

# Usefulness of Hebevital in the Treatment of Neutropenia in Patients with Oncopediatric Diseases

Caridad Verdecia Cañizares<sup>1,\*</sup>, Regla Caridad Broche Candò<sup>2</sup>, Oramis Sosa Palacios<sup>3</sup>, Talia Marrero Amores<sup>4</sup>

<sup>1</sup>Oncology Department, University Pediatric Hospital, William Soler Ledea, Havana, Cuba

<sup>2</sup>Professor and Assistant Researcher in Neonatology, William Soler Ledea Pediatric University Hospital, Cuba

<sup>3</sup>Assistant professor in Biostatistics, Researcher Pediatric University Hospital, William Soler Ledea, Cuba

<sup>4</sup>Specialist in Pediatrics, William Soler Ledea Pediatric University Hospital, Cuba

## ABSTRACT

**Introduction:** cancer represents an important health problem in the world, the treatment for its cure leads to neutropenia with or without fever in most of these patients, requiring the use of Hebevital to achieve an increase in the percentage of neutrophils. **Objective:** To describe the clinical and epidemiological characteristics and the therapeutic results of Hebevital in oncopediatric patients with chemotherapy-induced neutropenia. **Material and methods:** a descriptive, cross-sectional and retrospective study was carried out from January 1, 2010 to December 31, 2022, in the Oncosurgery service of the William Soler Ledea Pediatric Hospital. The sample consisted of 415 treatment-induced neutropenia patients. Results: the male sex predominated in 62.4% of the patients. The most affected age range was from 5 to 9 and from 15 to 18 years. The tumors that most occurred: Non-Hodgkin lymphoma and Hodgkin's disease. Grade II and III neutropenia predominated. Neutrophil count normalized in 80% of cases within 72 hours of Hebevital treatment. **Conclusions:** the prevalence of chemotherapy-induced neutropenia is high, with predominance of males and between the ages of 5-9 and 15-18 years. The main localizations were non-Hodgkin's lymphoma and Hodgkin's disease. Moderate and severe neutropenia were more frequent, and the neutrophil count returned to normal, 72 hours after subcutaneous treatment with Hebevital.

**Keywords:** Effectiveness of Hebevital, Neutropenia, Paediatrics.

## INTRODUCTION

Cancer patients are more exposed to infections due to their state of immunosuppression and the effects of the treatment established for their cure. It has been shown that these patients present affection of the natural defense mechanisms, for example, the skin and mucosa barriers are affected by the use of catheters, frequent venous punctures and mucositis secondary to cytostatic drugs. B and T lymphocytes, which are responsible for humoral and cellular immunity, respectively, are generally affected both in number and in their function, hence the increase in infections, associated with altered macrophage activity and tumor necrosis caused by treatment favor infections by opportunistic germs. It

**Vol No: 08, Issue: 08**

Received Date: July 20, 2023

Published Date: August 25, 2023

## \*Corresponding Author

**Dr. Caridad Verdecia Cañizares**

Oncology Department, University Pediatric Hospital, William Soler Ledea, Havana, Cuba

**Email:** caryverd@infomed.sld.cu

**Citation:** Cañizares CV, et al. (2023). Usefulness of Hebevital in the Treatment of Neutropenia in Patients with Oncopediatric Diseases. Mathews J Case Rep. 8(8):121.

**Copyright:** Cañizares CV, et al. © (2023). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

is stated in most of the publications that between 60% and 67% of patients undergoing anticancer treatment develop neutropenia with or without fever. They are predisposed to infection by various microorganisms [1,2].

Endogenous Granulocyte Colony Stimulating Factor (G-CSF) is glycoproteins that act on cells of the hematopoietic system, stimulating their proliferation, differentiation, and final activation. They are produced by monocytes, fibroblasts, and endothelial cells [2,3].

The improvements of the treatment, the advance in the diagnosis and the knowledge of new drugs have prolonged the life of the cancer patient; however, this is also related to the occurrence of adverse events. Sepsis in cancer patients, mainly undergoing chemotherapy, is an important cause of morbidity and mortality. Febrile neutropenia is an oncological emergency, which can be fatal if not promptly treated [1,3].

