GAMMA-GLUTAMYL TRANSPEPTIDASE IN DIAGNOSIS OF MALIGNANT BILIARY OBSTRUCTION

Pestra TC[1*]
Med-Diagnosis Lab, R & S, Manila, Philippines

Correspondence
Pestra Terre Chin. Med-Diagnosis Lab, R & S, Manila, Philippines
Email: Tukcheasovannah@gmail.com

Pestra TC. Gamma-glutamyl transpeptidase in diagnosis of malignant biliary obstruction. Diag Ther Stud. 2012; 1(3): 58 - 62.

ABSTRACT

Gamma-glutamyl transpeptidase (GGT) is a biliary enzyme that is useful in the diagnosis of obstructive jaundice. Also, it is more responsive to biliary obstruction than the other biliary enzymes. The purpose of this study was to determine the usefulness of GGT measurement in diagnosis of biliary obstruction. GGT was measured in the sera obtained from 100 patients with specific hepatobiliary diseases and 20 control subjects. The average value of this enzyme in patients with malignant extrahepatic obstruction was 93.35 ±14.16 U/L, significantly higher than that of patients with benign extrahepatic obstruction (62.33 ± 6.06 U/L), as well as patients with intrahepatic cholestasis and infiltrative liver cancers (66.29 ± 5.89 U/L and ; 65.95 ± 7.04, respectively). In addition, the average values of GGT in these four groups were significant higher than the average value of GGT in control group (25.00 ± 7.17 U/L). When 86 U/L was used as a cut-off value to discriminate between patients with malignant extrahepatic obstruction and the remaining hepatobiliary disorders, the sensitivity, specificity and accuracy of the test were 95 %, 100 % and 99 %, respectively. It is concluded that the GGT could be an additive useful marker in diagnosis of malignant extrahepatic obstruction.

Key words: Gamma-glutamyl transpeptidase, biliary, obstruction

INTRODUCTION

Gamma-glutamyl transpeptidase (GGT) is an enzyme that catalyses the transfer of gamma-glutamyl residues to amino acids or small peptides. GGT is intimately concerned in the synthesis and metabolism of glutathione through the gamma-glutamyl cycle. There is good evidence that this plays a role in the absorption of amino acids from the glomerular filtrate and from the intestinal lumen through a translocation mechanism [1].
In medical practice, it is a biliary enzyme that is especially useful in the diagnosis of obstructive jaundice, intrahepatic cholestasis, and pancreatitis [1]. Serum GGT was first reported by Szewzuk and Orlowski in 1960 as a clinical diagnostic procedure in the diagnosis of hepatobiliary diseases, afterwards, it has been used mostly as the marker of liver parenchymal disease and biliary obstruction [2 - 5].

GGT is an excretory enzyme, which is more specific for hepatic disease than is alkaline phosphatase. Also, it is more responsive to biliary obstruction than are aspartate aminotransferase (AST) and alanine aminotransferase (ALT) [6].
The purpose of this study was to determine the usefulness of GGT measurement in diagnosis of biliary obstruction. The study included different groups of patients who presented with jaundice such as infiltrative hepatic disorders (primary or metastatic tumor) and cholestatic disorders (e.g. intrahepatic and extrahepatic cholestasis).

MATERIALS AND METHODS

Subjects selection

The study population comprised 100 patients who attended a tertiary hospital during 1998 - 1999.
Group 1 consisted of 20 patients with malignant extrahepatic obstruction by cholangiocarcinoma or other periampullary tumors [aged 43-85 year, average 64.8 ± 14.5 year, M:F ratio 14:6]. All patients in this group had dilated intrahepatic and/or common bile duct on imaging study.
Group 2 consisted of 25 patients with nonmalignant extrahepatic obstruction [aged 18-78 year, average 50.7 ±15.4 year , ratio of males to females (M:F) 15:10]. Among these, 23 patients had stones obstructing the common bile duct and the remaining 2 patients each had a choledochal cyst. As in group 1, all patients in this group had dilated intrahepatic and/or bile duct on imaging study.
Group 3 consisted of 35 patients with intrahepatic cholestasis. [aged 23-80 years, average 48.3 ±19.6 years, M:F ratio 20:15]. All patients in this group had serum bilirubin>2 mg/dl and total alkaline phosphatase exceeded the upper limit level (279 U/L). There was also no evidence of biliary tract obstruction or hepatic infiltration on imaging study. The causes of cholestatic jaundice in this group included systemic infection (n=15), drug induced jaundice (n=5) and alcoholic hepatitis or cirrhosis (n=15).
Group 4 consisted of 20 patients with infiltrative hepatic disorders [aged 38-73 year, average 59.8±12.6 year, M:F ratio 16:4]. Fifteen patients had hepatocellular carcinoma, diagnosed by histology or imaging study combined with serum alphafetoprotein (AFP) level exceeding 400 ng/dl. The remaining three patients had liver metastasis, diagnosing based on imaging study combined with positive histology.
In addition, sera from 20 healthy subjects were included in this study to establish the control group.

