Liver Function Test in Cholestasis

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ABSTRACT Cholestasis is impaired bile flow that cause prolonged evacuation of conjugated bilirubin and other substances which are dependent of bile flow for its excretion. The liver function test is useful to determine the severity of disease, to follow up its progress, and to predict the prognosis. This study was performed restropectively from the medical record of cholestatic patients who were admitted to the Department of Child Health, Central Hospital of Denpasar, from January 1992 to December 1993. Among 34 patients with cholestasis, 27 (19 intrahepatic and 8 extrahepatic cholestasis) were included in this study. Although the means of transaminase enzymes (SGOT, SGPT) in intrahepatic cholestasis were higher significantly than those in extrahepatic cholestasis, the increase of these enzymes five times or more than normal was not different significantly. The means of GGT and alkaline phospatase (AP) in extrahepatic groups were higher significantly than those in intrahepatic groups, and the increase of GGT more five times than normal was different significantly as well. The means of total and conjugated bilirubin levels were higher in .extrahepatic group, but were not different significantly. **[Paediatr Indones 1995;35:180-184]**

Introduction

Cholestasis is impaired bile flow which results in prolonged elevation of conjugated bilirubin and other substances which are dependent on bile flow for its exretion. This disease does not only occur in early life, but also in later childhood with different causes.[1-3] In Britain, the incidence of neonatal cholestasis is reported to be 1 among 2500 livebirths. In RSAB Harapan Kita, Jakarta, 2 cases were reported among 2500-3000 livebirths in one year period. During 1991, 21 cases were admitted to the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta.[4,5]

Liver function test (LFT) is an important examination to establish early diagnosis of cholestasis, to differentiate intra-from extrahepatic cholestasis, to follow

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up the response of treatment, and to predict the prognosis. Liver function test, however, cannot determine the etiology of cholestasis.[5,6] It is important that clinicians establish early diagnosis for effective management. The aim of this study is to describe the results of LFT in patients with intra- or extrahepatic cholestasis who were admitted to the Department of Child Health, Central Hospital of Denpasar.

Methods

We reviewed the medical records of patients with neonatal cholestasis who were admitted to the Child Health Department, Central Hospital of Denpasar from January 1992 and December 1993. Subjects of this study were patients who were diagnosed to have intra- or extrahepatic cholestasis based on clinical manifestations (jaundice more than 2 weeks), laboratory examination (bilirubinuria, negative urobilin in urine, or increased conjugated bilirubin more than 2 mg/dl or more than 20% of total bilirubin), duodenal aspiration test (DAT), and ultrasonography in some cases.

Subjects were considered to have intrahepatic cholestasis if clinical and laborarory manifestations were consistent with cholestasis, and had positive DAT test. The diagnosis of extrahepatic cholestasis was established when clinical and laboratory findings were consistent with cholestasis and the result of DAT was negative in 3 consecutive examinations. We used 'The Technicon RA System Reagents' to determine all of LFT examinations (SGOT/AST, SGPT/ALT, gamma GT, alkaline phospatase, total bilirubin and conjugated bilirubin).

Chi-square or two-tailed t-tests were used to compare the differences between values of intra- and extrahepatic cholestasis.

Results

During the period of January 1992 till December 1993, 80 patients with jaundice were admitted to the Child Health Department, Central Hospital of Denpasar; 34 cases (42.5%) were diagnosed of having cholestasis (26 with intrahepatic and 8 with extrahepatic cholestasis). DAT was performed in all patients. Out of 26 cases in intrahepatic cholestasis group, only 19 were included in this study; 7 cases were excluded because of incomplete laboratory data. All of the extrahepatic cholestasis patients were included into this study.

Table 1. Characteristics of intra- and extrahepatic cholestasis

	Intrahepatic (n = 19)	Ekstrahepatic (n = 8)
Age on admission	45,9 days (13-90 days)	91 (20 days-8 months)
Sex (M/F)	14/5	3/5
Nutritional status (U/W)*	7/12	2/6

*) U/W: Undernourished/Well-nourished

Table 1 shows that the mean of age of the intrahepatic cholestasis patients (45.9

days) was younger than that of extrahepatic cholestasis patients (91 days). Most of patients with intrahepatic cholestasis (14/19) were male; in contrast, most of patients with extrahepatic cholestasis (5/8) were female.

