

The Evaluation of Hyperhydration for High Dose Melphalan in Stem Cell Transplantation

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BACKGROUND

Melphalan is commonly used cytotoxic drug in haematopoietic stem cell transplantation (HSCT). It is a part of conditioning chemotherapy regimens such as high dose melphalan (HDM), BEAM, FluMel or BuMel.

It is usually given with hydration with forced diuresis, however, the amount of fluid required for patients is unknown. Nationally and internationally, melphalan is given with normal hydration of 2 litres (L) or with hyperhydration of 4 to 6 L.

Melphalan is predominantly eliminated by spontaneous chemical hydrolysis. The relationship between renal function and melphalan elimination/ toxicity is unclear.

AIMS

To answer the following research questions;

RQ1. Is the practice of hyperhydration in patients receiving HDM autologous HSCT associated with decreased renal dysfunction? (Primary endpoint)

RQ2. Is the practice of hyperhydration in patients receiving HDM autologous HSCT associated with adverse events related to fluid overload? (Secondary endpoint)

METHODS

Study design

A retrospective cohort study comparing the endpoints between institutes using hyperhydration and not using hyperhydration:

- Royal Brisbane and Women's Hospital (RBWH) --- Hyperhydration 6L; versus
- The Townsville Hospital (TTH) --- Normal hydration 2L.

Patients

Inclusion criteria: Patients who have received HDM (200mg/m²) autologous HSCT for myeloma between January 2015 - September 2017 as a hospital inpatient.

Exclusion criteria: Patients received allogeneic HSCT or other types of autologous HSCT.

Data collection

The following data was collected from admission (day -2) to day 7 post HSCT:

- Demographical data;
- Daily creatinine (Cr);
- Daily weight and fluid balance; and
- Description of sepsis, overload and acute pulmonary oedema (APO).

Data analysis

Student t-tests or Fisher's exact tests were calculated to compare the two groups.

RESULTS

Table 1. Patients' demography

		RBWH (6L hyperhydration)	TTH (2L hydration)	p-value
Patient Number		N=54	N=34	
Age	Median	61	61	NS
	Range	41-71	48-69	
Gender	Female	N=23 (43%)	N=17 (50%)	NS
Baseline Creatinine	Median	76 (µmol/L)	73 (µmol/L)	NS
	Range	44-134 (µmol/L)	44-122 (µmol/L)	
Baseline Weight	Median	80 (kg)	77 (kg)	NS
	Range	53-122 (kg)	50-130 (kg)	

Table 2. Incidence of acute kidney dysfunction

Stage of Acute Kidney Impairment	RBWH (6L)	TTH (2L)	p-value
Stage 1: Cr=1.5-1.9 times or 0.3mg/dl (26.5micromol/L) increase	N=6 (11%)	N=2 (6%)	0.48
Stage 2/3	0	0	

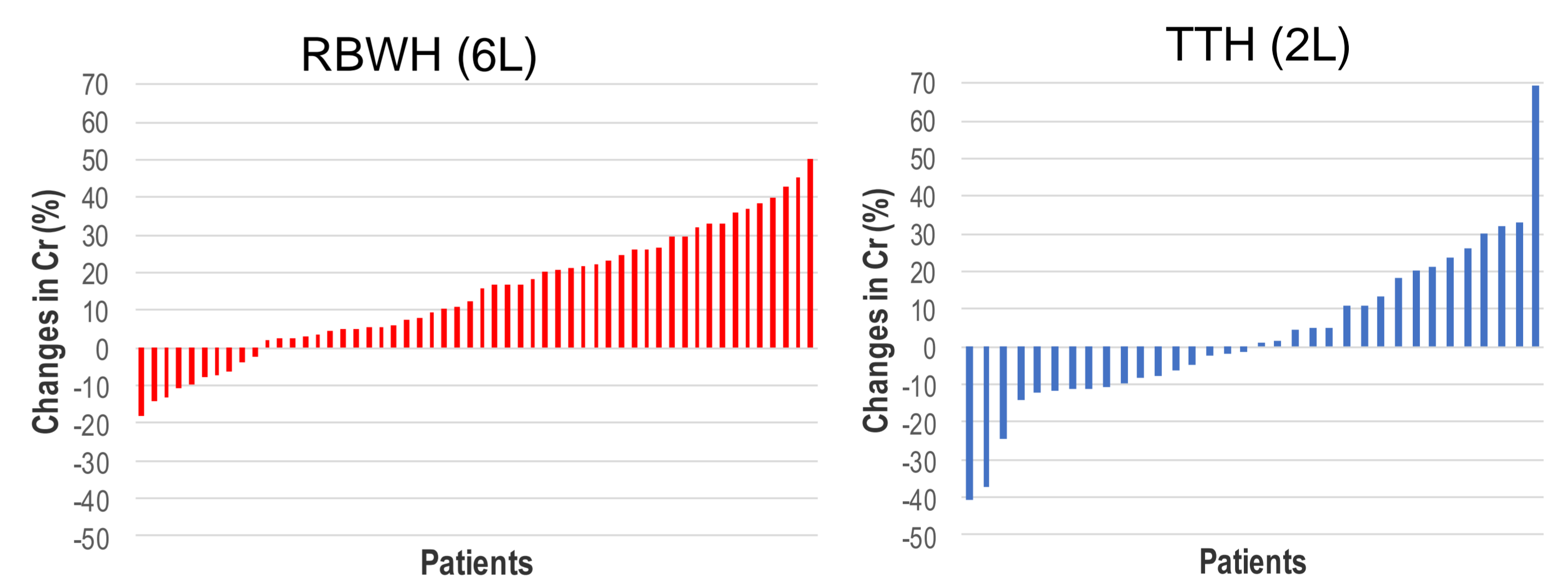


Figure 1. Each patient's Cr (Max)/ Cr (baseline) (%): Median changes =14% vs 0% (P<0.01)

Table 2..Incidence of acute kidney impairment

		RBWH (6L)	TH (2L)	p-value
Weight Gain	Median	1.75 kg	0.75 kg	NS
Weight gain \geq 3kg		N=13 (24%)	N=5 (15%)	NS
Clinical Overload		N=5 (9%)	N=2 (6%)	NS
Acute Pulmonary Oedema (APO)		Nil	Nil	
Other		2 patients required oxygen after hyperhydration	2 Patients had hypotension with sepsis	

Conclusions

In this study, hyperhydration (6L) with high dose melphalan did not show any benefits nor harm compared to standard hydration (2L).

Hyperhydration appears to be unnecessary with high dose melphalan. Further research is warranted.