Laboratory analysis

Blood samples were collected from subjects by evacuated blood collection system and sent to the clinical chemistry laboratory for further analysis. The laboratory setting is the clinical laboratory certified by ISO 9002:1994. All blood samples were analyzed for GGT by L-Gamma-Glutamyl-transferase method [6] (Boerhinger Manheim) using automated clinical chemistry analyzer, Hitachi 911 (Boerhinger Manheim). All analyses were performed according to the manufacturer instruction at room temperature.

Statistical Analysis

The data were expressed as average value (mean ± standard deviation) and percentage as their appropriateness. The analysis of variance and Scheffe test was used to test the difference among groups of patients.

RESULTS

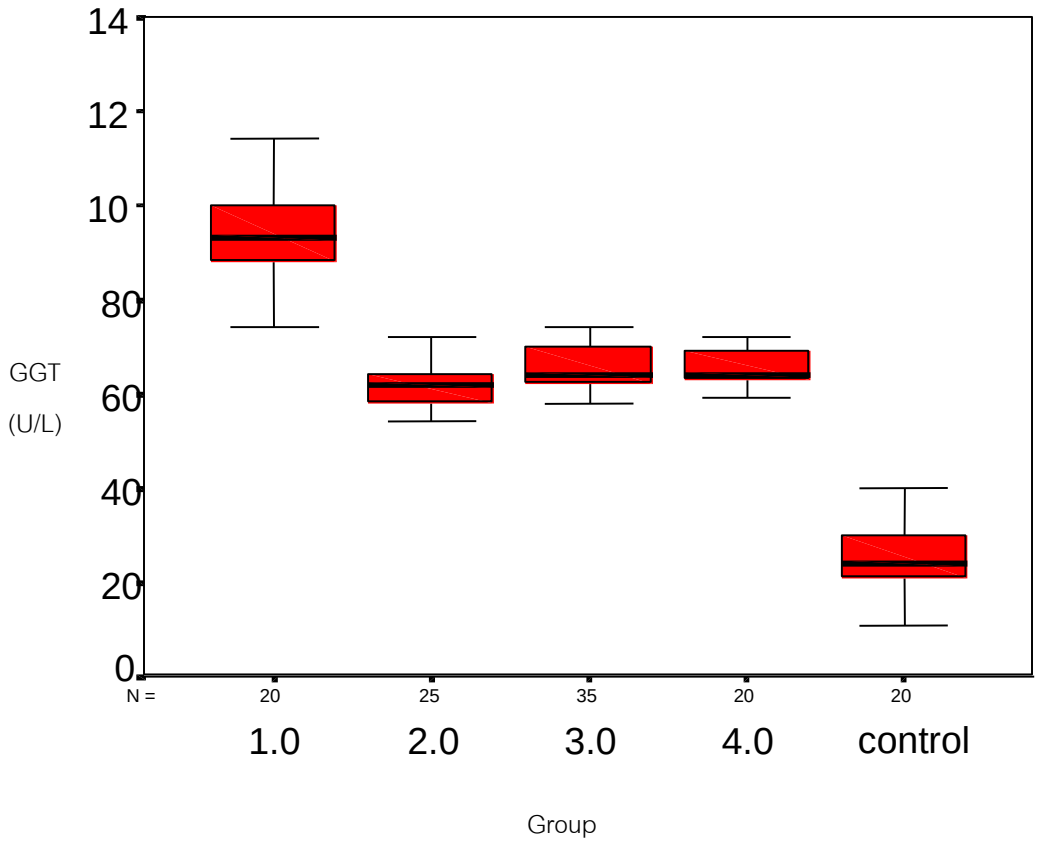
In our study, the average value of GGT in group 1 was 93.35 ±14.16 U/L, significantly higher than that found in the other three groups (group 2; 62.33 ± 6.06 U/L, group 3; 66.29 ± 5.89 U/L and group 4; 65.95 ± 7.04 U/L, ($p < 0.05$)). In addition, the average values of GGT in group 1,2,3 and 4 were significant higher than the average value of GGT in control group (25.00 ± 7.17 U/L) (Table 1 and Figure 1).

