Amifostine feasibility and efficacy in autologous stem cell transplantation for multiple myeloma

We prospectively compared 2 groups of multiple myeloma patients who had undergone autologous stem cell transplantation. The first group (group 1, n=30) received amifostine (740 mg/mq) whereas the second group (group 2, n=36) did not receive this treatment, before melphalan infusion, as cyto-protectant for mucosal damage. Our results demonstrated that amifostine did not reduce the incidence or grading of mucositis, but it influenced the use of total parenteral nutrition and of opioid analgesic therapy.

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Amifostine (Ethiol) is a phosphorylated aminothiol that protects bone marrow progenitors and other normal tissues from the toxicities of ionising radiations and several antineoplastics like alkylating agents, cisplatin, anthracyclines and taxanes.[1] Several clinical trials[2-3] suggested that amifostine could reduce mucosal damage after high dose chemotherapy following autologous stem cell transplantation for haematological diseases without compromising anti-tumour response. On the basis of this theory we compared, prospectively and not randomly, 2 groups of multiple myeloma patients who had undergone autologous stem cell transplant from November 1998 to December 2000 who either had received (group 1, n=30) or had not received (group 2, n=36) amifostine (740 mg/mq) 30 minutes before melphalan infusion used as single agent (200 mg/mq) or as part of the conditioning regimen (120 mg/mq). In fact, 20/30 patients (66%) in group 1 and 22/36 patients (61%) in group 2 received Busulfan (12 mg/kg) in addition to Melphalan (120 mg/mq). Pre-transplant treatment in all patients consisted of 4 cycles of VAD (vincristine, doxorubicine, dexamethasone). All the patients in group 1 gave informed consent prior to amifostine administration. None of them had amifostine-induced side effects. The two groups were similar in terms of age and sex, type and stage of disease, time from diagnosis to transplant and number of peripheral blood $CD34^+$ stem cells infused (Table 1). All of them were in major response at time of transplant. All patients engrafted without any difference in the 2 groups: median time to neutrophil count >1000/mm^3 was observed at day +11 (10-15) in group 1 and at day +12 (11-14) in group 2; median time to platelet count >30.000/mm^3 was observed at day +13 (8-21) in group 1 and at day +13.5 (11-14) in group 2. Similar was also the inpatients time [22 days (19-29) and 21.5 days (20-28), respectively] and the transfusion support [2.5 (0-8) and 3.5 (0-6), respectively for red cell infusions and 3.5[1-6] and 3.5 (1-7), respectively for platelets infusions]. The incidence of fever requiring intravenous antibiotics was similar: 20/30 patients (66%) in the first group and 25/36 patients (69%) in the other one. Regarding to mucosal damage and gastrointestinal complications, as summarised in Table 2, the only statistically significant difference was related to the use of total parenteral nutrition and the use of opioid analgesic therapy. We did not find any difference in mucositis onset and grading, emesis, diarrhoea and the use of anti-emetic drugs. Previous papers[3-6] showed that amifostine significantly improved the mucosal side effects of high dose chemotherapy in haematological malignancies as well as in solid tumours. In our experience amifostine did not seem to reduce the incidence of mucositis but essentially the necessity of nutrition and analgesic support. It could depend on the dose we used and also on the association in most of our patients with busulfan. Anyway, nevertheless the same incidence of mucositis in both groups, the reduction in supportive care costs should also be considered. These results clearly need larger randomised trials to confirm the efficacy of amifostine.

Table 1.

	GROUP 1	*GROUP 2*
PATIENTS	30	36
MALE/FEMALE	12/18	20/16
AGE	54 (48-65)	54 (46-66)
CD34+ * 106/kg	3.2 (1.7-9.8)	2.9 (1.9-4.1)
MONOCLONAL PROTEIN		
IgG/k	4	17
IgG/λ	12	10
IgA/λ	4	4
BJ	10	5
STAGE		
I	2	8
II	1	2
III	27	26
CONDITIONING REGIMEN		
Busulfan+Melphalan	20/30 (66%)	22/36 (61%)
Melphalan	10/30 (34%)	14/36 (39%)
MONTHS TO TRANSPLANT	11 (7-16)	11 (6-18)

Table 2.

	GROUP 1	*GROUP 2*
MUCOSITIS (TOTAL)	23/30 (76%)	23/36 (63%)
MUCOSITIS GRADE III-IV	6/30 (20%)	9/36 (25%)
EMESIS	10/30 (33.3%)	11/36 (30.5%)
DIARRHOEA	10/30 (33.3%)	14/36 (38.8%)
ORAL HSV	14/30 (46.6%)	14/36 (38%)
ORAL CANDIDA	0/30	1/36 (2.7%)
ANALGESIC OPIOID THERAPY*	7/30 (23%)	15/36 (41.6%)
Median Day Duration (Range)	6 (3-7)	8 (4-10)
PARENTAL NUTRITION*	7/30 (23%)	15/36 (41.6%)
ANTI-EMESIS DRUGS	8/30 (26.6%)	10/36 (27%)

** P value= 0.0217*

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