

Role of Advanced Glycation End Products and Antioxidants Vitamins A, C and E in the Development of Periapical Cyst

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Received: May 2020

Accepted: May 2020

ABSTRACT

Background: Oxidative stress has a main role in the pathogenesis of apical periodontitis (AP). Its non-enzymatic reaction mechanism is based on advanced glycation end product, antioxidants vitamins and trace elements. Objectives: To determine the role of advanced glycation end products and antioxidants vitamins A, C and E in the development of periapical cyst. **Methods:** Study was included fifty (50) consented patients with mean age 20-40 years visited dental outdoors. The criteria of recruiting patients was based on the presence of periapical granulomas with a Clinical Attachment Loss of > 3mm, depth is > 5mm with bleeding and radiolucencies. Whereas, twenty (20) healthy subjects with no history of any disease were taken as control. Blood sample was drawn from patients for the estimation of levels of serum AGEs and by standard ELISA kits and vitamin A, C and E were analyzed by measuring the absorbance by spectrophotometer (540nm). **Results:** It is observed that the levels of AGEs were significantly increased in patients in comparison to their controls (p-value 0.055). On the other hand, the levels of vitamin A (p-value \leq 0.044), vitamin C (p-values \leq 0.043) and vitamin E (p-values \leq 0.043) were significantly decreased in patients as compared to their counterparts. **Conclusion:** Study is concluded that besides other factors, advanced glycation end product and nutritional deficiency of vitamin A, C and D also have a role in progression of apical lesion. However further study is needed on large number of patients to reach a better conclusion.

Keywords: Apical lesion, advanced glycation end product, vitamins.

INTRODUCTION

Apical lesions (AL) consist of apical granulation tissue which lately form radicular cyst, lined with squamous epithelium.^[1] Oxidative stress has a main role in the pathogenesis of AP and radicular cyst. The mechanism of antioxidants is based on both non-enzymatic and enzymatic reactions including the role of enzyme superoxide dismutase, catalase etc. The non-enzymatic antioxidants may include advanced glycation end product, uric acid, coenzyme Q10 of substances taken from nutrients like fat and water soluble vitamins (Vitamin A, C and D and trace elements (folic acid and cysteine)).^[2,3]

In endodontic infection, toll like receptors are attached on the surface of bacterial cell stimulate the process of phagocytosis, production of reactive oxygen species (ROS), activation of cellular and humoral responses and synthesis of cytokines and matrix metallo proteinases which act as inflammatory mediators.^[4,5] Though the presence of ROS shows the defensive mechanism of body, still there is oxidative imbalance which may help in the synthesis and progression of AL, mainly due to damage at molecular level and signaling of redox system.^[6]

The antioxidant activities of vitamin C show its role in scavenging free radicals synthesis during inflammation. It detoxifies superoxide and perhydroxy radicals.^[7] It reduces ROS and helps protection against infection. Its deficiency is usually observed in old people. The subjects who are deficient to vitamin C are prone to develop periodontal disease.^[8]

Vitamin E as an antioxidant inhibits the synthesis of ROS during oxidation of fat. It is important for intensification of membrane of cell due to oxidative stress inflicted by lipid peroxides and may delay the occurrence of disease. Besides, vitamin E may have useful effect on periodontitis, reducing the inflammation occur locally and avoiding the loss of alveolar bone.^[9] It is found that vitamin A may also act as a pro-oxidant in giving reactive hydroxyl radical.^[10] It takes part in the synthesis of glycoproteins and supporting the strength of epithelial tissues in cavities.^[11]

Advanced glycation end products (AGE) is involved in diverse cellular mechanisms. Its formation is a significant abnormality that accompanies inflammation and other problems. The interaction of AGEs with the components of vessel wall increases the permeability of vessels and the production of ROS resulting enhanced expression of endothelial leukocytes adhesion, stimulate the process of inflammation and vascular perturbation in disease or modifying endothelial architecture.^[12,13]

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This study was therefore designed to observe the role of advanced glycation end products and antioxidants vitamins A,C and D in periapical or radicular.

MATERIALS AND METHODS

This cross-sectional comparative study was approved by Institutional Review Board (IRB). This study recruited fifty (50) patients (34 males and 16 females) with mean age 20-40 years, visited Dental out door after obtaining informed consent and recording of demographic information on predesigned proforma. The criteria of recruiting patients was based on the presence of periapical granulomas with a Clinical Attachment Loss (CAL)of > 3mm, Depth is > 5mm with bleeding and with a radiographic prove of periapical well-defined radiolucencies. Patients with history of currently taking antibiotic or any systemic disease (Diabetes, hypertension, cardiovascular, gastrointestinal disorders and liver disease), pregnancy or Lactation and smokers were excluded from the study. Twenty (20) healthy subjects (12 males and 8 females) with no absence of bleeding on probing, absence of CAL (Clinical attachment loss), absence of any periodontal disease and with probing depth of less than 3mm were taken as control.

