

ADMINISTRATION OF CYCLOSPHAMIDE FOR GVHD PROPHYLAXIS AFTER STEM CELL TRANSPLANTATION FROM UNRELATED DONOR AND INFECTIONS: A MULTI-CENTER EXPERIENCE

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Abstract

There is still no clear information about the incidence and consequences of infections with cyclophosphamide (PT-Cy) administration as prophylaxis of graft versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Objective

Revealing the incidence of pre-vaccination bacterial and viral infections (Cytomegalovirus (CMV), Herpes virus and BK-poliomavirus hemorrhagic-cystitis), infection related mortality and predictive factors associated with PT-Cy application after allo-HSCT was aimed.

Materials & Methods

Patients who underwent allo-HSCT from a 9/10-10/10 HLA tissue matched unrelated donor and administered cyclophosphamide for post-transplant GVHD prophylaxis from 3 centers between 2015 and 2020 were retrospectively reviewed. Infections that developed in the first 100 days after transplantation were recorded

Results

Forty-one patients, 25 male and 16 female, were included in the study. The mean age of the patients was 40.8 (21-67), with 23 AML, 11 ALL, 3 Non Hodgkin Lymphoma, 2 MDS, 1 biphenotypic leukemia and 1 Hodgkin Lymphoma diagnosis. HLA tissue compatibility was 9/10 in 32 patients and 10/10 in 9 patients. All patients received one of the myeloablative priming regimens (TBI (800-1200cGy)+Flu (30mg/m²x5), Cy (60mg/kgx2)+TBI (1200cGy), Treosulfan (10 gr/m²x3)+Flu (40mg/m²x4)). In GVHD prophylaxis, PTCy was administered at 72nd and 96th hours following transplantation in combination with calcineurin inhibitors ± methotrexate ± mycophenolate mofetil. Levofloxacin, valacyclovir, fluconazole, and trimethoprim-sulfamethoxazole were empirically given to all patients along with the transplant preparation regimen.

At least one episode of febrile neutropenia (FEN) developed in all patients during the transplantation process. More than one episode of FEN developed in 22% of the patients. One patient died due to septic shock on post transplant +9th day..

After a mean follow-up of 19 months, the incidence of CMV infection requiring treatment was 36.6% in the first 100 days and 41.5% at 1 year. All patients except 1 patient were CMV IgG positive before transplantation. While CMV reactivation was observed in 50% (15/15) of donor/patient CMV IgG (+/+), CMV reactivation was found in 30% (3/7) of the donor/patient CMV IgG (-/+) patients. Only one of these patients received antiviral therapy due to multiple reactivations.

Table 1.Infections after transplantation

Infections after Transplantation	n=41 (%)
Engraftman Time	
Neutrophil	+18.day (11-31)
Trombocyte	+22.day (9-48)
Febrile neutropenia	
1 attack	32(%78)
>2 attacks	9 (%22)
Septic Shock	1(%2.4)
CMV positivity	
+100 day	15(%36.6)
1. year	17 (%41.5)
CMV Reactivation Rates	
Donor/Rec CMV IgG(-/+)	3/10 (%30)
Donor/Rec CMV IgG(+/+)	15/30 (%50)
Donor/Rec CMV IgG(+/-)	0/1 (%0)
Donor/Rec CMV IgG(-/-)	
CMV Pneumonia	4(%9.8)
CMV Pneumonia related mortality	3 (%7.3)

In 4 patients, pneumonia developed due to CMV and 3 of them died. The rate of poliomavirus virus-associated cystitis was 7.3% (3/41).In the first year after transplantation, invasive fungal infection occurred in only 4 patients (9.8%), and herpes virus infection occurred in 1 patient. Three patients received tenofovir-entecavir treatment because of anti HBcIg positivity, and HBV reactivation was not detected in any of the patients.

Conclusion & Discussion

GVHD prophylaxis containing PTCy after allo-HSCT from an unrelated donor does not have an increased risk in terms of bacterial, viral or fungal infection and can be used safely.

References

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