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Effectiveness of therapeutic drug monitoring in patients undergoing allogeneic hematopoietic stem cell transplantation

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ABSTRACT

Background: Therapeutic drug monitoring (TDM) aims to prevent excessive immunosuppression, graft rejection, and the emergence of graft-versus-host disease (GVHD) and to control drug interactions. Estimates suggest that acute GVHD (aGVHD) occurs in 30-50% of patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT) and chronic GVHD (cGVHD) in 50 to 70%. **Objective:** To evaluate the effectiveness of TDM conducted by a clinical pharmacist on the quality of care for patients undergoing allogeneic HSCT to prevent GVHD and to improve clinical outcomes in comparison with historical controls. **Methods:** A cohort study of patients who underwent allogeneic HSCT was carried out from January 2015 to December 2017 (control group) and from January 2018 to December 2021 (TDM group). Patients were followed up for 2 years after HSCT. The exposed group received pharmaceutical TDM, considering the clinical pharmacokinetics of cyclosporine, tacrolimus, and busulfan, which was compared to a historical control group without TDM. **Results:** The control and TDM groups included 85 and 79 patients, respectively. Male patients predominated in this sample, the ages of whom ranged from 0 to 64 years. The incidence of GVHD in the overall cohort totaled 73.8% (n = 164). The incidence of aGVHD and cGVHD showed no significant difference between groups. Survival lasted for three more months (p = 0.04), and mortality was lower (risk ratio 0.55; p = 0.05) in the TDM group. **Conclusion:** TDM was associated with improved survival and reduced mortality, without significantly affecting the incidence of aGVHD or cGVHD.

Keywords: Hematopoietic stem cell transplantation; HSCT; Effectiveness; Therapeutic drug monitoring; Clinical pharmacist.

INTRODUCTION

In patients undergoing hematopoietic stem cell transplantation (HSCT), estimates suggest that acute graft-versus-host disease (aGVHD) occurs in 30-50% of patients and chronic GVHD (cGVHD) in 50-70%, depending on several factors, including conditioning protocols and immunosuppression.[1,2] The main immunosuppressants in the prophylaxis of GVHD are cyclosporine (CsA) and tacrolimus (TAC). These drugs have a narrow therapeutic window and a significant interindividual variability in blood concentrations. Busulfan (Bu), a chemotherapy drug present in several conditioning protocols, has similar pharmacokinetic characteristics and higher rates of relapse and rejection in patients with low exposure to it.[3] To keep these drugs within the therapeutic target and prevent toxicity, therapeutic drug monitoring (TDM) is recommended to adjust drug doses considering the serum level after the first dose.

Therapeutic drug monitoring adjusts doses based on drug blood concentration (pharmacokinetic monitoring) and biomarkers (pharmacodynamic monitoring) correlated with efficacy and toxicity (creatinine, blood potassium, and magnesium levels). TDM aims to avoid excessive immunosuppression, graft rejection, and GVHD emergence and to control drug interactions that can bring toxicity and critical adverse effects. This study aims to evaluate the effectiveness of TDM conducted by a clinical pharmacist on the incidence of GVHD and clinical endpoints in comparison with historical controls.