All blood samples were drawn under aseptic techniques, serum was obtained by centrifugation at 3000 rpm, labelled and aliquoted at -20 till further estimation of levels of serum AGEs by standard ELISA kits (made in USA). Whereas, vitamin A, C and E were analyzed and absorbance were measured by spectrophotometer (540nm). A standard graph was constructed using an electronic calculator.

Statistical Analysis:

Data was entered and analyzed by SPSS 20. Study variables were given as mean± SD. Variables of patients and controls were compared by student't' test. P-value ≤ 0.5 was significant.

Table 1: Comparison of levels of AGEs and of vitamin A, C and D in patients and their controls

Variables	Control(n=20)	Subject (n=50)	P - value
AGEs	1.66±0.10	2.31±0.55	0.055
Vit A	567±10.87	511±23.98	0.044
Vit C	0.44±0.05	0.39±0.39	0.043
Vit E	0.23±0.01	0.22±0.031	0.051

AGEs: advanced glycation end products; Vit A: vitamin A; Vit C: vitamin C; Vit E: vitamin E

RESULTS

Vitamin A levels measured in both healthy controls (567±10.87) and patients with radicular cyst (511±23.98) revealed a statistically significant decline in its concentration in diseased subjects when compared to healthy group (p-value ≤ 0.044). Similarly, the serum levels of vitamin C and vitamin E were also found to be decreased in patients having

radicular cyst, showing significant p-values ≤ 0.043 and 0.051 respectively. It is also observed that the levels of AGEs were significantly increased in patients in comparison to their controls [Table 1].

DISCUSSION

Antioxidant and health-endorse characteristics are related with anti-inflammatory, antihypertensive and immunomodulatory functions and preventing the body from oxidative stress. The antioxidant role of substances present in body and nutritional components may have an ability to scavenge ROS and prevent cell damage.^[14]

According to our study the levels of AGEs were significantly increased in patients in comparison to their controls. A study made sections of apical lesion and found that the infiltration of receptor of advanced glycation end product or RAGE express by the nitric oxide synthase forming cell, suggest that AGEs may have a role in injury of tissue and related periapical periodontitis.^[15] Another study reported that both AGE and its receptor stimulation the activation of cell and cause tissue injury.^[16] A later study reported that chronic AP patients had increased levels of oxidants, and reduced potential of antioxidant compared to normal subjects and endodontic therapy may restore the oxidative balance.^[17] It is observed that lymphocytes macrophages and endothelial cells of periapical lesion expressed increased receptor of advanced glycation end product.^[18]

We observed reduced levels of vitamin A, C and E in patients in comparison to their controls. Our study showed an indirect link of vitamin E with harshness of periodontitis in patients with decreased level of vitamin E, suggesting that for the health of periodontal side there is a need of proper dose of vitamin E.^[9,19] Another study reported that both vitamin C and vitamin E as an oxidant my control the process of auto-oxidation by interfering the propagation of free form of radicals or by blocking the production of free radicals and decrease oxidative stress and promote immunity.^[7]

Some properties of fat soluble vitamin E and other vitamin also make it less effective as an antioxidant such as its limited movement in cell membranes and hydrophobic nature as ROS are mainly released in hydrophilic environment.^[20] Bose et al., 2012 reported extremely low A, E and C levels in diseased individuals with oral premalignant lesions as well as poor antioxidant activity in contrast to controls.^[21] Dental caries which is one of the major chemical trauma to the odontogenic epithelium and in the long run is a cause of dental cyst formation has also been assessed in relation to salivary vitamins E and C, demonstrating decreased vitamin E and C levels in patients with dental caries showing their powerful antioxidant activity.^[22] Our calculation of serum vitamin A levels revealed some difference in values between the cases and controls thus showing decline

in vitamin A concentration in serum of diseased subjects when compared to healthy group. Our results are supported by a case control trial by Hamidreza et al., 2014 who compared salivary vitamin A, C and E levels of oral lichen planus (benign premalignant oral pathology) versus healthy controls revealing a significant drop in antioxidant vitamins of diseased participants.^[23]

CONCLUSION

It is concluded that besides other factors, advanced glycation end product and nutritional deficiency of vitamin A, C and D also have a role in progression of apical lesion. However further studies are needed on large number of patients to reach a better conclusion.

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How to cite this article: Malik TA, Javed S, Tauseef A, Sohail H, Akram T, Jabeen F. Role of Advanced Glycation End Products and Antioxidants Vitamins A, C and E in the Development of Periapical Cyst. *Ann. Int. Med. Den. Res*. 2020; 6(4):PH05-PH07.

Source of Support: Nil, **Conflict of Interest:** None declared