IMPROVEMENT IN ACUTE NEUROLOGICAL COMPLICATIONS RELATED TO STEM CELL TRANSPLANT IN SICKLE CELL DISEASE

LESSONS FROM OUR EXPERIENCE

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INTRODUCTION

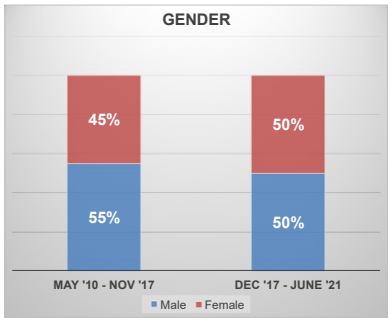
Central nervous system (CNS) complications during hematopoietic stem cell transplantation (HSCT) in sickle cell disease (SCD) patients are a major cause of morbidity, as: posterior reversible encephalopathy syndrome (PRES), seizures, strokes or subarachnoid haemorrhage (HSA). These complications can appear for several causes, but mostly due to variations on hemodynamic status of the patient. Conditioning regimen-related toxicity, graft-versus-host disease (GvHD) and the use of calcineurin inhibitors also play an important role.

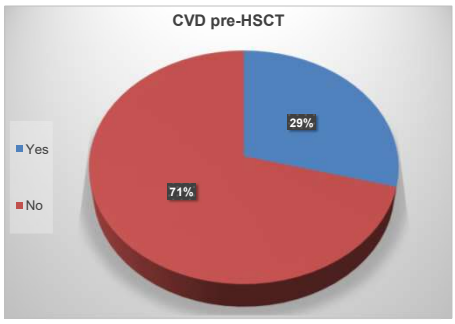
METHODS

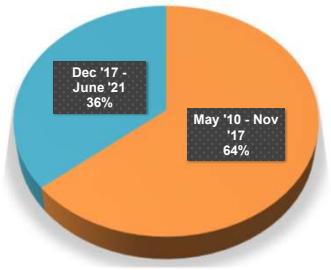
A retrospective single center study was conducted in children with SCD, allogeneic HSCT from an HLA-identical sibling donor since January 2010 to December 2021. Implementation of arterial blood pressure (ABP) Holter established in December 2017 providing a better understanding of patient's hemodynamic status and easing early treatment of arterial hypertension prior to HSCT. We analyze CNS transplant complications between two different periods: May 2010 to November 2017, and December 2017 to June 2021. A change on conditioning regimen was also established. Until June 2015 we used Bu, CFM and alemtuzumab. Afterwards, we changed to myeloablative but reduced toxicity conditioning: thiotepa, TREO, FLU, ATG. GvHD prophylaxis used until 2019 was CsA and MTX, changing later to tacrolimus and mycophenolate mofetile (MMF). Epidemiological and clinical parameters were collected. Data are presented as percentages and quartiles. For the comparison of the variables under study, a bivariate analysis with non-parametric *Fisher test* was used. *R Statistical Software* was used for the numerical analysis and *Survminer* to represent Kaplan-Meier curves.

RESULTS

48 allo-HCST were performed in 47 patients, median age 6.0 years (p25 2;p75 9).







- Prior to HSCT, 14/48 of HSCT had cerebrovascular disease (CVD: Moya-moya vasculopathy, silenct infarction, stroke or leukoencephalopathy); 64% (9/14) on first period and 36% (5/14) on second.

CEREBROVASCULAR DISEASE PRIOR TO HSCT:

- Moya-moya vasculopathy
- Silent infarction
- Stroke
- Leukoencephalopathy

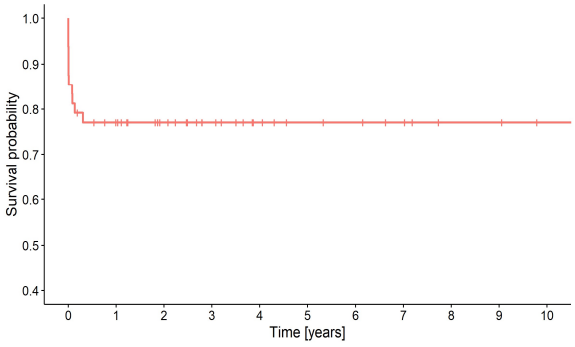
- **During HSCT**, 11/48 had acute CNS complications: 91% on first period (10/11); 9% on second (1/11).

	Seizures	HSA	PRES	Toxicity to CNI	Other
May '10 – Nov '17	9/10 (90%)	5/10 (50%)	5/10 (50%)		1/10 (10%)
Dec '17- June '21	-	-	-	1/11 (9%)	-

HTA was present in 89% of total HSCT and in 100% with post-HSCT CNS complications.

- Statistically **significant decrease on post-HSCT neurological complications on second period** was observed **compared to the first**, after the implementation of ABP Holter. Also, we **couldn't observe a statistically significant predisposition to have post-HSCT CNS complications according to their pre-neurological history**.

- **Global EFS of post-HSCT CNS complications** at the end of follow-up period (10.69 years) was **77%** (0.65-0.89).



	PERIODS OF TIME		
CNS complications post-HSCT	**PRE 11/2017[1]**	**POST 11/2017[1]**	*p*
Acute			0.002
No	13 (57%)	24 (96%)	
Yes	10 (43%)	1 (4.0%)	
Seizures			<0.001
No	14 (61%)	25 (100%)	
Yes	9 (39%)	0 (0%)	
HSA			0.020
No	18 (78%)	25 (100%)	
Yes	5 (22%)	0 (0%)	
PRES			0.049
No	18 (78%)	23 (100%)	
Yes	5 (22%)	0 (0%)	
NAs	0	2	
Others			>0.9
No	13 (93%)	18 (95%)	
Yes	1 (7.1%)	1 (5.3%)	
NAs	9	6	

	PRE-HSCT CNS COMPLICATIONS		
CNS complications post-HSCT	**NO**	**YES**	*p*
Acute			0.3
No	28 (76%)	9 (24%)	
Yes	6 (55%)	5 (45%)	
Seizures			0.10
No	30 (77%)	9 (23%)	
Yes	4 (44%)	5 (56%)	
HSA			0.14
No	32 (74%)	11 (26%)	
Yes	2 (40%)	3 (60%)	
PRES			0.2
No	30 (73%)	11 (27%)	
Yes	2 (40%)	3 (60%)	
NAs	2	0	
Others			>0.9
No	23 (74%)	8 (26%)	
Yes	2 (100%)	0 (0%)	
NAs	9	6	

CONCLUSION

Even with reduced-toxicity conditioning and the switch to tacrolimus, neurological events still happen. Recent modifications in our center, mainly **since the implementation of ABPH, have decreased acute CSN complications** and improved SCD event-free survival rates during transplant, with less toxicity, morbidity and mortality.

REFERENCES

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