METHODS

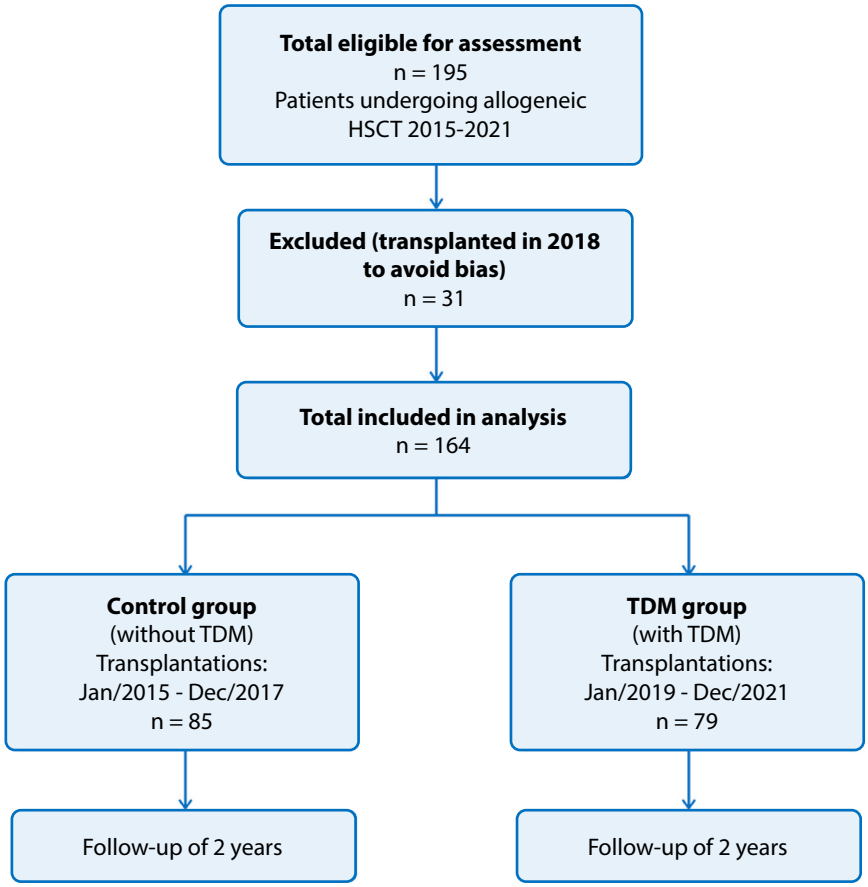
A cohort study with historical controls was conducted at the bone marrow transplant center of Hospital de Clínicas de Porto Alegre (HCPA), a public university hospital. The Research Ethics Committee approved this study (protocol number 2019-0138).

Inclusion criteria were adult and pediatric patients with malignant and non-malignant diseases who underwent related, unrelated, and haploidentical allogeneic HSCT from January 1, 2015, to December 31, 2021, who had been followed for 2 years after HSCT. Patients transplanted in 2018 were excluded to reduce the effect of the TDM learning curve and to better differentiate the groups.

Study flowchart is described in Fig. 1. The exposed group was composed of patients who underwent allogeneic HSCT from January 1, 2019, to December 31, 2021, with TDM of CsA, TAC, and Bu. The conditioning protocols included myeloablative, reduced-intensity, and non-myeloablative conditioning (MAC), with Bu commonly used in both myeloablative and reduced-intensity protocols. Exposure comprised TDM considering pharmacokinetic parameters. Patients who used GVHD prophylaxis protocols with CsA and TAC in oral and intravenous pharmaceutical forms and pediatric patients with IV Bu conditioning protocols also received monitoring.

In the TDM protocol, the PK/PD pharmacokinetic calculation was applied considering the serum dosages of CsA and TAC. The pharmacist calculated the next dose to be administered considering potential drug interactions, renal function, magnesium and potassium serum levels, and adverse effects. For Bu, adjustments were calculated according to the area under the curve, age, weight, height, body mass index, creatinine, aspartate transaminase, alkaline phosphatase, total bilirubin, alanine transferase, and conditioning protocol. The pharmacist informed the estimated dose and discussed drug adjustment with the medical team according to patients' conditions.

Patients who underwent allogeneic HSCT from January 1, 2015, to December 31, 2017, before TDM protocol implementation, were included in the control group. Drug adjustments followed the hematology and HSCT service routine (supplementary material), ignoring clinical pharmacokinetics.



Source: Elaborated by the authors.

Figure 1. Study flowchart.

Statistical analysis

The sample size was calculated according to Paz et al.,[4] carried out in the same population, which found incidences of aGVHD and cGVHD of 62.5% and 50.4%, respectively. Considering a 20% absolute reduction in GVHD in the TDM group, a statistical significance of 5%, and a power of 80%, the estimated sample totaled 194 patients (87 in each group).

