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BIOMARKERS AS A DIAGNOSTIC TOOL FOR PERI-IMPLANTITIS- A NEW PARADIGM REVIEW

Dental Science

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ABSTRACT

Diagnosis of peri-implantitis is still dependent on use of conventional diagnostic parameters which mainly includes mobility, BOP, probing depth (PD), bone loss. Main drawback of above clinical diagnostic parameters is that they lack the sensitivity and specificity, sufficient enough for early diagnosis of peri-implant tissue destruction, thus proper management can't be initiated before considerable supporting bone is lost and it leads to failure of implant. This review was aimed to analyse various studies based on biomarkers present in peri-implant crevicular fluid (PICF) which are released following bone destruction and inflammation, can serve as specific and sensitive parameters for early detection of peri-implantitis, so that proper management can be initiated much before considerable peri-implant tissue destruction has occurred.

KEYWORDS

BOP, PD, PICE.

INTRODUCTION

Dental implants made of titanium have become an imperative tool in the field of dentistry, as a replacement for teeth missing due to several disparate clinical conditions apart from crown and bridges. Over a period of a decade, survival rates of 95-98% has been reported. This high survival rate has persuaded dental surgeons to explore this method of oral rehabilitation.[1] An increase in the number of reported evidences of peri-implant inflammation have been affecting both soft and hard tissues, ultimately leading to implant loss. Analogous to gingivitis and periodontitis affecting the periodontium of natural teeth, peri-implant mucositis and peri-implantitis are terms given for inflammation and destruction of soft and hard tissues around an implant respectively.[2] Clinical and radiographic parameters, such as, bleeding on probing, probing depth, mobility, suppuration and marginal bone loss, are the ones which are mostly assessed for the diagnosis of peri-implantitis. But the drawback with these diagnostic parameters is that they lack the sensitivity. Early diagnosis of peri-implant destruction, helps in monitoring bone loss progression which aids in proper management before considerable amount of the supporting bone is lost. Focusing on disease entities like enzymes and biomarkers present in peri-implant sulcus fluid (PISF) released following bone destruction and inflammation should be the area of interest. To get more detailed informations regarding the pathogenesis of peri-implant diseases more research primarily focusing on relationship between certain biomarkers with health/disease should be conducted.[3] The aim of this review is to explore the new vistas of diagnostic parameters that can aid in early detection of peri-implantitis even in asymptomatic cases so that prompt treatment can be provided as early as possible.

Definition and pathogenesis

A progressive and irreversible condition of the soft tissues and the loss of bone around the ossointegrated dental implants which usually bears masticatory load, decreased osseointegration, suppuration and formation of deep pockets is referred to as Peri-implantitis. Padial-Molina et al. described peri-implantitis as cases with probing depth > 6 mm and with bone loss of ≥ 2 mm which can be seen radiographically.[4]

In implantology the tissue reaction seen in case of inflammation are similar to those confronted in cases of gingivitis and periodontitis. The plaque formation pattern on implant and teeth does not have any differences. Neutrophils are the first cells that are seen in the peri-implant pocket as soon as the buildup of plaque begins.

This occurs due to release of chemotactic peptides produced by the bacteria present in the vicinity of implants and natural teeth alike. As the process of damage of the epithelial cells by the bacteria continues, they bring about the release of more cytokines which further leads to attraction of leucocytes to the crevice.

These leucocytes eventually phagocytose the bacteria, thus eliminating the bacteria from the pocket. But with this if the neutrophil becomes saturated with bacteria, it subsequently degranulate to release toxic enzymes and further cause tissue damage.[5]

The efficiency of neutrophils and epithelial cells to control the infection is hampered, if there is overload of microbial plaque. In such cases inflammation around peri-implant tissue occurs which is clinically diagnosed as peri-implant mucositis. When the inflammation spreads from the marginal gingival into supporting peri-implant tissues, it results in bone destruction and loss of bone attachment; a process termed as peri-implantitis.[6]

Etiology

Quantification of incidence rate of peri-implantitis in patients with history of peri-implantitis was done by Zitmann et al, he states chances of peri-implantitis is almost 6 times more than in patients which have no history of periodontitis.[7]

Spectrum of pathogenic micro-organisms which can be detected in peri-implantitis includes:

- Aggregatibacter actinomycetemcomitans
- Treponema denticola
- Tannerella forsythia
- Prevotella intermedi
- Prevotella nigrescens
- Porphyromonas gingivalis
- Streptococcus constellatus

Risk Factors[8]

- Smoking
- History of periodontitis
- Poor oral hygiene and lack of compliance.
- Systemic diseases
- Iatrogenic causes
- Poor quality soft tissue at site of implantation.
- History of implant failure.
- cigarette smoking
- Implant overloading
- Faulty material and techniques
- Poor bone quality at the implant site

Square thread design implants with more than 10mm length shows higher rate of success.[9] Also rough implant surfaces (>2 microns) shows better osseointegration than smooth (<0.5 microns) or moderate surfaces (1–2microns).[10]

Conventional Diagnostic Parameters

Pain

Evaluation of pain or discomfort in implant cases are done by percussing with force up to 500 gm. Until and unless the implant is mobile and surrounded by inflamed tissues, or has rigid fixation which impinges on nerve, pain doesn't occur from implant body. If pain occurs during function it is placed under failure category.[11]

Mobility

Numerous studies suggested that advanced stage of peri-implantitis in which there is total loss of direct bone to implant interface is indicated by implant mobility.[4,11,12]

Probing

Periodontal probing using light pressure. (.25 Ncm) is one of the foremost and reliable tool for diagnosis of Per-implant tissue inflammation and for monitoring its progress.

