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IP Journal of Paediatrics and Nursing Science

Journal homepage: www.ipinnovative.com

Review Article

Biomarkers in dentin pulp complex

Shaik Ali Hassan[1,*], Sumit Bhateja[1], Geetika Arora[2], Francis Prathyusha[3]

[1]*Dept. of Dental, Manav Rachna Dental College, Faridabad, Haryana, India*
[2]*Inderprastha Dental College & Hospital, Ghaziabad, Uttar Pradesh, India*
[3]*Dr. Francis Maxillofacial and Dental Clinic, India*

ARTICLE INFO

Article history:
Received 05-06-2020
Accepted 16-06-2020
Available online 18-08-2020

Keywords:
Biomarkers
Periapical
BSP
MMP
Pulp.

ABSTRACT

Biomarkers are functional elements at the level of cells or molecules, play an important role in the health and disease. Tooth dentin-pulp complex houses several biomarkers at different stages of development, and the lack of these biomarkers yield developmental disorders. Furthermore, biomarkers play a very important role in the pathogenesis of dental caries, pulp and periapical pathoses in two ways - they is an important element in the process of detection of pathological and they assist in the accurate diagnosis of pathological conditions.

1. Introduction

The term "biomarker" is created from a portmanteau of "Biological markers" which refers to broad subcategory of medical signs that can be measured accurately and reproducibly.[1,2] National Institutes of Health Biomarkers the Working Group has defined the definition of a biomarker as a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention,[3] Basically, a biomarker can be considered as a response functional, psychological, biochemical or cellular level molecular interactions. Biomarkers are being widely used in research and has proven to be a boon in the medical field to assist in diagnosis and treatment.

2. Various Biomarkers

The dentin and pulp together form the dentin-pulp complex. The outermost cell layer at the boundary of pulp tissue and predentin consists of the odontoblasts, the cells that form and mineralize the dentin matrix[4]

3. Osteocalcin

Odontoblasts express a glycoprotein called osteocalcin (OCN) in the matrix of the dentine .[5] He is known to be one of reparative molecules and expression occurs in response to injury of the dental pulp. Itis believed to be collated with collagen fibers and is also found embedded in the tertiary dentin, where its expression occurs in response to the cavity preparation.[6] In addition, it is also considered as a marker for mature osteoblasts and has been used as markers of osteoblast-like differentiation mineralization odontoblast / on Stem cells from dental pulp.[7]

OCN is expressed before the start of the mineralization and is the highest non-collagenous protein in bone extracellular matrix. It is suggested to be essential in interceding.[7,8] osteoclast differentiation. OCN was found associated with proteins such as macrophage granulocyte macrophage colony-stimulating factor (GM-CSF) in cells forming bone. Expression NCBs occurs in the terminal differentiation of macrophages osteoblasts. It is expressed

* *Corresponding author.*
E-mail address: alishaikhassan@gmail.com (S. A. Hassan).

https://doi.org/10.18231/j.ijpns.2020.008

in response to the preparation of the cavity associated with the collagen fibers and is also found in the tertiary dentin.[9]

4. Osteonectin

It happens to be a major non-collagen matrix protein bone and dentin.[10] odontoblasts and beef, and odontoblasts predentine in human prenatal and postnatal samples were exposed . Its various roles in the initiation of mineralization was.[11] shown Because of their study, ON is indicated as a protein associated with the formation of collagen in mineralized tissues, such as bone and human dentin.

5. Dentin sialophosphoprotien

DSPP is the initial translation product DSPP envoy RNA (mRNA) which is then cleaved to the teeth and phosphoprotein dentin sialoprotein (DSP).[12–14] That primitive is considered to be Special dentin until detected on bone.[15] However, the expression of dentin is about 400 times that of bone. Being one of the non-collagenous proteins necessary foundation in the development of teeth and mineralization, it is mainly expressed in odontoblasts.DSPP role in dentinogenesis has been well demonstrated.[15] (Qin et al., 2002), so it remains a major marker for odontoblast differentiation. DSPP, osteocalcin and matrix extracellular phosphoglycoprotein (MEPE) grew up in a time expression Depending on the dental pulp cells (DPC) induced.[13,16–18] culture.

