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Short Communication

Neopterin Levels in Blood Serum and Bile in Acute and Chronic Liver Disease

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Introduction

Neopterin is released by macrophage in vitro, particularly when stimulated with interferon-gamma (IFN- γ) derived from activated T cells (7, 11, 15). Recent attention has been focused on neopterin as a marker for the activation of cell-mediated immunity, cell proliferation, and differentiation (1). Neopterin itself is biologically stable, and therefore the message induced during immune response is readily detectable. Neopterin is a marker for infectious diseases, especially viral diseases involving the macrophage system (3, 13, 14). Measurement of neopterin in body fluids turned out to be a sensitive diagnostic and prognostic parameter for monitoring patients with activated cellular immune system and has therefore been established in a variety of fields in clinical medicine, e.g., for monitoring patients with chronic infection, with malignant tumours and recipients of organgrafts (15). In liver diseases increased serum and urinary neopterin levels have been observed in patients with acute hepatitis, chronic hepatitis and liver cirrhosis (1). Weiss *et al.* supposed, that the liver is the source of constitutive neopterin concentrations and high concentrations of neopterin were detected in biliary fluid (16). The neopterin levels in the bile fluid are much higher than in serum. Hausen *et al.* suggested that the concentration of biliary neopterin seems to be more specific than serum or urinary concentrations for differentiating liver diseases (8).

Our aim was to investigate neopterin levels in bile of patients with cholelithiasis and viral hepatitis B as well as neopterin concentration in blood serum of the asymptomatic individuals with immuno-serological

signs of HBV infection.

Material and Methods

Examinations in bile were carried out in 35 patients (30 women, 5 men; aged 33~70), which were divided in the following groups: I-22 patients with cholelithiasis, the gallbladder bile for neopterin estimation was collected during surgical intervention, II-13 patients with viral hepatitis B, the gallbladder bile was obtained from duodenal tube. The diagnosis of particular patients was established on the basis of the whole anamnesis data, clinical course, as well as the biochemical and immunoserological investigation.

Examinations in blood serum were carried out in 85 people (25 women, 60 men; aged 23~70) which have been divided in the groups: III-6 clinically healthy HCV infected persons, IV-17 alcoholics asymptomatic HBsAg carriers, V-20 alcoholics without immuno-serological signs of HBV, HCV infection, VI-19 hemodialysed patients with HCV infection, VII-20 healthy individuals.

The examinations of immunoserological markers of HBV, HCV infection were performed by commercially available Abbott kits, HCV infection was confirmed using confirmatory test from ORTHO-Chiron Riba. The neopterin levels were estimated by radioimmunoassay (IMMUNtest Neopterin HENNING GMGH-Germany). The neopterin levels in the different groups were compared by Students t-test.

Results

Table I shows the mean neopterin levels in the bile of cholelithiasis patients and viral hepatitis B patients.

Table 1. Neopterin levels in the bile

Group	n	Neopterin nmol/l x ± SD	Statistical analyse
I	22	153 ± 87.5	I-II p<0.05
II	13	252.6 ± 184.6	

I-cholelithiasis patients

II-viral hepatitis B patients

Table 2. Neopterin level in blood serum in analysed groups of patients

Group	n	Neopterin nmol/l x ± SD	Statistical analyse
III	6	3.8 ± 1.9	IV-VII p<0.01
IV	17	7.2 ± 3.8	
V	20	6.5 ± 4.1	V-VII p<0.05
VI	19	202.4 ± 95.5	
VII	20	2.9 ± 0.4	VI-VII p<0.001

III-clinically healthy HCV infected persons,

IV-alcoholics, asymptomatic HBsAg carriers,

V-alcoholics without immuno-serological signs of HBV, HCV infection,

VI-haemodialysed patients with HCV infection,

VII-healthy individuals

The mean levels in the bile of cholelithiasis patients (group I) was 153.5 ± 87.5 nmol/l and this level was significantly higher than the neopterin concentrations of group II ($p<0.05$).

Table II shows the mean neopterin levels in serum in other analysed groups of patients. In each analysed group the mean neopterin concentrations were higher than in the control group. The highest neopterin level was in hemodialysed patients with HCV infection- 202.4 ± 95.5 nmol/l and was significantly higher than in the control group ($p<0.001$).

Conclusion

In the present study, serum and bile neopterin levels were examined in various infection diseases with the RIA kit (9). Neopterin has attracted interest as a clinically useful marker for cellular immune activation (4). Weiss *et al.* and our study suggested that large amounts of neopterin are excreted with the biliary fluids. Those results confirm data that these pteridine derivatives are synthesized in the liver constitutively, i.e. in absence of immunological stimulation (16).

In the present study, biliary neopterin levels in viral hepatitis B patients were significantly higher than those in cholelithiasis patients. Elevation of neopterin has been shown to indicate activation of cell-

mediated immune response in vivo. The present results may be explained by the fact that the B viral infection mediated cellular immune reactions.

In our study, serum neopterin levels in hemodialysed patients with HCV infection were the highest among the liver diseases. Fuchs *et al.* observed that the haemodialysed patients show significant signs of cellular immune activation (5) which agrees with, e.g., increased expression of IL-2 receptors on T-cells, and circulating gamma interferon (5). According to these results, the present results may be explained by the view that the high neopterin levels in uraemic patients in this study are mediated mainly by cellular immune reaction rather than directly by the virus.

Monitoring of neopterin concentrations allows the quantification of a specific aspect of the immune system (2, 6, 12). The strong correlation between neopterin concentrations and various viral diseases has established neopterin as an important marker for pathology of the disease (4, 10).

Our results indicate that serum and bile neopterin levels may be useful makers for cell-mediated immunity in liver disease, and that the immune system response in liver disease may be different for different pathogens.

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