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Clinical Utility of Enzymes, Electrolyte and Uric Acid in Different Stages of Chronic Pancreatitis

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Abstract:

Purpose: *- The present study examines the clinical utility of enzymes, electrolytes and uric acid in different stages of chronic pancreatitis admitted at Chandulal Chandrakar Memorial Medical College and Hospital Kachandur, Durg.*

Methods: *- A total number of 35 male subjects were selected at CCM Medical College Hospital Durg. 35 subjects are suffering from chronic pancreatitis average age range of 40 to 70 years. 35 subjects age, sex matched was selected for control group. Controls were clinically and physically normal and healthy. The study was conducted in the period of May 2015 to Feb 2017.*

Results and Conclusion: *- There were 35 patients suffering from chronic pancreatitis selected for study group and 35 normal healthy for control group. Levels of serum amylase, serum lipase, serum electrolytes and serum uric acid are given in following table no2. Most pancreatic function tests have high sensitivity and specificity to accurately diagnose patients with advanced CP. Serum lipase levels due to pancreatic disorders closely parallel the changes of serum amylase except that serum lipase may remain elevated longer than amylase (up to 2 weeks). Elevated serum amylase and lipase are strong evidence for a pancreatic process. When the serum amylase is elevated and the lipase is normal, non-pancreatic causes of the hyperamylasemia are more likely.*

Keywords: *- CP, AP, Amylase, lipase, Uric acid, Na, K, Ca*

Introduction

Pancreatitis is a rare disease in which the pancreas becomes inflamed. Pancreatic damage occurs when the digestive enzymes are activated and begin attacking the pancreas. In very severe cases, pancreatitis can result in bleeding into the gland, serious tissue damage, infection, and cyst formation. Severe pancreatitis can also cause damage if enzymes and toxins are released into the bloodstream, which can harm other vital organs such as the heart, lungs, and kidneys.

Chronic pancreatitis occurs most commonly after an episode of acute pancreatitis and is the result of ongoing inflammation of the pancreas. Chronic pancreatitis can be caused by prolonged alcohol use or smoking. It can also be caused by metabolic disorders. Very rarely, patients can have chronic pancreatitis that runs in families (hereditary pancreatitis). Patients with chronic pancreatitis may suffer with severe pain and loss of pancreatic function. This can cause abnormalities with digestion and blood sugar. Chronic pancreatitis is a long-standing inflammation of the pancreas that alters the organ's normal structure and functions.[1] It can present as episodes of acute inflammation in a previously injured pancreas, or as chronic damage with persistent pain or malabsorption. It is a disease process characterized by irreversible damage to the pancreas as distinct from reversible changes in acute pancreatitis.

Pathophysiology

Grossly, the pancreas may be enlarged or atrophic, with or without cysts or calcifications. The ducts may be dilated, irregular, or strictured. Essential pathologic features include irregular and patchy loss of acinar tissue, chronic inflammation, ductal changes, and fibrosis. These gross changes are end-manifestations of complex pathogenic mechanisms that are associated with gene mutations, metabolic and environmental factors.

Several past theories have been developed to explain the pathogenesis of chronic pancreatitis. The premise of the oxidative stress hypothesis is that reactive by-products of hepatic mixed function oxidase activity damage the pancreas through chronic reflux of bile into the pancreatic duct. The toxic-metabolic theory is that alcohol is directly toxic to the acinar cell through a change in intracellular metabolism. The stone and duct obstruction theory suggests that alcohol increases the lithogenicity of pancreatic juice and causes stone formation. Chronic contact of the stones with duct epithelial cells produces ulceration, scarring, and obstruction of the acinar glands. The necrosis-fibrosis theory

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emphasizes that acute and chronic pancreatitis represents a spectrum of disease. Inflammation from acute pancreatitis leads to scarring and extrinsic compression of the pancreatic ductules. Recently, research in the immunology of pancreatitis has demonstrated the primary role of pancreatic stellate cells.

