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Review Article

The Effect of Diabetes Mellitus on Dental Pulp Organ: A Review

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ABSTRACT

Diabetes mellitus (DM) is a systemic disease that brings numerous pathophysiological in the human body and oral complications are largely known and studied. Changes that occur in the dental pulp are of importance for the dentists, considering regular procedures outcome. The defense systems and neural connections of the dental pulp will be destroyed and disorganized. In the present article the literature concerning on complication, effect of Diabetes Mellitus on pulp and reparative response of dental pulp was reviewed.

Keywords: diabetes mellitus, oral complication and dental pulp organ

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INTRODUCTION

Diabetes mellitus (DM) is a complex and heterogeneous syndrome rather than a disease induced by genetic or gained alteration of insulin secretion and/or resistance to its peripheral action. It is characterized by derangement of glucose metabolism leading to secondary alteration of the other metabolisms: lipids, proteins, electrolytes, ions and vitamins ⁽¹⁾.

Diabetes mellitus can be broadly classified into two main types, Type1: insulin-dependent diabetes (IDDM) and Type2: non-insulin-dependent diabetes (NIDDM). Type 1 diabetes is characterized by beta cell destruction and absolute insulin destruction. It accounts for only 5-10% of those with diabetes. This form develops most frequently in children and adolescents, but is being increasingly noted later in life. While, Type 2 diabetes is also called as insulin resistance diabetes or non-insulin dependent diabetes characterized by insulin deficiency and accounts for 90-95% of those with diabetes. It occurs most frequently in adults, but is being noted increasingly in adolescents as well ⁽²⁾.

There are many complications may be occurring with uncontrolled diabetes patients, they have been

classified into as macro-vascular (atherosclerosis of coronary blood vessels, cerebral disease, etc.) or micro-vascular (diabetic retinopathy, diabetic nephropathy, etc.) ⁽³⁾. While the oral complication of which most commonly known are: xerostomia, infections, poor healing, increased incidence and severity of caries, candidiasis, burning mouth syndrome, gingivitis and periodontal diseases ⁽⁴⁾.

The poorly controlled insulin dependent diabetes had more gingivitis, attachment loss and gingival recession than controlled insulin dependent diabetes with a mean HBAI C of 9.2% ⁽⁵⁾.

There are also just few clinical and paraclinical studies concerning modifications appeared at dental pulp level. Bender et al. and Russel, in the early sixties have manifested interest for the first time for dental pulp study in diabetic patients ⁽⁶⁾.

Diabetes mellitus and pulpal diseases

Dental pulp is a connective tissue that has some unique characteristics. Namely, it has specific microcirculatory system without collaterals. Also, dental pulp is located within solid dentinal walls that cannot accept any significant change of its volume. These features make it very prone to irreversible inflammatory changes shortly after the impact of noxious stimuli. This can be significantly intensified in persons with diabetes mellitus known for their tissue vulnerability caused by macro- and micro-circulatory disorders ⁽⁷⁾.

Inflammation were more sever in diabetic rats than that in control rats, in apical periodontal ligament, also root resorption and alveolar bone resorption were more sever. These were other histological changes in pulpal and periapical tissues after pulpal exposure in streptozotocin induced diabetic rats ⁽⁸⁾.

It was noted that severe pulpitis with destruction of periodontal structures and bone loss along tooth roots in Akita mice ⁽⁹⁾.

limited dental collateral circulation, impaired immune response, increased risk of acquiring pulp infection (especially anaerobic ones) or, also necrosis toothache and occasional tendency towards pulp necrosis caused by ischaemia, all the mentioned are found in the Pulp diabetes patients. According to study in Akita mice, sever pulpitis with destruction of periapical structure and bone loss along tooth roots were noted. whereas the study revealed a marked reduction in plasma blood flow in dental pulp of rats with streptozotocin induced diabetes have therefore; conditions induced by diabetes such as periodontitis can affect the dental pulp via periapical way due to the dental pulp has limited or no collateral circulation ⁽¹⁰⁾.

It was showed that, there is angiopathies and thickened basement membrane of large and small blood vessels which impairs the leukocytic response and failure to deliver the humoral and cellular components of immune system. Vascular problems associated with diabetes also cause an increase in anaerobic infection, which may be attributed to reduced oxygen diffusion across the capillary wall. Infection becomes more severe and last longer because of neutrophil microbicidal suppression and synergism of aerobic and anaerobic bacteria, due to anoxia ⁽¹¹⁾.

