REVIEW

Residual ridge resorption – a review of etiology

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ABSTRACT

Residual ridge (RR) is a term used for the clinical alveolar ridge after healing of bone and soft tissues following tooth extraction. The residual ridge undergoes resorption, which is most rapid during the first six months; thereafter, the bone resorption continues throughout life at a slower rate, resulting in the removal of a large amount of the jaw structure. This unique phenomenon has been described as the residual ridge resorption (RRR). RRR has major nutritional, aesthetic, anatomic, functional and prosthetic implications. However, the etiology of residual ridge resorption is still not fully understood. Possibly, certain cytokines and genetic differences between individuals affect RRR process. Several studies have strongly pointed at a correlation between genes affecting healing of the periodontium and resorption of the residual ridge. Single nucleotide polymorphism studies on genes associated with the alveolar bone health may explain the etiology, define the risk and provide novel targets for personalized management of the disease. Further studies need to be undertaken to uncover the genetic susceptibility of edentulous patients to accelerated RRR. This article reviews the factors affecting the RRR.

KEYWORDS: Edentulism, residual ridge, residual ridge resorption, DNA polymorphisms in RRR

Citation: Gupta S et al. Residual ridge resorption – a review of etiology. Polymorphism 2019;2:107-113.

INTRODUCTION

Residual ridge (RR) is a term used for the clinical alveolar ridge after healing of bone and soft tissues, following tooth extraction. Post tooth extraction, the residual ridge alveolar bone undergoes a lifelong catabolic remodeling and consequently, the size of the residual ridge is reduced (Neufeld, 1958). The process is most rapid during the first six months, thereafter the bone resorption activity of the residual ridge continues throughout life at a slower rate, resulting in removal of a large amount of jaw structure (Hummel et al. 2002; Redford et al. 1996; Kapur et al. 1999; WHO Global Oral Health Data Bank & WHO Oral Health Country/Area Profile Programme, 2000; Atwood, 1971; Xie, 1997). This unique phenomenon has been described as residual ridge resorption (RRR). This bone resorption compromises the complete dentures-bearing area, making it difficult to produce prosthesis with good stability and retention (Atwood, 1971), as the function of removable prostheses relies greatly on the quantity and architecture of jaw bones. Poorly functioning complete dentures prosthesis would not fulfill its role in mastication or aesthetics, causing great discomfort to the patient (Eric J, TihacekSojic L, Bjelovic L, Tsakos G, 2017). Further, the dentist would have to frequently remake dentures for a patient with aggressive RRR, having obvious implications.

However, the etiology of residual ridge resorption is still not fully understood. Its extent and severity has been attributed to multiple aggravating systemic and oral factors. Systemic problems such as osteoporosis, hyperparathyroidism, dietary intake, hormonal imbalances, and local factors such as mechanical stress and tobacco consumption, (Pietrokovski, 2013) have been reported to play significant roles in the resorptive process. This elucidation however, has not led to predictable clinical results. Residual ridge resorption (RRR) has major nutritional, aesthetic, anatomic, functional and prosthetic implications (Klemetti, 1996). RRR has been reported till now to be a chronic, progressive and cumulative multifactorial disease. The extent of RRR differs across individuals and populations. Its etiology and variability are not fully understood. However, marked differences in bone response have been seen despite equalization of the above factors. Possibly, certain genetic differences between individuals modify their RRR response (Atwood, 1957).

Several investigators reported a possible link between periodontitis, osteoporosis and severe RRR (Wactawski-Wende et al., 1996; Daniel, 1983; Kribbs, 1990; Wactawski-Wende2001). These studies strongly point at a correlation between genes affecting healing of the periodontium and resorption of the residual ridge. However, very few studies have shown the impact of genetic variations on residual alveolar bone health. (Nishimura and Garret; 2004, Song and Lee; 2014, Kim et al; 2012, Peak J, Oh Y, Kim J, Lee JH; 2015, Emam et al.; 2019). This brief review aims to put together some important factors contributing to the etiology of RRR and the consequent implications.

