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Periodontitis as an Independent Factor in Pathogenesis of Erectile Dysfunction

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Erectile dysfunction (ED) is one of the most common sexual dysfunctions, which may be defined as persistent or recurrent inability of sufficient penile erection during sexual performance[1]. It is a major global men's health problem affecting more than 150 million individuals and is expected to still increase significantly owing to poor lifestyle factors[2]. ED adversely impacts the overall quality of life causing psychological distress, behavioral alterations due to unsatisfied sexual performances, and thus also disrupting a robust relationship with the partner. The incidence of ED increases dramatically from about 6% among men of 20-29 years of age to 50-70% in men of age between 40-79 years. This data has been suggested to get escalated to more than 320 million by the year of 2025[2].

ED, alike several other male infertility or subfertility problems, has multivariate causatives, ranging from physiological factors to environmental as well as sociodemographic factors[3]. Various infectious diseases have been reported to positively corelate with the incidence of ED[4]. In this regard, periodontitis, a highly prevalent gum infection causing damages to the soft tissue and tooth supporting bones, find substantial relevance[5]. Periodontitis is a multifactorial chronic inflammatory oral disease caused by dental plaque (mostly bacterial plaque) biofilm. In case of untreated periodontitis, loss of the dentition can occur. According to the Global Oral Health Programme, conducted by the World Health Organization (WHO), around 5-15% of the global population (34-45 years of age) suffer from

severe periodontitis[6]. Several systemic diseases have been found to be associated with chronic periodontitis that include diabetes, coronary heart disease, respiratory diseases as well as endocrine-related disorders like impaired pregnancy outcome, etc. This may be due to systemic colonization of periodontal pathogens and induction of inflammatory conditions. It may also impair male fertility parameters. Its association with ED is elusive but there is possibility of a positive correlation. Poor lifestyle with high alcohol consumption rate and/or smoking habits increase