Stages of pancreatitis[2,3]

First Stage - Chronic calcifying pancreatitis

Second stage - Chronic obstructive pancreatitis

Third Stage - Chronic autoimmune pancreatitis

Symptoms of pancreatitis

Most patients with acute pancreatitis have upper abdominal pain that radiates (spreads) to their backs. Patients may describe this as a "boring sensation" that is primarily aggravated by eating and slowly becomes worse. Their abdomens may be swollen and very tender. Patients may also have associated nausea, vomiting, fever, and an increased heart rate.[4,5]

- Constant pain that radiates to the back. In some patients, the pain may be disabling.
- Poor absorption of food, leading to weight loss. Patients may lose weight, even when their appetite and eating habits are normal. This poor absorption occurs because the body is not secreting enough pancreatic enzymes to break down the food normally.
- Diabetes may develop if the insulin-producing cells of the pancreas become damaged.

Causes of pancreatitis

Among the causes of chronic pancreatitis are the following[6]:

- Alcohol
- Autoimmune disorders
- Intraductal obstruction
- Idiopathic pancreatitis
- Tumors
- Ischemia
- Calcific stones

The relationship between etiologic factors, genetic predisposition, and the pace of disease progression requires further clarification, though recent research indicates smoking may be a high-risk factor to develop chronic pancreatitis.[7] In a small group of patients chronic pancreatitis has been shown to be hereditary. Almost all patients with cystic fibrosis have established chronic pancreatitis, usually from birth. Cystic fibrosis gene mutations have also been identified in patients with chronic pancreatitis but in whom there were no other manifestations of cystic fibrosis. Obstruction of the pancreatic duct because of either a benign or malignant process may result in chronic pancreatitis.[8]

Diagnosis

Pancreatitis is the medical term for inflammation of the pancreas. The pancreas produces digestive enzymes and the blood sugar-regulating hormones insulin and glucagon. Acute pancreatitis occurs suddenly and is most often caused by gallstones passing through the common bile duct. The common bile duct and the pancreatic duct join together to transport digestive enzymes and bile to the small intestine. A gallstone in the common bile duct can cause increased pressure in the pancreatic duct, leading to pancreatitis. Acute pancreatitis causes a spike in blood amylase and lipase levels.

Chronic pancreatitis refers to persistent inflammation of the pancreas, which is most frequently due to prolonged, excessive consumption of alcohol. Blood amylase and lipase are typically elevated with chronic pancreatitis[9,10]

Acute pancreatitis is primarily suspected when a patient has the symptoms mentioned above and has risk factors such as heavy alcohol use or gallstone disease. Confirmation of pancreatitis is done by measuring levels of the two digestive enzymes, amylase and lipase, in the blood. High levels of these two enzymes strongly suggest acute pancreatitis. As the patient recovers, the digestive enzyme levels decrease to normal.

Chronic pancreatitis is generally suspected when a patient has the symptoms mentioned above and has risk factors such as a heavy alcohol use. Diagnosis can be difficult but is aided by such techniques as pancreatic function tests and radiographic imaging of the pancreas. In more advanced stages of the disease, when poor absorption or diabetes are present, the doctor can use blood, urine, and stool tests to monitor the progression of the disease.[11]

Diagnostic tests include:

- Pancreatic function test, in which the pancreatic function is measured by determining if the pancreas is producing the appropriate levels of digestive enzymes
- Glucose tolerance test to measure damage to the cells in the pancreas that make insulin
- Ultrasound, which can produce images of the pancreas so that abnormalities may be seen
- Computed axial tomography scan (CAT scan), which can produce images of the pancreas so that abnormalities may be detected

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- ERCP (endoscopic retrograde cholangiopancreatography), an exam that shows the size and shape of the pancreas and its connections leading to the intestine
- Esophagogastroduodenoscopy with ultrasound (EUS), an examination in which images of the pancreas are obtained from inside the stomach and intestine using sound waves.

