The role of gene factors, hyperlipidemia and enteral microflora in the development of gallstone disease.

Hidayet Bilaloglu Isayev
M.A. Topchubashov Research Centre of Surgery

Galls-stones represent a mass of solid substance formed in gallbladder and more often consist of cholesterol (1). The excess of cholesterol or insufficient bile acid increases the evidence of gall-stones (2). Double investigation showed that genetic factors constitute 25% [95% of DI: 9-40%] of phenotypical variation of gallstone disease (3). Egil Ferkingstad, Asmundur Oddsson, Kari Stefansson (4) performed met-analysis of two genome studies in 27174 patients suffering from gallstone disease in Island and Great Britain. And they revealed 21 new variants of genome associated with gallstone disease in 20 loci. The findings obviously demonstrated that there are two different of low frequency missense variants in SLC10A2 encoding apical natrium-dependent transporter of bile acids (ASBT), and it may be assumed with reasonable confidence that they relate to high risk of gallstone disease. The main function of ASBT is a reabsorbing of bile salts (95%) out of terminal ileum in ileocysts and then bile salts are transported back in liver via enterohepatic circulation (5).

SLC10A2 encodes protein which reabsorbs bile salts out of ileum with its following participation in enterohepatic circulation. The authors revealed four new variants of low frequency sequences in (two are different variants) SERPINA1 and HNF4A relating to gallstone disease. Thus, we may conclude, that more low transporter of bile acids with the help of ASBT are accompanied by high risk of gallstone disease, and it became apparent the role of enteral compartment of enterohepatic circulation of bile acids was susceptible to gallstone disease.

In this respect, with the revealing of new variants related to gallstone disease, the authors indicated the role of enteral compartment of enterohepatic circulation of bile acids to predisposed gallstone disease.

Other researches demonstrate that there is no a direct way between lipid levels in serum and calculus formation in gallbladder that is coordinated with the studies by previous researches (61). However, in the opinion of other authors certain metabolic aspects of cholesterol may promote the development of gallstone disease (6, 7, 8).

We may conclude from this finding, that the variants of sequences having an effect on the levels of cholesterol secreted into bile or the ratio of cholesterol:bile acid seems to have some effect on the formation of gall-stone. Depending on the mechanism of gene action regulating cholesterol, allele associated with risk of gall-stone formation may not always reduce or increase the levels of cholesterol in serum. The reported associations confirm the role of variants of sequences in genes participating in homeostasis of cholesterol, in particular they release the enteral cholesterol of enterohepatic circulation in pathogenesis of gallstone disease. We may conclude that the variants of sequences having an effect on the levels of cholesterol secreting into bile or the ratio of cholesterol:bile acid are likely causes the formation of gall-stones.

Besides, on the other hand, the problems of the effect of ileum micro-flora in the process of enterohepatic circulation of bile acids to date are not yet solved.

Bile salts are steroid-containing and synthesized in hepatocysts. There are primary and secondary bile salts. The primary bile salts (cholate, kenodoxicholate) after adhesion to glycine (or taurine) are transformed into bile acids solved in water which introduce into enteral compartment with bile. Normal bile has 40% of cholate, 40%-kenodoxycholate and 20%-deoxycholate. The functions of bile salts are as follows: providing the normal bile outflow, adhesion to lipids in liver with the following outflow in enterum with bile, the maintenance of calcium ions in bile in adhesive state.

After the effect on primary bile salts of enteral micro-flora they transform in secondary salts. Out of latter ones deoxylate being resorbed was 20% of bile salt in bile. Moreover, bile salts perform three main functions. The bile salts are functioning in the following ratio: 40% of cholate + 40% - kenodoxycholate + 20% - deoxycholate.

hidayet@gmail.com