Alveolar bone loss pattern in obese patients
A systematic review

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Abstract

The purpose of this article (systematic review) was to test the assumption that: is there any difference in alveolar bone loss between individuals with ideal weight range and those who are within overweight / obesity, through which mechanism? An independent reviewer performed a literature search across the Cochrane Library, PubMed/ MEDLINE, and Scopus databases for papers listed in from 2009 until November 2019. Twelve articles were selected for review.

Both obesity and alveolar bone loss, going along with periodontitis, are attached to systemic inflammation, and probably they have a same pathophysiology. The products adipose tissue are implicating in activation of the inflammatory host reaction, which could increases the effect of overweight-population to alveolar bone damaged. However, the correlation between the inflammation reported in both obesity and periodontal disease is still unclear.

Keywords: Obesity, Periodontal diseases, Alveolar bone loss, high fat diet.

Introduction

The health may be affected by excessive fat accumulation in obesity and overweight (The World Health Organization WHO). Latest data indicate that the obesity prevalence has almost tripled since the seventies. Overall, estimations show that more of tow million people die every year due to diseases attached with obesity, and this is considered an epidemic in high-middle- and low- levels of growing countries. Around half of the world's population is predicted that will have obesity by the year 2030. High rates of mortality and morbidities such as cardiovascular diseases, type tow diabetes, and atherosclerosis are associated with obesity. It has newly been proposed that this situation is related with a low-grade inflammatory status, specified by an expansion in blood flowing inflammatory markers. This general inflammatory condition participates to immune response tampering and rising C-reactive protein (CRP) levels, of which is a systemic inflammation indicator. The authors:

Suvan et al. report that population with overweight/ obese have high tendencies to get alveolar bone loss contrasted to normal weight groups. This periodontal support demolition is probably attached to increased levels of inflammatory mediators like cytokines and periodontal pathogens germs in obese patients. A recent systematic review concluded that an increased waist circumference, obesity, overweight, and weight gain contribute to periodontal measures amplification. (1)

Also obesity is attached to the type II Diabetes Mellitus development (T2DM). Patients with T2DM have shown expanding tendency to fractured bone, likely due to their increased cortical porosity. Though, a high turnover on mineral bone composition is mostly responsible for cortical porosity, but patients with T2DM have decreased bone turnover. Modification in the systemic immunity advancement inflammatory stat must explain the clinical association between overweight, T2DM, and alveolar bone loss. The explanations for this association may be the Adipokines, especially Adipo-nectin and leptin5. The Leptin is regarded as a connection among immune systems and neuroendocrine. It must regulate a lot of physiological and pathophysiological procedures, particularly inflammation and immunity. Leptin and adiponectin can also control bone metabolism and be implicated in osteoporosis pathology.(3) Pro-inflammatory cytokines have osteoclastic effect in high levels. Also, high levels of leptin, usually associated with obesity, are risk factor for bone loss. Also Pro-inflammatory cytokines produced by adipose tissue, such as interleukin 6 (IL-6) or TNF Tumor Necrosis Factor α, exacerbate osteo-clastogenesis. Therefore, inflammation can impact the bone loss in obese patients (4). As previously sited, individuals with fat mass, regardless of body weight, had higher risk of bone diseases and fractures than normal ones. Osteoporosis-postmenopausal is closely associated with estrogen low level, and it includes periodontal manifestations, such as alveolar bone resorption, clinical attachment loss and tooth loss. (1, 2)

Materials and methods

The main question was: Is there any association between alveolar bone loss and overweight/obesity? Through which mechanisms?

Applied inclusion criteria: Articles published in French and English; randomized retrospective or prospective studies and controlled trials comparing alveolar bone loss degrees against individuals with overweight /obesity to those who are within the ideal weight range.

Search criteria and sources of information

In our research we used: Cochrane Library, Scopus databases and PubMed /MEDLINE. Pertinent articles were searched for publishing articles from 2009 until November 2019. Medical subject headings (MeSH, PubMed) and termsrelated to alveolar bone loss and obesity were combined using Boolean operators. The following search was conducted in each database: ("Obesity"[Mesh]) AND "Alveolar Bone Loss"[Mesh]

We exclude narrative animal studies and review articles.

Results

Details of the articles retrieved from searching are displayed in Fig -1-

12 articles were selected - an article was eliminated for in vivo study.

Discussion

The high obesity prevalence has drive to increased concerns regarding the health-related complications of this stat. Body fat high levels are attached to various inflammatory mediators, which result in a chronic low-grade inflammatory condition.

