Salivary cytokines expression during hematopoietic cell transplantation: is there association with oral toxicity?

Fernanda de Paula Eduardo, Leticia Mello Bezinelli, Mariana Henriques Ferreira, Marcella Gobbi, Flavia C. P. Rosin, Nelson Hamerschlak, Luciana Corrêa

The aim of this study is to determine the expression of salivary pro-inflammatory cytokines during the hematopoietic cell transplantation (HCT), and to verify whether there is an association between these cytokines with oral toxicity

Methods: We collected stimulated saliva from autologous and allogeneic HCT patients (n=72) at baseline (T0, before the HCT conditioning), during the neutropenia (T1), and after the marrow engraftment (T2). Salivary levels of IL-6, IL-1β, and TNF-α were quantified by ELISA assay. Data about conditioning regimen, time duration of neutropenia, oral mucositis, xerostomia, and body weight loss was collected.

Results: The levels of salivary IL-6, IL-1β, and TNF-α increased significantly at T1 compared to T0, with significant differences for IL-6 (p=0.039) and TNF-α (p<0.001). In an adjusted regression model analyzing the three cytokines, only high levels of IL-1β were significantly associated with a long duration of oral mucositis (OR=0.44, p=0.017) and xerostomia (OR=0.49, p=0.038). The highest levels of IL-1β at T1 were found in autologous HCT (OR=0.35, p=0.002), mainly after melphalan conditioning (OR=2.00, p=0.040). In addition, a significant association was found between body weight loss during the transplantation and high levels of salivary TNF-α at T0 (OR=2.35, p=0.010).

Conclusion: There is an increase in salivary pro-inflammatory cytokines at neutropenia. Among the analyzed cytokines, only salivary IL-1β exhibited a discrete association with oral mucositis and xerostomia. Salivary TNF-α at baseline was a predictive factor for body weight loss, suggesting that the saliva could signalize the systemic metabolic alterations caused by TNF-α during the HCT.

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