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Are myofibroblasts associated with gingival metabolic changes induced by cyclosporin, phenytoin and nifedipine?

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Drug-induced gingival overgrowth (GO) is a fibrotic condition mainly associated with cyclosporin, phenytoin and nifedipine. The gingival enlargement may be caused by a decrease in tissue breakdown and/or an increase in the synthesis of extracellular matrix (ECM) components. Several fibrotic pathologic conditions have been associated with myofibroblasts. The purpose of this experimental study was to analyze a possible correlation between myofibroblast and gene expression levels of collagen I, metalloproteinase (MMP) 1 and 2 during phenytoin, cyclosporine or nifedipine therapy. Gingival samples from the right maxillary canine area were obtained from twelve male monkeys (Sapajus ssp). The mesial part of each sample was assessed by reverse transcriptase-polymerase chain reaction (RT-PCR) for MMP1, MMP2 and collagen I gene expressions, while the distal one was histologically processed for α-SMA immunostaining. One week after the first biopsy, the animals were assigned to three groups that received daily oral doses of cyclosporine, phenytoin or nifedipine during 120 days. Further gingival samples were obtained on 52nd and 120th day of treatment from two animals of each group, at the opposite side of the first biopsy. Results showed that here was a general trend to lower levels of MMP-1 gene expression on 52nd day and increased levels on 120th day. Phenytoin led to increased levels of MMP-2 and collagen I gene expression on 120th day, whereas the opposite was observed in the nifedipine group.  $\alpha$ -SMA immunoreacion was negative in control and experimental groups. It may be concluded that altered MMP1, MMP2 and collagen gene expressions induced by cyclosporin, nifedipine and phenytoin are not associated with myofibroblast transdifferentiation in gingival samples of capuchin monkeys.

Descriptors: Gingival Overgrowth; Therapeutics; Cyclosporine; Phenytoin; Nifedipine.