

MELPHALAN INDUCED INTESTINAL MUCOSITIS IN HEMATOPOIETIC STEM CELL TRANSPLANT: RAPID RESPONSE TO SHORT COURSE OF ORAL BUDESONIDE

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Background: Approximately, 40% of patients receiving high dose melphalan (HDM) develop grade III or IV diarrhea (CTCAE 5.0) that promptly improves upon neutrophilic engraftment. Persistence of grade III-IV diarrhea beyond 24 hours post engraftment results in significant morbidity and prolongs hospitalization.

Methods: Histopathologic finding of colonic crypt inflammation in a patient with persistent diarrhea (first on table 1), led to use of short course of oral budesonide (BUD) resulting in rapid and sustained resolution of diarrhea. We here, document 20 such cases and discuss its role in reducing morbidity and duration of hospitalization. Persistent grade III-IV diarrhea 24 hours after neutrophil engraftment defined persistent diarrhea from melphalan. Infectious workup including stool examination for salmonella, shigella, rotavirus, cryptosporidium, clostridium difficile were performed.

Results: The median age of 20 patients was 66 (range, 44-74) years, (Females=10, Males=10). A total of 10 patients with multiple myeloma (MM) received melphalan 200 mg/m². A total of 4 MM patients 140 mg/m² (Age =3, renal failure =1) as did 6 patients with lymphoma/leukemia (table 1). Median time to neutrophilic engraftment following autologous stem cell transplant (ASCT) was day +12 (range, 9-13) days. Colonoscopy in one patient (first patient in table 1) confirmed patchy crypt apoptosis and crypt abscess formation. Standard supportive care including antidiarrheals offered no improvement. Oral budesonide (BUD) at 3-9 mg daily was introduced at median of 2 (range, -4 to 11) days after engraftment in 14 patients. Based on the established safety of post engraftment BUD, a total of 6 patients received BUD pre-engraftment. Median time for diarrhea improvement was 1-day (range, 1-7) days. The median duration of BUD administration was 2 (range, 1- 13) days. Median time to discharge from BUD initiation was 2 days (range 1-7). One patient was excluded from analysis as his stool tested positive for rotavirus; he too promptly responded to BUD. The median cumulative dose of BUD was 18 mg (range, 9-60).

Summary/Conclusions: We believe that reduction in gut inflammation by BUD improves melphalan induced intestinal mucositis. Neither pre-engraftment nor post-engraftment BUD produced any untoward effects from short courses of BUD. Oral BUD results in rapid resolution of lower GI toxicity of HDM, facilitates discharge and lowers cost of hospitalization.

Table-1

Patients Total	Diagnosis	Melphalan	Engraftment	Diarrhea	BUD		Discharge
		Dose	Day	Grade	Started Day		
						BUD	
65 F	MM	200/m2	+12	IV	+23	+30	42 mg
44 M	MM	200/m2	+12	III	+13	+14	9 mg
66 M	MM	200/m2	+12	III	+13	+14	9 mg
66 F	HL	140/m2 *	+10	III	+14	+16	18 mg
73 F	MM	140/m2	+12	IV	+14	+16	18 mg
60 F	DLBCL	140/m2*	+11	III	+14	+16	18mg
74 F	MM	140/m2	+12	IV	+13	+15	18 mg
66 F	DLBCL	140/m2 *	+10	III	+12	+14	18 mg
69 M	DLBCL	140/m2 *	+10	III	+17	+20	27 mg
66 M	MM	140/m2	+13	III	+13	+14	9 mg
66M	MM	200/M2	+13	III	+9	+14	30 mg
70M	DLBCL	140/m2*	+11	IV	+11	+21	60 mg
66 F	MM	200 mg/m2	+12	III	+12	+18	30 mg
57 M	MM	200 mg/m2	+12	IV	+11	+15	32 mg
64 M	MM	200 mg/m2	+12	III	+12	+16	18 mg
68 M	MM	140 mg/m2	+12	III	+17	+18	9 mg
52 M	MM	200mg/m2	+13	III	+9	+15	30 mg
62 F	MM	200mg/m2	+12	III	+7	+13	45mg
55 F	MM	200mg/m2	+12	III	+9	+12	27 mg
54 F	ALL	140mg/m2@	+18	III	+7	+19	18 mg

F= Female, M = Male, MM= Multiple Myeloma, HL= Hodgkin's Lymphoma, DLBCL= Diffuse Large B Cell Lymphoma. *BEAM conditioning component along with BCNU, Etoposide and Cytosine Arabinoside. @ Melphalan 140 mg with Fludarabine and post-transplant cyclophosphamide.