Assessing the Incidence of Elevation in Eosinophils with the Use of Dimethyl Fumarate in Multiple Sclerosis

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INTRODUCTION

Dimethyl fumarate (DMF) is an oral medication approved for the treatment of relapsing forms of Multiple Sclerosis (MS). In the pivotal MS studies involving DMF, a transient increase in mean eosinophils was seen during the first 2 months of therapy.

However, the incidence of this is not well reported, and its clinical significance is yet to be established.

STUDY AIMS

Our aims with this study were to:
1. Assess the incidence of elevation in eosinophils with the use of DMF in MS.
2. Begin to glean insight into its clinical relevance by assessing side effects and adverse events occurring among these patients.

METHODS

A retrospective chart review was conducted on all patients in our MS clinic who were prescribed DMF between March 2013 and March 2015 under routine care. Those who began treatment and had available pre- and post-dosing complete blood counts (CBC) that included levels of eosinophils were included in analysis. Patients were excluded if their pre-CBCs occurred more than 6 months prior to starting DMF. Elevation in eosinophils in this study was defined as ≥27% of all leukocytes on differential.

RESULTS

A total of 311 patients were prescribed DMF. Of these, 202 met criteria for inclusion, with 149 female patients (74%) and 53 male. Patient ages ranged from 18 to 75 years, with an average age of 47 years.

The incidence of elevation in eosinophils was 9.4% (19 of 202 patients). Elevated levels ranged from 7% to 19.5% of all leukocytes on differential. Of the 19 patients, 16 (84%) developed elevated eosinophils by the first post-CBC, an average of 2.4 months after starting DMF. Elevations were sustained for >1 year in only two patients and were otherwise transient. Thirteen of the 19 patients (68%) discontinued DMF; for six of them (46%), the reason was gastrointestinal side effects.

Only one patient had pre-existing elevated eosinophils (19.8% of all leukocytes on differential) while still on natalizumab. This patient experienced a normalization of eosinophils after switching to DMF therapy for their MS.

CONCLUSIONS

This study follows our initial study evaluating eosinophils in MS, as presented in 2015. To our knowledge, ours are among the first studies assessing the incidence of DMF-related elevations in eosinophils. Our data has several potential clinical implications:

First, it has been postulated that DMF-related gastrointestinal symptoms could be due to an eosinophilic, gastroenteritis-like syndrome. Whereas flushing is generally the most common side effect of DMF, in our study, gastrointestinal symptoms were the most common side effect among patients with elevated eosinophils and the most common reason for discontinuing DMF in these patients.

Second, a transient increase in eosinophils has been observed with fumaric acid esters, a similar compound to DMF which is used to treat Psoriasis. This has been attributed to elevations in IL-4, which stimulates eotaxin, an eosinophil-activating cytokine. IL-4 also decreases Th1 cells and increases Th2 cells.

Given that Th2 activation would be beneficial in MS, this increase in eosinophils might imply a positive treatment response and thus could be considered a biomarker. Further studies are needed to investigate this.

REFERENCES