Risk factors for digestive tract mucositis in myeloablative and non-myeloablative/reduced-intensity conditionings with busulfan prior to hematopoietic cell transplantation

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Introduction:

Busulfan is a major component of chemotherapy conditioning in hematopoietic cell transplantation (HCT). This alkylating agent is highly toxic at myeloablative doses, exposing HCT patients to risks of mortality. Non-myeloablative (NMA) and reduced-intensity conditioning (RIC) using busulfan have shown impaired toxicity. However, the toxicity of NMA/RIC in the digestive tract is poorly described.

Aim:

This study aimed to analyze whether myeloablative dose of busulfan is a risk factor for mucositis in the oral cavity (OM), oropharynx/esophagus, and gastrointestinal tract.

Pacientes adm Methods:

This is a retrospective study of consecutive adult HCT patients who attended the Hospital Israelita Albert Einstein (HIAE), Brazil, between 2012 and 2016 (n=100). We selected medical records from patients who underwent autologous and allogeneic HCT using intravenous busulfan in conditioning regimens prior to HCT. Exclusion criteria were patients younger than 18 years old; conditioning regimen without busulfan; medical records without adequate description of toxicity, especially mucositis; patients who refused to participate from the oral care protocol before, during, and after transplantation periods; and patients who died during the HCT.

This study was previously approved by our institution's ethical committee (Process number 2902-16).

Results:

OM severity (p=0.009) and time duration of mucositis in oropharynx/esophagus (p=0.022) were frequently higher in MAC than NMA/RIC. A myeloablative dose of busulfan was a risk factor for OM grade ≥ 2 (OR=4.8, p=0.002) and for mucositis in oropharynx/esophagus ≥ 5 days (OR = 2.64, p=0.035). A longer duration of mucositis in the oropharynx/esophagus was also associated with an increase in the prescription of opioids (OR=7.10, p<0.001). Overall survival (OS) in MAC was significantly higher than that in NMA/RIC (p=0.017).

Table 1 - Association of mucositis in the digestive tract with variables related to patient co-morbidities, disease status, conditioning regimen, characteristics of transplantation, GVHD prophylaxis, and opioids and total parenteral nutrition prescription.

	Signs and symptoms of mucositis		
	Oral mucositis $\geq$ grade 2	Oral mucositis ≥ 10 days	Mucositis in oropharynx/esophagus ≥ 5 days
Age ≥ 50 y	0.310	0.542	0.107
Charlson index ≥ 3	0.129	0.143	0.086
2 nd , 3 rd , 4 th remissions or active disease	0.355	0.016	0.283
Matched-unrelated donor	0.148	0.257	0.482
Busulfan + ATG	0.685	0.475	0.664
Busulfan plus Cy, and Mel	0.302	0.388	0.095
Myelosuppression	0.001	0.388	0.032
GVHD prophylaxis with methotrexate	0.465	0.435	0.761
Neutropenia ≥ 14 days	0.914	0.973	0.199
Opioids prescription	0.054	0.113	<0.001
Total parenteral nutrition prescription	0.794	0.081	0.811

Conclusion:

In conclusion, myelosuppression in regimens with busulfan are predisposed to a high risk of severe OM and to prolonged mucositis in the oropharynx/esophagus. OS was higher in the MAC group compared with the NMA/RIC group, but mucositis during transplantation was not associated with OS.

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