DOI: 10.22270/jmpas.V10I6.1524 ISSN NO. 2320–7418

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Review article

Genetic association of Hypoxia Inducible Factor (HIF) – 1 alpha gene and Residual Ridge Resorption of Jaw Bone

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ABSTRACT

Due to considerable alterations in individual bone structure, the residual ridge is constantly under the stress of bone resorption. In certain circumstances, this can cause disproportionate bone deterioration, making restorative dental management difficult. This inimitable curative procedure in the oral cavity is affected by specific factors in the oral tissue. A variety of HIFs are expressed during the healing of oral wounds in comparison to skin wounds. The target of this review article was to look at a cistron tic connotation among SNP of the HIF-1 α gene that is understood to own great genetic diversity, and also the residual ridge reabsorption (RRR). Hence, this review concentrates on the association and genetic basis of HIF α gene in residual ridge resorption.

Keywords: HIF-1, Single Nucleotide Polymorphisms, Residual Ridge Resorption.

Received – 21/07/2021, Reviewed - 10/09/2021, Revised/ Accepted- 06/11/2021

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INTRODUCTION

The extraction of a tooth is one of the most common dental treatments. Following a tooth extraction, the residual ridge continues the process of bone resorption due to abridged mechanical filling and the lack of dental ligaments. (1). The destroyed tissue integrity is restored within the first week, active bone formation begins, and the freshly formed bone gradually fills the socket over the next six months. Alternatively, the remaining ridge alveolar bone undergoes catabolic remodeling after six months, though it is most rapid in the first two months and slows down over time. (2).

The pathophysiology of residual ridge resorption is incompletely defined. The magnitude of decrease is associated of a mix of structural, physiological, and mechanical factors. During tooth extraction wound healing, the residual ridge is mostly made up of distinct oral soft tissues and alveolar bone, which can deteriorate if problems with cavity matrix production or cellular activity occur.(3). As a consequence, RRR can be caused by genetic regulatory factors that disturb the feature and measure of bone by modifying the genetic pattern. A pulled tooth may cause tissue hypoxia when damaged blood vessels, blood flow, and oxygen pressure in the surrounding area are reduced when blood vessels in the extraction socket are damaged.(4, 5). The homeostasis of oxygen in cells and in the body is largely controlled by the oxygen-inducible factor-1, or HIF-1.

It is a critical mediator of oxygen-dependent genes and some of the genes that HIF-1 targets are well defined.(6). In dentistry, residual ridge (RR) refers to the clinical alveolar ridge even after the healing of the bone and tissues around the tooth has been achieved. During the first six months, resorption of the enduring ridge is speedy; afterwards, the bone resorption endures at a slower rate for the rest of the person's lifespan, causing in the loss of a great measure of the jaw construction. Atrophic residual ridges have always been an obstacle for a successful prosthodontics treatment. (7). this distinctive phenomenon has been defined as the residual ridge resorption (RRR). RR has major nutritional, aesthetic, anatomic, functional and prosthetic implications.

Genetic factors were recognized recently since single nucleotide polymorphisms (SNPs) in genes involved in RRR have been identified in patients who have the condition. Researchers have found a strong correlation between genes affecting periodontal healing and the loss of residual ridges. The studies of SNPs in genes associated with alveolar bone health may provide useful information about its etiology, define the risk and offer new targets for treating the illness. (8-9). Research suggests that a very small number of studies have addressed genetic factors implicated in inter-individual differences in RRR development. (10).

Genetic association of residual ridge resorption

Numerous efforts were made to learn more about the patho physiology of resorption of thecontinuous residual ridge, but still no n oteworthy results were found.

The quantifiable comparison of the persistent residual bridgeresorption, on the other hand,reveals significant variabilityamo ng people under similar conditions, implying a possible genetic link. It is reinforced by massive literature evidence that genetic factors are highly associated with periodontitis, osteoporosis, and residual ridge resorption. However, the role of genes is essentially discussed in all the above studies. [(11)]. It is necessary to explore the genetic factors affecting ridge resorption, so as to determine whether this may be intervened with the function of genes in causing resorptive alterations is complicated and fascinating. Although numerous genes are implicated in producing pathological variations in residual ridge resorption, a substantial amount of study is still required to identify genes involved in developing and leading to progressive alterations. Almost every illness in humans is impacted explicitly or implicitly by genetic variability, which confers vulnerability, tolerance, or communication with ecological variables.[(12)].

