Oliwia Grochowska

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu

Infectious complications in children undergoing oncological treatment or hematopoietic cell transplantation

Summary

Introduction

Infectious complications are the most common cause of morbidity and mortality among children undergoing oncological treatment or hematopoietic cell transplantation. Patients with malignant tumours are particularly susceptible to bacterial, fungal, and viral infections. The multidirectional treatment regimens used in the therapy of childhood cancers contribute to the occurrence of risk factors predisposing to the development of infections. The most important of these include prolonged neutropenia and the use of central catheters.

Objectives

The aim of the study was to analyse the local aetiology and epidemiology of bacterial, fungal and viral infections in children undergoing anticancer therapy or hematopoietic cell transplantation and determining the effectiveness of their treatment.

Patients and methods

The analysis included a total of 983 patients hospitalized in the years 2012-2023 in the Department of Paediatrics, Haematology and Oncology and in the Department of Bone Marrow Transplantation for Children of the University Hospital No. 1 in the city of Bydgoszcz. Two groups of patients were distinguished: those treated for oncology without hematopoietic cell transplantation (PHO group) and those undergoing hematopoietic cell transplantation (HCT group). In the PHO group, microbiologically confirmed infections were identified in 458 patients, 215 of whom were girls and 243 boys. The largest percentage of patients with confirmed infections were patients with ALL (42.6%). In the HCT group, microbiologically confirmed infections were identified in 306 patients, including 128 girls and 178 boys. The highest percentage of patients with confirmed infections were patients with ALL (37.9%) and AML/MDS/JMML (23.2%).

The data were collected in two-year periods and the analysis was made retrospectively. The incidence of bacterial, fungal and viral infections was compared in the PHO and HCT groups. The analysis included the type of underlying disease and the type of transplantation (allo-HCT vs auto-HCT). The study assessed the risk factors for the development of infection and the risk of death. The effectiveness of the anti-infective therapy was assessed by event-free survival.

Results

Bacterial infections were the most common infectious complication in both, PHO and HCT groups (65,5% and 59,2%). In the PHO group fungal infection (33.7%) were the second, then viral infections (26.0%), while in the HCT group differently – viral infections occurred at a frequency of 48.3% and fungal at 38.7%. Considering the underlying disease**,** infectious complications were more common among children with haematological malignancies than children with solid tumours.

Among bacterial infections, Gram-negative infections predominated in both groups (PHO 51.8%, HCT 55.9%), and the most common isolated pathogen was *Escherichia coli* (PHO 37.7%, HCT 22.3%), while among Gram-positive bacteria, *Clostridioides difficile* (PHO 27.3%, HCT 24.1%). The most common clinical manifestation observed in both groups was UTI (PHO 37.0%, HCT 36.4%). Infections with multidrug-resistant bacteria were more common in the HCT group (42.4% vs 31.9%) and it was dominated among infections with Gram-negative species. Analysing patients undergoing hematopoietic cell transplantation, bacterial infections occurred more frequently in the allo-HCT subgroup than in the auto-HCT subgroup (64.4% vs 41.1%). The risk of developing bacterial infections was 1.7-fold higher in the PHO group and 2.6-fold higher in the allo-HCT group.

Fungal infections generally dominated in the HCT group, but the detailed analysis showed that possible IFD was diagnosed more often in the PHO group (21.1% vs 17.6%). In the PHO group, invasive fungal disease was most common among patients with AML (81.1%) and ALL (55.4%) but in the HCT group among patients with NHL (72.7%) and AML (62.7%). Infections did not occur among children with Hodgkin's disease in either the PHO or HCT groups. Proven and probable IFD occurred among 12.7% of PHO patients and 21% of HCT patients. In the group of children undergoing hematopoietic cell transplantation, fungal

infections were much more common after allo-HCT than auto-HCT (25.4% vs 8.4%), and the risk of infection was 7-fold higher in the allo-HCT group.

The analysis of viral infections showed that the most common infections in the PHO group were ADV (9.2%), rotavirus (8.1%) and SARS-CoV-2 (6.9%). In the HCT group, the aetiology was different and the most common infections were CMV (28%), EBV (23.2%) and BKV (9.9%). The same proportions were observed among allo-HCT patients and for them the risk of developing a viral infection was 30-fold higher than for children after auto-HCT.

Based on the risk factor analysis, it was found that among HCT patients, allogenic hematopoietic cell transplantation was a risk factor for any type of infection, while in the PHO group, the diagnosis of acute leukaemia was a risk factor for fungal infections.

The analysis of treatment effects showed that for all types of infections, survival was better among PHO patients. In both, the PHO and HCT groups, the lowest survival rates were observed for fungal infections. Transplant therapy and IFD were shown to be risk factors for death.

Conclusions

Summing up the collected data, the most common infectious complication among children treated by anticancer therapy and undergoing hematopoietic cell transplantation was bacterial infections. The cumulative frequency of bacterial infections was higher among PHO group, fungal and viral infections among HCT group. Regardless of the type of infection, complications were more common among patients with hematological malignancies than with solid tumors. Considering patients undergoing a transplant procedure, infections occurred significantly more often among allo-HCT group than among patients undergoing auto-HCT. In all types of infections, survival was higher among PHO group than in the HCT group, and the lowest survival rates were noted for fungal infections.