

Short-Term Side Effects of Azathioprine in Patients with Inflammatory Bowel Disease

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ABSTRACT

Introduction: Inflammatory bowel disease (IBD), such as ulcerative colitis, Crohn's disease, and indeterminate colitis, is a complex, chronic inflammatory disorder of the gastrointestinal tract with diverse clinical symptoms and complications. Purine analogs, including azathioprine (AZA) and 6-mercaptopurine, are immune-suppressive medications commonly employed to induce and maintain remission in IBD. However, their use is constrained by the potential for side effects, which have been reported to occur in 5% to 30% of patients, with severe and potentially fatal bone marrow suppression affecting 2% to 5% of individuals. Research has indicated that 25.8% of patients discontinued AZA due to side effects, and 6.6% required dose reduction. Given the limited global studies and lack of similar research in Iran identifying the short-term side effects of AZA and the factors, our study aimed to evaluate the short-term side effects of AZA in IBD patients based on laboratory findings.

Methods and Materials: This prospective cohort study was conducted at a gastroenterology clinic in Isfahan in 2022. The study population included all IBD patients treated with AZA (1-1.5 mg/kg) and followed for six months to monitor treatment response and adverse effects. SPSS was used in this study to analyze the data. The normality of data normality was assessed using the Kolmogorov-Smirnov test with Lilliefors correction. Parametric tests (Student's t-test and ANOVA) were employed for normally distributed data, while non-parametric tests (Mann-Whitney and Kruskal-Wallis) were applied for data that did not meet this assumption. When expected frequencies were low, categorical data were analyzed using Pearson's chi-square or Fisher's exact test. Logistic regression was applied for combined result analysis using IBM-SPSS v.20.

Results: The analysis included 50 IBD patients. The average age was 37.5 for men and 40.1 for women. The mean disease duration was approximately nine years, and the average treatment duration in this study was about five months. Among the patients studied, the incidence of side effects from initiating AZA treatment to ending one year of follow-up was 24%. The side effects observed included leukopenia, thrombocytopenia, elevated ALT levels, and increased creatinine levels.

Conclusion and Discussion: AZA side effects can be dose-related, such as myelosuppression, infections, and malignancies, or dose-independent hypersensitivity reactions such as fever, rash, arthralgia, hepatitis, and gastrointestinal disturbances, which typically occur 2 to 4 weeks after the initiation of treatment. Myelosuppression is the most common reason for dose reduction or discontinuation of AZA. A profound potential side effect of AZA is bone marrow suppression, which is linked to low thiopurine methyltransferase activity due to genetic polymorphisms. Regular monitoring during therapy is essential. Pancreatitis, a rare but serious side effect, was not observed, suggesting its low incidence should not deter AZA use. AZA remains a cost-effective, widely available treatment for IBD, and its manageable side effects warrant its continued use in clinical practice.

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