Table 1. Level of serum GGT in the studied subjects.

Group	Average value of serum GGT (U/L)
1	93.35 ±14.16*
2	62.33 ± 6.06
3	66.29 ± 5.89
4	65.95 ± 7.04
control	25.00 ± 7.17

* significant higher than group 2,3 and 4 ($p < 0.05$)

Figure 1. Level of serum GGT in the studied subjects.



Comparing the GGT level in group I and the other groups, the ideal cut-off point for a diagnostic value of the GGT was determined by selection of multiple points from the receiver-operating characteristic (ROC) curve. The point considered best was 86 U/L. At this level, it had a sensitivity and specificity of 95 % and 100 %, respectively and the accuracy was 99 %.

DISCUSSION

The mechanism by which different physiological states and disease processes cause an elevation of the serum GGT has been generally accepted that it originates in tissues that undergo metabolic stimulation [8]. Presently, the most universal application of serum GGT assay is in diagnosis of liver and biliary tract disease [9]. Concerning the mechanism of the serum elevation in cholestatic diseases, it is found that the increase in serum GGT activity is mainly of biliary cell origin and does not originate from hepatocytes [8].

It is widely believed that higher values occur in biliary obstruction than in parenchymal disease [9]. Also, it is more specific to biliary obstruction comparing to other biliary enzymes (e.g. ALP) [1,4,6,9]. However, the magnitude of abnormalities and the overlap of values in individual cases in different biliary obstruction categories are not clearly documented so recommendation for this purpose is still controversy [1,4,6,9 - 10].

Here, we performed a study was to determine the value of serum GGT activity in diagnosis of biliary obstruction. According to our results, there was a clear significant difference of GGT activity between control and cholestatic subjects. This can confirm the usefulness of this enzyme determination in diagnosis of biliary obstruction [1 - 2]. In interest, we found the significant higher average value GGT activity than that of patients with benign extrahepatic obstruction, as well as patients with intrahepatic cholestasis and infiltrative liver cancers.

The biochemical determination of GGT is technically easy and reliable. The technique is inexpensive and can be performed by automated clinical chemistry analyzer. Although it cannot provide the structural detail of the pathology as the imaging technology (e.g. CT scan) it can be used as a useful additive marker in diagnosis of malignant extrahepatic obstruction.

COMPETING INTERESTS

I have not received in the 5 past year reimbursements, fees, funding or salary from organization that may in anyway gain or lose financially from the publication of this paper. I do not hold any stocks or shares in organizations that may gain or lose financially from publication of this paper. I have not any other financial competing interests.

REFERENCES

1. Stein TA, Burns GP, Wise L. Diagnostic value of liver function tests in bile duct obstruction. J Surg Res. 1989; 46: 226 – 9.

2. Reichling JJ, Kaplan MM. Clinical use of serum enzymes in liver diseases. Dig Dis Sci. 1988 33: 1601 – 14.
3. Friedman LS, Martin P, Munoz SJ. Liver Function tests and the objective evaluation of the patient with liver disease. In: Hepatology: a Textbook of Liver Disease (Edited by Zakim D, TD Boyer TD). Philadelphia, WB Saunders, 1996, 791 – 833.
4. Maggiore G, et al. Diagnostic value of serum gamma-glutamyl transpeptidase activity in liver diseases in children. J Pediatr Gastroenterol Nutr. 1991; 12: 21 – 6.
5. Baden H, et al: Diagnostic value of Gamma-Glutamyl Transpeptidase and Alkaline Phosphatase in liver metastases. Surg Gynecol Obstet. 1971; 133:769 – 73.
6. Lum G, Gambino SR. Serum Gamma-Glutamyl Transpeptidase activity as an indicator of disease of liver, pancreas, or bone. Clin Chem. 1972; 18: 358 - 62.
7. Persijn JP, van der Slik W. A new method for the determination of gamma-glutamyltransferase in serum. J Clin Chem Clin Biochem. 1976; 14: 421 – 7.
8. Bulle F, et al. Mechanism of gamma-glutamyl transpeptidase release in serum during intrahepatic and extrahepatic cholestasis in the rat: a histochemical, biochemical and molecular approach. Hepatology. 1990; 11:545 – 50.
9. Goldberg DM. Structural, functional, and clinical aspects of gamma-glutamyltransferase. CRC Crit Rev Clin Lab Sci. 1980; 12: 1- 58.
10. Ruppin DC, Frydman MI, Lunzer MR. Value of serum gamma-glutamyltransferase activity in the diagnosis of hepatobiliary disease. Med J Aust. 1982; 1: 421 - 4.