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FREE RADICALS STATUS IN TEMPOROMANDIBULAR JOINT DISORDER- A LITERATURE REVIEW

B. Saravanan[1], R.Devaki Vijayalakshmi[2], S.Karthik[2], P.Jayamathi[3]

[1]Department of Oral and Maxillofacial surgery, TamilNadu Govt Dental College, Chennai
[2]Department of Orthodontics and Dentofacial Orthopaedics, Meenakshi Ammal dental College, Maduravoyal
[3]Department of Biochemistry, Meenakshi Ammal dental College, Maduravoyal

E-mail of Corresponding Author: gjayamathe@gmail.com

ABSTRACT

Increased production of reactive oxygen species (ROS) contributing to oxidative stress, significantly influences many diseases including temporomandibular joint (TMJ) disorder. Temporomandibular joint disorder (TMJD) is an inflammatory disease which emphasizes that mechanical stresses lead to the oxidative stress of articular tissues. But, studies on the defense mechanism against oxidative stress in the pathogenesis of TMJD have received little attention. Hence, we made a novel attempt to review the pathogenesis of TMJD to explore the possible role of ROS in the degenerative TMJ disease.

INTRODUCTION

Temporomandibular joint (TMJ) is a synovial joint located between the mandibular fossa of the temporal bone and the condylar process of the mandible with an articular disk interposed between them. Deviations in this intimate relationship between the bony surfaces and the articular-disc often leads to disorders of the TMJ. TMJ disorders are a heterogeneous collection of signs and symptoms that can be generally characterized by the presence of pain, temporomandibular joint noise and limitation of jaw movement[1]. Studies suggest that upto 70% of patients seeking treatment for TMJ disorder have articular disk displacement leading to degenerative changes in the TMJ. Clinical management of these patients depends upon whether the disease process is self- limiting or not. Therefore it is necessary to differentiate an adaptive state from a disease process before a therapeutic measure is instituted; as only an astute discernment of the underlying molecular changes encompassing a degenerative event in the TMJ can provide a beneficial and comprehensive structure to the interventional regimen planned for the patient.

Pathogenesis of Temporomandibular joint disorder

Few studies carried out in the molecular mechanisms involved in degenerative TMJD, suggests that mechanical stresses lead to the oxidative stress of articular tissues. Milam[2] showed various models of degenerative TMJ disease and postulated that excessive mechanical stress could be of a magnitude sufficient to damage tissues directly or indirectly, triggering a cascade of molecular events leading to disease in susceptible individuals. These events involve the production or release of various kinds of reactive oxygen species, reactive nitrogen species, cytokines, various other

inflammatory mediators, and collagen degrading enzymes. Under normal circumstances, these molecules may be involved in the remodeling of articular tissues in response to changing functional demands. However, if functional demands exceed the adaptive capacity of the TMJ or if the affected individual is susceptible to maladaptive responses, then a disease state will ensue.

Though the pathophysiology of TMJ syndrome is not entirely understood, it is believed that the etiology of TMJ dysfunction syndrome is likely to be multifactorial and arises from both local insults and systemic disorders. Local problems frequently arise from articular disc displacement and hereditary conditions affecting the structures of the joint itself, such as hypoplastic mandibular condyles. Endothelial cells and synovial cells in the TMJ when subjected to mechanical stress promotes oxidative stress of articular tissues[3]. In normal, healthy individuals, the metabolic process results in balanced levels of reactive oxygen species (ROS) and antioxidants. If the normal oxidant/antioxidant balance is disturbed, it can result in a proliferation of free radicals. Recent scientific research have shown that oxidative stress not only aggravates the inflammation in oral tissues, but also is a contributing factor to systemic inflammatory diseases, including rheumatoid arthritis and cardiovascular disease[4].

Hyaluronic acid forms the central axis of proteoglycans and it maintains the viscosity of synovial fluid within joints. Following exposure to free radical systems, this polymer fragments (Hyaluronic acid)[5] leads to destabilization of connective tissues and loss of synovial fluid viscosity. A number of natural defense mechanisms exist for limiting oxidative damage[6]. In TMJ diseases, it has been suggested that ROS alter the molecular configuration of hyaluronic acid, and also produces degradation of collagen and proteoglycans of the articular cartilage[7&8].