Due to obliterative endartitis, pulp ages rapidly in patients with diabetes mellitus ⁽¹¹⁾. Calcifications were more frequently and, often sickle shaped in type 2 diabetics. Though pulpal were found in both diabetics and other systemic disease. Thus; there were higher incidence of pulpal calcification in type II diabetes and other systemic disease.as showed by Nayak et al. ⁽¹²⁾.

Moreover, Bissada and Sharawy have observed calcified bodies in the pulp of diabetics. Similarly, there were more pulp stones in type I diabetics (35.6%) than in non-diabetics (10%) in first maxillary molars of the present study. Prevalence of the pulp stones was similar in males and females as reported by Ranjitkar et al. ⁽¹³⁾.

Also, there are other changes in the mesiodistal crown widths, crown and pulp widths at the cervix of first maxillary molars and heights of the mesial pulp horns of first mandibular molars in diabetics were greater than in non-diabetics but these are not important for clinical assessment ⁽¹⁴⁾.

The higher frequency of tooth extraction after endodontic therapy in patients with DM as result of

lower success rate of root canal treatment that suggested by Wang et al. ⁽¹⁵⁾.

Pathophysiology of dental pulp affection in Diabetes mellitus

Hyperglycemia which results in increase of tissue oxidative stress which causes the main pathophysiological mechanism of changes during DM. This changes mitochondrial overproduction of superoxides. This is one of the physiological changes in DM ⁽²⁾.

This leads to activation of specific pathophysiological mechanisms, signed to be direct promoter of histological changes. Activation of protein kinase C and formation of glycosylated end products are the main mechanisms to provoke changes in levels and function of different GF, contributing profoundly to the specific diabetic pathology ⁽²⁾.

Vascular endothelial growth factor (VEGF) is also the most prominent GF responsible for diabetic complications. In physiological conditions it is responsible for vasculogenesis, angiogenesis and processes associated with them. ⁽¹⁶⁾ The levels and function of VEGF is altered in tissues and organs during DM. There are tissues with up-regulation of this GF leading to complications with extensive pathological hyper-angiogenesis such as diabetic retinopathy. On the other hand there are tissues where VEGF is down-regulated causing complications based on insufficient blood supply such as wound healing difficulties ⁽¹⁷⁾.

Diabetic mellitus also provokes changes in TGF- β superfamily members ⁽²⁾. Bone morphogenetic protein 2 (BMP-2), one of the members of this GF group, has significant influence on a specific pathological change in DM. Namely, BMP-2 is up-regulated in walls of diabetic blood vessels causing differentiation of osteoblasts and ectopic vascular calcifications. This is the main mechanism for atherosclerosis and similar changes in vascular beds to occur in DM ⁽¹⁸⁾.

In 2012, Ilić et al, analyzed human diabetic dental pulp and found significant changes in levels of VEGF and BMP2, GF's important for pulp reparative response ⁽¹⁹⁾. Vascular endothelial growth factor is of great importance for microcirculatory system of dental pulp ⁽²⁰⁾. as well as immunohistochemical identification ⁽²¹⁾. Increased expression of VEGF has been noticed during some pathological conditions of dental pulp such as inflammation, injury and hypoxia ⁽²²⁾.

While, GF is responsible for odontoblast differentiation of pulp stem cells and for up-regulation of odontoblast secretion in primary, secondary and tertiary dentinogenesis ⁽²³⁾.

Changes in these GF levels could be of special interest, when analyzing the effect of DM on pulp reparative response, which is known, that GF is responsible for regulation of odontoblast secretion in primary, secondary and tertiary dentinogenesis. Also responsible for odontoblasts differentiation of pulp stem cells. Inadequate reaction of dental pulp on noxious stimuli is provoked when GF level is altered in DM, which was in concordance with Garber et al. investigations ⁽²⁴⁾. This investigation provided that, on rat models there were evidences that DM impede dental pulp reparation. This investigation also provided that reaction DM of dental pulp on capping procedures may be very unpredictable, which is a fact proven from practice

Reparative response of dental pulp

The primary role of pulp is to produce dentin, but it is well known that tissue has several functions: nutritive, sensory, defensive and reparative. Ability to repair is of special clinical interest because it has fundamental influence on all therapeutic procedures aiming to maintain pulp vitality ⁽⁷⁾.

