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Study of Serum Homocysteine Status in Patients with Acute Pancreatitis in a Medical College & Hospital of Odisha

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Abstract:

Homocysteine plays a established role in coronary artery disease. It also plays a siginificant role in inflammation and malignancy as studied experimentally. Few have suggested that a relationship might exist between pancreatitis and homocystinuria, possibly due to occlusive vascular disease of the pancreas. As of now, serum homocysteine levels in pancreatic disease have not been studied effectively. We aimed to analyze the homocysteine status in patients with acute pancreatitis, and the changes of the serum homocysteine level at the acute onset of the disease. 25 acute pancreatitis patients and 25 healthy subjects were studied. Serum homocysteine, vitamin B_{12}, folate, amylase, lipase, C-reactive protein, total cholesterol, HDL and LDL cholesterol, triglycerides, blood urea nitrogen, white blood cells and creatinine were measured in the two groups of subjects. Levels of homocysteine were significantly increased in patients with acute pancreatitis along with increase in levels of serum creatinine, blood urea nitrogen, WBC counts, amylase, lipase, and C-reactive protein. Also reduced creatinine clearance was also noted in these patients, however was not statistically significant. Serum total cholesterol, HDL and LDL cholesterol concentrations were apparently similar between the two groups of subjects. Hence our study suggests that homocysteine has a role in acute pancreatitis. Increased serum homocysteine levels in acute pancreatitis could be used a marker, as one of the diagnostic criteria for acute pancreatitis. In conclusion, this particular study is showing that patients with acute pancreatitis have higher serum homocysteine levels than healthy subjects.

Keywords: homocysteine, homocystinuria, pancreatitis

Introduction:

Homocysteine is a non-protein α-amino acid. It is a homologue of the aminoacid cysteine, differing by an additional methylene bridge (-CH2-). It is biosynthesized from methionine by the removal of its terminal methyl group. Homocysteine can be recycled into methionine or converted into cysteine with the aid of certain B-vitamins. A high level of homocysteine in the blood (hyper homocysteinemia) makes a person more prone to endothelial cell injury, which leads to inflammation in the blood vessels, which in turn may lead to atherogenesis, which can result in ischemic injury.[1] Hyperhomocysteinemia is therefore a possible risk factor for coronary artery disease. Coronary artery disease occurs when an atherosclerotic plaque blocks blood flow to the coronary arteries, which

supply the heart with oxygenated blood. Hyperhomocysteinemia has been correlated with the occurrence of blood clots, heart attacks and strokes, though it is unclear whether hyperhomocysteinemia is an independent risk factor for these conditions. Hyperhomoscyteinemia has also been associated with early pregnancy loss[2] and with neural tube defects.[3] Some studies suggested that there is a relationship between pancreatitis and homocystinuria, possibly being secondary to occlusive vascular disease of the pancreas.[4] High homocysteine levels may be the cause of acute pancreatitis with endothelialdysfunction and impaired microvascular circulation. Pancreatic microvascular perfusion failure may be a primary reason for clinical and experimental acute pancreatitis.[5,6] Our study was aimed to analyze serum homocysteine status in acute pancreatitis patients in a medical college of Odisha.

Materials and Method:

Our study was a prospective case-control study. 25 patients with acute pancreatitis, admitted to Medicine ward and ICU of Hi-tech Medical College & Hospital, Bhubaneswar, Odisha were taken as case group. The control group consisted of 25 healthy subjects from Odisha general population. Informed consent was obtained from both the patients and the control subjects. The diagnosis of acute pancreatitis was based on the typical clinical signs of abdominal pain, vomiting or nausea, serum amylase of more than 3 times the upper reference limit, and/or positive ultrasonography or computed tomography scan. The severity of acute pancreatitis according to the Atlanta criteria was mild in all 25 patients. After detailed physical examination, venous blood was taken within 24 hours from admission and sent to central laboratory for evaluation of plasma homocysteine and serum vitamin B12, folate, amylase, lipase, C-reactive protein (CRP), serum HDL and LDL, cholesterol, triglycerides, blood urea nitrogen (BUN), white blood cells (WBC) and creatinine. Vitamin B12 and folic acid levels were assessed in order to exclude cases of vitamin deficiency. Creatinine clearance was calculated using the Cockroft and Gault formula:

Creatinine clearance (mL/min) = (140 - age (year)) x weight (kg) / (0.81 x serum creatinine(µmol/L)). For women this value was multiplied by 0.85. Serum folate and vitamin B12 were measured by radio-assay. Total homocysteine concentrations were determined in EDTA plasma by high performance liquid chromatography. Immediate plasma seperation was carried out after blood sampling, and the plasma was kept at 4°C.

Statistical Analysis:

The results were expressed as mean ± SD. Two-tailed P values less than 0.05 were considered statistically significant. Differences between cases and the control subjects were analyzed using the unpaired t test. SPSS 11 for Windows statistical package was used for statistical analysis.

Results:

The results are shown in Table 1. The plasma levels of homocysteine were significantly higher in acute pancreatitis patients than in healthy subjects while no significant differences were detected in vitamin B12 and folate. There were no significant differences in serum total, HDL, and LDL cholesterol concentrations between the two groups of subjects while trygliceride, BUN and WBC counts were significantly higher in acute pancreatitis patients. Moreover, the acute pancreatitis patients had serum creatinine levels significantly higher than the control subjects. The creatinine clearance was also impaired in these patients. Finally, amylase, lipase, and CRP were significantly higher in acute pancreatitis patients than in control subjects.