Role of free radicals

Free radicals play a vital role in the pathogenesis of degenerative joint diseases[2]. Although oxygen free radicals participate in many physiological processes, they can be harmful to tissues when their action is left uncontrolled. Both cellular and extracellular molecules may be destroyed[9]. A susceptible site for peroxidation is cellular membrane which leads to increased production of lipid peroxides an indicator of inflammation. Cai et al[9] measured the activity of oxygen free radicals in the synovial fluid (SF) of the TMJD patients and observed that the concentration of lipid peroxides were significantly higher in the TMDJ patients than in the normal control subjects.

The pro-inflammatory mediators such as cytokine, IL-l (Interleukin -1), affects various cells in TMJ compartments, thereby inducing inflammation[10], activation of collagen- as well as proteoglycan degrading enzymes, followed by the inflammatory process, causing deleterious effects in the TMJ.[11]

Currently, the importance of reactive oxygen species such as superoxide and hydroxyl radicals as causative agents of inflammation has been recognized[12]. Previous studies have shown that superoxide is an important mediator of inflammation and tissue injury[13,14]. Superoxide can degrade synovial fluid and collagen, depolymerize hyaluronic acid and convert arachidonic acid, a membrane lipid into biologically active mediator, which results in further tissue injury[14.]

Nitric oxide, which is an endothelium-derived factor, regulates blood pressure, vascular tone, neural signaling and

immunological functions. It may function as a inflammatory mediator in the TMJ region. Recently, increased nitric oxide production has been shown to play a role in the pathogenesis of synovitis in the TMJ. Nitric oxide concentration in TMJ fluid is closely associated with inflammatory changes and painful TMJ.[15]

Antioxidant system

The antioxidant mechanisms are the evolutionary designs that avidly react and annihilate ROS before they inflict oxidative damage to tissues and cells[16]. ROS can cause DNA and protein damage, initiate lipid peroxidation, oxidize α1- antitrypsin and stimulate the release of proinflammatory cytokines[16].

Milam et al [3] reported that free radicals in normal TMJs might not cause TMJ disease if endogenous free radical scavenging mechanisms (antioxidant enzymes) prevent their accumulation. However, if the scavenging capacity of affected articular tissues is exceeded by an overwhelming production of free radicals, significant tissue damage could occur. Nitzan et al[17] reported that TMJ with oxidative stress may indicate increased exposure to free radicals and a decrease in antioxidant potential capacity of the system, or a combination in synovial fluid. This insufficient scavenging activity leaves free radicals to cause further damage and prevent the re-establishment of a normal lubrication system in various joint components.

Antioxidants available in supplement form include the enzymes superoxide dismutase (SOD), catalase and glutathione peroxidase, vitamin A, beta-carotene, and vitamins C and E, and the trace mineral selenium[18]. SOD can protect the joint against the toxic effect of the superoxide radical by catalyzing its dismutation to molecular oxygen and hydrogen peroxide. Sumii et al[19] reported that SOD activity in the SF from patients with rheumatoid arthritis was higher than that of the normal group. This result may imply that inflammation exaggerates the SOD synthesis as a defense mechanism against overwhelming superoxide radicals. Lin et al[20] have provided preliminary evidence that SOD is effective at reducing symptoms in patients with TMJ disorders who had not previously responded to exhaustive trials of conventional therapy. SOD helps to protect the cells from the damage of free radicals, and revitalizes the cells [21]. It has been reported that SOD, catalase, and glutathione peroxidase activities in erythrocytes from patients with rheumatoid arthritis were scored much lower than those from patients with osteoarthritis, suggesting that the erythrocytes in rheumatoid arthritis patients might be more susceptible to ROS damage[22]. Guven et al[23] studied the activity of superoxide dismutase (SOD) in the synovial fluid of patients with TMJD, measured the relationship between the activity of SOD and the severity of the disease, and concluded that the reduction of SOD activity may result from insufficient scavenging capacity of free radicals [23]. However, SOD activity in SF does not differ between rheumatoid arthritis and osteoarthritis, though it is higher than that of the normal group[19].

Cai et al[9] measured the activity of oxygen free radicals and the level of antioxidant enzyme superoxide dismutase (SOD) in the synovial fluid (SF) of TMJD patients found that the levels of SOD activity were significantly higher in the TMJD patients than in the normal control subjects.

CONCLUSION

Studies on the defense mechanism against oxidative stress in the pathogenesis of TMJ disorders have received little attention.

Further investigations and studies are required to determine the role of antioxidants that scavenge the free radicals in TMJ disorders. This might also offer a potential for the development of new treatment regimen, including application of metal chelaters and radical scavengers specific for the pathophysiology of TMJD.

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