Reparative response of dental pulp is modified by morphological and functional pulp status (younger or older subjects, specific location, previous history of reparation process, etc). Reparative response depends on the type and intensity of harmful stimuli ⁽²⁵⁾.

Specificity of pulp tissue compared to other connective tissues is dentin production up regulated during the repair process known as tertiary dentinogenesis. The layers of dentin are deposited on the pulp-dentinal interface, particularly towards noxious stimuli. The aim of this process is to protect pulp tissue by blocking harmful effects. The prerequisite for this process is localized, controlled and mild inflammation that will allow spreading blood vessels and providing adequate nutrient supply for up-regulated pulp secretory activity ⁽²⁶⁾.

Tertiary dentinogenesis may progress in two completely different ways depending on the intensity of noxious stimuli. In mild to moderate stimuli (for example shallow caries lesion) odontoblasts, specific secretory cells of dental pulp, may survive and increase their activity forming layers of tertiary dentin ⁽²⁷⁾.

Cells will form layers of new dentin in complex process known as reparative dentinogenesis. In case of strong stimuli, odontoblasts will not survive as result, Progenitor pulp cells will activate, migrate and differentiate into odontoblast like cells and these cells will form layers of new dentine. This process is called reactionary dentinogenesis ⁽²⁸⁾.

Various signaling molecules regulate both reactionary and reparative dentinogenesis. Although the process of tertiary dentinogenesis is well recognized and described, cellular and molecular mechanisms of its regulation are still not fully identified. It is known that specific cells conduct tertiary dentinogenesis. The cell lines involved in up-regulated dentin production are odontoblasts or odontoblast-like cells. The origin of the later ones is still unclear, but they are most probably derived from progenitor pulp cells (stem cells, Rougett pericytes, etc) ⁽²⁹⁾.

CONCLUSIONS

Diabetes Mellitus is a chronic condition and now prevalent among people of all ages because of its multiple causes of occurrence. It has many complications in all the human body. Dental Caries is the most common oral complication. So Dental Caries in Diabetic patients may lead to pulpal and periapical diseases. So there is a relationship between diabetes mellitus and pulpal diseases.

REFERENCES

1. Moța M. Compendiu. Diabet zaharat, nutriție, boli metabolice. Ed. Medicală Universitară, Craiova, 2001.
2. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. *Nature*. 2001; 414:813-820. [DOI: 10.1038/414813a] [PMID: 11742414]
3. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. *Nature*. 2001; 414:813-820. [DOI: 10.1038/414813a] [PMID: 11742414]
4. Lamster IB, Lalla E, Borgnakke WS, Taylor GW. The relationship between oral health and diabetes mellitus. *J Am Dent Assoc*, 2008, 139(Suppl):19S-24S.
5. Seppala B, Seppala M, Ainamo J. A longitudinal study on insulin dependent diabetes mellitus & periodontal disease. *J Clin Periodontol* 1993; 20: 161-5.
6. Moraru A, Gheorghita M, Dascalu I, et al. Histological and immunohistochemical study on the dental pulp of patients with diabetes mellitus. *J Rom Morphol Embryol*. 2017, 58:493-499.
7. Jugoslav I. diabetes mellitus and reparative response of dental pulp. *J Serbian Dent*. 2016, 63 :85-90.
8. Kohsaka T, Kumazawa M, Yamasaki M, Nakumara H. Periapical lesions in rats with streptozotocin induced diabetes. *J Endod* 1996; 22 : 418- 21.
9. Chih-Ko Y, Stephen H, Mohan, E et al. "Hyperglycemia and xerostomia are key determinants of tooth decay in type 1 diabetic mice", *HHS Public Access, Lab Invest*. 2012.