Treatment of Pancreatitis

Some cases of severe pancreatitis can result in death of pancreatic tissue. In these cases, surgery may be necessary to remove the damaged pancreatic tissue. An acute attack of pancreatitis usually lasts only a few days, unless it is caused by gallstones. An acute attack of pancreatitis caused by gallstones may require removal of the gallbladder or endoscopic surgery of the bile duct.[12]

Pancreatic surgery can be performed as a laparoscopic or "minimally invasive" procedure. During laparoscopic surgery, five or six small (5 to 10 millimeter) incisions (cuts) are made in the abdomen. The laparoscope and surgical instruments are inserted through these incisions. The surgeon is guided by the laparoscope, which transmits a picture of the internal organs on a monitor. The advantages of laparoscopic surgery include smaller incisions, less risk of infection, pain, and scarring, and a more rapid recovery. The need for surgery is determined by the severity of the pancreatitis. After the gallstones are removed and inflammation subsides, the pancreas usually returns to normal.[6,13]

Chronic pancreatitis can be somewhat difficult to treat. Doctors will primarily try to relieve the patient's pain and improve the nutritional and metabolic problems that result from loss of pancreatic function. Patients are generally given pancreatic enzymes and insulin, since these substances are not being secreted or released by the pancreas. Pancreatic enzyme pills are usually prescribed to be taken before meals to aid in nutrient absorption. A low-fat diet may also be helpful. Surgery may be necessary to relieve abdominal pain, restore drainage of pancreatic secretions, treat chronic pancreatitis caused by blockage of the pancreatic duct, or to reduce the frequency of attacks. Patients must stop drinking alcoholic beverages, follow their physician's and dietitians dietary recommendations, and take the proper medications in order to have fewer and milder attacks of pancreatitis.[14,15]

Epidemiology

The annual incidence of chronic pancreatitis is 5-12 per 100,000 persons; the prevalence is 50 per 100,000 persons.[16] New cases of chronic pancreatitis develop in about 8 per 100,000 people a year and currently affect about 50 per 100,000 people in the United States.[17]

Material and Method

A total number of 35 male subjects were selected at CCM Medical College Hospital Durg. 35 subjects are suffering from chronic pancreatitis average age range of 40 to 70 years. 35 subjects age, sex matched was selected for control group. Controls were clinically and physically normal and healthy.

Table1. Distribution of Study group subjects

Groups	No of Subjects
Normal Healthy Group	35
Chronic Pancreatitis patients	35
Age group	40-70
Stage I	15
Stage II	12
Stage III	08
Age wise Distribution of Patients	
40-50	12
51-60	16
61-70	7
Heavy alcohol Drinking	35
Alcohol drinking with Smoking	24

Sample Collection

5 ml blood sample was collected in plain dry test tube. Serum sample was obtained by centrifugation and sample were immediately separated into another plain dry test tube and stored at -08^0 C. Serum sample was used to estimate serum amylase, serum lipase, serum electrolytes, serum uric acid levels were also carried out in serum samples of all the subjects. Estimation of Serum amylase carried by using Somogyi's Amyloclastic photometric end point method.[18] Serum lipase carried out by using turbidimetric method.[19] Serum electrolyte estimated on flame photometer and serum uric acid level estimated by using caraways method[20]

Data Analysis

Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student –t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.05$ were considered statistically significant.

Observation, Results and Discussion

There were 35 patients suffering from chronic pancreatitis selected for study group and 35 normal healthy for control group. Levels of serum amylase, serum lipase, serum electrolytes and serum uric acid are given in following table no2

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Table2: Shows the activity of biochemical parameters in different stages of chronic pancreatitis and control group.