Data were collected from medical records and entered into Research Electronic Data Capture (REDCap).[5,6] Statistical analysis was performed using IBM SPSS Statistics 22, applying Pearson's chi-square test for categorical variables in comparing group characteristics. The chi-square test was used to compare the characteristics related to the transplant, and the non-parametric test (Mann-Whitney *U* test) was used for continuous variables. The chi-square test was applied to compare the proportion of clinical outcomes (global incidence of GVHD, incidence and severity of aGVHD and cGVHD, and cumulative mortality). Hospitalization time was analyzed by the Mann-Whitney *U* test. To assess the effectiveness of TDM on clinical outcomes, the crude relative risk was calculated and adjusted in a generalized linear model (Poisson's regression with a robust estimator). Survival in the groups was analyzed by Cox regression, estimating crude and adjusted risk ratios for the type of HSCT, cell source, conditioning intensity, human leukocyte antigen (HLA) compatibility, and age. In selecting potential confounding factors, the risk factors for aGVHD = in the literature[1] and those unequally distributed between the groups with $p < 0.20$ were considered. The same criteria were applied in the multivariable model for cGVHD. Significant differences were considered at $p < 0.05$.

RESULTS

From January 2015 to December 2017, the control group included 85 patients, whereas from January 2019 to December 2021, the TDM group included 79 patients. Table 1 illustrates the patient selection process and group allocation. Males predominated in the sample, and the ages ranged from 0 to 64 years. The overall incidence of GVHD in the cohort (n = 164) totaled 73.8%.

Table 1 describes group characteristics. Haploidentical HSCT was more frequent in the TDM group than in the control group, whereas related and unrelated HSCT occurred more often in the control group. Cell source was bone marrow in most exposed patients. Other sociodemographic and clinical characteristics failed to significantly differ. Table 2 describes transplant-related characteristics. Most patients underwent MAC. In total, 106 patients showed platelet engraftment, of whom the time to platelet engraftment was longer in controls.

Table 1. Characteristics of the sample.

	TDM (n = 79)	Control (n = 85)	p-value
Male, n (%)	45 (57.0)	52 (61.2)	0.58
Age (years)			0.31
< 10	22 (27.8)	18 (21.2)	
10 a < 20	18 (22.8)	28 (32.9)	
≥ 20	39 (49.4)	39 (45.9)	
Type HSCT			< 0.00
Haploidentical	29 (36.7)	13 (15.3)	
Related	19 (24.1)	34 (40.0)	
Unrelated	31 (39.2)	38 (44.7)	
Cells source			< 0.00*
Bone marrow	49 (62.8)	72 (92.3)	
Peripheral blood	29 (37.2)	3 (3.8)	
Cord blood	0 (0.0)	3 (3.8)	
HLA compatibility			0.14
Partial (less than 10 × 10)	47 (72.3)	44 (60.3)	
Complete	18 (27.7)	29 (39.7)	
Diagnosis			0.21
Acute myeloid leukemia	19 (24.1)	21 (24.7)	
Acute lymphoid leukemia	21 (26.6)	21 (24.7)	
Myelodysplasias/myeloproliferative disease	8 (10.1)	14 (16.5)	
Primary immunodeficiency	2 (2.5)	4 (4.7)	
Medullary failure	11 (13.9)	8 (9.4)	
Genetic disease Lymphomas Others	4 (5.1) 3 (3.8) 11 (13.9)	9 (10.6) 5 (5.9) 3 (3.5)	

* p-value may be overestimated due to a cell with zero frequency. Source: Elaborated by the authors.

Table 3 describes outcomes, and Table 4 shows crude and adjusted risks. The incidence and severity of aGVHD and cGVHD were similar between groups. Crude analysis showed a non-statistically significant lower incidence of deaths (p = 0.094) and higher survival at 24 months (difference of 3 months; p = 0.097) in the TDM group, as shown in Tables 3 and 4. The incidence of graft failure was 30.4% in the TDM group and 44.7% in the control group (p = 0.059) (Table 3). Length of hospital stay failed to differ between groups. The proportion of patients readmitted due to viral infections (mostly cytomegalovirus [CMV] and Epstein-Barr virus [EBV] infections) was higher in the TDM group, and readmissions due to bloodstream and fungal infections were less frequent. Figure 2 shows the adjusted survival curve in groups with and without TDM.