Fat tissue accumulated in adipocytes and hepatocytes secretes inflammatory mediators such cytokines like IL-629 and TNF Tumor Necrosis Factor alpha (TNF-a). Indeed, fat tissue acts as an endocrine organ and mostly consists of internal and subcutaneous adipose tissue, first one of which constitutes nearly 20% of body adipose tissue and consists mainly of abdominal adipose tissue. Besides, studies results have indicated that macrophage infiltration in fat tissue is associated with the chronic inflammatory state found in obesity. (5, 6)

Mechanism of bone metabolism in obesity

The excessive fat tissue, in overweight body, is considerate like an endocrine organ. It can product inflammatory mediators after macrophage accumulation in white adipose tissue. (Kawasaki et al. 2012, Lee 2014) (Amar et al. & Leeman, 2007; L.-Czernik et al., 2015). For example, bone trabecular density was decreased in high-fat diet-induced by Potikanond and colleagues in 2016. Other studies show a direct correlation with chronic systemic inflammation because of bone inflammation process observed in obese-induced insulin-resistant rats (Blasco-Baque et al., 2012, Cavagni et al., 2015, Li, Lu et al., 2015, Muluke et al., 2015). Many findings declare that general inflammation, a high inflammatory tone in blood circulation, may be an important element in bone inflammation as well as bone porosity in obese stat. Increased levels of tumor necrosis factor TNF, cytokines,

interleukin (IL)-1β and IL-6 in blood circulation compounded osteo-clastogenesis (New creation) , the process of stem cell differentiation into osteoclasts, following in bone resorption procedure (Blasco-Baque et al., 2012, Lu et al., 2015, Weitzmann et al., 2013). Several researches showed that following the general inflammation, increased osteoclastogenesis could occurs through the up-regulation of macrophage colony stimulating factor (M-CSF), the chemical receptor activator of nuclear factor (NF)-κB ligand (RANKL), and finally an increase in all downstream cytokines mediators, which directly activate osteoclastogenesis in the osteoclast precursor cells (Yamashita et al., 2015). (7)

Increased shift from the osteoblasts to adipocytes has been observed in cases of obesity (Luo et al., 2015). Both adipocytes and osteoblasts came from mesenchymal stem cells and their differentiation is disturbed by the long-view consumption of a high-fat nutrition (Luo et al., 2015, Shu et al., 2015). In adverse to Luo's study, Shu and colleagues found that osteoblast activity increased in cases of obesity, along with high adipogenesis (Shu et al., 2015). (6) The increase in osteoblast activities in Shu's study might be in part due to a compensatory effect of increased osteo-clastogenesis at the time-point they analyzed. Additionally, obesity is found to be associated with the reduction of osteoblast cell survival, the impaired osteoblastic insulin signaling and decreased bone formation rate (Potikanond et al., 2016, Pramojanee et al., 2013) (8). After those findings, bone resorption and metabolism are finaly affected by obesity and fat tissue substance degradation. (7, 8)

Moreover, overweight / obesity are attached with the change in the levels of material called "adipokines" affiliated to the fat tissues degradation. (9) Also, studies had found increased "Leptin" and decreased "Adiponectin" (inflammation mediators) levels have been detected in the obese patient (Leal & Mafra, 2013). These two principal inflammation elements (including Leptin and adiponectin) play important roles -direct and indirect- in both bone metabolic disorders and bone metabolism (Ducy & col., 2000, Elefteriou & col., 2004, Holloway et col., 2002, Oshima et al., 2005). (5) Leptin has important roles in decreasing appetite, inducing inflammation in adipose tissues and increasing energy expenditure (Leal & Mafra, 2013). However, the precise leptin effect on bone physiological metabolism is still misunderstood. It has been shown that the previous leptin levels of each person played a role in the various outcomes of leptin on bone metabolism, that explain differences in fat tissue quantity of invidious (Cao, 2011) (7, 8, 10). In non-obese stat, levels of the physiological Leptin are thought to be responsible for directly enhancing bone mass density by increasing osteoblastogenesis and decreasing osteo- clastogenesis (Cornish & al., 2002, Holloway & al., 2002). Nonetheless, high blood leptin level "hyperleptinemia" in nutrition inducing obesity has been accused to increase "systemic" inflammatory responses (Loffreda et al., 1998) so indirectly reduce bone mass osteodensity (Fujita, Watanabe, & Maki, 2012; Shu et al., 2015). Hyperleptinemia also increased pro-inflammatory reaction