Bone metabolism and RRR

It is postulated that RRR varies with the quantity and quality of the bone of the residual ridges. The quantum and rate of resorption is dependent on the bone density of the ridge, i.e., the denser the bone the slower will be the rate of resorption. Hence efforts are needed to maintain the density of jawbone post-extraction. Jawbone has its own specific metabolism and undergoes continuous changes. At no time during life is the bone static, as it undergoes constant rebuilding, resorption and remodeling, subject to functional and metabolic stresses (Neufeld, 1958). To accomplish these functions, bone resorption is carried out by osteoclasts and bone formation by osteoblasts. In equilibrium the two antagonistic actions (of osteoblasts and osteoclasts) are in a balance. During the growth phase, the bone anabolic

activity exceeds catabolic activity while during the maximum period of adult life; the two activities are in equilibrium. However, during old age, the bone catabolic activity exceeds anabolic activity. Alveolar bone loss has been associated with age-related macular degeneration (AMD), especially in men (Karesvuo et al., 2013). AMD was in turn associated with systolic blood pressure and diabetes, and patients with AMD had fewer teeth and more alveolar bone loss (Karesvuo et al., 2013). On the other hand, in women teeth extracted early in life during the rapid phase of bone metabolism were less susceptible to loss of alveolar height, than individuals losing teeth in middle or old age (Klemetti, 1995). It has been reported that the resorption of residual ridge is enhanced by the tenure of edentulousness, wearing of dentures, tobacco use and some other metabolic factors (Pietrokovski, 2013). Multivariable regression analysis showed that patients using tobacco or having diabetes were significantly associated with moderate to severe bone loss (Chatzopoulos et al., 2018).

RRR and osteoporosis

Osteoporosis is a common bone disease involving gradual loss of mineral content and mass of the bones and has been widely studied in the vertebra, femur, and radius, which are prone to spontaneous fractures. Osteoporosis is characterized by reduction of bone mass and the micro-architectural deterioration of bone tissue leading to enhanced bone fragility, with consequent increase in fracture risk. (Wactawski-Wende et al., 1996). According to the clinical and pathophysiologic views, osteoporosis may be classified as Type I and II osteoporosis. Type I osteoporosis is defined as the specific consequence of post-menopausal estrogen deprivation, and characteristically presents bone mass loss mainly in the trabecular bone. On the other hand, type II osteoporosis reflects a composite of age related changes in intestinal, renal and hormonal functions, affecting both cortical and trabecular bones. Pathologic fractures also occur in the mandible and it is conceived that osteoporosis can also affect resorption rates of the mandible to the point of pathologic fracture (Sones et al., 1986). The extent of RRR is proportional to the time lapsed after teeth have been extracted as well as the age of the patient. The maxillary residual ridge has been reported to be significantly smaller in postmenopausal osteoporotic women while their edentulous mandible remained the same as age related controls (Kribbs, 1990). Studies have exhibited that postmenopausal women with lower bone densitometric scores show a tendency to a knife-edged lower alveolar ridge. (Nishimura et al, 1992). This may occur in combination with a small maxillary ridge which may be a disadvantage to successful rehabilitation using a conventional removable prosthesis.

Although resorption constantly takes place in the remodeling of bones as they grow, increased osteoblastic activity makes up for the bone destruction. Since osteoblasts are hypoactive in osteoporosis, increased osteoblastic activity is unable to keep up with the increased osteoclastic activity. The normal equilibrium may be upset and pathologic bone loss can occur, if bone resorption is increased and/or bone formation is decreased. Osteoclastic activity occurs primarily on the surface of the residual ridge and hence there is a three-dimensional change in the shape of the ridge. When bone resorption occurs at the labial and lingual surfaces of the residual ridge in, preference to the occlusal surface it results in a knife-edged ridge (Klemetti, 1995). Hence in geriatric edentulous patients, type I and type II osteoporosis may contribute significantly to RRR. Since bone metabolism is dependent on cell metabolism, anything that influences cell metabolism of osteoblasts and osteoclasts is important.

Osteoclasts are the bone-resorbing cells and their formation is coordinated by the interplay of receptor activator of nuclear factor-κB ligand (RANKL) and osteoprotegerin (OPG) (Suda et al.

1999). RANKL binds directly to RANK on the surface of pre-osteoclasts and osteoclasts, stimulating both the differentiation of osteoclast progenitors and the activity of mature osteoclasts. On the other hand, OPG is a soluble molecule and a naturally occurring inhibitor of osteoclast differentiation. OPG binds to RANKL with high affinity and prevents RANKL from interacting with RANK (Lacey et al. 1998). As RANKL and OPG are believed to be key factors regulating bone metabolism, it is to be expected that they are also involved in bone destruction in edentulous patients (Nicu et al., 2012). It has been reported that dietary supplementation with Calcium and Phosphorous after tooth extraction can retard RRR. However, the effect of topical medication, especially with Ayurveda/herbal preparations, has not been reported.