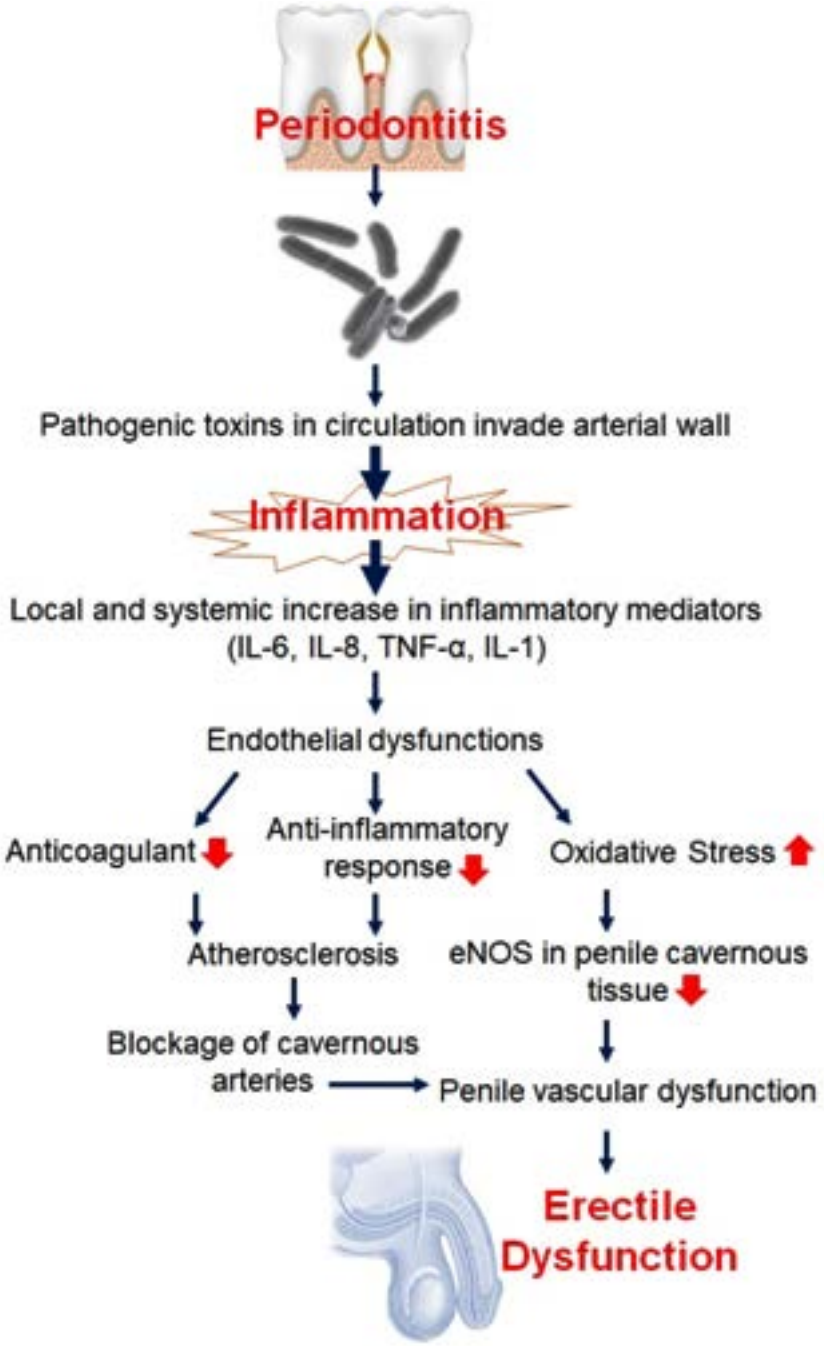

Fig. 1. The possible mechanism of periodontitis-induced erectile dysfunction

the susceptible to both ED and oral inflammatory disease like periodontitis[7, 8]. Both these diseases predispose to endothelial dysfunction and affect the overall well-being of the patient[5]. Several recent studies contributing to endothelial cell dysfunctions have tried to draw a link between ED and periodontal disease[5] but still they are not in accord with the shreds of evidence. On the other hand, participation of several common important cytokines as well as growth factors in the etiopathology of both diseases kindles research interest to explore the mechanism of their association[9]. Hence, in this letter, we have tried to leave some messages for further research to establish the relationship between ED and periodontal disease.

Eltas *et al*., conducted a three months study to put forth that periodontal treatment leads to significant improvement in both periodontal health and International Index of Erectile Dysfunction (IIEF) score in the study group compared to the control group ($P<0.05$)[10]. Improvement in endothelial cell function and reduced pro-inflammatory cytokine Tumor Necrosis Factor-α (TNFα) levels, are considered for treatment of patients with several systemic diseases associated with progressive periodontitis[11]. Surprisingly, gingivectomy or flap surgery in periodontitis patients showed lesser prevalence of ED as compared to the patients without any treatment at all for chronic periodontitis[7]. Thus, dental extraction can lead to reduction in inflamed tissue, but it may debilitate the circumstance of ED, induced by chronic periodontal inflammation[12]. Besides cytokines, other pro-inflammatory markers like nitric oxide (NO), increases both in ED and in periodontal disease[13]. The question may arise that why does ED occur during periodontal diseases? During chronic periodontitis, increased level of TNF α is a known fact which has been shown to decrease the expression of endothelial nitric oxide synthase (eNOS) gene leading to reduction in NO production (Fig 1)[14-15] thereby possibly also affecting male reproductive functions that are NO dependent. Beside these, insulin-like growth factor I (IGF-I) has opposite effect to TNF as it combines with platelet-derived growth factor (PDGF) and transforming growth factor (TGF) to cause regeneration towards normal periodontal state during periodontitis treatment[16]. The possible interactions between IGF-1 and TNF is further complicated by a report that IGF-1 can inhibit TNF signaling[17]. These cross-talks among the periodontitis inflammatory markers with endocrine milieu and growth factors, suggest a potential connection between periodontitis with sexual disorders like ED. According to few studies, it is evident that ED has association with periodontal diseases but the exact reason for their co-occurrence is still unknown.

A possible hypothesis can be drawn from the above evidences to elucidate how periodontitis may initiate pathogenesis leading to ED. The periodontal pathogens, e.g. Porphyromonas gingivitis may invade the systemic circulation followed by homing into the arterial wall and induction of systemic inflammatory condition. Local and systemic inflammation caused by chronic periodontitis is associated with increased levels of inflammatory mediators, such as IL-6, IL-8, TNF a and IL-1, which may induce atherosclerosis and in turn endothelial dysfunctions. On the other hand, endothelial dysfunctions may lead to compromised vascular anti-inflammatory responses as well as anti-coagulation properties and increased production of reactive oxygen species (ROS). ROS generation overwhelms the vascular antioxidant capacities and disrupt the activities of eNOS. Thus, atherosclerosis together with reduced eNOS activities pave the way to blockage of the cavernosal arteries and impair the functions of the penile vasculature which may potentially cause ED (Fig 1).

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