Table 2. HSCT-related characteristics by group.

	TDM (n = 79)	Control (n = 85)	p-value
Conditioning regimens			0.06
MAC	41 (51.9)	45 (52.9)	
RIC	16 (20.3)	7 (8.2)	
Non myeloablative	22 (27.8)	33 (38.8)	
GVHD prophylaxis			0.32
CsA + MTX	24 (30.4)	26 (31.0)	
TAC + MTX	12 (15.2)	23 (27.4)	
MMF + CsA	8 (10.1)	3 (3.6)	
MMF + TAC	5 (6.3)	6 (7.1)	
CY post + TAC + MMF	14 (17.7)	10 (11.9)	
CY post + CsA + MMF	7 (8.9)	5 (6.0)	
Others	9 (11.4)	11 (13.1)	
Anti-thymocyte globulin (ATG)	35 (44.3)	40 (47.1)	0.72
Cells infusion			
CD 34 × 10^6/kg			
Mean (SD)	5.52 (2.66)	4.79 (3.16)	0.12*
Median (P25, P75)	5.10 (3.40;7.82)	3.94 (2.69;6.39)	
TNC 5.8 × 10^8/kg			
Mean	6.13 (SD 4.31)	2.59 (SD 4.33)	< 0.00*
Median (P25, P75)	5.37 (3.53;8.50)	0 (0;3.80)	
Neutrophil engraftment (days)			
Mean (SD)	17.73 (8.35)	18.72 (6.31)	0.41*
Median (P25, P75)	16 (14;20)	19.00 (15.75;22.25)	
Platelet engraftment (days)			
Mean (SD)	21.32 (7.77)	25.02 (8.10)	0.02*
Median (P25, P75)	19.50 (16;25.25)	22.00 (18;30)	
Length of hospital stay (days)			
Mean (SD)	65 (37.54)	59.46 (35.01)	0.33*
Median (P25, P75)	53 (43;79)	50.00 (39.50;71.50)	
Chimerism D+30			0.99
Complete (≥ 95%)	59 (84.3)	62 (83.8)	
Mixed (5% a < 95%)	8 (11.4)	9 (12.2)	
Autologous (< 5%)	3 (4.3)	3 (4.1)	
Chimerism D+60			0.39
Complete (≥ 95%)	53 (86.9)	37 (77.1)	
Mixed (5% a < 95%)	7 (11.5)	9 (18.8)	
Autologous (< 5%)	1 (1.6)	2 (4.2)	
Chimerism D+100			0.10**
Complete (≥ 95%)	56 (90.3)	42 (76.4)	
Mixed (5% to < 95%)	6 (9.7)	12 (21.8)	
Autologous (< 5%)	0 (0.0)	1 (1.8)	

ATG: complete chimerism above 95%, from 5% to 95% mixed, less than 5% autologous; MMF: mycophenolate mofetil; MTX: methotrexate; RIC: reduced intensity conditioning; non-MAC: CY + fludarabine + 2Gy TBI; SD: standard deviation; TNC: total nucleated cells. * Mann-Whitney *U* test; ** p-value may be overestimated due to a cell with zero frequency. Source: Elaborated by the authors.

Table 3. Outcomes incidence according to the groups.

