Case-Control Study of Outcomes of Autologous Stem Cell Transplantation in Jehovah's Witness Multiple Myeloma Patients

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ABSTRACT

Multiple myeloma (MM) is a hematological neoplasm characterized by the abnormal proliferation of plasma cells in the bone marrow**.** Autologous stem cell transplantation (ASCT) after high-dose chemotherapy is the standard of care for intermediate and high-risk MM. Several cell lines drop during ASCT and require a blood transfusion. Jehovah's Witness (JW) patients present unique management challenges as they refuse blood transfusion due to religious beliefs. Therefore, most of JW receives a single ASCT. Tandem transplantation has rarely been reported in JW. Consequently, we sought to analyze the comparative safety outcomes of single or tandem ASCT in JW vs. non-JW patients. We performed a retrospective case-control study of eight single and five tandem ASCTs in JW compared with non-JW control in a 1:2 ratio at the University of Arkansas for medical sciences Little Rock, AR, between 1990 to 2021. The bleeding complication, the outcome of ASCT, the induction chemotherapy regimen, the number of CD34 collected and transfused, mortality, engraftment time for white blood cells, platelets, and re-hospitalization in 30 and 100 days were compared. There was no significant difference between tandem/ single ASCT in JW vs. non-JW. Therefore single/tandem ASCT can be safely performed in JW patients.

BACKGROUND

- JW is a Christian religious community that refuses blood transfusion or related products.
- There are 8.7 million people worldwide, with 2.5 million living in North America. [1]
- Physicians encounter management and ethical issues while treating JW patients, mainly when it involves solid organ transplant, surgery, autologous, and allogeneic stem cell transplantations.[2]
- Ford et al. reported single ASCT in 68 JW patients with multiple myeloma [3].
- R. Khan et al. reported 4 tandem ASCT in JW patients [4].
- We are reporting the safety and outcome of 5 JW patients who received tandem and 8 single ASCT compared to non-JW control.

METHODS

In a retrospective case-control study, we compare the data of 5 JW patients who received tandem and 8 single ASCT to similar non-JW control for outcomes and safety with a 1:2 ratio from 1990 to 2021.

Matching (1:2) is done based on age, date of MM diagnosis, race/ethnicity, performance status, International Staging System (ISS) stage, and number of ASCT. Patient characteristics for tandem ASCT with control are summarized in the table 1, and single are outlined in table 2, respectively. Melphalan dose ranged from (100 mg/m2 to 200 mg/m2) based on individual patient characteristics. Patients received tobo-filgrastim when ANC (absolute neutrophil count) <1.5, along with appropriate antibacterial and antifungal prophylaxis, till engraftment in all ASCT.

Table 1. Tandem Transplant. Comparison of cases to controls with respect to demographic, laboratory, and outcome measures. Medians and interquartile ranges are presented forn continuous variables and percents and counts are presented for categorical variables. Wilcoxon rank-sum tests were used to test continuous variables, while Fisher's exact tests were used for categorical variables.

Variable		Case (N=5)	Control (N=10)	P-value
Age		49.0 (46.0, 52.0)	49.5 (44.5, 52.5)	>0.99
AA		20.0% (1)	20.0% (2)	>0.99
Female		40.0% (2)	40.0% (4)	>0.99
ISS				
	1	60.0% (3)	60.0% (6)	>0.99
	2	20.0% (1)	20.0% (2)	
	3	20.0% (1)	20.0% (2)	
B2M		2.9 (2.2, 5.3)	2.3 (2.1, 4.3)	>0.55
LDH		181.0 (102.0, 321.0)	199.0 (165.0, 272.0)	>0.86
Calcium		8.8 (8.6, 9.8)	9.2 (8.9, 9.8)	>0.61
HGB		11.6 (11.0, 12.9)	11.6 (9.2, 12.5)	>0.67
Albumin		3.8 (3.7, 3.8)	3.9 (3.4, 4.4)	>0.74
ECOG	0	60.0% (3)	40.0% (4)	>0.60
	1	20.0% (1)	60.0% (6)	
	2	0.0% (0)	0.0% (0)	
	3	20.0% (1)	0.0% (0)	
Creatinine		1.0 (0.9, 1.1)	1.1 (0.9, 1.3)	>0.16
GFR		82.8 (64.9, 87.9)	65.7 (57.9, 75.3)	>0.09
ICU Transfer		0.0% (0)	0.0% (0)	>0.99
Transfusion		20.0% (1)	80.0% (8)	<0.005
CD34 Collected		34.0 (21.0, 38.0)	21.3 (20.0, 34.9)	>0.66
CD 34 Infused		10.8 (10.6, 13.2)	8.8 (7.8, 9.5)	<0.01
Hospitalization within 30 days		20.0% (1)	0.0% (0)	>0.33
Hospitalization within 100 days		40.0% (2)	10.0% (1)	>0.25
Response				
	sCR	0.0% (0)	20.0% (2)	
	CR	20.0% (1)	40.0% (4)	
	VGPR	40.0% (2)	20.0% (2)	
	PR	20.0% (1)	20.0% (2)	
	NR	20.0% (1)	0.0% (0)	
VG Response		60.0% (3)	80.0% (8)	>0.56

Table 2. Single Transplant.

