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Review Article

Ischemia Modified Albumin in Periodontal Diseases: Review Article

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Abstract

Background and Objective: Reactive oxygen species (ROS) had a central role in the progression of many chronic and inflammatory diseases. Periodontitis is associated with hyperactivity of polymorphonuclear leukocytes (neutrophils), which are considered the predominant source of ROS. Several studies suggested that periodontitis could precipitate both local and systemic oxidative stress. Ischemia modified albumin (IMA) is a distinctive and significant indicator for patients suffering from various acute and chronic conditions associated with an increase of ROS. The present study aimed to review the role of IMA in periodontal diseases and express the efficacy of periodontal therapy on the levels of IMA according to available research articles. The data for this review article was collected from several electronic databases (PubMed, Scopus, Google Scholar, and others). The review was designed as follows: introduction, IMA as a marker for several systemic diseases, IMA in periodontal diseases, and discussion of this knowledge.

Conclusion: The serum levels of IMA could be a sensitive potential biomarker for the development of periodontal diseases and possibly significantly decreased by periodontal therapy. Further research is crucial to investigate the IMA in gingival crevicular fluid (GCF) and saliva in different stages of periodontitis in both systemically health and diseased patients.

Keywords: Ischemia Modified Albumin; Serum; Periodontitis

Abbreviations

ROS: Reactive Oxygen Species; IMA: Ischemia Modified Albumin; LPS: Lipopolysaccharides; NADPH: Nicotinamide Adenine Dinucleotide Phosphate; HOCL: Hypochlorous; OH: Hydroxyl radical; H2O2: Hydrogen Peroxide; BOP: Bleeding on Probing; GAP: Generalized Aggressive Periodontitis; CP: Chronic Periodontitis; NUG: Necrotizing Ulcerative Gingivitis; NUP: Necrotizing Ulcerative Periodontitis; GCF: Gingival Crevicular Fluid; CAL: Clinical Attachment Loss; hsCRP: High-Sensitive C-reactive Protein.

Introduction

Periodontal diseases comprise a group of chronic inflammatory processes mainly categorized into gingivitis and stages of periodontitis. Presence of different anaerobic bacteria, including *Porphyromonas gingivalis, Treponema denticola, Tannerella forsythia,* and *Prevotella intermedia*, in conjunction with other periodontopathogens in dental plaque biofilm, it can result in inflammation and destruction of teeth-supporting tissue, leading to loss of attachment, resorption of alveolar bone, and tooth loss may be expected

[1,2]. The virulence factors of periodontal pathogens comprise; lipopolysaccharides (LPS), proteolytic enzymes, and other enzymes, in addition to several bacterial metabolites that challenge the host immune response and exaggerate the periodontal tissue destruction [3].

In recent decades, reactive oxygen species (ROS) had more consideration due to their key role in the progression of numerous inflammatory diseases [4]. Periodontitis is generally associated with the activation of neutrophils, which generate ROS during inflammatory processes [5]. After the challenge by pathogenic bacteria, neutrophils produce O^-_2 through the metabolic pathway named "respiratory burst" catalyzed by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase during phagocytosis of microorganisms. The O^-_2 is then converted to many radical and non-radical derivatives, for example, hypochlorous acid (HOCl), hydroxyl radical (OH), hydrogen peroxide (H_2O_2), and singlet oxygen ($^1O_2$) [6]. During physiological circumstances, ROS are efficiently neutralized by antioxidants, which prevent ROS-mediated tissue injury. The ROS can directly cause tissue damage, include damaging of DNA and protein, lipid peroxidation, and oxidation of important enzymes; temporarily, they can function as signaling molecules or mediators of inflammation [7].

Several studies investigated peripheral blood neutrophils in periodontitis patients and observed that their activity of producing ROS is mostly compared to neutrophils from healthy persons [8-10]. For example, higher levels of malondialdehyde (MDA), hydrogen peroxide, and oxidative DNA damage have been described in patients with periodontitis [11]. The pathogenesis of periodontal tissue destruction is thought to involve oxidative stress [12]. The oxidative stress levels were significantly higher in the periodontal disease groups than in the gingivitis groups and healthy groups; the oxidative stress showed a direct trend associated with the severity of periodontal diseases and bleeding on probing (BOP) [13]. The ROS are involved in the ischemia of tissues in several diseases that have an interrelationship with periodontitis including cardiovascular disorders, diabetes mellitus, in addition to liver and kidney diseases [14-17].

Albumin is one of the most common proteins in the human body, ranging about 40% in the bloodstream. It also has a significant component of most extracellular fluids, including lymph, interstitial, cerebrospinal fluids, gingival crevicular fluid, and saliva [18-20]. Ischemic attacks precipitate a change in albumin properties associated with oxidative stress, ROS, and acidosis [21]. The biochemical modifications and degradation induced by oxidative stress in albumin lead to the production of a variant form called Ischemia Modified Albumin (IMA) [22].

The IMA has been projected as an early biomarker for many diseases associated with ischemia and oxidative stress [23]. In the last decade, some studies observed the possible role of IMA as an inflammatory and diagnostic biomarker in periodontal diseases [24-27]. The present research pointed to review the potential role of IMA in development of various periodontal diseases based on available published articles.