cytokine production and alveolar bone altering inflammation in the periodontitic experiments in which invidious were fed with a normal diet (Li, Huang, Liu, Hou, & Meng, 2015). Adiponectin plays a role in an anti-inflammatory process by indirectly increases bone mass via the inhibition of osteoclastogenesis (Leal & Mafra, 2013) (Oshima et al., 2005). A lot of studies exhibited adiponectin direct effects on bone mass in various conditions (Pu et al. 2016, Yamaguchi et al. 2007, Zhang et al., 2014) (5). An example of this is founding when Yamaguchi and colleagues (2007) demonstrated that "adiponectin" pro-inlammation product, resulted from the activation of periodontogenic bacterial lipo-polysaccharides (*Actinobacillus actinomycetemcomitans*) which could stopped osteoclastogenesis in cell lines by deleting the transcription factor "NF-κB", important element for osteoclast formation. Adiponectin develops osteoblastogenesis in human jaw bone marrow mesenchymal strain cells (2016). Moreover, by reducing an inflammatory process and osteoclastogenesis in the diet-induced obese experiment subjects, Adiponectin could improve alveolar bone loss (Zhang et al., 2014) (7, 12). Associated together, levels circulating adipokines alterations, including increased leptin and decreased adiponectin, in high-fat level nutrition -induced obesity may play an important role in bone physiological metabolism and bone loss pathology. (6, 7, 13)

Obesity / overweight -insulin resistance and alveolar bone loss

Jaw bone density loss was showed in several animal studies, indicated by decreased alveolar bone height or decreased bone mechanical and chemical properties, including bone strength, bone mineral density (BMD), and bone histo-morphometry, may be affected by diet nutrition-induced overweight with or without insulin resistance (12) (Amar et al., 2007, Blasco-Baque et al., 2012, Cavagni et al., 2013, Cavagni et al., 2015, Fujita and Maki, 2015, Li. Lu & al., 2015, Muluke & al., 2015, Pramojanee & al., 2013, do Nascimento et al., 2013). Furthermore, Moura-Grec and colleagues in 2014, in their meta-analysis and systematic review reported that in periodontal pathology, through an unfamiliar mechanism, obesity was associated with chronic inflammation of the tissue surrounding the teeth causing alveolar bone loss and bone inflammation (in twenty five out of thirty one studies) (Moura-Grec, Marsicano, Carvalho, & Sales-Peres, 2014). Clinical studies showed also that an increase in body weight could exacerbate the strictness of periodontitis (Cavagni et al. 2015, Verzeletti; Gaio, Linhares, & Rosing, 2012). Muluke and colleagues (2015) found that increased plasma fatty acid levels together with increased body weight enhanced alveolar bone loss after "*Porphyromonas gingivalis"* infection. All of those results suggest that high-fat feeding-induced obesity can activate alveolar bone loss and aggravate the severity of periodontitis. (7, 12, 14)

However, there are tow 2 controversial reports regarding the contribution of overweight to alveolar bone lysis. First, Priesnitz and colleagues in 2008 showed that four months of consumption of a cafeteria style-alimentation did not promote the progression of alveolar bone lysis(Priesnitz Simch, José Gaio, & Kuchenbecker Rösing, 2008). Although that several study showed there were only 13% different, in body weight between the control and experimental groups, which was relatively small and not statistically significant. Moreover, the insulin levels were not shown in the results (5). These findings could also suggest that the combination of obesity and insulin resistance might exacerbated be alveolar bone loss. Secondly, Cavagni and colleagues in 2013 (Cavagni et al., 2013) demonstrated the effect of a cafeteria-diet on spontaneous periodontal disease without any mechanical or bacterial induction. That study showed that obesity alone increased the incidence of periodontal tissue breakdown without bone loss. Therefore, it is possible that the obesity-derived tissue inflammation occurred prior to bone loss. (7)

Issue

Recent data suggest that obesity has a negative impact on bone health possibly via the alteration of food-diet and host immune status. Body health and food quality, an imbalance of the resident gut micro-organism population, instigated by a long-term high-fat feeding consumption results in an increased inflammatory level both locally and systemically. These chronic inflammatory stats have been proposed as pivotal factors for the subsequent bone loss and lysis found in the obese patients. The diminished bone mass following a chronic high-fat and high-sugar nutriments consumption is caused by an increased osteo-clastogenesis and decreased osteoblastogenesis. The other plausible explanations are altered “serum adipokines”, increased Leptin and decreased adiponectin levels which could both directly and indirectly affect bone metabolism in overweight patient.