Antineoplastic drugs induce apoptosis mechanisms through damage caused to their deoxyribonucleic acid, as well as cell growth inhibition, affecting tumor cells and also acting on healthy tissues. The most common opportunistic infections are fungal, with *Candida albicans* being the most frequent germ. On the other hand, vascular catheter infections used to administer the treatment also constitute one of the entry doors for microorganisms, mainly *Staphylococci* and *Streptococci*. Therefore, in the presence of fever in these patients, the first thing to do is a blood culture, in search of these germs. Another frequent infection is herpetic stomatitis after mucositis in patients receiving chemotherapy, with the presence of painful ulcers on the oral mucosa. Herpes zoster reactivation is common in these patients [3-5].

With the use of Hebevital, the reduction and incidence of neutropenia is achieved, its duration is decreased, mainly in patients with immunosuppressive treatment, who are going to receive a bone marrow transplant [1]. On the other hand, it facilitates autogenous mobilization of stem cells to the peripheral blood or accelerates hematopoietic recovery after chemotherapy, thus reducing the use of antibiotics and the hospital stay of the patient [1,2,4].

Patients with malignant diseases, mainly solid childhood tumors, are admitted to our hospital. We have been using domestically manufactured granulopoietic colony-stimulating factor or Hebevital for some time, so we decided

to carry out this study to see the response to it over a period of time certain.

**Objective:** To describe the clinical and epidemiological characteristics and the therapeutic results of Hebevital in oncopediatric patients with chemotherapy-induced neutropenia treated at the Oncosurgery service of the "William Soler Ledea" Pediatric University Hospital, from 2010 to 2022.

## MATERIAL AND METHODS

A descriptive, cross-sectional and retrospective study was carried out from January 1, 2010 to December 31, 2022 at the Oncosurgery service of the William Soler Ledea Pediatric Hospital.

The universe consisted of 625 patients treated with malignant diseases in the Oncosurgery service. The sample consisted of 415 patients diagnosed with neutropenia during cytostatic treatment.

Patients were identified from the databases of the hospital registry of the Oncosurgery service and the medical records were reviewed. Empirical method: observation (documentary review)

The neutrophil count was measured and the clinical method was used as a particular method.

**Inclusion criteria:** Patients between the ages of 0 and 18 years were included.

All patients with a diagnosis of chemotherapy-induced neutropenia who received subcutaneous treatment with Hebevital were selected.

**Exclusion criteria:** Allergy to the product or to any component thereof.

The variables evaluated were:

Epidemiological variables: age and sex

Clinical variables: histological diagnosis and degree of neutropenia during treatment

Therapeutic variable: normalization time of the neutrophil count in hours.

The degree of neutropenia was used according to the neutrophil count defined by the Spanish Society of Internal Medicine (SEMI).

**Degree of neutropenia:**

Neutropenia	Absolute Neutrophil Count
Light (grade I)	1500-1000 cells x mm <sup>3</sup>
Moderate (grade II)	500-1000 cells x mm <sup>3</sup>
Severe (grade III)	Less than 500 cells x mm <sup>3</sup>
Severe (grade IV)	Less than 100 cells x mm <sup>3</sup>

The results obtained are reflected in the following tables:

**Table 1.** Patients with neutropenia treated with Hebevital according to sex and age. William Soler Ledea Pediatric University Hospital, 2010-2022

Age and Sex	n	%
Age intervals (years)		
0-4	20	4,8
5-9	134	32,3
10-14	127	30,6
15-18	134	32,3
Sex		
Female	156	37,6
Male	259	62,4
total with neutropenia	415	66,4*
Total with malignant diseases	625	

Source: Clinical History

As can be seen in table number 1, the male sex was the one that predominated in 62.4% of the patients, the most affected ages were the range between 5 and 9 years and that of 15 and 18 years with 32.3% respectively, followed in order of frequency by the range from 10 to 14 years with 30.6%, while the age group from 1 to 4 years presented with 4.8% of the cases. Of 625 patients who received chemotherapy treatment, neutropenia occurred in 415 patients (66.4%).

**Table 2.** Patients with neutropenia treated with Hebevital according to histological type of tumor. William Soler Ledea Pediatric University Hospital, 2010-2022

Histological type of the tumor	n	%
Non-Hodgkin lymphoma	128	30.8
Hodgkin's disease	109	26.2
soft tissue sarcoma	56	13.4
Neuroblastoma	46	11.0
Nefroblastoma	42	10.1
Hepatoblastoma	34	8.2
Total	415	100.0

Source: clinical history

As shown in Table 2, the oncopediatric diseases most involved in neutropenia were non-Hodgkin lymphoma in 30.8% of the cases followed by Hodgkin's disease in 26.3% of the cases, soft tissue sarcomas represented 13.5% of cases and less frequently neuroblastoma, nephroblastoma and hepatoblastoma representing 11.1%, 10.1% and 8.2%

respectively.