6. Thyrotropin-Releasing Hormone -Degrading Enzyme

This is known as pyroglutamyl peptidase II and shows the absolute functional specificity for substrates, TRH.[19,20] It is oriented extracellular, a membrane-associated peptidase (ectopeptidase) and a function to stop the peptide-mediated cell signaling. TRH-DE has been found in the dental pulp by microarray analysis and real time RT-PCR analysis of.[20] TRH-DE mRNA expression in dental pulp stem cells / progenitor (CD105 + and CD31- Side population (SP) cells were enhanced by induced nerve cell. Its presence in the process of neuronal The dental pulp is confirmed by immunohistochemistry and in situ hybridization. In addition, the TRH-DE mRNA was expressed in pulp regeneration 28 days after transplant CD31- SP cells into a root canal after pulpectomy.

7. Matrix metalloproteinase

MMPs are synthesized by cells of connective tissue such as as fibroblasts, osteoblasts, and odontoblasts and secreted into the extracellular matrix. Several matrix metalloproteinases (MMP) have been identified in the dentin and pulp by polymerase chain reaction (PCR) and immunohistochemistry.[21–23] MMPs have have been classified into six groups based on their structural homology and their substrate specificity as collagenase (MMP-1, MMP-8, MMP-13 and MMP-18), gelatinases (MMP-2 and MMP-9), stromelysins (MMP-3, MMP-10 and MMP-11), MMP transmembrane or MT-MMP (MMP-14, MMP-15, MMP-16, MMP-17, MMP-24 and MMP-25), and others (MMP-12, MMP-19, MMP-20, MMP-21, MMP-22, MMP-23, MMP-27 and MMP-28).[22]

Some MMPs have been identified in human mineralization dentin, ie collagenase MMP-8[24] gelatinases (25) and enamelysin.[23] MMP MMP-20 is present in the saliva and the dentin is host-derived and activated at acidic pH resulting from the release of lactate of cariogenic bacteria.[25,26] At neutral pH, the effect of MMP in remodeling of the extracellular matrix. tissue damage always colligated with aberrant expression of MMP.MMP role in various physiological processes in the dentin-pulp complex has good roles including organizational understood. The matrix prior to mineralization, the mineralization controls, peritubular dentin formation, and changes in the matrix during aging.[27]

8. Bone sialoprotein

BSP has been contained within the mineralized dentin and modulation of MMP-2. use the collected RNA was isolated from the pulp tissue of both health and caries, it has been observed that there is 8-fold up-regulation in gene expression in the pulp BSP teeth with active caries.[28] However, the expression of the pulp tissue MMP-2 in response to the caries process remains unknown. Immunohistochemical analysis of extracted third molars and premolars did not reveal any detection of MMP-2 and BSP in tubular lumen of sound dentin. Therefore, both BSP and MMP-2 may involved in host defense mechanisms that lead to calcification areas affected by caries.

9. Biomarkers in dental pulp complex in diseases

Infection, exposure, trauma and chemicals may result in losses pulp vitality. As a result of these tooth injury, the signal for progenitor stem cells were sent to stimulate the differentiation, proliferation, and migration as part of reparative dentinogenesis. Influx and macrophage recruitment of polymorphonuclear (PMN) is the beginning In response to bacteria and their metabolites. In addition to fibroblast proliferation and angiogenesis, macrophage infiltration, lymphocytes and plasma cells are a typical feature in more chronic conditions. MMPs have also been identified for both pulp and periapical.[29–31] inflammation. This group of enzymes responsible for degradation of extracellular matrix (ECM), as seen in inflammationpulp and periapical region. The destruction of the ECM generated by component of intracellular bacteria, bacterial metabolites, and other molecules, leading to the formation

of periradicular lesions.[32]

Basically, MMP is a group of structurally related but endopeptidases expressed in genetically distinct normal tissues at low levels, but regulated inflammation. That also interesting to note that the levels of MMP-8, which is usually higher in the case of periapical exudate, reduced significantly after the first visit root canal treatment.[33] IHC staining showed MMP-8 in the pulp and periapical granulomas with PMN become larger cell types to express MMP-8.

