ABSTRACT

Function of gut mucosal barrier: methodology and modulation

Right function of the intestinal barrier is essential for maintaining the homeostasis of the inner environment and it serves as a mechanical barrier against penetration of macromolecular compounds and microbes from outer environment. Impaired gut mucosa cannot effectively protect from invasion of infectious microorganisms, antigens from food, bacteria, viruses and xenobiotics into the subepithelial gut layer. Excessive interaction among the immune system and antigens from intestinal lumen can lead to immune mediated damage of the organism. Damaged intestinal barrier plays an important role in the pathogenesis of inflammatory and autoimmune diseases, like inflammatory bowel disease, diabetes, celiac disease and rheumatoid arthritis. The aim of this study was to define methods for measuring intestinal permeability, which would reflect the gut barrier damage. We were trying to detect the gut damage caused by indomethacin (non-steroidal anti-inflammatory drug), alcohol and bacterial LPS by measuring the intestinal permeability for 4,4 kDa FITC-dextran. We were also evaluating changes in gene expression of tight junction proteins, IL-6 and iNOS in mice after intraperitoneal administration of LPS, which induces septic shock. Another goal was to evaluate the effect of probiotic bacteria components on the intestinal barrier function. On mice model of DSS colitis we have found out, that preventive administration of probiotic bacteria *L. casei* ameliorates the state of intestinal barrier. We have proved using the imunofluorescence method that production and localization of tight junction proteins remains the same in the group with *L. casei* as in the healthy mice. These results were confirmed by RT-PCR. Further we have compared the intestinal permeability of adult and young breast feeding germ free mice after administration of indomethacin. There was no statistically significant difference in permeability among adult mice, however there was a statistically significant difference in increased intestinal permeability in young germ free mice compared to conventional young mice.

Conclusion: Results are showing the importance of the intestinal barrier and its damage stands at the beginning of many inflammatory and immune system mediated diseases. Further analyzing of environmental factors and searching for compounds which could influence the intestinal permeability and understanding the mechanisms of its damage can help in prevention and successful treatment. For example a lysate of probiotic bacteria *L.*

casei is improving the intestinal barrier, it was confirmed in experimental model of DSS colitis. Our results show that the bacterial colonization of gastrointestinal tract can influence the intestinal permeability, which changes soon after birth.

Key words: intestinal barrier function, probiotics, intestinal permeability, FITC-dextran, germ free mice, LPS, septic shock, indomethacin