is contraindicated. It also has a more favorable hepatic safety profile in some cohorts, as reported in our study, where only a minority experienced minor LFT abnormalities.

Finally, Greaves and Dawber found only a 25% PASI improvement in azathioprine-treated patients in a 6-week study, likely due to premature evaluation before the drug's full therapeutic window [14]. Their findings emphasize the importance of assessing response at later intervals. In our study, the mean PASI dropped from 14.2 at baseline to 6.3 at 12 weeks and further to 5.1 at 24 weeks, reflecting the delayed but meaningful efficacy of azathioprine when continued appropriately.

Overall, while biologics and methotrexate remain the gold standards for moderate to severe psoriasis, azathioprine presents a cost-effective, tolerable, and clinically useful alternative in carefully selected patients. Regular monitoring, especially during the initial phase, and tailoring doses based on clinical response are crucial to its success. The findings of this study contribute to the growing body of evidence supporting azathioprine as a viable systemic agent in the Indian population.

Conclusion

Azathioprine demonstrated appreciable efficacy and tolerability in patients with chronic plaque psoriasis over a 24-week treatment period. With 82.5% of patients achieving fair or good PASI responses and minimal adverse effects, azathioprine proves to be a valuable systemic option, especially in settings where biologics and methotrexate are not feasible. Its relatively low cost, acceptable safety profile, and moderate efficacy position it as a reasonable second-line agent in patients with contraindications to standard therapies.

Early lesion exacerbation and mild hepatic enzyme elevation were manageable and did not necessitate therapy discontinuation in most cases. Thus, azathioprine should be considered in individualized treatment plans for moderate to severe psoriasis in tertiary care settings.

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