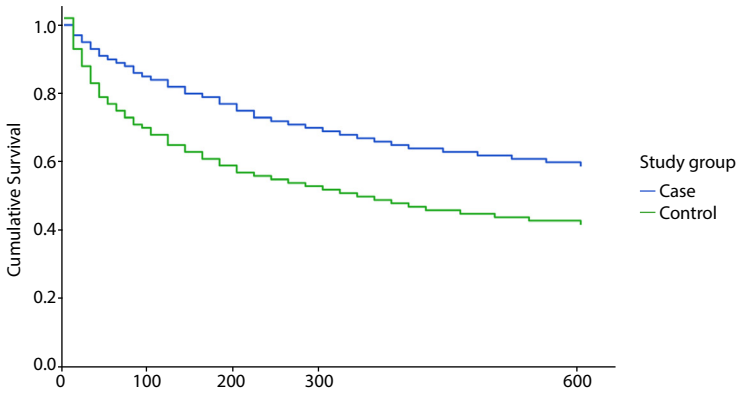
	TDM (n = 79)	Control (n = 85)	p-value
GVHD*			
aGVHD	41 (51.9)	40 (48.2)	0.64
cGVHD	19 (24.1)	19 (22.4)	0.80
Grade aGVHD			0.64
1	12 (31.6)	14 (35.0)	
2	16 (42.1)	19 (47.5)	
3 or 4	10 (26.3)	7 (17.5)	
Grade cGVHD			0.74
Mild	8 (42.1)	9 (47.4)	
Moderate to severe	11 (57.9)	10 (52.6)	
Death within 2 years	27 (34.2)	40 (41.1)	0.09
Survival at 24 months, average (95%CI)	17.23 (15.11-19.36)	14.55 (12.32-16.78)	0.09
Graft failure	24 (30.4)	38 (44.7)	0.05
Readmission due to infection			
Sepsis	25 (31.6)	40 (47.1)	0.04
Fungal infection	8 (10.4)	23 (27.1)	0.00
Bacterial	44 (26.4)	41 (48.2)	0.29
Viral**	48 (61.5)	34 (40.0)	0.00

Source: Elaborated by the authors. * Four missing among those who made GVHD; ** CMV and EBV.

Table 4. Multivariable analysis for clinical outcomes in the TDM group when compared to the controls.

	Crude risk	Adjusted risk	95%CI	p-value
aGVHD*	1.05	0.90	0.61-1.35	0.62
cGVHD**	1.08	1.08	0.60-1.95	0.80
2-year mortality***	0.73	0.55	0.31-0.99	0.05
2-year survival***	0.67	0.45	0.21-0.95	0.04
Readmission for infection				
Sepsis***	0.67	0.54	0.27-1.07	0.76
Fungal***	0.27	0.58	0.21-1.60	0.28
Bacterial***	0.48	1.44	0.94-2.20	0.09
Viral***	1.54	1.48	0.98-2.24	0.06

* Adjusted for cell source, conditioning intensity, HLA match, and age; ** Adjusted for HLA matching, age, and previous GVHD; ***Adjusted for HSCT type, cell source, conditioning intensity, HLA match, and age. Source: Elaborated by the authors.



Source: Elaborated by the authors.

Figure 2. Adjusted survival analysis according to the exposition groups.

A sub-analysis of Bu usage evaluated the outcomes most related to drug exposure: graft failure and neutrophil engraftment (Table 5). Among patients (n = 61) who received Bu, the graft failure rate totaled 23% in the TDM group (n = 22) and 36% in the control group (n = 39; p = 0.42). Neutrophil engraftment occurred in 99% of TDM patients, compared to 90% of controls (p = 0.65).

Table 5. Graft failure and neutrophil engraftment according to TDM stratified by Bu exposure.

	TDM group	Control	Total	p-value
Bu use	22	39	61	
Graft failure	5 (23)	14 (36)		0.42
Neutrophil engraftment	21 (99)	35 (90)		0.65
No Bu use	57	46	103	
Graft failure	19 (33)	24 (52)		0.07
Neutrophil engraftment	52 (91)	43 (93)		0.72

Source: Elaborated by the authors.

DISCUSSION

In this cohort study of patients who underwent allogeneic HSCT and were followed up for 2 years, the CsA, TAC, and Bu TDM conducted by a clinical pharmacist failed to reduce the incidence of aGVHD and cGVHD. However, overall survival in the TDM group was approximately 3 months higher than in the control group.

