TLR4, SIBO AND GUT MICROBIOTA IN PATIENTS WITH HYPERLIPIDEMIA

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Abstract category: 7.4.: Metabolic/genetic disorders

Introduction: Toll-like receptor 4 (TLR4) is a pattern recognition receptor that functions as a lipopolysaccharide (LPS) sensor, and its activation results in the production of several pro-inflammatory and antibacterial cytokines. TLR4 is normally expressed in various cell types, including hepatocytes, and represents a link between intestinal microbiota, endotoxemia, and liver damage. LPS, a major component of the outer membrane of Gram-negative bacteria, and the exogenous ligand for TLR4. SIBO is mainly associated with gram-negative microbiota in the intestine with LPS increasing simultaneously. It could lead to the early deconjugation of bile acids and enterohepatic circulation disturbing with an impact on lipid metabolism in the liver. Additionally, gut microbiota composition is one of the factors that are associated with dyslipidemia.

Aims & Methods:

This study aimed to determine the TLR4 serum level in patients with hyperlipidemia. Furthermore, the aim was to find the association of TLR4 with gut microbiota and SIBO.

145 patients with hyperlipidemia (average age 45.2±2.7) with an average BMI of 25.12±0.88 were examined in Danylo Halytsky Lviv National Medical University (Lviv, Ukraine). 82 control subjects (average age 47.38±1.9), with an average BMI of 24,71±0.59. All control subjects had normal lipid range and no history of coronary disease. All patients of both groups underwent the biochemical tests for lipid metabolism and liver function. Determination of microbial composition at the level of major microbial phyla was carried out by identification of Bacteroidetes, Firmicutes, and Actinobacteria DNA with quantitative real-time PCR (qRT-PCR), using genetargeted primers. The examination of lactulose breath test was proved to patients of both groups. Quantative detection of TLR4 in the serum was realized by using the Cusabio Elisa kit.

Results:

TLR4 serum level was 2.67±1,05 ng/mL in hyperlipidemia group (normal range 1,25-2,5 ng/mL), 1.23±0.99 ng/mL in controls. SIBO prevalence was

59,8% in main group, 35% in control. Bacteroidetes in main group amounted to $40.70\pm25.43\%$, Firmicutes - $39.43\pm23.77\%$, Actinobacteria - $8.95\pm9.41\%$, while in the control group - Bacteroidetes was $52.98\pm13.62\%$, Firmicutes - $33.85\pm12.47\%$, Actinobacteria - $5.36\pm1.76\%$. Firmicutes/Bacteroidetes index in the hyperlipidemia group was 2.98 ± 1.6 , in control - 0.75 ± 0.54 . The correlational relationship was marked between TLR4 and Firmicutes (r=0,71), TLR and Actinobacteria (r=0,65) and TLR and F/B index (r=0,73). Moreover, the association was between TLR4 and cholesterol (r=0,46), ALT (r=0,56), LDL (r=0,49), uric acid (0,52) and albumin (r=-0.79). Actinobacteria was in strong positive correlation with TG (r=0,67) and cholesterol (r=0,51). Positive correlational relationship between SIBO and TRL4 in patients with hyperlipidemia was marked (r=0,53).

Conclusion: Based on these results, we can suggest that microbiota composition could be the factor that is associated with TLR4 activation with further liver cholesterol metabolism disturbing. SIBO prevalence in patients with hyperlipidemia was remarkably higher than in patients of control group (59,8% vs. 35%). TLR4 increasing leads to Actinobacteria and Firmicutes/Bacteroidetes index growth, which simultaneously impacts cholesterol, ALT, and triglycerides increasing. TLR4 and SIBO are in a correlational relationship in patients with hyperlipidemia (r=0,53). Thus, gut microbiota composition disturbing and SIBO could be the risk factors for dyslipidemia.

Nothing to disclose: Yes

Keyword 1: microbiota

Keyword 2: hyperlipidemia

Keyword 3: SIBO

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