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Mexican Biosimilar Filgrastim for Autologous Hematopoietic Stem Cell Mobilization and Transplantation

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ABSTRACT

Background: Following the release of the initial presentation of filgrastim (granulocyte colony-stimulating factor), several biosimilars have been developed worldwide. **Objective**: To study the efficacy of a Mexican biosimilar granulocyte colony-stimulating factor in a single transplant center. **Methods**: In a group of 19 consecutive patients with multiple sclerosis given autografts, we employed granulocyte colony-stimulating factors to mobilize stem cells from the bone marrow to the peripheral blood, either the original granulocyte colony-stimulating factor (n = 10) or a Mexican granulocyte colony-stimulating factor biosimilar (n = 9). **Results**: The efficacy of both agents was similar in mobilization capacity, white blood cell count rise, stem cell collection, and kinetics of auto-engraftment. **Conclusion**: We conclude that both granulocyte colony-stimulating factor agents were similar in their efficacy to mobilize stem cells and usefulness in autografts. (REV INVES CLIN. 2016;68:181-3)

Key words: Biosimilar, Filgrastim. G-CSF. HSCT.

INTRODUCTION

The human recombinant granulocyte colony-stimulating factor (G-CSF) filgrastim has been used in the mobilization and transplantation of $CD34^+$ peripheral blood hematopoietic stem cells (PBHSC) as well as in the prophylaxis of chemotherapy induced neutropenia. The first G-CSF employed in clinical practice was Neupogen® (Amgen, Thousand Oaks, CA, USA); however, the introduction of generics and biosimilars later on has resulted in saving the world's healthcare budget an enormous amount of money[1].

Recently, a biosimilar filgrastim agent has been developed, produced, and used in Mexico (Filatil®, Probiomed, Atzcapotzalco, Mexico). To assess its efficacy, we conducted an observational, randomized, prospective, longitudinal study in a single center in Mexico in patients with multiple sclerosis (MS) to assess the efficacy and safety of two G-CSF agents, the original

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Table 1. Arithmetic mean (range) of the variables analyzed in the patients given granulocyte colony-stimulating factor agents (Neupogen® or Filatil®)

	Neupogen®	Filatil®	p value
Number of patients	10	9	
Total WBC after mobilization and before apheresis, × 10^9/l	17 (2-39)	23 (1-45)	0.41
Granulocyte count before apheresis, × 10^9/l	14 (1-31)	18 (0.5-40)	0.39
Number of apheresis needed to obtain > 1 × 10^6/kg $CD34^+$ PBHSC	1 (1-2)	1 (1-2)	0.66
Number of $CD34^+$ PBHSC obtained per apheresis, × 10^6/kg	2 (1-10)	2 (1-4)	0.29
Number of $CD34^+$ PBHSC grafted, × 10^6/kg	3 (1-10)	2 (1-6)	0.16
Days to recover above 0.5 × 10^9/l granulocytes	9 (6-12)	10 (8-11)	0.97

All the differences are statistically non-significant employing Fisher´s exact test.
PBHSC: peripheral blood hematopoietic stem cells; WBC: white blood cell.

G-CSF and the Mexican biosimilar G-CSF, in both the mobilization and transplantation of $CD34^+$ PBHSC.

METHODS

The PBHSC mobilization schedule was done with cyclophosphamide (Cy) and filgrastim (G-CSF). Intravenous Cy (50 mg/kg) was delivered in a 120-minute period on days −11 and −10. Subcutaneous G-CSF (10 µg/kg twice daily) was delivered on days −9 to −1. Apheresis was performed on day − 2 to obtain at least 1 x 10^6 viable $CD34^+$ cells/kg. As conditioning, intravenous Cy (50 mg/kg) was delivered on days −2 and −1 followed by MESNA, ondansetron, dexamethasone and pantoprazole. G-CSF 5 µg/kg once daily was re-started on day +3 until granulocyte recovery was above 0.5 x 10^9/l.

RESULTS

Nineteen consecutive patients with MS (12 females) with a median age of 47 years (30-65) were prospectively randomized to be given G-CSF, either the original G-CSF (n = 10), or the Mexican biosimilar. At the end of the deployment, the total white blood cell count (WBC) as well as the absolute granulocyte count was similar for the two groups of patients. The number of aphereses needed to obtain at least 1 x 10^6 viable $CD34^+$ cells/kg, as well as the number of $CD34^+$ PBHSC obtained in each apheresis, was similar for patients given either G-CSF. The time to recover above 0.5 x 10^9/l granulocytes was also similar for both G-CSF agents. Bone pain presented in four patients in the original G-CSF group and in three in the biosimilar group. Table 1 summarizes these results; the differences observed were statistically non-significant employing Fisher´s exact test.

DISCUSSION

In patients with hematological malignancies, comparisons of efficacy between different G-CSF agents are difficult since many variables may introduce bias, such as the underlying disease and hence the type and amount of chemotherapy previously delivered to the patients[2-4]. In this group of MS patients, there was no history of previous exposure to chemotherapy and the comparisons may be more valid, despite the low number of individuals studied[5]. In this study, we found no differences in efficacy between the original G-CSF and the Mexican biosimilar; these results support the idea that the two G-CSF agents are equally effective in mobilizing and autografting $CD34^+$ PBHSC. Along this line, Danylesko, et al.[2] have shown the usefulness of a biosimilar human G-CSF made in Israel (Tevagrastim®), whereas Nahon, et al.[3] employed Zarzio®, another biosimilar G-CSF made in France, and both agents were found to be equally effective compared to Neupogen®. In a different study published by Sivgin, et al.[6], the biosimilar Leucostim® induced a significantly higher count of peripheral blood $CD34^+$ compared with the Neupogen® group. The efficacy of biosimilar G-CSF versus Neupogen® in multiple studies worldwide has proven to be equivalent and to provide a cost-effective strategy in all instances[7-11].

The information obtained from this study should be added to that coming from other trials concerning the usefulness of G-CSF biosimilars worldwide.

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