Role of inflammatory mediators in RRR

Periodontal pathogens persist in the oral cavity of edentulous subjects who have had periodontal disease, even after the extraction of all teeth and in the absence of other hard surfaces in the mouth (Fernandes et al., 2012). Periodontitis is a chronic bacterial infection that affects the gingival and the bone supporting the teeth. The host inflammatory response stimulated by bacterial plaque leads to tissue damage and bone resorption. Osteoimmunology is a major area of research interest. Researchers have tried to explain the mechanism of host immune response involving cytokines and bone biology. The bone loss ranges from small resorption area due to periodontitis affecting a single site of the tooth, to large resorption area involving several or all teeth. A few serum factors have been correlated with periodontitis. Serum calcium (Amarasena et al., 2008), IL-17 (Duarte et al., 2010), IL-6 (Guentschetal et al., 2009; Marcaccini et al., 2009; Nakajima et al., 2010; Raunio et al., 2007; Renvert et al., 2009), TNF-α (Duarte et al., 2010; Nakajima et al., 2010), MMP -3, -8, -9 (Marcaccini et al., 2009; Passoja et al., 2008), cortisol (Ishishaka et al., 2008) and osteocalcin (Yoshihara et al., 2009) have been correlated with inflammation associated with periodontitis, but their correlation with jaw bone resorption is poorly understood.

The relationship between clinical parameters and concentrations of the proinflammatory cytokine IL-6 and the anti-inflammatory cytokine IL-10 in the saliva of totally edentulous patients with overdentures indicated that IL-6 and IL-10 could be together used as markers of periodontitis, and that their levels gives additional information about the potency of an organism's integrated immune response for maintenance of inflammatory balance (Liskmann et al., 2006). Some other inflammatory mediators, mainly prostaglandins, have also been regarded as key players in increasing the rate of RRR using animal studies (Nishimura et al., 1988). However, the direct cause-effect direct relationship between prostaglandin-mediated bone resorption and resorption of the residual ridge has not been successfully demonstrated (Devlin & Ferguson, 1991). The inflammatory markers of RRR are poorly defined and mechanisms governing this process are far from been understood completely. Thus there is a need to identify the cytokine signalling factors that trigger the process post tooth extraction, with a view to identifying novel interventions to prevent/delay the RRR process.

Genetic influences on RRR

The alveolar ridge receives mechanical load continuously from the periodontal ligament connected to the teeth and it diminishes dramatically as a consequence of dental extraction; thus it is believed that the continuing pattern of alveolar bone resorption is related to this change. The reduced partial pressure of oxygen is the most prominent event from the reduced mechanical load. Vascular Endothelial Growth Factor (VEGF), regulated by hypoxia

inducible factor-1 (HIF-1) is reported to have a close association with angiogenesis and bone turn over, where partial oxygen pressure has changed. The regulatory network of activation and suppression of RRR is known, with IL-6 stimulating the bone resorption process and IL-10 opposing the resorption. Similarly, RANKL and PTH are known to participate in bone resorption, while osteoprotegerin and calcitonin (acting via calcitonin receptor) oppose bone resorption. Genetic variations in these regulatory elements may significantly affect jawbone health by affecting the rate of bone remodeling. One base pair in every 100 to 300 base pairs of the genome sequence varies among humans, suggesting that genetic diagnosis using the single nucleotide polymorphisms (SNPs) may provide a novel opportunity to differentiate edentulous patients(Nishimura and Garret, 2004) and predict their susceptibility to RRR. Studies looking into the impact of genetic variations on jawbone health are particularly lacking, and a thorough literature search identified few studies that tested the association between genetic variations and RRR. Song and Lee (2014) investigated the association between SNPs in vascular endothelial growth factor and RRR in 120 subjects with the edentulous mandible in the Korean population. The study reported a notable association of rs1570360 and haplotype A-C-C with RRR. The investigators claim it as a novel genetic marker for identifying people susceptible to severe RRR after dental extraction.