Previous studies on TDM have mostly analyzed the proportion of serum levels within the therapeutic target, a substitute for clinical outcomes. They generally show that patients with TDM more successfully maintain target serum levels and have lower toxicity.[7-10] The observational study by Gawedzki and Collins[2] compared adult patients undergoing allogeneic HSCT before and after an immunosuppression protocol with TDM (conducted by the clinical pharmacist). On D+30, the rate of patients at the therapeutic level totaled 64% and 68% in the pre-protocol and protocol groups (p = 0.35), respectively. D+100 showed no differences. The total number of adverse events (nephrotoxicity, hypertension, and neurotoxicity) was higher in the pre-protocol group (p = 0.03). The studied sample was small, and the reduction of nephrotoxicity, hypertension, or neurotoxicity alone was insignificant. Clinical outcomes, such as engraftment, incidence of GVHD, and relapse, showed no significant reductions. This study also found no reduction in the incidence of GVHD.

A study[11] on differences between haploidentical HSCT and HLA-identical sibling HSCT found that the cumulative incidence of overall mortality after haploidentical HSCT was higher than after HLA-identical sibling HSCT (38.7% vs. 33.3%, p = 0.012). We found a lower mortality in this group than that study. Although the number of haploidentical HSCTs was higher in the TDM group than in the control group in our study, mortality was lower, reinforcing the benefit suggested for TDM conducted by a clinical pharmacist.

A cost-effectiveness, non-randomized, retrospective study[12] with pediatric patients aged from zero to 18 years in a single center evaluated two strategies of monitoring and dose adjustment of CsA up to D+ 100. From 2014 to 2016 (n = 90), a pharmacist implemented the TDM approach, combining a blood test and a population pharmacokinetic model. From 2017 to 2018 (n = 54), due to a lack of human resources, physicians empirically adjusted CsA doses. The other care procedures were the same in both periods, and the characteristics of the groups were similar. When assessing the incidence of aGVHD during the first 100 days after HSCT, the incidence of aGVHD was 68.1%, 11.6% of which were severe. This rate is higher than the rate in our study, which included children and adults. They also observed that, in addition to the type of donor, performing CsA TDM was a protective factor (odds ratio = 0.86) for viral infection, whereas, in our study, the group with TDM had a higher risk of hospitalization due to viral or bacterial infections. This result may be associated with the number of haploidentical HSCTs (36.7%) during monitoring. Haploidentical HSCT generally uses

cyclophosphamide (CY) post-HSCT on D+3 and D+4, in combination with a calcineurin inhibitor (TAC) and TDM, for GVHD prophylaxis, combining immunomodulatory effects with immunosuppression.[13,14] However, prolonged post-engraftment immunosuppression may increase infectious complications and side effects associated with the calcineurin inhibitor.[15] In our study, the adjusted analysis suggests TDM protection against rehospitalization due to bloodstream infection. A better adjustment of GVHD prophylaxis may have influenced the results. Studies[16,17] have described the period up to D+30 after HSCT as that with the highest risk of infections. During this period, the TDM of calcineurin inhibitors is essential to maintain patients at the therapeutic target and improve immune control without increasing the risk of GVHD.

The incidence of severe GVHD in the cost-effectiveness analysis study described above[12] was 7.8% vs. 18.5% in the groups with TDM and without TDM, respectively ($p = 0.053$), in addition to a reduction in the incidence of viral infections (36.7% vs. 79.6%, $p < 0.01$), suggesting a clinical benefit of TDM. Our study observed a greater number of haploidentical HSCTs, which justifies, according to the literature,[18-20] the use of MAC as it enables various drug combinations, such as Bu/CY, fludarabine/TBI, and fludarabine/Bu. We performed a subanalysis for Bu usage due to its role in conditioning regimens prior to transplantation. Its pharmacokinetic profile is more directly associated with outcomes related to engraftment quality and graft function, such as neutrophil recovery and graft failure, unlike calcineurin inhibitors, which are primarily used for GVHD prophylaxis. Our study neither evaluated the incidence of infections during transplant hospitalization nor observed a reduction in the incidence of severe aGVHD. One difference between the studies is the length of follow-up, which was longer in this study, with a reduction in mortality and a 3-month increase in survival.

