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Pharmacology Oral Session

36 - Pharmacology

O173

ANALYSIS OF THE PATIENT-PHARMACIST INTERACTION THROUGH AN MHEALTH PLATFORM IN THE MANAGEMENT OF ALLOGENEIC STEM CELL TRANSPLANT RECIPIENTS (MYMEDULA STUDY)

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Background: Polypharmacy is an important issue after allogeneic stem cell transplant (allo-SCT). Mobile health (mHealth) tools can improve therapy management and provide personalized care by an interdisciplinary team, including clinical pharmacists.

The objective of this analysis is to describe the patient-pharmacist interaction in the allo-SCT setting through an mHealth platform.

Methods: Prospective, non-randomized single-center pilot study, carried out in a tertiary university hospital, by an interdisciplinary team (Study code: IIBSP-EME-2019-44, approved by the hospital's ethics committee).

A web page and a mobile application were designed. Patients using the mHealth tool were able to register their symptoms/adverse events, medication, and other variables such as vital signs, physical exercise, or food intake. A patient-healthcare professional messaging service was available. Patients could also access a library with general information about their condition and videos of how their healthcare team could help them.

Two clinical pharmacists, involved in the allo-SCT team, provided pharmaceutical care to these patients. They reviewed the messages sent to the pharmacists' team and the treatments registered by the patients. Pharmacists could validate or reject the treatments entered; after validation, patients could activate and view the treatment in their medication list.

The variables collected were the number of drugs reviewed by pharmacists, medication adherence, and patient-pharmacist messages. The subject of the messages was classified into 5 categories: queries about treatment, interactions, visit request, technical questions about the mHealth tool and general messages from pharmacists.

Results: Between October 2021 and January 2022, 28 volunteer allo-SCT recipients participated in the pilot study. Pharmacists reviewed 297 drugs introduced by 22 patients. There were 210 (70.7%) drugs introduced and activated, being the mean number of drugs per patient 9.5 (range 1–24). There were 87 (29.3%) drugs not activated by patients; 52 (59.8%) validated but with a pharmacist observation, 32 (36.8%) validated but not activated by any apparent reason and three (3.4%) rejected by a pharmacist, because the dose was wrong, the drug was already stopped or because the drug was considered not safe for the patient. At the end of the pilot study, 27 patients answered the ARMS-e adherence questionary, although only 4 patients registered their adherence to treatment in the platform, three with adherence over 80% and one patient less than 20%.

Pharmacists sent a total of 118 messages to 28 patients, 19.7% of the total messages sent by the healthcare team. The mean number of messages per patient was 4.2 (range 1–16). Pharmacists received 65 messages from 24 patients, 31% of the total of messages received by the healthcare team. The mean number of messages per patient was 2.7 (range 1–11).

Conclusions: Pharmacist involvement in the care of allo-SCT patients through an eHealth tool, facilitated the revision of medication and how patients were taking it. It helped providing pharmaceutical care, increasing communication, solving non-

urgent consultations, and identifying areas of concern in the allo-SCT setting.

Clinical Trial Registry: Study code: IIBSP-EME-2019-44.

Disclosure: The study has the collaboration of the pharmaceutical company Amgen S.A. which assumed the cost of the technological development and those derived from the implementation of the tool. Amgen had no influence on the study design, data collection or data analysis.

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O174

BUSULFAN TARGET EXPOSURE ATTAINMENT IN CHILDREN UNDERGOING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION: A SINGLE DAY VERSUS A MULTIDAY THERAPEUTIC DRUG MONITORING REGIMEN

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Background: Previous studies have shown a clear relation between busulfan exposure and clinical outcomes in children undergoing allogeneic hematopoietic cell transplantation (HCT), warranting therapeutic drug monitoring (TDM) of busulfan. The objective of this study was to evaluate the effect of day 1 TDM-guided dosing (regimen d1) versus days 1 + 2 TDM-guided dosing (regimen d1 + 2) on attaining adequate busulfan target exposure.

Methods: In this observational study, we included all children who received an allogeneic HCT with intravenous once daily busulfan over 4 days as part of the conditioning regimen at the University Medical Centre Utrecht or the Princess Máxima Center for Pediatric Oncology between July 31th 2014 and November 12th 2021. The primary outcome was attainment of the therapeutic busulfan target (cumulative area under the curve [AUC0-∞] 80–100 mg*h/L). Dose adjustment was based on the estimated AUC of the preceding dosing day(s). Additional TDM was performed in the event of large dose adjustments (≥25%). The choice of TDM regimen was solely based on the first day the busulfan dose was administered (regimen d1 + 2 occurred when conditioning started on a Saturday). In all patients, blood sampling was performed on day 4 for evaluation. The AUC0-∞ was estimated using nonlinear mixed effect modeling with a validated model that adjusted for (interoccasion) variability in clearance and volume of distribution. Busulfan target exposure was compared between both TDM regimen groups using a propensity score adjusted logistic regression model. The variance between the TDM regimens was compared using the F-test. Patients were stratified for age (categorical).

