Protein Expression Profiles of Collagen Turn-Over in Gingival Overgrowth Induced by Immunosuppressive Agents after Liver Transplantation

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Abstract

Background: In recent years, liver transplantation has become an accepted treatment for end-stage liver disease. Tacrolimus (FK506-TAC) is a potent immunosuppressive agent used as an alternative to Cyclosporine A (CsA) to prevent graft rejection and treat autoimmune diseases. Although TAC may cause unwanted systemic side effects, such as nephrotoxicity and neurotoxicity. Unlike CsA, it does not appear to induce marked gingival over-growth (GO), which is one of the undesired side effects associated with CsA therapy. Objective: To compare the effect of CsA and TAC on the collagen turn over pathway at the molecular level, by investigating the degree of expression of Transforming Growth Factor (TGF-β1), Platelet Derived Growth Factor (PDGF-B), Matrix Metalloproteinase-2 (MMP-2) and Matrix Metalloproteinase-9 (MMP-9) in human gingival connective tissue of patients receiving immunosuppressive agents after liver transplantation.

Materials and Methods: Gingival tissue samples were obtained from patients undergoing therapy with TAC (n=6), CsA (n=6) as well as control tissues from systemically healthy control (n=6). Formalin fixed paraffin embedded tissue sections of all the studied cases were immuno-stained by using labeled streptavidin-biotin (DAB) technique, using monoclonal antibodies against TGF-β1, PDGF-B, (MMP-2) and (MMP-9). Sections were assessed; positive reading appeared as membrane and cytoplasmic brownish staining for (MMP-2), (MMP-9), TGF-β1 and PDGF-B.

Results: comparison of the type of expression (focal or diffuse) among the studied groups, showed statistically significant diffuse expression of TGF-β1, PDGF-B, (MMP-2) and (MMP-9) in CsA group when compared with less focal expression of the same cytokines in TAC group (P value ≤0.05). Also, statistically significant focal expression of the same cytokines was analyzed in TAC group when compared to control (P value ≤0.05).

Conclusions: We could conclude that the molecular mechanisms responsible for CsA-induced GO may involve significant up regulation of essential polypeptides and growth factors (TGF-β1, PDGF-B, MMP-2 and MMP-9) when compared to TAC effect, illustrating its potential effect targeting collagen homeostasis, and suggesting that the elimination of CsA and its replacement by TAC could be an important aspects on the reduction of GO problem, via improving the oral health in patients receiving liver transplantation.

Keywords: gingival overgrowth, immunosuppressive agents, liver transplantation.