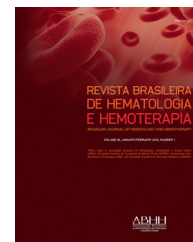




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### Original article

# Herpes zoster after autologous hematopoietic stem cell transplantation

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#### ABSTRACT

**Background:** The autologous hematopoietic stem cell transplantation procedure involves immunosuppression of the patient. Thus, the patient has an elevated risk for several diseases, such as infections with the varicella-zoster virus. Prevention protocols have been proposed based on the use of acyclovir from the first day of conditioning, and maintaining this drug for 30–100 days after the procedure or for as much as one year. The objective of this work was to evaluate the incidence of herpes zoster after autologous transplantations related to the early suspension of acyclovir.

**Methods:** A retrospective study was carried out based on the collection of data from 231 medical records of transplant patients in the Bone Marrow Transplant Unit of the teaching hospital of the Universidade Federal de Juiz de Fora in the period between 2004 and 2014.

**Results:** Fourteen (6.1%) patients had herpes zoster in the post-transplant period on average within six months of the procedure. Patients with multiple myeloma (64.3%) were the most affected. There was a statistically significant difference in the age of the patients, with older individuals having a greater chance of developing the infection ( $p$ -value = 0.002). There were no significant differences for the other variables analyzed.

**Conclusion:** The early suspension of acyclovir can be safe in patients who receive autologous hematopoietic stem cell transplants. However some groups may benefit from extended prophylaxis with acyclovir, particularly older patients and patients with multiple myeloma.

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## Introduction

Autologous hematopoietic stem cell transplants (HSCT) are usually recommended as a recovery therapy for patients who receive myeloablative chemotherapy.<sup>1</sup> The immunosuppression caused by the conditioning leaves the patient at a high

risk of acquiring different types of diseases. Infections are an important cause of morbidity in this process.<sup>2</sup> These patients therefore receive prophylactic medications, the most common of which are antibiotic, antiviral and antifungal agents.

Viruses, usually of the herpes family, such as the herpes simplex virus (HSV), cytomegalovirus (CMV) or varicella-zoster

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virus (VZV), are some of the most common causes of infections in the period after HSCT.<sup>3</sup>

Herpes zoster (HZ) is a painful vesicular eruption that is typically restricted to one or two dermatomes. It is the result of the reactivation of latent VZV virus in nervous ganglia, usually many years after the primary infection.<sup>4</sup> Infections caused by the varicella-zoster virus are quite common after HSCT, occurring in approximately 20–30% of patients submitted to autologous transplants within one year after transplantation.<sup>4–6</sup> Studies have shown that the occurrence of HZ is more common after the third month after transplant, with an incidence peak in the fourth month.<sup>5</sup>

The use of acyclovir as prophylaxis against the reactivation of herpes is considered standard care during neutropenia in autologous HSCT patients.<sup>7</sup> Different protocols include the prophylactic use of acyclovir on the first day of chemotherapy (conditioning), maintaining its use until Day 30–100 after HSCT in the absence of immunosuppression.<sup>8</sup>

In the Bone Marrow Transplant Unit of the Universidade Federal de Juiz de Fora (UFJF), the start of prophylaxis with acyclovir occurs on the first day of chemotherapy, and is suspended when the neutrophil count is greater than 500 cells/mm<sup>3</sup>, i.e. when engraftment occurs, resulting in less time of use than recommended. The present study therefore aims to evaluate the incidence of infection by the herpes virus in patients submitted to autologous HSCT in respect to the early suspension of acyclovir.

## Methods

This retrospective study compared the incidence of HZ in patients submitted to autologous HSCT with early interruption of prophylactic acyclovir compared to the usual scheme of one year reported in the literature.

The medical records of 221 patients submitted to HSCT in the period between 2004 and 2014 at the Bone Marrow Transplantation Unit of the UFJF, were analyzed retrospectively. Of these, nine patients underwent two transplants, totaling 230 procedures.

### Data collection and variables

The data were collected from medical records. Data collection occurred in the period from March to September 2014. For the characterization of the population, data was collected related to gender, age, diagnosis, presence or absence of diabetes, in addition to the occurrence of death. Additionally, the occurrence of herpes before and after HSCT and other variables of interest were studied including the time of use of acyclovir, duration of neutropenia, length of hospitalization, use of corticosteroids or thalidomide after an outbreak of herpes, and the time of onset of the disease after the transplant. Although some records presented prior serology for HZ, many patients were not tested and thus the analysis of this variable was not performed.

All patients submitted to autologous BMT, independent of the baseline disease, received prophylactic acyclovir at a dose of 500 mg/m<sup>2</sup>/day divided in 2–4 doses per day according to the period in which the procedure was performed. Prophylaxis

was starting on the first day of conditioning and suspended when the neutrophil count was greater than 500 cells/mm<sup>3</sup>.

After hospital discharge, the patients were monitored on an outpatient basis for a period of 24 months in the transplant service of the UFJF.

Data collection was only started after approval by the Research Ethics Committee of the UFJF (# CAAE 25735614.3.0000.5133).

## Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences software (version 19.0 for Windows). The Chi-square test was used for categorical variables and Student's t-test for numerical variables, means and medians. A *p*-value <0.05 was considered statistically significant.

## Results

Two hundred and thirty medical records were analyzed. The mean age was 48.73 years (range: 4–79) and most patients were male (58.7%). The most commonly found diagnosis in the transplant service was multiple myeloma, totaling 52.2% of hospital admissions. The average length of hospital stay of the patients was 20.78 days. The characteristics of the population are described in Table 1.

Few patients had some type of associated comorbidity, with diabetes mellitus being the most common, occurring in 7.4% (*n* = 17) of the patients.

Eight patients (3.5%) had had HZ before hospitalization to perform the HSCT, only one of whom (0.43%) also presented HZ after the HSCT. Fourteen (6.1%) patients presented HZ after the HSCT; there were no significant differences in the evaluated variables between patients who had HZ after the HSCT and those that did not (Table 2). The average time of onset of the HZ outbreak was 164.6 days after the transplant (median: 144; range: 49–330 days).

Of the 14 patients who had HZ in the post-HSCT period, only one was taking corticosteroids/thalidomide during the onset of the infection (7.21%). Furthermore, only one patient

**Table 1 – Characteristics of the population.**

Variable	n	Percentage (%)
<i>Gender</i>		
Male	135	58.7
Female	95	41.3
<i>Diagnosis</i>		
Multiple myeloma	120	52.2
Lymphomas	97	42.2
Other diseases	13	5.7
<i>Diabetes</i>		
Presence	17	7.4
Absence	213	92.6
<i>Death</i>		
Yes	67	29.1
No	163	70.9

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