A single nucleotide polymorphism (SNP) occurs when an alternative base happens in aninhabitant at an incidence larger than 1%. In a study on 120 Korean patients with edentulous mandibles, Song and Lee investigated the relationship between rs1570360 and haplotype A-C-C and residual ridge resorption (RRR)[(13)]. The investigations indicate it as a novel genetic marker for identifying people at risk of austere RRR following tooth extraction. Furthermore, Al Sheikh et al. discovered both a relationship among SNPs in the IL10 and NOD2 genes, and also that the genotypes of the various SNPs influence health and bone resorption in a study. [(14)]. Discovering SNPs in susceptible genes would thus not only help us to get an enhanced information of disease progressions and their associated consequences, but it would also pave the way for more effective RRR therapeutic opportunities.

The significant genes

Few studies have looked at SNPs in diverse genes, such as cytokine and growth factor genes, fibroblast growth factor receptor (FGFR1), matrix metallo proteinases (MMPs), and hypoxia-inducible factor-1 (HIF-1), in order to uncover the involvement of genetic variables in the progression of RRR. SNPs in the matrix metalloproteinase-1 (MMP-1) gene promoter and RRR in the edentulous jaw were identified by Sundar et al.[(12)].

HIF alpha gene SNP in residual ridge resorption

It is thought that the Hypoxia-Inducible Factor (HIF)-1 protein complex shows a significant role in the body's response to low oxygen levels, also known as hypoxia. In hypoxic areas, such as localized ischemia and tumors, HIF-1 is an important gene for homeostasis, which promotes vascularization. As a transcription factor, HIF-1 acts on hundreds of target genes. In addition, it plays a role in immune responses, as well as homeostasis, vascularization, and anaerobic metabolism. HIF-1 contains of α and β subunits. The alpha subunit, which controls HIF-1 activity, is controlled by oxygen tension.

Because the HIF-1 gene is important for managing oral wounds after tooth extraction and has a lot of genetic variability, mutual SNPs in HIF-1 might have a role in the entry of severely resorbed mandibular ridges. SNP 1772C>T is one of the two common HIF-1α mutations (1772C>T and 1790G>A). It is a coding SNP that results in an amino acid change from proline 582 to serine in the HIF-1 gene's ODD domain of exon 12. Researchers study this SNP extensively in an attempt to find out whether it is associated with cancer, ischemic heart disease, osteonecrosis, chronic obstructive pulmonary disease, and diabetes and how it affects the performance of elite athletes in power-oriented sports. RRR occurs at different rates in different people as a result of wound healing after tooth extraction. Relative hypoxia is a key factor in wound healing success. In hypoxic conditions, HIF-1 is shielded from degradation and activates a series of genes that allow cells to adapt to hypoxia. As a result, coding SNPs in the HIF-1 gene may change the hypoxia responsiveness of various cells, resulting in a distinct wound healing phase after tooth extraction. This might result in an accentuated RRR pattern. According to Peak et al, an SNP at 1790G>A (rs11549467) can be utilized as a marker to predict the prognosis of the alveolar ridge after tooth extraction. [(15)].As a result, a suitable treatment approach may be devised, with unnecessary spending avoided. 1772C>T (rs11549465) was discovered to be a predictor for future residual alveolar ridge condition in an Egyptian research. [(16)].

CONCLUSION

Disease-induced bone loss, dental decay, and defects are becoming a worldwide concern with a high incidence, negatively impacting the fitness and advantage of life of the entire population. In many cases, it's better to intervene in the disease rather than remove its cause from the gene. It is important that dentists recognize the clinical characteristics of these rare conditions early on since they are the first people to identify them. HIF-1 functions, target genes, and activation pathways are being better understood, enabling the development of novel treatments for diseases like residual ridge resorption. In spite of the gray areas in the understanding of HIF-1, it remains a highly priority target for drug development. There is promising evidence that modulating the HIF-1 pathway could have a significant impact on treatment, impacting millions of people who suffer from such diseases.

CONFLICTS OF INTEREST - There are no conflicts of interest.

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How to cite this article

Mahendirakumar Nagarajan, Vijitha D, Sriram Kaliamoorthy, Paranthaman Srinivasan, 2021. HIF-1, Single Nucleotide Polymorphisms, Residual Ridge Resorption. Jour. of Med. P'ceutical & Allied. Sci. V 10 - I 6, 1524, P- 3831-3833. doi: 10.22270/jmpas.V10I6.1524