Journal of Istanbul University Faculty of Dentistry
Volume: 48, Number: 3 Pages:75-81, 2014

THE TWO-WAY RELATIONSHIP BETWEEN OBESITY AND PERIODONTITIS

Obezite ve Periodontitis Arasındaki Karşılıklı İlişki

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Received: 24/02/2014
Accepted: 19/06/2014

ABSTRACT

Periodontitis and obesity are two chronic inflammatory diseases. Since obesity and periodontitis are associated with systemic inflammation, these two situations are linked by common pathophysiology. TNF-alfa and IL-6 are cytokines that are involved in the pathophysiology of both obesity and periodontitis. The levels of these cytokines increase with obestiy and periodontitis. Resistin is produced by immune cells and therefore, is related to the activation of inflammatory processes. Increased resistin serum levels have been associated with periodontitis. Adipose tissues also secrete some anti-inflammatory factors, such as adiponectin. Plasma levels of adiponectin are decreased in individuals who are obese, compared with persons who are normal weight. Furthermore, evidence suggests a trend toward decreased adiponectin serum levels and reduced adiponectin function in individuals with periodontitis. In conclusion, periodontitis and obesity are diseases that are associated through various cytokines, proteins, vitamins, etc.

Keywords: *Periodontitis, obesity, TNF-alpha, IL-6, resistin*

ÖZ

Periodontitis ve obezite iki kronik enflamatuar hastalıktır. Obezite ve periodontitis sistemik enflamasyonla ilgili olduklarından bu iki hastalığın ortak patofizyolojiye sahip olduğu söylenebilir. TNF-alfa ve IL-6 obezite ve periodontitisin patofizyolojisinde yer alan sitokinlerdir. Bu sitokinlerin seviyeleri obezite ve periodontitis ile birlikte artar. Resistin immun hücreler tarafından üretilir ve bu yüzden de enflamatuar sürecin aktivasyonunda yer alır. Resistinin pro-enflamatuar özellikleri TNF-alfa ve IL-6 salınımı ve adiponektinin anti-enflamatuar etkilerinin bozulmasıdır. Periodontitiste serumda resistin seviyesi artmaktadır. Aynı zamanda adipoz dokular da adiponektin gibi bazı anti-enflamatuar faktörleri salgılamaktadır. Obez bireylerde normal ağırlıktaki bireylere göre plazmada azalmış adiponektin seviyeleri görülmektedir. Ayrıca bilimsel kanıtlar periodontitisli bireylerde serum adiponektin seviyesinin ve fonksiyonunun azaldığını göstermektedir. Sonuç olarak, periodontitis ve obezite çeşitli sitokinler, proteinler, ve vitaminler aracılığıyla birbirleri ile ilişkili iki hastalıktır.

Anahtar kelimeler: *Periodontit, obezite, TNF-alfa, IL-6, rezistin*

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Introduction

Obesity is considered as a chronic low-grade inflammatory disease because of changes occuring in adipose tissue (1-4). Obesity, which is characterized by excess adipose tissue, results in elevated levels of pro-inflammatory cytokines and hormones named adipokines, resulting in an imbalance between increased inflammatory stimuli and decreased anti-inflammatory mechanisms, leading to persistent low-grade inflammation (5). It affects over 35% of the adult population of the USA, and obesity-related illnesses have emerged as the leading cause of preventable death worldwide, according to the World Health Organization (6). Obesity's secondary morbidities include increased risk of cardiovascular disease, type 2 diabetes and cancer, in addition to increased occurence and severity of infections. Sedentary lifestyle and weight gain caused by consumption of a high-fat diet contribute to the development of obesity, with individuals having a body mass index (BMI) score greater than or equal to 30 (7).

Periodontitis is a chronic infectious disease caused predominantly by bacteria that release endotoxins that activate pro-inflammatory cytokines interleukin (IL)-1 and tumor necrosis factor alpha (TNF-alfa), among other interleukins, which affect the tissues supporting the teeth and induce loss of alveolar bone, cementum, and periodontal ligament (6).

Periodontitis and obesity are two chronic inflammatory diseases which have been proved by several studies that they are associated with each other. Since obesity and periodontitis are associated with systemic infammation, it may be said that these two situations are linked by common pathophysiology (1).

Obesity's Effects on Periodontal Tissues

Individuals with obesity have higher levels of circulating TNF-alfa and interleukin-6 (IL-6), which are also secreted from adipose tissues and are involved in the pathophysiology of both obesity and periodontitis. Moreover, serum levels of these cytokines decrease with weight loss (8). The adverse effects of obesity on the periodontium may be mediated by impaired glucose tolerance (9), dyslipidemia (10) and more likely by inflammatory cytokines and adipokines such as TNF-alfa (4), IL-6 (11) and adiponectin (12) or leptin (13). The high concentration of TNF-alfa may exacerbate preexistent periodontal disease through the stimulation of fibroblasts that promote the synthesis of degrading enzymes and the stimulation of osteoclasts that activate bone resorption (1). In a recent study by Nassar et al. the cafeteria diet induced obesity in rats led to greater alveolar bone loss, as assessed radiographically suggesting that obesity can contribute to further progression of periodontal disease (6). Recent evidence suggests that adipose tissue is a reservoir of inflammatory cytokines. Thus it is plausible that the increase of adipose tissue results in increased activation of the inflammatory host response, making the obese individual more susceptible to periodontal disease (6). TNF-alfa is a pro-inflammatory cytokine that provides an evident link between obesity and inflammation (14) and seems to play an important role in the progression of periodontitis (15). Increased cytokines, such as TNF-alfa, IL-6 and acute-phase respondents such as C-reactive protein(CRP) (16), contribute to the development of a low-grade systemic inflammation and may enhance periodontal tissue destruction (17). Plasminogen activator inhibitor 1 (PAI-1) is another cytokine that takes place in the pathogenesis of obesity

