Effect of Phenytoin and Cyclosporine on connective tissue enzymes in gingival fibroblasts of adult and children

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Abstract

Background: Gingival overgrowth (GO) is a common side effect of antiepileptic, immunosuppressive and calcium channel blocker drugs. Cyclosporine and phenytoin are amongst the most widely used drugs associated with GO. Gingival fibroblasts seem to have a significant role in the production of certain enzymes after administration of the drugs contributing to GO. Previous studies have shown a higher prevalence of GO in children and adolescents. The aim of this study was to compare normal human gingival fibroblasts with those exposed to Cyclosporine or phenytoin in measuring the production levels of certain enzymes that could have a possible role in GO.

Materials and Methods: samples were obtained from the gingival biopsies of seven adult and seven pediatric patients and were cultured into plates. With the growth of fibroblast cells, they were treated with or without either Cyclosporine or phenytoin. Reverse transcriptase-polymerase chain reaction (RT-PCR) was used to determine the expressed levels of R-EGF, Cathepsin B, L, Lysyl oxidase, COL1, TGF β1, MMP-1,2 and TIMP1.

Results: According to RT-PCR analyses, the expressed levels of R-EGF, Cathepsin B, L, Lysyl oxidase, COL1, TGF β1, MMP-1,2 and TIMP1 were affected by Cyclosporine and phenytoin. TGF-β1, TIMP, Cathepsin B and EGF showed comparable values in the adult and pediatric groups. TGF-β1 was the only mediator produced by both drugs in adults and children. Phenytoin lead to TIMP production and cyclosporine induced cathepsin B gene production at both age groups.

Conclusions: Different expressed levels of enzymes after treatment of the gingival fibroblasts of adults and pediatrics with phenytoin or Cyclosporine could be the reason for the higher severity of GO in children. More studies need to be performed on the pathogenesis of GO at different age groups.

Key words: Cyclosporine, phenytoin, fibroblast