



RESEARCH ARTICLE

TERIPARATIDE - THE FUTURE OF HOST MODULATION AND PERIODONTAL REGENERATION? A SHORT REVIEW

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Abstract

Periodontal disease is multifactorial and infectious, and can lead to loss of the dentition. Multiple treatment modalities have been used and experimented upon over several years. The main objective of periodontal therapy is to arrest the bone loss and help in its regeneration. Teriparatide is a type of recombinant human parathyroid hormone, which can aid in alveolar bone regeneration in treating periodontal conditions. This review discusses the mechanism and applications of teriparatide in periodontics and its potential use in host modulation and periodontal regeneration.

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Introduction:-

Periodontitis is a complex condition that results in tooth loss. It has a complicated etiology that involves a vulnerable host and a bacterial assault. To treat periodontitis, a number of medicines have been utilised as an adjuvant to non-surgical periodontal therapy. As more is discovered about the significance of the host response, novel techniques for periodontal disease management are emerging. Our growing understanding of inflammation and how to manage it, has opened up various avenues for researchers to investigate new periodontal therapy options. The activation of the host's immuno-inflammatory response to the bacterial onslaught is the primary cause of soft and hard tissue deterioration in periodontal disease. The expression of endothelial host-derived inflammatory mediators such as cytokines and lipids by neutrophils, monocytes, lymphocytes, and fibroblasts characterises the underlying molecular mechanisms of this reaction. Periodontal disease is characterised by increased amounts of MMPs, cytokines, and prostanooids in the periodontal tissue, according to Page et al. in 1999. (1) The goal of host modulation therapy is to re-establish the appropriate balance of pro-inflammatory or destructive mediators and anti-inflammatory or protective mediators.

History And Background:-

Various pharmacological drugs have been explored for their potential functions as host modulators in the therapy of periodontal disease throughout the last two decades. Antiproteinases (represented by tetracyclines), anti-inflammatory medications (non-steroidal anti-inflammatory drugs, statins, omega 3 fatty acids), and bone-sparing therapies are the three types of host-modulating agents studied in periodontal therapy (which are represented by antiresorptive agents such as bisphosphonates). A fourth group, dubbed as "bone-forming medicines," have recently been proposed, which includes teriparatide. Teriparatide, often known as rPTH (recombinant human parathyroid hormone), is a biosynthetic human parathyroid hormone made up of the first 34 amino acids. (2)

The anabolic effects of parathyroid hormone on bone have been known since the early 1900s. Interest in its clinical application for bone regeneration in localised osseous defects and fractures has recently gained acceleration. PTH's

impact on bone growth and remodelling in the craniofacial region has been demonstrated in animal models and gene ablation models, providing a solid basis for its usage in oral and maxillofacial bone regeneration. Teriparatide has shown promise in preliminary clinical investigations for periodontal regeneration and the therapy of osteonecrosis of the jaw caused by bone antiresorptive medications.(3)

Mechanism Of Action:

Teriparatide and PTH exert their biological effects through high-affinity membrane cell-surface receptors that are G-protein dependent. Both osteoblasts and renal tubular cells produce these receptors, and both compounds bind to them with the same affinity and have identical physiological effects on bone and kidney. Binding of ligand activates protein kinase-1, cyclic adenosine monophosphate, protein kinase-C, and phospholipase-C, resulting in an increase in the number of active osteoblasts, a decrease in osteoblast apoptosis, and most likely, recruitment of bone lining cells as newly formed osteoblasts, thereby increasing bone strength, mass, and diameter, as well as serum and urinary levels of bone formation and resorption markers.(2)

Teriparatide In Periodontal Regeneration:

Jung et al. in 2007(3) analysed the effect of matrix bound parathyroid hormone on bone regeneration and found significant new bone formation but there was no more bone to implant contact. In a study conducted by Moore et al.(4) to evaluate the osteogenic potential of Teriparatide on various parts of human skeleton, mandible was found to have maximum activity rate. Bashutski et al. (5) evaluated the effect of Teriparatide on periodontal regeneration in patients with severe periodontitis. They used 20µg dose along with calcium and vitamin D supplement daily for six weeks and found significant improvement in clinical and radiographic outcomes. Similarly, Yun et al. (6) administered PTH systemically in a rat model and found stimulated local bone formation, whereas a local delivery of PTH by using β -tricalcium phosphate was not as much effective like systemic delivered PTH. Valderrama et al. evaluated role of parathyroid hormone bound to a synthetic matrix in guided bone regeneration around dental implants placed in dog's mandible and found that covalently bound PTH to a synthetic, RGD (arginine-glycine-aspartic acid) -modified Poly Ethylene Glycol hydrogel marginally results into improved bone formation at 2 weeks of healing compared to the use of PEG alone. Kuchler et al. investigated the effects of teriparatide on the osseointegration of titanium implants in 24 individuals and reported higher median values of NBV/TV (new bone-volume-per-tissue-volume (NBV/TV) and NBIC (new bone-to-implant-contact) in teriparatide groups in comparison to control group. This was the first histological data on the osseointegration of titanium study implants in individuals treated with teriparatide. In another case report, Bashutski et al.(7) studied the effect of teriparatide on periodontal bone regeneration. They administered teriparatide in conjunction with traditional open-flap debridement surgery and found that teriparatide offers potential for the regeneration of bone in severe intrabony defects resulting from chronic periodontitis. In a recent clinical trial, Takedachi et al.(8) discussed about the present status of periodontal regeneration and concluded that FGF-2 and teriparatide both has stimulatory effect on bone regeneration and may be helpful in future.

Discussion:-

The primary goal of using teriparatide for craniofacial defects or periodontal regeneration is to enhance healing. So, in such a condition the timing for the application of teriparatide in relation to the stages of bone healing becomes critical. A current concept in the mechanism of teriparatide action is related to its effect to stimulate processes associated with bone formation before it stimulates processes associated with bone resorption. This sequence of events has led to the concept of the anabolic window; the period of time when teriparatide is maximally anabolic. Optimal duration for teriparatide therapy needs further exploration. The most reasonable answer to this is probably not beyond six months because the normal bone healing time range is around six months. However, the treatment time should be short to minimize the adverse effects like hypophosphatemia, hypercalcemia or more extent to osteosarcoma. In some clinical studies the duration ranged from 4 to 8 weeks. Next future requisite is to standardize the form of application of teriparatide in periodontal regeneration. The drug delivery mode should be non-invasive, reliable, easy to use and comfortable to both patients as well as to the operator. (9) Although, Wei et al. and Liu et al. have tried to develop local delivery form of teriparatide and found positive results too, but in contrast, Yun et al. did not find local delivery form as superior like systemic form. Therefore, more clinical studies are required to formulate a more effective form of teriparatide which is non-invasive as well as cost effective too. So, for periodontal regeneration there is a clear need for improved therapeutics which can target localized osseous healing as desired. (10)

Conclusion:-

With the introduction of teriparatide i.e., an anabolic drug in a periodontist's armoury, a new door of periodontal regeneration has been opened. Its use as an adjunct to traditional gold standard non-surgical periodontal therapy seems to be a novel therapeutic approach. There are numerous concerns about the safety, efficacy, optimal dosage and drug delivery approaches, hence large-scale clinical studies are required to eliminate such concerns and to facilitate the use of Teriparatide in periodontal regeneration.

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