Conflict of interest

All of contributing the authors declares that there is no conflict of interest.

Figure list

Fig 1: list of selected articles

	Authors	Title	Journal	Reference	Year
1.	Monteiro JLGC, Pellizzer EP, Araújo Lemos CA, deMoraes SLD, do Egito	Is there an association between overweight/obesity and dental implant complications?	Int J Oral Maxillofac Surgery	Sep;48(9):1241-1249 doi:10.1016/j.ijom.2019.01.015	2019

	Vasconcelos BC. (5)	A systematic review and meta-analysis.			
2.	Sales-Peres SHC, Groppo FC, Bonato RCS, Sales-Peres MC, Haiter-Neto F, Chaim EA. (2)	ALVEOLAR BONE PATTERN AND SALIVARY LEPTIN LEVELS AMONG PREMENOPAUSAL OBESE WOMEN.	Arq Bras Cir Dig.	Feb 7;32(1):e1422. doi: 10.1590/0102-672020180001e1422.	2019
3.	Alkhudhairy F, Vohra F, Al-Kheraif AA, Akram Z. (6)	Comparison of clinical and radiographic peri-implant parameters among obese and non-obese patients: A 5-year study.	Clin Implant Dent Relat Research.	Oct;20(5):756-762. doi: 10.1111/cid.12633.	2018
4.	Al-Hamoudi N, Abduljabbar T, Mirza S, Al-Sowygh ZH, Vohra F, Javed F, Akram Z. (8)	Non-surgical periodontal therapy reduces salivary adipocytokines in chronic periodontitis patients with and without obesity.	J Investig Clin Dentistry.	May;9 (2):e12314. doi: 10.1111/jicd.12314	2018
5.	Vohra F, Alkhudhairy F, Al-Kheraif AA, Akram Z, Javed F. (9)	Peri-implant parameters and C-reactive protein levels among patients with different obesity levels.	Clin Implant Dent Relat Resesearch	Apr;20(2):130-136. doi: 10.1111/cid.12556.	2018
6.	Eaimworawuthikul S, Thiennimitr P, Chattipakorn N, Chattipakorn SC. (7)	Diet-induced obesity, gut microbiota and bone, including alveolar bone loss.	Arch Oral Biology.	Jun;78:65-81. doi: 10.1016/j.archoralbio.2017.02.009.	2017
7.	Pradeep AR, Nagpal K, Karvekar S, Patnaik K. (3)	Levels of lipocalin-2 in crevicular fluid and tear fluid in chronic periodontitis and obesity subjects.	J Investig Clin Dentistry.	Nov;7(4):376-382. doi: 10.1111/jicd.12165.	2016
8.	Abduljabbar T, Al-Sahaly F, Kellesarian SV, Kellesarian TV, Al-Anazi M, Al-Khathami M, Javed F, Vohra F.(10)	Comparison of peri-implant clinical and radiographic inflammatory parameters and whole salivary destructive inflammatory cytokine profile among obese and non-obese men.	Cytokine.	Dec;88:51-56.	2016
9.	Renvert S, Persson RE, Persson GR.(11)	Tooth loss and periodontitis in older individuals: results from the Swedish National Study on Aging and Care.	J Periodontology.	Aug;84(8):1134-44. doi: 10.1902/jop.2012.120378	2013
10.	Gorman A, Kaye EK, Apovian C, Fung TT, Nunn M, Garcia RI.(12)	Overweight and obesity predict time to periodontal disease progression in men.	J Clin Periodontology	Feb;39(2):107-14. doi: 10.1111/j.1600-051X.2011.01824.x	2012
11.	de Moura-Grec PG, Marsicano JA, Rodrigues LM, de Carvalho Sales-Peres SH.(13)	Alveolar bone loss and periodontal status in a bariatric patient: a brief review and case report.	Eur J Gastroenterol Hepatology.	Jan;24(1):84-9. doi: 10.1097/MEG.0b013e32834bebb3	2012
12.	Modéer T, Blomberg C, Wondimu B, Lindberg TY, Marcus C.(14)	Association between obesity and periodontal risk indicators in adolescents.	Int Journal Pediatr Obes.	Jun;6(2-2):e264-70. doi: 10.3109/17477166.2010.495779.	2011

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