Biochemical Parameters		Control Group	Normal range	Stage I	Stage II	Stage III
Age Group		40-60		40-52	48-60	55-70
Serum Amylase U/L		53.9 ± 23.72	23-85	266 ± 197	96 ± 79	22 ± 11
Serum Lipase U/L		94.2 ± 34.59	0-160	282 ± 98	126 ± 78	19 ± 9.2
Uric acid mg/dl		4.9 ± 2.13	3.5-7.0	18.6 ± 1.6	19.6 ± 1.4	15.6 ± 3.9
Serum Electrolyte	Na(mEq/ L)	139 ± 4.27	136-145	144 ± 5.3	139 ± 3.9	140 ± 4.2
	K (mmol/ L)	4.72 ± 1.93	3.5-5.0	4.9 ± 1.7	4.1 ± 0.98	4.0 ± 0.86
	Ca (mg/dl)	2.36 ± 0.38	2.20-2.55	3.78 ± 1.45	2.37 ± 0.87	1.47 ± 1.01

Serum Amylase

Amylase is the pancreatic and salivary gland enzyme responsible for digesting carbohydrates. The level will increase 2 to 12 hours after the beginning of symptoms of acute pancreatitis and peaks at 12 to 72 hours afterward. It may rise 5 to 10 times the normal level and will usually return to normal within a week but in chronic pancreatitis or long-term inflammation of the pancreas activity of should not come in normal range before treatment. Pancreatitis is likely if the level reaches 3 times above the upper limit of normal. Amylase also may be monitored in people with chronic pancreatitis; it will often be moderately elevated until the cells that produce it are destroyed, at which point blood levels of amylase may be decreased. Normally, a total amylase test is requested. Sometimes, the isoenzyme tests are requested individually to distinguish pancreatic and non-pancreatic causes of increased amylase. Normally amylase won't get into circulation due to the barrier effect of cells lining the small tubules of pancreatic glands. Pancreas also produces proteolytic enzymes which break down proteins but they don't digest the protein of pancreatic cells itself because of presence of anti- proteinases in pancreas and various other protective mechanisms.

In present study we observe that the level of amylase is highly significantly increased in stage I of pancreatitis as compared to normal healthy control group because of the subject drinking alcohol, its level were 266 ± 197 in stage I, but disease progressed and stopping alcohol the level goes down in normal range or below normal range in stage II 96 ± 79, in stage III 22 ± 11 and in control group 53.9 ± 23.72 respectively. In our study we observed that 4 patients out of 15 having normal amylase activity but lipase activity is highly increased found in these patients. Activity of amylase increased in chronic pancreatitis because there is intra-pancreatic activation of proteinases due to various factors like ischemia, infections, trauma, anoxia etc. This leads to digestion of pancreatic tissue and barrier which prevents the enzymes getting into circulation is broken. But another study published in 1995 shows that the lower level of normal (LLN) are routinely detected in patients with CP. If such LLN amylase is detected, advanced chronic pancreatitis with significant, if not severe pancreatic exocrine insufficiency can be expected.[21]

Serum Lipase

Lipase is the pancreatic enzyme that, along with bile from the liver, digests fats. Lipase is another enzyme commonly used to diagnose chronic pancreatitis. Lipase is more sensitive and more specific than amylase for the diagnosis and prognosis of chronic pancreatitis.[22,23] In some assays that detect non-pancreatic lipase, milder elevations may occur as a result of non-pancreatic disorders. In people with pancreatitis, lipase may rise to several times than its normal level and remain elevated longer than amylase. The levels of lipase in our study group were 282 ± 98, 126 ± 78, 19 ± 9.2 in different stages and the activity in normal control group was 94.2 ± 34.59. Like with the amylase test, pancreatitis is diagnosed if the lipase level reaches 5 times above the upper limit of normal. As cells are destroyed with chronic pancreatitis and as lipase production drops to less than 10% of the normal level, steatorrhea will form. As chronic pancreatitis progresses, amylase and lipase may be normal or decreased, even during acute attacks.