Ischemia modified albumin as a marker for several systemic diseases

IMA has been proposed as an early biomarker for various diseases associated with ischemia and oxidative stress, for instance, myocardial infarction and cerebrovascular accidents, diabetes mellitus and renal failure, also neural and obstetric disorders [23]. The IMA was documented as an early marker of myocardial ischemia [28], a marker for acute coronary syndrome [29], a biomarker in hypertensive retinopathy [30], and a sensitive marker of myocardial Ischemia after percutaneous coronary intervention [31]. Glycaemia control and vascular complications in Type 2 diabetes mellitus [23], and chronic kidney disease [32]. Furthermore, the IMA is considered a unique marker of global metabolic risk in schizophrenia and mood disorders [33]. Recently, Erre., *et al*. (2024) concluded that the IMA is a promising biomarker of endothelial dysfunction in rheumatoid arthritis patients [34].

Ischemia modified albumin in periodontal diseases

Periodontal diseases are characterized by chronic inflammation and the production of oxidative stress, the potential role of IMA biomarker may be existing [35].

A few studies conducted the IMA levels in periodontal diseases. A preliminary clinical trial by Tayman., *et al*. (2016) evaluated the IMA serum levels in necrotizing ulcerative diseases, they reported that IMA levels were higher in patients with acute and sub-acute phases of necrotizing ulcerative periodontitis (NUP) than in patients with NUG and baseline IMA levels were also higher in both NUP and necrotizing ulcerative gingivitis (NUG) patients than in control subjects and concluded that the higher levels of IMA in necrotizing periodontal disease; can be used as a measure of disease activity [24]. Likewise, the serum levels of IMA examined by Karacaoglu and Tayman (2017), they recorded that the IMA levels were significantly higher in the generalized aggressive periodontitis (GAgP) group compared to the control group and serum IMA level is a valuable indicator for GAgP [25]. Moreover, the evaluation of IMA serum levels in chronic periodontitis (CP) and the impact of nonsurgical periodontal therapy on that biomarker was conducted by Tayman., *et al*. (2018) they found that levels of IMA were higher in CP patients and decreased after periodontal management, IMA is a marker indicating systemic inflammation during periodontal disease and might be suggested as a useful indicator of periodontal disease [26].

Recently, Karcı and Savas (2025) investigated the impact of periodontitis on serum levels of IMA in healthy periodontal subjects (group 1) compared to stage II (group II) and III/IV (group 3) periodontitis patients. They resulted that statistically significant difference was found between Stage III/IV and II periodontitis patients with a highest level was detected in Stage III/IV and consider as a potential biomarker in inflammatory periodontal status [27].

Discussion

Periodontitis is accompanied by hyperreactions of peripheral blood neutrophils, which are theoretical to be the predominant source of ROS. New clinical studies suggested that hyperactivity of neutrophils is possibly a host-immune response to the inflammation of periodontitis, which could be genetically predisposed [11,35,36]. Numerous studies suggested that periodontitis could contribute to both local and systemic oxidative stress [6,7,11,36].

Concerning to the relation of IMA to periodontitis, the published studies established the interrelationship between them [24-27]. The main conclusions for these studies suggested that IMA is considered a promising indicator for disease activity in necrotizing ulcerative periodontal disease, GAgP, and chronic periodontitis, also correlated to high-sensitive C-reactive protein (hsCRP), and healthy periodontal subjects versus stage II and III/IV periodontitis patients.

The efficacy of periodontal therapy on the serum levels of IMA in CP patients was studied by Tyman., *et al*. 2018. They reported that the levels of IMA and hsCRP were significantly decreased after six weeks of nonsurgical periodontal therapy and concluded that IMA levels may be related to the systemic influence of CP. Furthermore, IMA may also be used to indicate the clinical outcomes in the management of CP patients [26].

For limitations of literatures, some issues are present: The investigated levels of IMA include the systemic level (serum) only, thus, the detection of IMA should be studied in local secretory levels of both gingival crevicular fluid (GCF), saliva and possibility in periodontal tissues of periodontitis subjects. Regarding to the recent classification of periodontitis (2017), periodontitis was classified into several stages (Stage I-IV) according to the severity of clinical attachment loss (CAL) and level of alveolar bone loss [38]. For recommendation, the investigation of local and systemic levels of IMA within the various stages of periodontitis and the effectiveness of periodontal therapy is very suggested to clarify the possible role of IMA in severity and progression of periodontal diseases.

Finally, based on the previous scientific knowledge, the IMA is a unique indicator of oxidative stress in numerous systemic diseases, and the evaluation in systemically influenced periodontitis patients appears to be an exciting field of research.

Conclusions

Based on the available published articles, the IMA might be a promising diagnostic systemic marker of periodontal diseases and significantly possibly influenced by periodontal therapy. Further research is mandatory to investigate the levels of ischemia modified albumin in GCF and saliva, and for clarification of its actual role in development and progression of the periodontal diseases. Fur-

thermore, effectiveness of periodontal treatment on various stages of periodontitis in systemically diseased and healthy individuals seemly to be required.

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Conflict of Interest

None declared.

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