

Title: Incidence of Skin Changes in Patients with Myasthenia Gravis Prescribed Mycophenolate or Azathioprine

Objective:

To examine the impact of mycophenolate mofetil (MMF) and azathioprine (AZA) on the incidence of development of skin lesions in patients with myasthenia gravis (MG).

Background:

International consensus guidelines for the management of MG recommend the use of nonsteroidal immunosuppressive agents, such as MMF and AZA. It has been reported that AZA increases the risk of malignancies. Limited information exists on the risk of skin cancer in MG patients treated with MMF.

Methods:

This is a single center, cohort study of patients with MG. Retrospective chart review was conducted to gather demographic data, MG history and management. Patients were contacted via EHR patient message, telephone, and/or during clinic appointment to request participation in a standardized survey to assess skin lesion history. Patients were assigned to either non-exposed or exposed groups, determined by treatment with MMF or AZA for ≥ 12 months. Statistical analysis was performed using chi-square for categorical data and logistic regression to analyze the relationship between age and MMF/AZA exposure on incidence of skin lesions.

Results:

Of 194 total patients in MG clinic population, 142 patients met inclusion criteria and were contacted to request participation. Majority (67%) were white, with median age of 67 years (IQR 48-74), and 56% identifying as female. A total of 103 patients (72%) responded to the survey, with 63 patients (61%) in the exposed group and the remaining 39% either naïve to these agents or exposed for < 12 months. Of those surveyed, 51 and 14 patients had been exposed to MMF or AZA, respectively, including 2 patients who had been exposed to both agents.

Per the patient-reported survey, we found that 8 (16%) and 5 patients (36%) developed skin lesions after initiation of MMF and AZA, respectively. Of those exposed, only 6 patients (10%) reported a malignant lesion. Of the non-exposed patients, 16 patients (40%) reported historical or current skin lesions, including 10 (25%) who reported a malignant lesion. The incidence of skin lesions was significantly lower in the exposed group compared with the non-exposed cohort ($X^2=4.536$, $p=0.033$). When adjusting for current age, it was found that the odds of experiencing skin lesions was lower in the patients exposed to MMF or AZA compared with the non-exposed group (OR=0.383, 95% CI 0.149 - 0.959).

Conclusions:

Based on this large MG cohort survey study, we found that the incidence of reported skin lesions in patients exposed to MMF or AZA was statistically lower than the incidence of reported lesions in patients not exposed to these medications. After adjusting for current patient age, the incidence of skin lesions reported in the exposed group compared with the non-exposed group remains significantly lower. Two potential factors could explain these findings: variable sun exposure in MG populations due to risk of MG exacerbation and/or refused treatment with AZA/MMF after being counseled on potential risk of skin malignancies. Prospective studies with detailed dermatological evaluation may be essential for further investigation of the skin cancer risk in MG patients treated with AZA and MMF.