and periodontitis. PAI-1 is the main inhibitor of plasminogens. It is produced by liver and endothelial cells, and its production is controlled by lipids and TNF-alfa. It was shown that plasma levels of PAI-1 were increased in obese individuals (18) and enhanced PAI-1 levels in the visceral adipose tissue increased agglutination and caused ischemic vascular disease (19). In addition, enhanced TNF-alfa may lead to an increase in PAI-1 levels for obese individuals (18). This increased levels of PAI-1 may induce agglutination of blood; agglutination of blood in the microvasculature decreases blood flow to the gingiva in obese people, facilitates the progression of periodontitis, and raises the risk of ischemic vascular disease (20). Leptin is an adipose tissue-secreted protein that regulates food intake and energy spending (21) and stimulates the production of other pro-inflammatory cytokines (22-24). Studies have demonstrated association between severity of periodontitis and local and circulating levels of leptin (25-26). Although originally identified in adipose tissue, resistin is also produced by immune cells and therefore, is related to the activation of inflammatory processes. The pro-inflammatory properties of resistin include the secretion of TNF-alfa and IL-6 (27) and the impairment of the anti-inflammatory effects of adiponectin (28). Increased resistin serum levels have been associated with periodontitis (9, 29). In a study by Zimmermann et al. (30), serum resistin levels are upregulated in groups of obese periodontitis and normal weight periodontitis patients, suggesting that periodontal inflammation may modulate the systemic levels of this pro-inflammatory marker independent of obesity. In addition to the aforementioned pro-inflammatory adipocytokines, adipose tissues also secrete some anti-inflammatory factors, such as adiponectin. Plasma levels of adiponectin are decreased in individuals who are obese, compared with persons who are normal weight. Furthermore, evidence suggests a trend toward decreased adiponectin serum levels and reduced adiponectin function in individuals with periodontitis.

Effects of Periodontitis on Obesity

Periodontitis mainly influences the circulating levels of resistin and adiponectin, whereas obesity and periodontitis affect the circulating levels of leptin in favor of pro-inflammation, suggesting a role of both conditions in the systemic inflammatory burden (30). Lipopolysaccharide derived from periodontal pathogens, such as Porphyromonas gingivalis existing in periodontal pockets, increases circulating TNF-alfa (31), which induces insulin resistant and atheromatous change (32, 33). This may be a possible reason for the relationship between poor periodontal status and obesity. Elevated serum CRP level suggesting systemic inflammatory status enhances the risk of cardiovascular disease (34-36) and is associated with obesity (37).

Link Between Obesity and Periodontitis: Data from Epidemiological Studies

In a study carried out by Zimmermann et al. (30), resistin serum levels were higher whereas adiponectin levels were lower in periodontitis patients than in healthy patients. The normal weight and periodontally healthy patients presented the lowest serum leptin levels. In addition high serum levels of two pro-inflammatory adipocytokines, leptin and IL-6, are associated with individuals presenting obesity and periodontitis. These findings indicate that obesity and periodontitis can, independently or jointly, alter the local and systemic levels of adipocytokines, mostly in favor of pro-inflammation (30). In another

study which compared the non-surgical periodontal treatment effects between patients with and without obesity, statistically significant decreases were observed in TNF-alfa, IL-6, and leptin levels within the group with obesity and only in IL-6 levels within the group without obesity. Conversely hsCRP levels did not change in either group (8). The findings in this study demonstrate that non-surgical periodontal treatment promotes significant improvements in all the clinical parameters in both groups. These observations are consistent with previous reports that obesity did not act as a negative modifying factor on the periodontal healing after non-surgical periodontal treatment. In conclusion the clinically successful non-surgical periodontal treatment decreases the systemic inflammation by reducing the circulating levels of TNF-alfa, IL-6, and leptin and is associated with alleviation of insulin sensitivity in patients with obesity but yields no significant changes in the lipid profile. However, in the group without obesity, a significant decrease was observed only in the circulating levels of IL-6 (8). In a study by Chaffee et al. (38), there appears to be stronger obesity-periodontitis association in women, non-smokers, and younger individuals than in the general adult population. In a meta-analysis by Dalla Vecchia CF et al. (39), obesity was significantly associated with periodontitis among females, with obese females showing an 80% higher chance of having periodontitis than females of normal weight. The association of periodontitis with obesity was stronger in female non-smoker. Hence, female nonsmokers were 3.4 times more likely to be diagnosed with periodontitis compared to female non-smokers with normal weight. Vitamin D has an important role in bone growth and maintenance, which might be beneficial for maintaining periodontal health. Recently, it has been suggested to have positive effects on periodontal diseases, tooth loss, and gingival inflammation not through its effects on bone metabolism but through anti-inflammatory mechanisms. Hence adequate serum values of vitamin D could be important in the prevention and treatment of periodontal diseases (40). In a research by Teles et al. (40), there were positive correlations between adiponectin/vitamin D and between IL-6/leptin, negative correlations between IL-6/vitamin D and leptin/vitamin D, but no associations between serum analytes and clinical or microbial parameters. In another study by Akman et al. (41), serum triglyceride levels were positively correlated with plaque index, probing depth, and clinical attachment level. There were negative associations between clinical periodontal parameters and HDL-C. Periodontal findings were also found to increase with the increasing BMI (42).

Conclusion

In conclusion, periodontitis and obesity are diseases that are associated with each other through various cytokines, proteins, vitamins, etc. They are both inflammatory diseases and can be associated with each other. IL-6, TNF-alfa, adiponectin, leptin, resistin are some important molecules that take place through interaction between these diseases. Additional studies are needed in order to fully understand the relationship between obesity and periodontitis.

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