The limitations of this study include its retrospective data collection from medical records in the control group and the loss of some information. The incomplete recording of adverse events impaired safety assessment. Additionally, the control and exposed groups are not contemporaneous. Thus, other more recent changes may have influenced the results, the interpretation of which requires caution. The longer hospitalization time in the TDM group may be associated with changes in nursing care routines, such as incorporating new patient assessment scores. Hospital discharge criteria changed, and better patient care may have impacted mortality and survival time. Another characteristic of the group exposed to monitoring was its concomitance with the COVID-19 pandemic. From 2019 to 2021, the number of transplants decreased, and hospital infection prevention routines changed. On the other hand, the evaluation of clinical outcomes, the 2-year post-transplant follow-up, and the sample size constitute the strengths of this study.

CONCLUSION

Although this study did not demonstrate a reduction in GVHD incidence in the TDM group, the findings highlight the important role of the pharmacist in guiding dose adjustments based on serum drug levels while also considering clinically relevant variables in the allogeneic HSCT setting. In addition, the results suggest potential benefits regarding mortality reduction and improved 2-year survival.

CONFLICTS OF INTEREST

Nothing to declare.

AUTHORS CONTRIBUTIONS

Conceptualization: Zuckermann J. **Investigation:** Zuckermann J, Castro BM, Ruschel RG, Beltrami LB, Fonseca RP, Silva PO, Scherer FF. **Methodology:** Zuckermann J, Castro BM, Moreira LB. **Analysis:** Zuckermann J, Castro BM, Araújo BV, Daudt LE, Paz AA, Moreira LB. **Data Curation:** Zuckermann J, Castro BM, Ruschel RG, Moreira LB. **Project Administration:** Zuckermann J. **Funding Acquisition:** Moreira LB. **Writing:** Zuckermann J. **Supervision:** Zuckermann J, Moreira LB. **Final Approval:** Zuckermann J.

DATA AVAILABILITY STATEMENT

Data will be provided upon request.

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DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

The authors declare that no artificial intelligence tools were used in the preparation, writing, or editing of this manuscript.

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REFERENCES

1. Vigorito AC, Moreira MCR, Silva MM, Tavares RCBS, Corre MEP, Funke VAM, et al. Guidelines for diagnosis and classification of chronic graft-versus-host disease. São Paulo: Sociedade Brasileira de Transplante de Medula Óssea; 2017. [cited 2022 Dec 1]. Available from: https://sbtmo.org.br/consensos-sbtmo/
2. Gawedzki P, Collins J. Impact of the implementation of a pharmacist-driven immunosuppression drug monitoring protocol for hematopoietic stem cell transplant recipients. J Oncol Pharm Pract. 2021;27 (8):1907-13. https://doi.org/10.1177/1078155220975088
3. Ghiculescu R. Therapeutic drug monitoring: which drugs, why, when, and how to do it. Aust Prescr. 2008;31 (2):42-4. https://doi.org/10.18773/austprescr.2008.025
4. Paz A, Fischer G, Schittler M, Pezzi A, Valim V, Dahmer A, et al. Donor characteristics and hematopoietic stem cell transplantation outcome: experience of a single center in Southern Brazil. Hematol Transfus Cell Ther. 2018;40 (2):136-42. https://doi.org/10.1016/j.htct.2017.11.008
5. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap): a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42 (2):377-81. https://doi.org/10.1016/j.jbi.2008.08.010
6. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software partners. J Biomed Inform. 2019;95:103208. https://doi.org/10.1016/j.jbi.2019.103208
7. Tian JX, Zhang P, Miao WJ, Wang XD, Liu XO, Liao YX, et al. Tacrolimus levels in the prophylaxis of acute graft-versus-host disease in the Chinese early after hematopoietic stem cell transplantation. Ther Drug Monit. 2019;41 (5):620-7. https://doi.org/10.1097/FTD.0000000000000645
8. Tafazoli A, Dadashzadeh S, Mehdizadeh M, Parkhideh S, Tavakoli-Ardakani M. Evaluation of cyclosporine pharmacokinetic, monitoring, and dosing parameters for GVHD prophylaxis in hematopoietic stem cell transplant (HSCT) recipients. Iran J Pharm Res. 2019;18 (Suppl 1):302-14. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7393056/
9. Corrêa PM, Zuckermann J, Fischer GB, Castro MS. Immunosuppressive serum levels in allogeneic hematopoietic stem cell transplantation: pharmaceutical care contribution. Pharm Pract (Granada). 2016;14 (2):683. https://doi.org/10.18549/PharmPract.2016.02.683