Enzyme linked immunosorbent assay has shown that MMP-1 levels are below the limit of detection in healthy and inflamed pulp, while the level of MMP-9 was significantly increased in inflamed human dental pulp. In contrast, levels of MMP-2 and MMP-3 reduced the inflamed pulp symptoms than with a normal pulp.[34] This suggests a major role of MMP-9 in the degradation of inflamed human dental pulp tissue. Role MMP-9 in the inflamed pulp was then supported by another report.[35] Another study also noted that MMP-9 mRNA gene is increased in the inflamed pulp.[34] Furthermore, in-situ localization of MMP-9 expression in specimens showed significantly pulp higher expression of MMP-9 in the inflamed pulp compared to clinically healthy pulp. Increased activity of MMP-9 and MMP-2 has also has been shown in the gingival sulcus fluid teeth with periapical lesions.[35] Thus, the use of MMP-9 and MMP-2 as a biological markers can be proved. Furthermore, periapical granuloma showed higher MMP-9 and MMP-13 activity compared with[34] radicular cysts. Osteocalcin role in the pulp pathoses not clearly explained until recently, when it was shown that the expression of osteocalcin was higher in comparison with irreversible reversible pulpitis pulpitis,[8] Osteocalcin is reparative molecules in the dental pulp and in terms of improvement, it is localized in the cell and the surrounding matrix areas of calcification in the cells surrounding the blood vessels. However it's not in normal tissue. These findings correlated positively with angiogenic markers such as vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), supporting role in the repair of pulp.

10. Biomarkers as diagnostic tool

As there is a significant expression of MMPs pulp and pathological inflammation, MMP analysis of periapical exudate can an option to demonstrate and monitor the activity of inflammatory and as an indicator of the success of root canal treatment that has previous periapical lesions. There is a strong denotation that MMP-8 periapical inflammation appear on the site because it is still on display in second visit root canal treatment regardless of the deletion pulp networks and canals cleaned during the first appointment that implies that the active phase of periapical inflammation sites still exist. The loss of partial onset inflammation and healing is reflected by the lack of MMP-8 in exudates during root canal third visit. Therefore, the level of MMP-8 could serve as Biochemical indicators to assess the inflammatory status of the periapical tissues. MMP measurement of the root canal during treatment serves as a potential prospect as a diagnostic tool to assess periapical inflammatory conditions. MMP-9 also serves as potentially unreliable marker as levels significantly improve in pulp inflammation.[35] The presence of molecular differential expression in the cyst or granuloma has the potential to provide information to distinguish between periapical cysts of granuloma before executing Endodontic procedures as cysts have a lower healing rate.[36] Zehnder et al is the first to provide clinical relevance for the use of MMP-9 as a marker for the pulp pathoses.[37–39] They performed a study to improve the diagnosis of the pulp to assess the level of MMP-9 in dentin fluid diagnosed with irreversible symptoms pulpitis and healthy peers. In order to perform non-invasive assessment of pulp, dentin fluid collection of dentin wounds can be done after the cavity preparation. After access cavity is prepared, sterile folded polyvinylidene difluoride (PVDF) membrane filters used to collect fluid dentin of dentin open and the fluid is then charged MMP-9 assay neon. This particular assay has been claimed has a sensitivity that is superior to conventional ELISA for functions based substrate turnover effect in the liberation of the fluorophore. In conclusion, dentin fluid samples from dental symptoms had significantly higher MMP-9 levels compared for healthy pulp.

11. Source of Funding

None.

12. Conflict of Interest

None.

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Author biography

Shaik Ali Hassan Dental Surgeon

Sumit Bhateja HOD

Geetika Arora Reader

Francis Prathyusha BDS

Cite this article: Hassan SA, Bhateja S, Arora G, Prathyusha F. **Biomarkers in dentin pulp complex**. *IP J Paediatr Nurs Sci* 2020;3(2):34-37.