Results: We included 141 patients, of which 76.6% ($n = 108$) were monitored with TDM regimen d1 and 23.4% ($n = 33$) with TDM regimen d1 + 2 (Table 1). The patient characteristics were equally distributed across both TDM regimen groups. In regimen d1, 84.3% ($n = 91/108$) attained a therapeutic busulfan AUC, while in regimen d1 + 2, 90.9% ($n = 30/33$) attained a therapeutic AUC (adjusted odds ratio for non-therapeutic AUC = 0.47, 95% confidence interval 0.12–1.77). In the total population and age groups, target attainment and the variance of the AUC0-∞ did not significantly differ between TDM regimens (Fig. 1).

			Therapeutic AUC (mg*h/L)		Non-therapeutic AUC (mg*h/L)			
			80–100		<80 or >100			
		N patients	%	n	%	n	adjOR	95% CI
Total population	Regimen d1	108	84.3%	91	15.7%	17	Ref	
	Regimen d1 + 2	33	90.9%	30	9.1%	3	0.47	0.12–1.77
0–2 (y)	Regimen d1	29	79.3%	23	20.7%	6	Ref	
	Regimen d1 + 2	5	100.0%	5	0.0%	0	NE	
2–5 (y)	Regimen d1	18	77.8%	14	22.2%	4	Ref	
	Regimen d1 + 2	6	83.3%	5	16.7%	1	0.41	0.03–6.26
5–12 (y)	Regimen d1	28	92.9%	26	7.1%	2	Ref	
	Regimen d1 + 2	13	84.6%	11	15.4%	2	2.83	0.30–26.41
12–18 (y)	Regimen d1	33	84.8%	28	15.2%	5	Ref	
	Regimen d1 + 2	9	100.0%	9	0.0%	0	NE	

Table 1. Target attainment of busulfan for both therapeutic drug monitoring (TDM) regimens, stratified for age (0–2, 2–5, 5–12, and 12–18 years). adjOR = odds ratio adjusted for gender, body weight, disease status (malignant/non-malignant), serotherapy regimen (anti-thymocyte globulin) and the conditioning regimen, AUC = area under the curve, CI = confidence interval, NE = not estimable, Ref = reference.

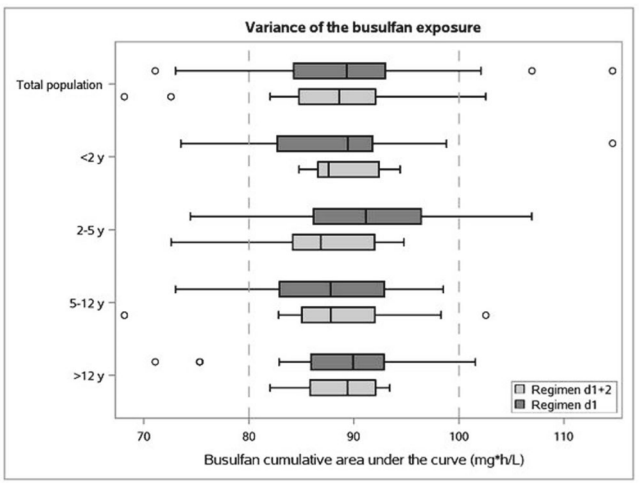

Figure 1. Variance of the busulfan cumulative exposure (target cumulative area under the curve = 80–100 mg*h/L) for both therapeutic drug monitoring (TDM) regimens, stratified for age (0–2, 2–5, 5–12, and 12–18 years). The variance did not differ significantly between TDM regimens (F-test).

Conclusions: In conclusion, day 1 TDM-guided dosing of busulfan may be sufficient for attaining adequate target exposure.

Disclosure: Nothing to declare.

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O175

ASSOCIATION OF CYCLOSPORINE TROUGH CONCENTRATIONS AND THE INCIDENCE OF ACUTE GRAFT VERSUS HOST DISEASE IN PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Cyclosporine (CsA) is recommended for the prevention of acute Graft-versus-Host Disease (aGvHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT), with a target range for CsA trough blood concentrations of 200–300 ng/mL. Some studies suggest greater CsA effectiveness with higher CsA exposure. Our aim was to assess CsA trough concentrations achieved in our center between days −3 to +100, and to determine if higher concentrations were associated with a lower rate of clinically significant aGvHD (grade 2–4).