Table 1: Comparison of different parameters in cases and controls

Parameters Reference	Reference Range	Cases (Mean ± SD)	Controls (Mean ± SD)	P value
Homocysteine (µmol/L)	5-12	21.6 ± 8.5	7.6 ± 2.1	<0.001
Vitamin B12 (pmol/L)	180-810	400 ± 220	412 ± 225	0.849
Folate (nmol/L)	6-36	10.3 ±4.5	10.5 ± 3.3	0.858
Amylase U/L	25-115	1324 ± 580	60.5 ± 15	<0.001
Lypase U/L	114-286	2800 ± 1200	140 ± 25	<0.001

CRP (mg/L)	0-5	80.2 ± 30.6	3.5 ± 1.3	<0.001
Total cholesterol (mg/dL)	0-200	182.6 ± 24.5	181.5 ± 35.2	0.898
HDL cholesterol (mg/dL)	30-85	40.2 ± 7.3	39.2 ± 5.5	0.586
LDL cholesterol (mg/dL)	0-130	110.8 ± 8.6	105 ± 30.5	0.364
Triglycerides (mg/dL)	35-135	205 ± 20.3	120.8 ± 18.5	<0.001
BUN mg/dL	7-18	28.6 ± 4.3	17.6 ± 6.3	<0.001
WBC (cells x10^9/L)	4,600-10,200	16,000±3200	7500±1200	<0.001
Creatinine (µmol/L)	0-1.3	1.25 ± 0.16	0.95±0.15	<0.001
Creatinine clearance (mL/min)	100-120	76.1 ± 24.5	95.6 ± 20.5	0.003

Discussion:

Acute pancreatitis is an inflammatory disease associated with auto digestion of the pancreas due to intra-pancreatic activation and the release of digestive enzymes, but there is increasing evidence that pancreatic ischemia plays an important role in this disease. Pancreatic microvascular perfusion failure may be a reason for clinical[8,9,10] and experimental acute pancreatitis.[5,6] Reduction in the pancreatic circulation aggravates pancreatic damage in the course of acute pancreatitis.[6] It is well-known that a disturbance of pancreatic microcirculation leads to the formation of thrombi in capillaries, the activation of leukocytes, the release of proteolytic enzymes and the formation of oxygen-derived free radicals and pro inflammatory cytokines. Makins et al[11] suggest that there is a relationship between pancreatitis and homocystinuria, possibly being secondary to occlusive vascular disease of the pancreas. High homocysteine levels may be a cause of acute pancreatitis with endothelial dysfunction and impaired microvascular circulation. In addition, it may lead to complications as per Sircar et al[12] report cardiogenic shock due to acute pancreatitis after hyperhomocysteinemia.

In our study, we found that the plasma homocysteine level was increased in patients with acute pancreatitis as compared to normal controls. The hyperhomocysteinemia was probably due to disturbed methylation. A relationship between hyperhomocysteinemia and acute pancreatitis has not been studied previously. However, Batra S.[13] suggested that homocystinuria is an uncommon metabolic cause of pancreatitis, and pancreatitis is an unusual manifestation of homocystinuria. Batra quoted that pancreatic disease in homocystinuria is preventable and that recurrent disease is amenable to therapy which reduces homocysteine concentrations. They would recommend that homocysteine concentrations be included in the metabolic workup of chronic relapsing pancreatitis. We agree with suggesting that, in acute pancreatitis, recurrent acute pancreatitis may be related to hyperhomocysteinemia in the presence of normal folate and vitamin B12 levels. Another explanation for high homocysteine levels was insufficient renal function.

The healthy kidney plays a major role in homocysteine clearance and metabolism, as it does with other amino acids. Hyperhomocysteinemia in renal disease is related to reduce plasma homocysteine clearance. The underlying cause of this reduction is unknown but involves a defect in renal and/or extrarenal clearance.[14] In our study, BUN and serum creatinine values were significantly higher in acute pancreatitis patients than in the control group. Plasma homocysteine levels in acute pancreatitis subjects increased with a decrease in creatinine clearance when compared to the control subjects. The inverse relationship between homocysteine levels and the glomerular filtration rate is related to reduce renal function suggesting that increased plasma homocysteine levels may be useful as a marker of decreased glomerular filtration rate when assessing high risk patients.

Lien et al[15] observed a close relationship between total plasma homocysteine and creatinine in iatrogenic hypothyroidism. They found a progressive and parallel increase in total homocysteine and serum creatinine in hypothyroidism. Homocysteine and serum creatinine responses were explained by the hypodynamic circulation and renal failure in hypothyroidism. And acute pancreatitis also decreases the glomerular filtration rate as in hypothyroidism, which is related to serum creatinine, but also closely associated with plasma homocysteine. We observed higher plasma homocysteine and lower creatinine clearance in acute pancreatitis patients as compared to healthy

subjects. In conclusion, a decreased glomerular filtration rate in acute pancreatitis is related to decrease renal homocysteine clearance.

Conclusion:

This study shows that plasma homocysteine is significantly increased in patients with acute pancreatitis and a decreased creatinine clearance was found in these patients. Additional research is needed to better understand the effect of homocysteine levels in acute pancreatitis.

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