CYCLOSPORINE EFFECTS ON HYPEROXIA-INDUCED LUNG DAMAGE IN NEONATAL RATS

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Cyclosporine is one of the most frequently used drugs for immunosuppression in organ transplantation and it may be excreted into breast milk. Controversial effects have been reported on the lung after cyclosporine treatment in experimental animals. Some studies reported in cell cultures bronchial epithelial-mesenchymal transition, with increased expression of fibronectin, collagen and vimentin, and, in adult rats, inflammatory infiltration of the lung, bronchiolar associated lymphoid tissue hyperplasia, perivasculitis, reduction in mucus production and decrease in mucociliary transport velocity. Conversely, some authors observed that in adult mice and rats, pretreatment or simultaneous treatment with cyclosporine reduce hyperoxia-induced histopathological and functional changes, such as neutrophil infiltration, capillary congestion, edema, hyaline membrane formation and reduction in lung compliance. There are no data instead about the possible effects of cyclosporine exposure in hyperoxia-induced pulmonary changes in the newborn. Thus, in the present study, we evaluated the effect of cyclosporine in young rats after 60% hyperoxia exposure in the first two weeks of postnatal life, i.e., an experimental model of bronchopulmonary dysplasia (BPD). Experimental categories included I: room air for the first 5 postnatal weeks with daily injection of saline from postnatal day (PN) 15 to PN35; II: room air with daily injection of 15 mg/kg ciclosporin from PN15 to PN35; III: 60% oxygen from PN0 to PN14 and then daily injection of saline, i.p., during the following three weeks; IV: 60% oxygen from PN0 to PN14 followed by daily injection of ciclosporin from PN15 to PN35. Analysis of alveolarization (number of secondary alveolar crests, mean alveolar size) was morphometrically performed, together with morphological study of the connective components with azan-Mallory and Weigert-van Gieson stainings. Hyperoxia resulted in significant reduction in secondary crests, and significant increase in the mean alveolar size and thickness of the alveolar septa. In normoxia, cyclosporine exposure caused a significant reduction in the number of secondary crests, although without significant change in mean alveolar size, and a slight increase in the connective components of the alveolar septa. Conversely, cyclosporine treatment did not significantly modify the hyperoxia-induced changes in the number of secondary crests and mean alveolar size, and in the connective components. In conclusion, our data show that cyclosporin does not significantly modify alveolarization parameters in an experimental model of BPD, although in normoxia it may cause reduction in the number of secondary alveolar crest and slight increase in the connective components. Further analyses will be necessary to better evaluate possible lung effects of cyclosporine during breastfeeding, i.e., in the presence of lower drug levels than in the present preliminary study.