Streszczenie w języku angielskim

Gut-blood barrier permeability to bacterial metabolites under pathophysiological conditions

The gut-blood barrier is a multilayer system that controls the passage of nutrients, bacterial metabolites, drugs, and other exogenous compounds from intestinal lumen to the bloodstream. The integrity of the barrier may be impaired in gastrointestinal, as well as in cardiovascular and some metabolic diseases where intestinal perfusion is impaired due to hemodynamic or vascular changes. This may result in easier access of biologically active compounds, such as gut bacterial metabolites, to the bloodstream and may affect functioning of entire organism. Therefore, the permeability of the gut-blood barrier and increase in bacterial metabolites concentration may be a marker of both intestinal and extraintestinal diseases.

Intestinal bacteria produce a number of biologically active compounds such as methylamines or short-chain fatty acids. They can have both beneficial and adverse effects on the body. For example, it has been shown that the increase in plasma level of trimethylamine oxide (TMAO), formed in the liver from trimethylamine (TMA, a bacterial metabolite), is positively correlated with cardiovascular risk. The mechanisms of the TMAO increase in blood remain unclear. Increased passage of TMA through the gut-blood barrier may be a key factor. So far, little is known how the morphological and functional changes that occur in the intestines in systemic disorders affect the gut-blood barrier permeability for bacterial metabolites.

The aim of presented studies was to develop an optimal method to assess the function (permeability) of the gut-blood barrier which does not require administration of exogenous marker and is independent of individual factors such as diet. Another aspect was to investigate the changes in bacterial metabolites concentration associated with aging and hypertension.

An in vivo method for evaluating the gut-blood barrier and liver metabolism of bacteria-derived products in rats has been developed (Publication No. 1). Furthermore, a non-invasive method was tested in the animal model of colitis and in patients with inflammatory bowel disease. Intestinal permeability was determined based on the ratio of metabolite concentration in blood to fecal concentration. The method only requires a sample of stool and peripheral blood, therefore it is relatively non-invasive and simple. At the same time it is

independent of individual factors, such as diet or composition of the bacterial flora. The increased permeability for bacterial metabolites (short-chain fatty acids) in rats and patients with colitis in comparison to control groups has been confirmed. In addition, these changes were positively correlated with standard intestinal function markers (Publication No. 2).

Morphological and functional changes in intestines, including permeability to TMA, which are associated with aging (in Sprague Dawley and Wistar Kyoto rats in different age), as well as hypertension-induced changes (in Spontaneously Hypertensive Rats) were assessed. Moreover, the therapeutic potential of enalapril (angiotensin converting enzyme inhibitor) in restoring the physiological function of the gut-blood barrier has been investigated.

Both hypertensive rats and older rats showed increased TMA colon permeability, which was accompanied by morphological and hemodynamic changes in the colon (Publication Nos. 3 and 4). Rats treated with enalapril showed improvement in pathological changes induced by hypertension. Therefore, the gut-blood barrier is a potential target for angiotensin converting enzyme inhibitors.

In conclusion, functional changes of the gut-blood barrier can be effectively assessed using the presented method by the ratio of bacterial metabolites concentrations. The method is non-invasive, therefore, it can be used in both experimental and clinical practice. In addition, cardiovascular diseases such as hypertension may be characterized by increased gut-blood barrier permeability to bacterial metabolites. This in turn may negatively affect the underlying disease. Furthermore, the increase in cardiovascular risk associated with aging may be partially caused by the increase in plasma concentration of toxic metabolites due to intestinal damage.

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