Changes of salivary antioxidant enzymes during hematopoietic cell transplantation: implications to oral mucositis and xerostomia

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Introduction: The aim of this study was to investigate the levels of salivary antioxidant enzymes during hematopoietic cell transplantation (HCT), and their association with oral toxicity.

Methods: Stimulated saliva of patients who underwent autologous and allogeneic HCT (n=72) was collected at baseline (T0, before the HCT), neutropenia (T1), and after marrow engraftment (T2). Activity of superoxide dismutase (SOD) and levels of catalase (CAT) and glutathione reductase (GR) in the saliva were also determined. Association tests of these enzymes with oral mucositis and xerostomia were performed.

Characteristics of the patients

	Total (n=72)
Sex – n (%)	
Male	38 (52.8)
Female	34 (47.2)
Age – mean (±SD)	46.0±17.2
Primary disease – n (%)	
Hodgkin lymphoma	4 (5.6)
Non-Hodgkin lymphoma	16 (22.2)
ALL	5 (6.9)
CLL	1 (1.4)
AML	7 (9.7)
CML	4 (5.6)
Multiple myeloma	12 (16.7)
Myelofibrosis	3 (4.2)
Myelodysplastic syndrome	6 (8.3)
Others	14 (19.4)

Characteristics of the transplantation.

	Total (n=72)
Type of transplantation	
Autologous	35 (48.6)
Allogeneic	23 (31.9)
Haploidentical	14 (19.4)
Conditioning – n (%)	
Bu/Flu (tiotepa, ATG or TMI)	19 (26.4)
Bu/Cy	4 (5.6)
Bu/Mel	1 (1.4)
Mel/Flu/TBI	8 (11.1)
Mel	12 (16.7)
Cy/Eto/Mel	2 (2.8)
BEAM/R-BEAM	15 (20.8)
Cy/Flu/TBI	6 (8.3)
Cy/methylprednisolone/ATG	3 (4.2)
Flu/TBI	2 (2.8)

GVHD prophylaxis	
Tacrolimus/MTX with or without ATG	17 (23.6)
Tacrolimus/MMF/CY	10 (13.9)
MMF/CSA with or without ATG	5 (6.9)
MTX/CSA	5 (6.9)
Time of neutropenia – mean (±SD)	11.6±6.0
Body weight loss (%) – mean (±SD)	4.4 ± 3.0

Characteristics of the oral toxicity

Oral mucositis	Total (n=72)
Time duration (in days) – mean±SD	23.4±4.8
Maximum degree – n (%)	
0	9 (12.5)
1	31 (43.0)
2	24 (33.0)
3	7 (9.7)
4	1 (1.3)
Xerostomia	
Frequency	25 (34.7)
Time duration (in days) – median (range)	0 (0-21)

Results:

Logistic regression analysis with oral mucositis as dependent variable and antioxidative enzymes (at T1)* as independent variables.

Duration of oral mucositis	OR	CI 95%	P value
First model			
Catalase	1.92	0.89-4.11	0.095
Glutathione reductase	0.65	0.30-1.40	0.274
Superoxide dismutase	0.38	0.17-0.82	0.001
Second model			
Superoxide dismutase	0.45	0.21-0.93	0.031

Logistic regression analysis with xerostomia as dependent variable and antioxidative enzymes (at T1)* as independent variables.

Xerostomia	OR	CI 95%	P value
First model			
Catalase	0.47	0.21-1.05	0.066
Glutathione reductase	2.42	1.07-5.52	0.034
Superoxide dismutase	2.91	1.30-6.51	0.009
Second model			
Glutathione reductase	2.30	1.03-5.15	0.042
Superoxide dismutase	2.55	1.17-5.52	0.017

Logistic regression analysis with oral mucositis as dependent variable and antioxidative enzymes (at T0)* as independent variables.

Xerostomia	OR	CI 95%	P value
First model			
Catalase	0.84	0.40-1.75	0.650
Glutathione reductase	1.91	0.76-4.78	0.166
Superoxide dismutase	2.48	1.18-5.25	0.017
Second model			
Superoxide dismutase	2.71	1.32-5.55	0.006

Logistic regression analysis with xerostomia as dependent variable and antioxidative enzymes (at T2)* as independent variables.

Xerostomia	OR	CI 95%	P value
First model			
Catalase	0.43	0.17-1.05	0.064
Glutathione reductase	2.79	0.98-7.93	0.053
Superoxide dismutase	4.84	1.93-12.10	<0.001
Second model			
Superoxide dismutase	3.39	1.50-7.65	0.003

Conclusion: Expression patterns of salivary SOD, CAT, and GR during HCT periods are different, with a trend to SOD activity increase and CAT and GR reduction. SOD activity increase is related to a long duration of oral mucositis and xerostomia, suggesting that some protective antioxidant activity persists even in conditions of intense oral toxicity.

Ackwoledgments: We thank the São Paulo Research Foundation (FAPESP, Proc. # 2016/03650-4) and AmigoH for their financial support.

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