A STUDY ON ORAL GLUCOSE TOLERANCE TEST IN CIRRHOSIS

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ABSTRACT

BACKGROUND

Overt diabetes mellitus (diabetes mellitus) and impaired glucose tolerance test has been reported 21%-30% and 60-80% respectively in patients with liver cirrhosis.[1]

The aim of the study is to assess the prevalence of impaired glucose tolerance among cirrhosis patients with normal blood sugar and to improve their long-term survival by early detection of impaired glucose tolerance by OGTT and timely institution of treatment.

MATERIALS AND METHODS

This study was conducted among 100 cirrhosis patients attending Gastro Clinic at Government Rajaji Hospital, Madurai. Patients with overt diabetes, complication of cirrhosis such as bleeding manifestation, hepatic encephalopathy, spontaneous bacterial peritonitis and moderate-to-severe ascites were excluded from the study.

RESULTS

In our study, the frequency of glucose metabolism disorder was 64%, of which 46% were IGT and 18% were diabetes mellitus. Such a high incidence of latent glucose metabolism disorder in cirrhosis was revealed with the routine use of OGTT. This test should be recommended routinely for cirrhosis patients for early detection of glucose metabolism disorder.

CONCLUSION

In our study, the frequency of glucose metabolism disorder was 64% among 46% were IGT and 18% were diabetes mellitus. This 64% was revealed after OGTT, which indicates of high incidence of latent glucose metabolism disorder in cirrhosis.

KEYWORDS

OGTT, Cirrhosis, Glucose Metabolism Disorder.

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BACKGROUND

Diabetes mellitus may arise from a progressive disorder of insulin secretion in the presence of liver and muscle resistance to insulin.[2] Diabetes mellitus is related to liver cirrhosis in two ways-

1. Type 2 diabetes mellitus (type 2 diabetes mellitus) (often associated with metabolic syndrome) causes non-alcoholic fatty liver disease (steatosis, steatohepatitis, liver cirrhosis and hepatocellular carcinoma).
2. Diabetes mellitus may develop as a complication of liver cirrhosis, which is known as "hepatogenous diabetes." As liver disease advances, diabetes mellitus becomes clinically evident. Type 2 diabetes mellitus and hepatogenous diabetes are associated with an increased risk of complications of chronic liver diseases and mortality.

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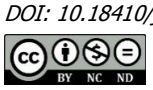

The liver has an important role in carbohydrate metabolism since it is responsible for blood glucose levels by means of glycogenolysis and gluconeogenesis. In the presence of hepatic disease, the metabolic homeostasis of glucose is impaired as a result of insulin resistance, glucose intolerance and diabetes. Insulin resistance in muscle and adipose tissue combined with hyperinsulinaemia is responsible for impaired glucose tolerance and diabetes in cirrhosis.[3] On the other hand, subclinical abnormal glucose tolerance disorders, such as impaired glucose tolerance or diabetes mellitus (called subclinical since they are detected only by means of an oral glucose tolerance test), maybe observed in 45% and 22%, respectively, of patients with liver cirrhosis with no history of diabetes. Therefore, the prevalence of diabetes mellitus and Impaired Glucose Tolerance (IGT) maybe underestimated when only Fasting Plasma Glucose (FPG) levels are taken into account. Usually, it is found to be normal due to hyperinsulinaemia. Various ill effects of impaired glucose tolerance are-

1. Progression of hepatic failure by lipid peroxidation of accumulated fat due to hyperinsulinaemia.
2. Frequent infection due to immune suppression by diabetes.

3. Chance of variceal bleed will be high due to splanchnic hyperaemia by postprandial hyperglycaemia, which will increase portal pressure.
4. Development of hepatocellular carcinoma will be high in diabetes with cirrhosis. So, it is necessary to find out impaired glucose tolerance in early stage, because-
    a. At the time of diagnosing diabetes in cirrhosis, the patient might be in advanced liver stage where most of the antidiabetics drugs are contraindicated.
    b. Frequent hypoglycaemic episodes with insulin therapy. So, oral glucose tolerance test, which will find the impaired glucose tolerance in early stage of cirrhosis may improve the prognosis of these patient by instituting lifestyle modification.

MATERIALS AND METHODS

This study was conducted among 100 cirrhosis patients attending Gastro Clinic at Government Rajaji Hospital, Madurai. Patients with overt diabetes, complication of cirrhosis such as bleeding manifestation, hepatic encephalopathy, spontaneous bacterial peritonitis and moderate-to-severe ascites were excluded from the study. Informed written consent was obtained from all the patients. Information regarding age, sex, history of diabetes, family history of diabetes, duration of cirrhosis, complication of cirrhosis (variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome), aetiology of cirrhosis (alcoholic if alcohol consumption >80 g in men and >40 g in female for 10 years, viral if HBsAg or anti-HCV AB positive and all other aetiology are categorised as others) were collected. Serum bilirubin, serum albumin, liver enzymes, prothrombin time and random blood sugar was obtained and Child-Pugh score (A, B and C) and MELD score (INR, serum bilirubin and creatinine) were calculated.

All patients underwent ultrasonographic examination of the abdomen and findings like cirrhosis such as contracted liver with coarse irregular surface, diameter of portal vein and also portal flow, caudate lobe hypertrophy and atrophy of third segment were recorded.