Bleeding on probing is a salient parameter that is suggestive of soft-tissue inflammation and micro-ulceration. Mucositis showed increase bleeding on probing at 67% sites while peri-implantitis showed increased bleeding on probing at 91% sites in an experimental study.[13]

Bone Loss

Intra-oral periapical radiographs and panoramic radiographs are recommended for peri-implantitis diagnosis.[4,12] However three-dimensional radiographs, aids in evaluating buccal and lingual/palatal bone walls along with mesial and distal ones.

Padial-Molina et al.[4] suggested the threshold of bone loss > 2 mm to diagnose peri-implantitis, while Misch et al.[14] suggested the threshold of > 4 mm.

New Paradigm

A biomarker is fundamentally an indicator of a biological state and it helps in differentiating normal and pathological processes3. In present scenario, researches are emphasizing on utilizing biomarkers as diagnostic tool as they can indicate disease presence much before considerable clinical damage has occurred. But, to establish this relationship much more research is needed to be done3. Saliva and gingival crevicular fluid/ peri-implant crevicular fluid (PICF) are the main sources from which biomarkers sample can be obtained. Non-invasive nature of obtaining samples and repeatability are the main advantages of utilizing biomarkers as a diagnostic tool.

Cytokines can be defined as soluble proteins that bind to specific receptors on target cells and initiate intracellular signaling cascades which via altered gene regulation results in phenotypic changes in cells. Effectiveness at low concentration and transient nature of production is characteristic feature of interleukins. Their induction mode can be either autocrine or paracrine in nature. The PICF levels of 13 different cytokines (IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-17, IFN-γ, PGE-2 and TNF-α) have been compared in different clinical peri-implant conditions. Majority of studies had targeted IL-1β and TNF-α as the potential diagnostic biomarkers. IL-β and TNF-α contributes in osteoclast formation and bone resorption. IL-1β exerts its effect mainly by regulating the degradation of plasminogen system extracellular matrix components and also modifying activity of collagenase in wound healing and inflammation. Reduction in the progression of tissue inflammation and tissue breakdown have been shown by inhibition of IL-1β.[15] TNF-α belongs to pro-inflammatory cytokine category which is secreted majorly by monocytes and macrophages. Its mechanism of action consists of collagenase secretion by fibroblasts, bone resorption by activation of osteoclasts, and has been also associated with periodontal tissue destruction in periodontitis.

MMPs belongs to endopeptidases group which has modifying actions on cell proliferation, differentiation, migration, apoptosis and is also responsible for degradation of various extracellular matrix proteins.[16] MMP-1, MMP-3, MMP-8, and MMP-13 are some of the important MMPs which were included in the studies assessing PICF in different peri-implantitis lesions. According to various studies, MMPs were reported to be positively correlated with clinical inflammatory conditions around implants.[16]

Myeloperoxidase (MPO) can be described as a leukocyte-derived anti-microbial enzyme found in primary granules of leukocytes in high concentrations. Reactive oxidant species formation gets catalyzed by MPO.[17] Studies have reported significantly higher amounts of MPO in PISF collected around peri-implantitis lesions.[18]

Elastase, an enzyme which is released from human leukocytes and contributes in the process of tissue damage during inflammation, has been found in significantly higher amounts in PISF around implants with peri-implantitis compared with healthy controls. Prostaglandin E2 (PGE2) a vasodilator increases vascular permeability at inflammation sites and also causes bone resorption. There is a study which reports that PGE2 showed positive correlations with gingival index and PD.[19]

Cathepsin-K, is a protease enzyme which is released after tissue injury and accelerates inflammatory process. Yamalik et al.[20] conducted a study in which he indicated that Cathepsin- K can be used as biomarker to assess peri-implantitis as there is a positive co-relation of Cathepsin – K with the volume of PISF peri- implant inflammatory lesion which has bone loss.

CONCLUSION

At present Peri-implantitis diagnostic parameters are mainly clinical and radiographical, but these parameters lack specificity and doesn't lead to early prompt diagnosis of Peri-Implantitis. Hence in most cases significant amount of damage has already occurred before diagnosis of Peri-implantitis is done. Inflammatory mediators present in PISF can assist in the early diagnosis of Peri-implant inflammatory conditions, so that prompt treatment can be started before extensive damage and alteration to peri-implant tissue occurs. So there is need of more studies to be conducted for establishing a standardized set of methods and protocol based on inflammatory mediators for more specific and sensitive diagnosis of peri-implantitis.

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