In vitro cytoprotective effects of melatonin on zoledronic acid-treated human mesenchymal stem cells.

M.R. Pecci LLoret¹, M.P. Pecci LLoret¹, J. Guerrero Gironés¹, M. Vallés-Bergada¹,², M. González García¹,², J.F. Martínez-Lage¹, J.E. Rodríguez-Lozano¹,², D. García-Bernalz, J.E. Millán-Riveroz, P. Romecín-Duránz, M.A. Ros-Rocaz, M.C. Algueróz, R. Oñate-Sánchez², M. Vera-Sánchez², J.M. Moraleda²

¹ Faculty of Medicine. University of Murcia.
² Hematopoietic Transplant and Cellular Therapy Unit, Hematology Department, Virgen de la Arrixaca Clinical University Hospital, IMIB, University of Murcia, Spain.

INTRODUCTION AND AIM: Bisphosphonate-related osteonecrosis of the jaw (BRONJ) in patients receiving zoledronic acid (ZA) is a common complication after tooth extraction [1]. Moreover, melatonin has been proposed as a therapeutic drug for the oral cavity due to its antioxidant and anti-inflammatory properties [2]. The aim of this in vitro study was to evaluate the cytoprotective effects of melatonin on ZA-treated human mesenchymal stem cells from periodontal ligament (PDLSCs) and bone marrow (BMMSCs).

METHODS: PDLSCs and BMMSCs were cultured in presence of ZA, melatonin or ZA in addition to melatonin for 72h. Proliferation of cells was assessed by MTT whereas their mesenchymal phenotype was analyzed by flow cytometry.

RESULTS: Dose-response MTT experiments showed that PDLSCs presented lower ZA resistance than BMMSCs, as well as a different behavior to the simultaneous treatment of ZA and melatonin. Using PDLSCs, high doses of melatonin (≥300 μM) significantly increased PDLSCs proliferation up to 5 μM ZA, whereas a lower concentration were enough to increase BMMSCs proliferation in presence of ZA doses >10 μM. Furthermore, PDLSCs displayed a slight CD90 and CD105 downregulation and CD73 upregulation in response to ZA, which was more pronounced in response to melatonin. Moreover, ZA or ZA plus low doses of melatonin induced a decrease of expression of CD90, CD105 and CD73 on BMMSCs, while a higher concentration recovered CD73 levels.

CONCLUSION: These results suggest that melatonin has a cytoprotective effect of ZA-treated human PDLSCs and BMMSCs. Thus, cytoprotective agents as melatonin could be used as a preventive medication to avoid undesirable complications of bisphosphonate therapy such as BRONJ.

References