The degree of neutropenia that prevailed was grade II and III in most cases, mainly associated with intense treatments required in current schemes for lymphomas and soft tissue sarcomas.

**Table 3.** Time to normalization of the neutrophil count with Hebevital. "William Soler Ledea"  
Pediatric University Hospital, 2010-2022

Normalization time (hours)	n	%
≤72	332	80
>72 -144	75	18
>144	8	2
Total	415	100

Source: clinical history

As shown in Table 3, the neutrophil count returned to normal in the first 72 hours after starting treatment with Hebevital in 80.0% of the cases, the neutrophil count recovered after 72 hours and before 144 hours in the 18.0% of the cases and only 2.0% of the patients required more than 144 hours to achieve normalization of the neutrophil count. Thus showing the effectiveness of Hebevital

## DISCUSSION

Febrile neutropenia is a heterogeneous clinical entity that includes patients with highly variable risks and can develop serious medical complications, which can cause a decrease in the intensity of the treatment dose, thus decreasing therapeutic efficacy [1-3].

There are few works related to the topic in pediatric age, in our environment. Forteza et al. [1] carried out a similar study in pediatric patients from January 1, 2006 to December 31, 2016, at the National Institute of Oncology and Radiobiology, where they evaluated demographic, clinical, and therapeutic variables, including 512 cancer patients treated at their service and of them 369 presented neutropenia 72% of the cases. The predominant tumors were lymphomas and sarcomas and demonstrated a good response to treatment with granulocyte-stimulating factor or Hebevital [1].

Cordero et al. [4] carried out a study similar to ours where they evaluated the effectiveness of granulocyte colony-stimulating factor in patients with febrile neutropenia, coinciding that the most affected sex is male and the ages of longest duration in adolescents and young adults from 15 to 39, in comparison with those under 0 to 9 years of age whose durability was shorter, with an average use of granulocyte

colony-stimulating factor of 6 days until neutropenia emerged, with grade III and IV neutropenia predominating [4]. However, in our study, grade II and III neutropenia predominated and most of our patients emerged from neutropenia within 72 hours of starting treatment with Hebevital.

García-Carbonero et al. [5] in a randomized multicenter clinical trial in 2001, prospectively evaluated the efficacy of adding the use of granulocyte colony-stimulating factor (G-CSF) to antibiotic therapy in patients with solid tumors, encompassing 210 patients assigned to antibiotic groups. and another with antibiotic plus G-CSF, demonstrating that the duration of neutropenia, antibiotic therapy, hospitalization, and hospital costs were lower [5].

It is essential to assess which pathogen is most likely to be involved in order to initiate the most appropriate treatment, a priori. Thanks to advances in diagnostic methods, microbiology, the development of new and more effective antibiotics and better knowledge of the risk factors in each patient, it allows the development of a more individualized treatment, but, on the other hand, the use of more invasive therapies with a greater risk of immunosuppression, as well as the progressive development of resistance to classical antimicrobials, make this problem appear more frequently [3-5].

Knowledge of neutropenia as the factor that most frequently predisposes to infection in cancer patients. The concurrence of other factors such as the alteration of mucocutaneous barriers either due to the invasive effect of the tumor itself, as well as due to treatments, involvement of the oral mucosa

(mucositis) and the use of vascular catheters. Exposure to hospital pathogens and alterations in other mechanisms of the cellular or humoral immune system increase this risk and worsen the prognosis. Between 48 and 60% of neutropenic patients present a febrile syndrome during the course of the infection and 20% may present a neutrophil count of less than 500 cells per mm<sup>3</sup> and develop bacteremia during the course of treatment [2,4-6].

In the review carried out on the subject, most of the authors state that the most frequent germs detected in the infection of patients with neutropenia are coagulase-positive *Staphylococcus*, *Staphylococcus aureus*, beta-hemolytic *Streptococcus* and *Viridans Streptococcus*, *Enterococci*: mainly *E. faecalis*. Gram-negative aerobic bacilli cause 30% of bacteremia and the most frequent microorganisms are: *E. coli*, *Klebsiella Pneumonie*, *Pseudomona aeruginosa*. Anaerobic germs cause less than 5% of infections. *Bacterioides fragilis* and *Clostridium spp* [3,7-9].