Another study identified that edentulous patients with the minor allele of ss518063493 in FGFR1OP2/wit3.0 gene may be associated with excessive atrophy of edentulous mandible whereas patients with rs840869 in FGFR1OP2/wit3.0 gene were not associated with excessive atrophy in the Korean population (Kim et al., 2012). Another genetic association study between single nucleotide polymorphisms of the HIF-1α gene and RRR of the edentulous mandible in Korean population showed a positive association. (Peak J, Oh Y, Kim J, Lee JH, 2015). A genetic association study between single nucleotide polymorphisms of matrix metalloproteinase-1 (MMP-1) gene promoter and RRR of edentulous mandible reported a significant positive correlation (Sundar et al., 2015). Similarly, genetic variation due to SNP in the hypoxia inducible factor-1α (HIF-1α) gene was found to be significantly associated with severe form of mandibular ridge resorption in edentulous patients (Emam et al., 2019). It could be exciting to investigate the relationship of genetic variations in key genes controlling the process of bone remodeling so as to identify genetic markers that affect the rate of RRR.

The Indian Perspective

In economically weak, aged edentulous patients, RRR is a major cause of morbidity. The frequent redoing of prostheses due to RRR adds significantly to their economic distress. It has been established that RRR rate varies significantly between different subjects and among the several causes for this disparity, genetic and biochemical factors may be majorly implicated. In highly populated developing countries like India, the population of elderly people above 60 years constitutes >8%. They have multifactorial causes of oral health morbidity. An estimated 80% of the elderly reside in rural India, out of which ~40% are economically weak and nearly 73% are illiterate (Shah, 2001). A cross-sectional study undertaken on geriatric patients (60 years and above) indicated that the prevalence of edentulism was as high as 75%, with a substantial gender difference (69% in men and 81% in women). Only 10% of the subjects had all natural teeth, while 80% wore removable dentures. The remaining 10% had neither natural teeth nor prostheses. Amongst these, 50% percent of the subjects needed a repeat prosthesis, 60% needed extractions and 25% required conservative treatment (Chhabra et al., 2013). Poor oral health was mainly due to lack of awareness, neglected care, and economic barriers. Hence RRR is a major national health issue that needs to be redressed.

Discussion

Residual ridge resorption is a prevalent and debilitating problem for edentulous patients and is chronic, progressive, cumulative multifactorial disease. Various systemic and oral factors attribute to the severity of the problem (Xie, 1997). Though the etiology of this problem is not fully understood, it has been documented that the extent of RRR differs across individuals and populations. Some of the significant players in the alveolar bone loss could be metabolic/systemic diseases like osteoporosis, inflammation, hyperparathyroidism, diabetes, malnutrition, hormonal imbalances, along with genetic and some local factors, such as mechanical stress and tobacco consumption (Pietrokovski, 2013). A critical balance between bone catabolism by osteoclasts and bone anabolism by osteoblasts maintains the alveolar ridge, which gets disturbed by age-related metabolic disturbances in the bone such as diabetes (Klemetti, 1995). Geriatric edentulous patients with type I and type II osteoporosis, have a greater tendency for RRR due to osteoclastic activity on the surface of their residual ridge, causing knife-edged ridges (Wactawski-Wende et al., 1996).

On the other hand, periodontitis associated inflammation with increased production of pro-inflammatory cytokines and prostaglandins is suspected to enhance the ridge resorption rate (Nishimura et al., 1988). Recently, genetic causes of RRR have gained the attention of clinicians and researchers. It is well known that one base pair in every 100 to 300 base pairs of the genome sequence varies among humans, suggesting that genetic diagnosis using single nucleotide polymorphisms (SNPs) may provide a novel opportunity to differentiate edentulous patients and predict their susceptibility to RRR (Nishimura and Garret, 2004). Limited genetic studies have indicated the association of genetic variation in FGFR1OP2/wit3.0, MMP-1 and HIF-1α genes with severe RRR (Nishimura and Garret; 2004, Song and Lee; 2014, Kim et al; 2012, Peak J, Oh Y, Kim J, Lee JH; 2015, Emam et al.; 2019). Since RRR has major aesthetic, anatomic, functional and prosthetic implications its management becomes important (Klemetti, 1996).

Conclusion

Hence, RRR is a multifactorial problem that may cause great morbidity in aged, edentulous patients; and requires due management. Genetic single nucleotide polymorphism studies critically associated with alveolar bone health may provide novel targets for personalized management of the disease. Further studies need to be undertaken to uncover the genetic susceptibility of edentulous patients for better management of RRR.

Acknowledgments

Samiksha Gupta is thankful to the Indian Council of Medical Research (ICMR), New Delhi for the grant of Senior Research Fellowship (3/1/2(25)/Oral/14/NCD-II).

Conflict of interest

The authors declare no competing or conflict of interest.

Authors' contributions

SG, SVS, and DA extensively reviewed the subject, collected relevant literature and wrote the manuscript. SVS edited the manuscript.

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