10. Pishipati Vinayak Kalyan Chakravarthy, "Diabetes mellitus: An endodontic perspective", <http://www.ejgd.org>, 2016; 23.
11. Bender LB, Bender LB . Diabetes mellitus & dental pulp. J Endod 2003; 29:383 -9. 13.
12. Nayak M, Kumar J, Prasad L. A radiographic correlation between systemic disorders and pulp stones .Indian J Dent Res. 2010 ; 21:369-73.
13. Ilguy D, Ilguy M, Bayirli G. The size of dental pulp chamber in adult diabetic patients", OHDMBS. 2004.3; III: 38-41.
14. Pratha A, Jayalakshmi S. Relationship between diabetes mellitus and pulpal Infection and eriapical diseases.. Sci Res. 2016 ; 8: 794-6
15. Wang CH, Chueh LH, Chen SC, Feng. et al. Impact of Diabetes Mellitus, Hypertension, and Coronary Artery Disease on Tooth Extraction after Nonsurgical Endodontic Treatment. J Endod. 2011; 37 :1-5. [DOI: 10.1016/j.joen.2010.08.054] [PMID: 21146066].
16. Ferrara N. Vascular endothelial growth factor: basic science and clinical progress. Endocr Rev. 2004; 25:581-611.[DOI: 10.1210/er.20030027] [PMID: 15294883]
17. Wirosko B, Wong TY, Simo R. Vascular endothelial growth factor and diabetic complications. Prog Retin Eye Res. 2008; 27(6):608-621. [DOI: 10.1016/j.preteyeres.2008.09.002] [PMID: 18929676]
18. Bostrom KI, Jumabay M, Matveyenko A, Nicholas SB, Yao YC. Activation of Vascular Bone Morphogenetic Protein Signaling in Diabetes Mellitus. Circ Res. 2011; 108(4):446-U123. [DOI: 10.1161/CIRCRESAHA.110.236596] [PMID: 21193740]
19. Ilić J, Radović K, Roganović J, Brković B, Stojić D. The Levels of Vascular Endothelial Growth Factor and Bone Morphogenetic Protein 2 in Dental Pulp Tissue of Healthy and Diabetic Patients. J Endod. 2012; 38(6):764-768. [DOI: 10.1016/j.joen.2012.03.016] [PMID: 22595109]
20. Matsushita K, Motani R, Sakuta T, Yamaguchi N, Koga T, Matsuo K, et al. The role of Vascular Endothelial Growth Factor in human dental pulp cells: induction of chemotaxis, proliferation, and differentiation and activation of the AP-1-dependent signaling pathway. J Dent Res. 2000; 79:1596-1603. [DOI: 10.1177/00220345000790081201] [PMID: 11023281]
21. Guven G, Altun C, Gunhan O, Gurbuz T, Basak F, Akbulut E, et al. Co-expression of cyclooxygenase-2 and vascular endothelial growth factor in inflamed human pulp: An immunohistochemical study. J Endod. 2007; 33(1):18-20. [DOI: 10.1016/j.joen.2006.07.014] [PMID: 17185121]
22. Tran-Hung L, Laurent P, Camps J, About I. Quantification of angiogenic growth factors released by human dental cells after injury. Arch Oral Biol. 2008; 53(1):9-13. [DOI: 10.1016/j.archoralbio.2007.07.001] [PMID: 17764655]
23. Casagrande L, Demarco FF, Zhang Z, Araujo FB, Shi S, Nor JE. Dentinderived BMP-2 and Odontoblast Differentiation. J Dent Res. 2010; 89(6):603-608. [DOI: 10.1177/0022034510364487] [PMID: 20351355].
24. Garber SE, Shabahang S, Escher AP, Torabinejad M. The Effect of Hyperglycemia on Pulpal Healing in Rats. J Endod. 2009; 35(1):60-62. [DOI: 10.1016/j.joen.2008.09.010] [PMID: 19084126]
25. Smith A. Pulpal Responses to Caries and Dental Repair. Caries Res. 2002; 36:223-232. [DOI: 10.1159/000063930] [PMID: 12218270] .
26. Cooper PR, Takahashi Y, Graham LW, Simon S, Imazato S, Smith AJ. Inflammation-regeneration interplay in the dentine-pulp complex. J Dent. 2010; 38(9):687-697. [DOI: 10.1016/j.jdent.2010.05.016] [PMID: 20580768].
27. Smith A, Cassidy N, Perry H, Begue-Kirn C, Ruch J, Lesot H. Reactionary dentinogenesis. Int J Dev Biol. 1995; 39:273-280. [PMID: 7626417].
28. Lesot H, Begue-Kirn C, Kubler MD, Meyer JM, Smith AJ, Cassidy N, et al. Experimental induction of odontoblast differentiation and stimulation during reparative processes. Cell Mater. 1993; 3:201-217.
29. Harichane Y, Hirata A, Dimitrova-Nakov S, et al. Pulpal Progenitors and Dentin Repair. Adv Dent Res. 2011; 23(3):307-312. [DOI: 10.1177/0022034511405322] [PMID: 21677084]