Pancreatic lipase is secreted into the duodenum through the duct system of the pancreas. Its concentration in serum is normally very low. Under extreme disruption of pancreatic function, such as pancreatitis or pancreatic adenocarcinoma, the pancreas may begin to autolyse and release pancreatic enzymes including pancreatic lipase into serum. Thus, through measurement of serum concentration of pancreatic lipase and amylase can be used for chronic pancreatitis diagnosed.[24]

Serum Electrolytes

Hypercalcemia can lead to acute pancreatitis.[25] Causes include hyperparathyroidism, malignancy (often in the setting of bony metastases or multiple myeloma), vitamin D toxicity, sarcoidosis, familial hypocalciuric hypercalcemia, and total parenteral nutrition and infusions of preoperative high-dose calcium during cardiopulmonary bypass.[26]

In our present study we found that the levels of calcium were 3.78 ± 1.45, 2.37 ± 0.87, 1.47 ± 1.01 in stage I, stage II and stage III respectively and in normal healthy control group is level was 2.20-2.55. The activity of serum calcium was highly increased in stage I because of recurrent acute pancreatitis can progress to chronic pancreatitis, as described by the necrosis-fibrosis theory. The South Indian

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study has proposed that presence of hypercalcemia correlated to PHPT among patients susceptible to tropical chronic pancreatitis (TCP), a form of chronic calcific nonalcoholic pancreatitis may cause an unmasking of preclinical and subclinical diseases.[27] Hypercalcemia leads to the formation of pancreatic calculi and by modifying pancreatic secretion, may lead to protein plug formation.[28] The resultant ductal obstruction can lead to subsequent attacks of acute or chronic pancreatitis.[29]

In present study we observe that there was no significance change found in stage II and stage III Na and K level, slightly in stage I in some patients the level of electrolytes were increased found. In acute pancreatitis the levels were increased found. There is no documentary supports found to this study.

Serum Uric Acid

Cigarette smoking and alcohol consumption are the major factor for pancreatic dysfunction in patients with chronic pancreatitis. In the course of acute pancreatitis may lead to organ damage resulting in their failure. The chronic renal failure can cause disturbances in the exocrine pancreas. The study population consisted of 35 patients with chronic pancreatitis and 35 healthy subjects classified as the control group. The study population was divided into smokers with alcohol drinker and only alcohol drinker. It has been shown 2.4 times higher uric acid concentration in the serum of smoking with alcohol consumption patients with chronic pancreatitis (18.6± 1.6, 19.6 ± 1.4, 15.6 ± 3.9) and in compared to normal control group (4.9 ± 2.13). The results show that cigarette smoking may be an important factor in potential changes in uric acid levels in patients with chronic pancreatitis. In addition, reduced protein catabolism is the result of progressing exocrine pancreatic dysfunction in both smoking and non-smoking patients with chronic pancreatitis. Similar findings observed by Sliwińska-Mossoń M[30] shown that the concentration of creatinine in the groups was in the range of reference values, but in non-smoking and smoking control group that is higher in comparison with patients (respectively 0.97 +/- 0.17 and 0.79 +/- 0.14 [mg/dl] , p = 0.0004; 1.00 +/- 0.14 and 0.78 +/- 0.23 [mg/dl], p = 0.0416). It has been shown 1.5 times higher uric acid concentration in the serum of smoking patients with chronic pancreatitis (245.67 +/- 79.73 micromol/l) compared to non-smoking control group (173.67 +/- 50.08 [micromol/l]). There was a significant difference between the mean value of urea nitrogen (BUN) in terms of the concentration of creatinine (index of BUN/creatinine) in the group of non-smoking healthy persons (13.38 +/- 4.53) and the average index of BUN/creatinine ratio in a group of nonsmoking and smoking patients with pancreatitis (respectively, 2.73 +/- 0.56, p < 0.0001 and 2.40 +/- 0.77, p < 0.0001).

Conclusion

Most pancreatic function tests have high sensitivity and specificity to accurately diagnose patients with advanced CP. Serum lipase levels due to pancreatic disorders closely parallel the changes of serum amylase except that serum lipase may remain elevated longer than amylase (up to 2 weeks). Elevated serum amylase and lipase are strong evidence for a pancreatic process. When the serum amylase is elevated and the lipase is normal, non-pancreatic causes of the hyperamylasemia are more likely.

There are clinical symptoms indicative of chronic pancreatitis; however, none of them are specific or even pathognomonic. They should make a physician think of the pancreas as a source of the patient's symptoms. Laboratory tests are also indicative at best: there is no biochemical positive test proving the diagnosis of CP.

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