OGTT was done on 100 patients as per the WHO guidelines. The patients were asked to fast for nearly 12 hours and then FBS was collected. Then, they were asked to take 75 g of oral anhydrous glucose mixed with 200 mL of water. After 2 hours, nearly 5 mL of blood was drawn and sent for analysis. Those having 2 hour PG <140 mg/dL, 140-200 mg/dL and >200 mg/dL were considered as normal, IGT (impaired glucose tolerance), diabetes, respectively. In this study, patients who were having 2 hour PG >140 mg/dL were considered as glucose metabolism disorder (both IGT and diabetes mellitus). The data collected during the study was formulated into a master chart in Microsoft office excel and statistical analysis was done with help of computer using statistical software package SPSS V. 17 for windows. Using this software, frequencies, range, mean, standard deviation and 'p' were calculated through Student's t-test, one-way ANOVA, Pearson correlation and Chi-square test. P value of <0.05 was taken as significant.

RESULTS

OGTT	Number of Cases
Normal	36
IGT	46
Diabetes	18

Table 1. Number of Cases

		OGTT
Duration of Cirrhosis	**Normal**	**GMD (IGT/DM)**
<20 (8)	5	3
21-40 (69)	26	43
41-60 (23)	5	18

Table 2. OGTT with Duration of Cirrhosis

		OGTT
Child-Pugh Score	**Normal**	**GMD (IGT/DM)**
A (43)	21	22
B (57)	15	42

Table 3. Child-Pugh Score and OGTT

		OGTT
MELD	**Normal**	**GMD (IGT/DM)**
<10 (26)	7	19
11 and 12 (28)	15	13
13 and 14 (36)	10	26

Table 4. MELD and OGTT

Middle-aged males predominated the study. OGTT was able to find out nearly 64 glucose metabolism disorder. Among that, 46 were quoted as IGT (46%) and 18 as diabetes mellitus (18%). So, OGTT revealed nearly 64% of cirrhotic patients who had normal blood sugar as duration of cirrhosis, Child-Pugh score and MELD score went high, incidence of glucose metabolism disorder also went high.

DISCUSSION

Hepatogenous diabetes is a common complication of cirrhosis. The liver plays a very important role in glucose metabolism. Thus, in the presence of chronic liver disease, the homeostasis of glucose metabolism is impaired and results in glucose intolerance and diabetes mellitus (diabetes mellitus) type 2. About 50%-80% of cirrhotic patients have IGT and 30%-40% develop diabetes mellitus, sometimes diabetes mellitus in cirrhosis maybe subclinical, since fasting serum glucose maybe normal. In these cases, it is necessary to perform an Oral Glucose Tolerance Test (OGTT) to detect an impairment of glucose metabolism. Also, diabetes mellitus increases the risk of complications of cirrhosis and reduces survival rate. Moreover, these patients have increased peripheral resistance and altered adipocyte sensitivity. To compensate for Insulin Resistance (IR), pancreatic insulin secretion increased.[4,5]

Diabetes mellitus can increase fibrosis, incidence of hepatocellular carcinoma and resistance to antiviral therapy in patients with cirrhosis. Diabetes mellitus maybe involved in the progression of liver fibrosis and inflammation through diverse mechanisms- it is likely that adipokine production (such as leptin and tumour necrosis factor-alpha, which activate inflammatory pathways exacerbating liver injury) is increased by insulin resistance. Leptin and oxidative stress

associated with liver inflammation may activate Transforming Growth Factor-Beta 1 (TGF-B1), which is one of the most potent profibrogenic cytokines produced in the liver. TGF-B1 activates hepatic stellate cells, which are the major source of collagen and extracellular matrix proteins.

Diabetes mellitus increases the incidence of severe infections by inducing immunosuppression.[6] Cirrhotic patients with diabetes mellitus have a higher prevalence of infections compared to nondiabetic ones. Spontaneous bacterial peritonitis was more frequent in patients with cryptogenic cirrhosis (which is associated with diabetes mellitus) compared to those with cirrhosis of other causes. These infected patients had higher mortality due to sepsis, liver failure and hepatorenal syndrome. In addition, diabetes mellitus may increase the risk of variceal bleeding, as postprandial hyperglycaemia that occurs in diabetic patients produces splanchnic vasodilatation and increases the flow and pressure of the portosystemic venous system. Also, oesophageal variceal bleeding increases the risk of infection and death by inducing bacterial intestinal translocation. Diabetes mellitus has also been associated with increased risk of hepatic encephalopathy.

Hepatogenous diabetes is less associated with retinopathy,[7] cardiovascular and renal complications and more frequently associated with hypoglycaemic episodes as a result of impaired liver function, liver disease abnormalities (low intravascular coagulability, low cholesterol, lower prevalence of hypertension) as well as shorter duration of diabetes mellitus may explain relatively lower rate of diabetic complication in chronic liver disease.

Subclinical forms of Impaired Glucose Tolerance (IGT) or diabetes mellitus (diabetes mellitus) may influence survival of nondiabetic cirrhotic patients.[8] Previously, it had been demonstrated that clinically overt diabetes mellitus is associated with low survival of cirrhotic patients. This issue is important since a high proportion of cirrhotic patients (about 70%) without history of diabetes mellitus and with normal fasting plasma glucose have subclinical abnormal glucose tolerance. The use of oral glucose tolerance test for early recognition and treatment of diabetes mellitus may improve prognosis of these patients. Serum albumin level, Child-Pugh B and C and high MELD scores were other independent negative predictors of survival.

CONCLUSION

In our study, the frequency of glucose metabolism disorder was 64% among 46% were IGT and 18% were diabetes mellitus. This 64% was revealed after OGTT, which indicates of high incidence of latent glucose metabolism disorder in cirrhosis. Among parameters duration of cirrhosis, family history of diabetes and severity of liver disease (Child-Pugh and MELD) were the independent risk factors for haematogenous diabetes. Aetiology of cirrhosis does not show statistically significant correlation with glucose metabolism disorder in cirrhosis even though alcohol and hepatitis C impairs insulin secretion.

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