Michigan neuropathy screening for assessing diabetes in participants and correlation to the immune response

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ABSTRACT

Background: Diabetes Mellitus (DM) as a chronic disease makes some influence to all organic systems in the body. Some of these changes affect nervous system (different kinds of neuropathies), and some kind of immune response to these disorders could be expected. Michigan Neuropathy Screening Instrument (MNSI) is used to assess distal symmetrical peripheral neuropathy in DM.

Aims: This research study aimed to assess the population of diabetic patients with MNSI and to check the influence of the duration of DM on the immune response. Inflammatory markers (CRP; Le; SE) and cytokines (IL-6, Il-1β, TNF-α, TGF-β) were used as a measure of the immune response.

Methods: The study included 100 participants with Diabetes Mellitus type 2 (men and women) and 30 healthy participants as a control group. All participants were examined through the regular examination in General Hospital Tešanj, BiH. The participants were divided into 3 groups, by criteria DMT2 duration and a control group. The first group included 32 participants with DMT2 less than 10 years duration (group A); second group included 35 participants 10-20 DMT2 duration (group B) and the third group included 33 participants more than 20 years DMT2 duration (group C). The control group included 30 healthy participants. All diabetic participants were examined by MNSI to check neuropathy status and to check distribution through the groups (sensitivity 93.3%, specificity 25%). Cut-off values of MNSI were: ≤2.5 points without neuropathy; 2.5-7- neuropathy I stage, ≥7.5 neuropathy stage II. The ELISA test was performed for the measurement of cytokines.

Results: The results of MNSI examination have shown that: 7 diabetic participants had ≤2.5; 31 participants had 2.5-7 p, and 54 had ≥7.5 (Picture 1). Groups A (n=4) and B (n=3) had a similar number of participants without neuropathy. Groups B (n=22) and C (n=20) had a similar number of participants with stage II neuropathy (Picture 2). No significant difference between groups in MNSI was found. Statistically significant correlations were found in group A between MNSI and IL-6 (R=0.402, p=0.025); IL-6 and CRP (R=0.784, p=0.0001); CRP and MNSI (R=0.500, p=0.034) (Table 1). No statistically significant corelations were found in B and C groups between MNSI and inflammatory markers (Table 2, 3). Also, statistically signficant correlations were not found between HbA1C and MNSI, inflammatory markers and cytokines.

Discussion: Previous studies conducted to assess the impact of hyperglycemia on diabetic neuropathy (1, 2, 3, 4) and the inflammatory environment (5, 6, 7) in the body, have shown a positive correlation. However, there was no study that measured the impact of different periods of DM on these processes. This study is unique because the MNSI score showed a significant correlation with IL-6 and CRP only in the group of participants with less than 10 years of DM duration. MNSI examination showed an increase in the number of participants with neuropathy across groups, and according to these results a correlation with other inflammatory cytokines, especially TGF-β1, was expected (8, 9, 10). Subsequent studies should look at the effect of drugs on inflammatory cytokines, which treat glycaemia and concomitant diseases.

References

1. Ramirez H, Patel SB, Pastar I. The role of TGF β signaling in wound epithelialization. Wound care. 2014; 3:7.
2. Ye L, Yunlong H, Zhao L, Li Y, Sun L, Zhou Y, et al. IL-1 β and TNF-α induce neurotoxicity through glutamate production: a potential role for neuronal glutaminase. J Neurochem. 2013;125(6): 897-908.
3. Xu F., Zhang Ch., Graves T.D. Abnormal cell response and role of TNF-α in impaired Diabetic wound healing. BioMed Research International. 2013; Article ID 754802, 9 p.
4. 4Satoh J, Yagihashi S, Toyota T. The Possible Role of Tumor Necrosis Factor- α in Diabetic Polyneuropathy. Experimental Diab. Res. 2003; 4:65-71.
5. Kristiansen OP, Mandrup-Poulsen T. "Interleukin-6 and diabetes: the good, the bad, or the indifferent?" Diabetes. 2005; 54(2):S114–24. doi:10.2337/diabetes.54.suppl_2.S114. PMID 16306329.
6. Qiao Y, Chen Y, Pan Y, Tian F, Xu Y, Zhang X, et al. The change of serum tumor necrosis factor alpha in patients with type 1 diabetes mellitus: A systematic review and meta-analysis. Plos ONE 12(4): e0176157.
7. Shaker G, Sadik NAH. Transforming growth factor and monocyte chemoattractant protein-1 as prognostic markers of diabetic nephropathy. Hum Exp Toxicol. 2013; 32(10):1089-96.
8. Tsukaguchi K, Yoneda T, Yoshikawa M, Tokuyama T, Fu A, Tomoda K et al. Case study of interleukin-1 beta, tumor necrosis factor alpha and interleukin-6 production peripheral blood monocytes in patients with diabetes mellitus complicated by pulmonary tubercolosis. Kekkaku. 1992; 67(12):755-60.
9. Costa de Souza K, Abbott Galvao Ururahy M, Costa Oliveira YM, Bezerra Loureiro M, Vital da Silva HP, Hernandes Botolin R et al. Low bone mineral density in patients with type 1 diabetes: association with reduced expression of IGF1, IGFR and TGF-B1 in peripheral blood mononuclear cells. Diabetes Metab Res Rev. 2016; 32(6):589-95.
10. Hussain G, Rizvi SA, Singhal S, Zubair M, Ahmad J. Serum levels of TGF-β1 in patients of diabetic peripheral neuropathy and its correlation with nerve conduction velocity in type 2 Diabetes Mellitus. Diabetes Metab Syndr. 2016;10(1):S135-9.