

The role of Toll-like receptors in pathogenesis of insulin resistance and ovarian dysfunction in girls with obesity

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Menstrual function disturbances are recorded 6 times more frequently in case of the alimentary obesity than in girls with the normal BMI. It is known that obesity leads to pimelitis, which affects metabolic and secretory functions of the adipose tissue and plays a key role in the development of insulin resistance (IR). New data confirming the role of violations of innate immunity in the pathogenesis of IR. Toll-like receptors (TLRs) are essential components of the innate immune response and are therefore one of the key factors involved in recognizing and defending against invading pathogens.

The objective of our research - the study of the role of some proinflammatory cytokines, TLR-2 and TLR-4 in the pathogenesis of ovarian dysfunction in adolescent with obesity.

Methods. The content of leptin, adiponectin, IL-1?, MCP-1, TNF-? in 2 groups of overweight adolescent girls was established by the ELISA. The group I included 43 adolescents with oligomenorrhea and IR, group II - 31 patients with regular cycle, without IR. The control - 25 healthy girls without obesity. The determination of TLR-2 and TLR-4 expression on monocytes of the peripheral blood was performed by the method of two-color flow cytometry.

Results. It was established that in 2 groups of patients the levels of leptin increase and adiponectin decrease as compared to the control. The increase of MCP-1 levels maintains the process of adipose tissue inflammation.

In the I group as compared with the control and group II there were apparent changes in the form of statistically significant increase of TLR-2 and TLR-4 expression on monocytes ($p < 0.05$). Besides, we registered the increase of the production of IL-1? and TNF-? ($p < 0.05$).

Conclusion. TNF-? and IL-1? stimulate leptin secretion, inhibit adiponectin expression and are the key molecules in metabolic disturbances related to obesity. The increase of MCP-1 level as a strong chemoattractant for monocytes and activated ?-lymphocytes maintains the process of adipose tissue inflammation. Consequently, in case of obesity products of adipocytes increase the secretion of proinflammatory cytokines, which can change the metabolic and secretory activity of adipocytes; it results in the further growth of the inflammatory reaction, development of the IR and ovarian dysfunction. The activation of the innate immunity receptors may result in the increase of the cytokine formation and pimelitis that promote the development of the IR and ovarian dysfunction.

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