Although in our study we did not have the objective of evaluating the germs that cause sepsis in the course of neutropenia, in the reviewed publications on the subject they state that fungal infections: the most frequent are *Candida albicans* and *Candida tropicalis*. Respiratory viruses are also present in the case of immunosuppression: adenovirus, respiratory syncytial virus, parainfluenza, influenza A and B, rhinovirus; and herpes viruses: HVS, VZV, CMV, EBV [10-13].

Sobrevilla et al. carried out a study on the evaluation of the safety and efficacy of Filgrastim in the treatment of post-chemotherapy or radiotherapy febrile neutropenia in oncohematological patients, as well as the effects derived from treatment with this product, obtaining similar results to ours [14].

## CONCLUSIONS

We can conclude from our study that the prevalence of chemotherapy-induced neutropenia in our patients was high. The male sex was the most affected and in percentage terms, it is distributed in a similar way in the age intervals 5-9 years, 10-14 and 15-18 years. The onco-pediatric diseases most involved in neutropenia in this study were non-Hodgkin's lymphoma and Hodgkin's disease, since intense multidrug chemotherapy schemes are used. Moderate and severe neutropenia predominated, and neutrophil counts normalized in most patients 72 hours after initiation of subcutaneous treatment with Hebevital.

## ACKNOWLEDGEMENTS

None.

## CONFLICT OF INTEREST

No conflict of interest in this publication.

## REFERENCES

1. Forteza M, García D, Pérez M, Alert J, Renó J. (2019). Use of Hebevital in Oncopediatrics of the National Institute of Oncology and Radiobiology, 2006-2016. *Rev Cubana Farm.* 2019;52(3):1-11.
2. Mirón M, Estrada O, González VJ. (2022). Home intravenous antimicrobial treatment protocols. Chapter XXII. Infections in patients with Neutropenia. SCUB13712REV062008.
3. Blaney SM, Peter C, Helman Lee J, Adamson PC. (2022). Pizzo & Poplack's Pediatric Oncology 8th Edition. Netherlands: Wolters Kluwer. ISBN: 978-1975124793.
4. Cordero H, Staël J, Jerves M, Martínez FR. (2018). Response to Granulocyte Colony Stimulating Factors in Febrile Neutropenia events in Oncology patients at the Solca-Cuenca Cancer Institute. *Rev Oncol Eq.* 28 (3):219-231.
5. García-Carbonero R, Mayordomo JI, Tornamira MV. (2021). Granulocyte colony-stimulating factor in the treatment of high-risk febrile neutropenia: a multicenter randomized trial. *J Natl Cancer Inst.* 93(1):31-38.
6. Fish JD, Lipton JM, Lanzkowsky P. (2021). *Lanzkowsky's Manual of Pediatric Hematology and Oncology 7th Edition.* United States: Academic Press. ISBN-13 978-0128216712.
7. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, Infectious Diseases Society of America, et al. (2011). Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. *Clin Infect Dis.* 52(4):e56-e93.
8. Gaviria LM. (2016). Clinical impact of levofloxacin prophylaxis in neutropenic patients with haematological malignancies. *Colombian Medical Act.* 41(4):219-220.
9. Rivas Llamas JR. (2016). Febrile neutropenia: the hematologist's point of view. *Mexican Gazette of Oncology.* 15(4):212-221.
10. Abelle MLC, Caballero IA. (2020). Sepsis in patients with solid tumors undergoing chemotherapy. *Science and Health.* 4(3):53-61. DOI: 10.22206/cysa.2020.v4i3.pp53-61.

11. Gea-Banacloche JC. (2017). Rituximab-associated infections. *Semin Hematol.* 47(2):187-198.
12. Beyar-Katz O, Dickstein Y, Borok S, Vidal L, Leibovici L, Paul M. (2017). Empirical antibiotics targeting gram-positive bacteria for the treatment of febrile neutropenic patients with cancer. *Cochrane Database Syst Rev.* 6(6):CD003914.
13. Mendoza PBRM, Pineda HSE. (2021). Respiratory infection in children with cancer in a hospital in Medellín. *Cuban Journal of Pediatrics.* 93(1):e939.
14. Sobrevilla P, Castañeda N, Bustamante E, Molina A, Revilla J. (2009). Evaluation of the safety and efficacy of Filgrastim in the management of post-chemotherapy or radiotherapy febrile neutropenia in oncohematological patients: clinical experience report. *Mexican Gazette of Oncology.* 8(2):69-74.