Biochemical, Immunological and Histochemical Study of Cyclosporin-A Induced Gingival Enlargement in Kidney Transplanted Patients

A thesis
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Abstract

Background

Proliferative types of gingival lesions have been found to be associated with the administration of several drugs, namely phenytoin, nifedipine and cyclosporin. Cyclosporin is a potent immunosuppressive agent that used in organ transplantation to prevent allograft rejection. One of major side effects of cyclosporin is gingival enlargement with incidence of approximately 30% in renal transplant patients. The etiology of cyclosporin-induced gingival enlargement is still uncertain till now.

Aim of the Study

The present study was designed to find out any possible correlation between the severity of gingival enlargement with age, sex, daily dosage, and duration of cyclosporin intake. Also to investigate changes in serum and saliva levels of essential elements, enzymes, immunoglobulins and serum C-reactive protein, beside study the alkaline phosphatase enzyme activity of gingival tissue in cyclosporin-induced gingival enlargement, non-enlarged gingiva received cyclosporin, gingivitis patients , and normal healthy individuals.

Methods

The sample population comprised of 120 males and females aged from 17-66 years. This sample was divided into 4 groups, each one contain 30 subjects:

- Group 1: cyclosporin-induced gingival enlargement.
- Group 2: non-enlarged gingiva under cyclosporin treatment.

- Group 3: plaque-associated gingivitis.
- Group 4: normal healthy individual.

Serum and saliva samples were collected and then analyzed for estimation essential elements: Zinc (Zn), Copper (Cu), Magnesium (Mg), Calcium (Ca) and Inorganic phosphate (P), by using flame atomic absorption spectrophotometry (AAS). The levels of alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) were analyzed using colorimetric analysis. Immunoglobulins levels in serum and saliva were determined by using single radial immunodiffusion technique. Serum C-reactive protein was analyzed using rapid Latex precipitation technique. Histopathological study with histochemical analysis of the activity of alkaline phosphates enzyme in gingival tissue were done by taking a gingival biopsy.

Results and Discussion

In the present results , the highest percentage of CsA-induced gingival enlargement was seen in males of young age groups. Age and duration of CsA intake had no significant correlation with the severity of gingival enlargement. Daily dosage of CsA therapy had a significant influence on the severity of enlarged gingiva.

The serum and salivary elements (Zn, Mg and P) were significantly reduced ($P<0.05$) in gingival enlargement group (G1) in comparison to non-enlarged group (G2), gingivitis group (G3) and normal group (G4), where as Cu, Ca and Cu/Zn ratio were significantly increased.

Calcium and inorganic phosphate are the only essential elements that showed a significant effect in relation to the duration of CsA intake in G1. Only calcium showed a significant influence by sex distribution.

Salivary Zn and Cu levels are the only trace elements that presented a statistical significant effect with age.

The serum and salivary ALP and LDH levels exhibited a highly significant elevation ($P<0.0001$) in G1 if compared to G2, G3 and G4. Serum and saliva ALP and LDH among patients with enlarged gingiva declared a statistically significant effect on sex distribution and duration of drug intake.

An obvious reduction of serum and salivary levels of immunoglobulins (IgA, IgG and IgM) in G1 compared to other groups.

No significant effect ($P>0.05$) had been found in immunoglobulin levels on the distribution of sex, age and duration of CsA intake in G1.

Patients with CsA- induced gingival enlargement presented the highest percentage of positive results of C-RP.

Histochemical analysis of ALP enzyme activity showed intense stain for ALP activity in all epithelial layers of enlarged gingiva .The highest optical density was recorded in CsA-induced gingival enlargement in basal and spinous layers.

Conclusion:

From these results it can be concluded that a number of markers show promise as sensitive measures of disease prognosis and the effectiveness of therapy. At this time , essential elements, enzymes, immunoglobulins, and C-reactive protein, can be used as a monitor for healthy and patients with different periodontal disease. Saliva may be used alone or as a supplementary to serum tests for confirmation of any finding. Furthermore, analysis of saliva may offers an efforts-effective approach to assessment in controlling progression of periodontal disease in large populations.