Methods: We conducted a retrospective database study in consecutive adults undergoing myoabalative allo-HSCT during the years 2018–2020 at the Rambam Health Care Campus and received CsA for at least 2 weeks after the transplant. We extracted from the electronic medical record demographic and clinical characteristics, data on CsA dosing and trough blood concentrations, and aGvHD and its severity. For each patient, we calculated the weighted mean CsA trough concentration (CsA_{wa}) for different time periods between day −3 to +100, interpolating between consecutive measurements. We compared CsA_{wa} and other parameters between patients with and without grade 2–4 aGvHD until day +100, and used logistic regression analysis to examine whether CsA_{wa} was associated with aGvHD after adjustment for multiple covariates.

Results: We included 146 patients (60% male, median age [interquartile range, IQR] = 54 [40, 63] years). The most common indication for transplant was acute leukemia (69%), and the most common conditioning regimen was busulfan/fludarabine. 47% had matched related donors. Rate of grade 2–4 aGvHD was 45.2%. There were no significant differences in demographic and clinical parameters between patients with and without aGvHD. Mean CsA (SD) trough concentrations were at the lower limit of the target range in the first days of therapy, but there was no significant difference in CsA_{wa} trough concentrations between patients with and without aGvHD at any time point: at day 0, 185 (85) and 198 (96) ng/mL, $p = 0.4$; during day 0–3, 203 (81) and 216 (86) ng/mL, $p = 0.2$; during the first week, 223 (61) and 240 (73) ng/mL, $p = 0.2$; during the first 2 weeks, 254 (51) and 268 (56) ng/mL, $p = 0.2$; and during the first 4 weeks, 288(46) and 291(34) ng/mL. In multivariate linear regression analyses, CsA_{wa} during various time intervals was not associated with grade 2–4 aGvHD.

Conclusions: In our cohort, CsA trough concentrations were below target in the first days after transplantation, but the average concentrations increased to >250 ng/mL during the second week. Average CsA concentrations in various time periods during the first 100 days post-transplant were not associated with aGvHD. Future studies examining the association of more intensive CsA dosing regimens (designed to achieve target exposure earlier after transplantation) on aGvHD will be of interest.

Disclosure: Nothing to declare.

33 - Quality Management

O176

AUTOMATING OUTCOME ANALYSIS FOR SCT PATIENTS: THE YEARLY OUTCOME REVIEW TOOL

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Background: For quality management after hematopoietic stem cell transplantation (HSCT), yearly outcome review is required by standards such as JACIE or FACT, but comes with substantial effort and associated costs.

Methods: To reduce the effort required to perform these analyses, we created the Yearly Outcome Review Tool (YORT), a graphical tool that works on a single-center export file in the EBMT registry format. It allows users to define filters to select which patients to analyze, and groups to compare patients by.

It compares demographics, performs survival analysis for overall and event-free survival, reports engraftment, uses competing risk analysis to investigate relapse rate and relapse-free survival, and analyses complications including acute and chronic Graft versus Host Disease (GvHD).

The tool works using R and Shiny, is available as an R package, and offers a standalone installer for users without R experience. It uses an extensible, modular design, facilitating additions without modifying its source code. It allows users to export the data retrieved for analyses in Excel or SPSS.

To demonstrate the capabilities of the tool, we analyzed outcome of pediatric patients transplanted at the Willem Alexander Children's Hospital between 2019 and 2021.

Results: In the tool, we defined filters to select patients with a first allogeneic HSCT, an age below 18 at time of transplant, and a transplant between 2019 and 2021. We grouped by graft source and main diagnosis categories. All following analyses are performed using the tool.

Primary diagnosis was a primary immune deficiency in 26 patients, a hemoglobinopathy in 23 patients, bone marrow failure in 16, and Glanzmann thrombasthenia in 1 patient. Overall survival was 94% at 100 days and 92% at 1 year. Differences between diagnoses were in line with literature, with 80% survival for histiocytic disorders and 96% for hemoglobinopathies at 1 year.

Event free survival, defined as survival without relapse, disease progression or subsequent transplants, was 92% at 100 days, 86% at 1 year and 77% at three years, without difference between groups. Relapse rate and non-relapse mortality was not analyzed due to the primary diseases included.

Furthermore, the tool reported on acute and chronic GvHD, engraftment of neutrophils and of platelets, and acute and chronic GvHD. Since no patients were transplanted for malignancies, we did not analyze relapse and non-relapse mortality.

We distributed the tool to 5 HSCT centers, who tested the tool and provided feedback, and completed a security impact assessment.

Conclusions: We created YORT, a tool which performs standardized outcome analyses on an unmodified file in the EBMT registry format which can be exported by centers

entering data in the registry. We extensively tested it, and passed a security impact assessment. The tool reduces the effort required to perform an outcome analysis, and allows users to easily adjust the population analyzed and groups compared.

We hope this tool will both increase the quality and standardization of outcome analyses performed, as well as increase data quality by improving data usefulness for centers entering data, and allowing centers to identify anomalies and incomplete data easily.

Disclosure: Nothing to declare