Variable		Case (N=8)	Control (N=16)	P-value
Age		66.0 (65.8, 67.5)	67.5 (65.8, 69.0)	>0.99
AA		62.5% (5)	62.5% (10)	>0.99
Female		50.0% (4)	62.5% (10)	>0.99
ISS	1	62.5% (5)	62.5% (10)	
	2	37.5% (3)	37.5% (6)	>0.99
	3	0.0% (0)	0.0% (0)	
B2M		2.9 (2.8, 3.8)	2.8 (2.2, 4.1)	>0.64
LDH		134.5 (107.5, 156.2)	166.0 (153.5, 173.8)	<0.05
Calcium		9.6 (9.0, 9.9)	9.1 (8.9, 9.3)	>0.32
HGB		11.3 (10.6, 11.6)	11.2 (9.5, 13.2)	>0.92
Albumin		3.5 (3.3, 3.8)	3.7 (3.7, 3.8)	>0.17
ECOG	0	37.5% (3)	31.2% (5)	>0.99
	1	62.5% (5)	62.5% (10)	
	2	0.0% (0)	6.2% (1)	
	3	0.0% (0)	0.0% (0)	
Creatinine		0.9 (0.9, 1.0)	0.9 (0.8, 1.3)	>0.66
GFR		64.9 (64.9, 68.1)	64.9 (53.6, 68.6)	>0.73
ICU Transfer		25.0% (2)	6.2% (1)	>0.24
Transfusion		0.0% (0)	81.2% (13)	<0.0003
CD34 Collected		23.2 (14.5, 29.5)	30.1 (15.9, 34.6)	>0.61
CD 34 Infused		5.8 (4.6, 7.0)	5.1 (3.9, 7.2)	>0.60
Hospitalization within 30 days		50.0% (4)	43.8% (7)	>0.99
Hospitalization within 100 days		50.0% (4)	50.0% (8)	>0.99
Response				
	sCR	0.0% (0)	12.5% (2)	
	CR	50.0% (4)	31.2% (5)	
	VGPR	37.5% (3)	43.8% (7)	
	PR	12.5% (1)	12.5% (2)	
	NR	0.0% (0)	0.0% (0)	
VG Response		87.5% (7)	87.5% (14)	>0.99

RESULTS

JW MM patients received ASCT in the study period (8 single, 5 tandem) compared with 26 non-JW MM patients (16 single, 10 tandem).

For JW patients who received single ASCT, the median age was 66 (range:65.8-67.5 years), 50% were female and 62.5% were black. Average CD34 stem cells collected/infused were 23/5.8 million cells in JW compared to 30.1/5.1 million in non-JW, respectively. For JW patients who received tandem ASCT, the median age was 49 (range:46-52 years); 50% were female and 62.5% were black. Average CD34 stem cells collected/infused were 34/10.8 million in JW compared to 21.3/8.8 million in non-JW, respectively.

JW's lowest hemoglobin and platelet levels were 6.6 g/dl and 3000 k/uL, respectively. 100-day mortality for all patients was 0%. Multivariable analysis showed no significant difference in 30 days/100 days re-hospitalization, primary and/or minor bleeding, adverse events, and response to treatment (very good partial response or better).

White blood cell engraftment is defined as sustained peripheral blood neutrophil count>500x106/L for three days. This was not statistically significant as shown in the table 3 and 4

Table 3. Tandem transplants. Medians and interquartile ranges are presented. Wilcoxon rank-sum tests are used to compare groups

Variable	Case	Control	P-value
ANC Days_1	13.0 (10.0, 13.0)	11.5 (11.0, 13.0)	0.9499
ANC Days_2	10.0 (9.0, 10.0)	11.0 (11.0, 11.0)	0.0632
Platelet Days_1	14.0 (13.0, 16.0)	14.5 (12.0, 15.0)	0.3809
Platelet Days_2	12.0 (11.0, 12.0)	13.0 (13.0, 14.0)	0.0742

Table 4. Single transplant. Medians and interquartile ranges are presented. Wilcoxon rank-sum tests are used to compare groups.

Variable	Case	Control	P-value
ANC Days	11.0 (11.0, 11.2)	11.0 (11.0, 11.2)	0.9437
Platelet Days	12.5 (12.0, 14.0)	14.0 (13.0, 14.2)	0.3030

CONCLUSIONS

- ASCT offers OS and PFS benefits in MM but may need red cell and platelets transfusion up to 29 % and 71%, respectively.[5] Delaying or deferring transfusions poses a significant risk. Most MM patients are anemic at the time of diagnosis making chemotherapy or transplant challenging in JW patients. Tandem ASCT has better progression-free survival and overall survival in patients with high-risk cytogenetics and extramedullary disease when compared to single ASCT in MM. [6] Supportive therapy agents like tranexamic and Romiplostim can be used.[7]
- Although ASCT in JW MM patients may be riskier compared to the general population out study found no statistically significant difference in safety between tandem/ single ASCT in JW vs. non-JW patients. Following a strict algorithm like higher baseline blood counts, blood conserving strategies, erythropoietin use, antifibrinolytics for mucosal bleeding, iron folate and B12 supplementation can be helpful.

References

1. Rashid et al Curr Opin Anaesthesiol. 2021;34(2):125-130. doi:10.1097/ACO.0000000000000096
2. Bodnaruk ZM . Transfus Med Rev. 2004;18(2):105-116. doi:10.1016/j.tmrv.2003.12.004
3. Ford PA. Community Oncology. 2006;3(12):776-780. doi:10.1016/S1548-5315(11)70948-2
4. Khan et al Bone Marrow Transplant. 2018;53(11):1428-1433. doi:10.1038/s41409-018-0132-6
5. BMC Cancer | Full Text. Accessed September 10, 2022.
6. Biol Blood Marrow Transplant. 2019;25(11):2134-2142. doi:10.1016/j.bbmt.2019.07.004
7. - Journal of Gastroenterology and Hepatology - Wiley Online Library. Accessed September 10, 2022
8. British Journal of Haematology. 2013;161(5):738-740. doi:10.1111/bjh.12284

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