10. Bognàr TT, Kingma JSJ, Smeijsters EHE, van der Elst KCMK, de Kanter CTMK, Lindemans CAC, et al. Busulfan target exposure attainment in children undergoing allogeneic hematopoietic cell transplantation: a single day versus a multiday therapeutic drug monitoring regimen. Bone Marrow Transplant. 2023. https://doi.org/10.21203/rs.3.rs-2507097/v1

11. Yan C H, Xu L P, Wang F R, Chen H, Han W, Wang Y, et al. Causes of mortality after haploidentical hematopoietic stem cell transplantation and the comparison with HLA-identical sibling hematopoietic stem cell transplantation. Bone Marrow Transplant. 2016;51 (3):391-7. https://doi.org/10.1038/bmt.2015.306

12. Beyron C, Ceraulo A, Bertrand Y, Bleyzac N, Philippe M. Impact of a Bayesian individualization of cyclosporine dosage regimen for children undergoing allogeneic hematopoietic cell transplantation: a cost-effectiveness analysis. Ther Drug Monit. 2021;43 (4):481-9. https://doi.org/10.1097/FTD.0000000000000886

13. Carnevale-Schianca F, Caravelli D, Gallo S, Becco P, Paruzzo L, Poletto S, et al. Post-transplant cyclophosphamide and tacrolimus-mycophenolate mofetil combination governs GVHD and immunosuppression need, reducing late toxicities in allogeneic peripheral blood hematopoietic cell transplantation from HLA-matched donors. J Clin Med. 2021 11;10 (6):1173. https://doi.org/10.3390/jcm10061173

14. Williams L, Cirrone F, Cole K, Abdul-Hay M, Luznik L, Al-Homsi AS. Post-transplantation cyclophosphamide: From HLA-haploidentical to matched-related and matched-unrelated donor blood and marrow transplantation. Front Immunol. 2020; 11:636. https://doi.org/10.3389/fimmu.2020.00636

15. Zeiser R. Prevention of graft-versus-host disease. In: UpToDate [Internet]. Waltham (MA): UpToDate; 2022. [cited 2022 Jul 16]. Available from: https://doi.org/10.1056/NEJMc1716969

16. Stanojevic M, Bertaina A, Bonfim C, Ciccocioppo R, Cohen S, Purtill D, et al. Viral infection in hematopoietic stem cell transplantation: an International Society for Cell & Gene Therapy Stem Cell Engineering Committee review on the role of cellular therapy in prevention and treatment. Cytotherapy. 2022;24 (9):884-91. https://doi.org/10.1016/j.jcyt.2022.05.010

17. Pereira MR, Pouch SM, Scully B. Infections in allogeneic stem cell transplantation. In: Principles and practice of transplant infectious diseases. Cham: Springer; 2019. p. 209-26. https://doi.org/10.1007/978-1-4939-9034-4_11

18. Sengsayadeth S, Savani BN, Blaise D, Mohty M. Haploidentical transplantation: selecting optimal conditioning regimen and stem cell source. Semin Hematol. 2016;53 (2):111-4. https://doi.org/10.1053/j.seminhematol.2016.01.012

19. McCurdy SR, Luznik L. How we perform haploidentical stem cell transplantation with posttransplant cyclophosphamide. Blood. 2019;134 (21):1802-10. https://doi.org/10.1182/blood.2019001323

20. Van der Stoep MYEC, Oostenbrink LVE, Bredius RGM, Moes DJAR, Guchelaar HJ, Zwaveling J, et al. Therapeutic drug monitoring of conditioning agents in pediatric allogeneic stem cell transplantation: where do we stand? Front Pharmacol. 2022;13:826004. https://doi.org/10.3389/fphar.2022.826004