Table 2 summarizes the difference of the results of LFT in both groups. It can be seen that the means of the transaminase enzymes (SGOT, SGPT) in intrahepatic group were significantly higher than those in extrahepatic group; i.e., 411.3 (SD 135.3) and 169.6 (SD 125.1) for SGOT; and 315.9 (SD 56.9) and 126.5 (SD 97.8) IU for SGPT, respectively. Furthermore, it appears that the means of the alkaline phospatase level in the extrahepatic groups were significantly higher than those in the intrahepatic group, i.e., 627,3 (SD 196.8) and 473.0 (SD 44.2) IU respectively, while the mean of the GGT level in the extrahepatic group was significantly higher than that in the intrahepatic group, i.e., 574.8 (SD 117.9) vs. 139.9 (SD 40.6). The means of the total bilirubin and the conjugated bilirubin in extrahepatic group were higher than those in the intrahepatic group, i.e., 10.5 (SD 3.5) mg/dl vs. 7.8 (SD 2.7) mg/dl for extrahepatic and 9.6 (SD 3.5) mg/dl vs. 7,0 (SD 2,9) mg/dl for intrahepatic cholestasis. The difference of the means of total bilirubin and conjugated bilirubin in both groups were not significant.

However, the increase of the transminase serum enzyme five times than normal in both groups, did not differ significantly (See Tables 3 and 4). In extrahepatic group the increased GGT level five times or more than normal was found in 75% of cases, while in the intrahepatic group only 36,8%. The difference between the two groups was statistically significant ($p < 0,05$).

Table 2. Distribution of mean SGOT, SGPT, alkaline phospatase, GGT, total and conjugated bilirubin levels in intrahepatic and extrahepatic cholestasis

	Intra (n = 19) (SD) [Range]	Extra (n=8) (SD) [Range]	p (t-test)
SGOT (IU)	411,2 (135,2) [31 - 1551]	160,6 (129.0) [39 - 702]	< 0,05
SGPT	315,9 (57,0) [19 - 423]	126,5 (97,8) [17 - 319]	< 0,05
AP	473,0 (44,2) [79 - 1841]	627,3 (196,8) (242 - 694)	< 0,05
GGT	139,9 (40,6) [41 - 356]	574,8 (117,9) [806 - 1498]	< 0,05
Total bilirubin	9,6 (3,5) [3,7 - 17,9]	10,5 (3,5) [5,0 - 14,8]	< 0,05
Conj. bilirubin	7,0 (2,9) [2,3 - 12,7]	7,8 (2,7) [3,7 - 12,3]	> 0,05

Table 3. Distribution of increased SGOT level

	Intrahepatic (n = 19)	Extrahepatic (n = 8)	p
≥ 5 x N	7	3	> 0,05
< 5 x N	12	5	

$X^2 = 0,21$

Table 4. Distribution of increased SGPT level

	Intrahepatic (n = 19)	Extrahepatic (n = 8)	p
≥ 5 x N	8	2	> 0,05
< 5 x N	9	6	

$X^2 = 0,67$

Table 5. Distribution of increase of GGT level

Increase of GGT	Intrahepatic (n = 19)	Extrahepatic (n = 8)	p
≥ 5 x N	7	6	< 0,05
< 5 x N	12	2	

$X^2 = 4,99$

Discussion

The liver function test (LFT) is used to determine impaired of bile flow, to follow up and predict the prognosis, to differentiate intra- or extrahepatic cholestasis, but not to recognize the etiology of cholestasis. The transaminase enzymes level (SGOT, SGPT) usually increase early and rapidly in abnormality of the hepatic parenchym. SGPT is found in hepatic cell cytoplasm only, but SGOT is also found in skeletal muscle and cardiac cells.[1,6,8] If the hepatic cell destructed, the membrane cell permeability will increase and finally cause leakage of the cytoplasm component to the circulation;[6-8] it can be ten times than normal level in intrahepatic cholestasis, but in extrahepatic cholestasis, it can be normal in early stage and increases similar to in intrahepatic in terminal stage.[5,10]

In our study, we found that the means of SGOT and SGPT in intrahepatic group were higher than those in extrahepatic group. Both of the means were different significantly ($p < 0,05$). These findings were consistent with Ferry's et al finding. They found that the means of the transaminase level were higher in intrahepatic cholestasis than those in extrahepatic cholestasis, but the different was not statistically significant.[10]

The increase of the transaminase levels of more than five times tend to be found more frequently in intrahepatic cholestasis.[4] In this study, we found that the increase of the transaminase level more than five times or higher were observed more frequently in intrahepatic than in extrahepatic cholestasis, but the different was not statistically significant. This finding might be caused by the wide variation of laboratory result and late stage of extrahepatic cholestasis patents.

Alkaline phospatase (AP) is an enzyme with wide distribution in the body. In the liver, alkaline phospatase and GGT take place in billiary canaliculi.[6,9] They will increase in impaired hepatic extretion, but GGT is more sensitive. In extrahepatic cholestasis, GGT can be increase five times or more than normal.[11,12]

In our study, we found that the means of AP and GGT in extrahepatic cholestasis were higher significantly than those in intrahepatic cholestasis. Besides that, the increase of GGT five times or more than normal in extrahepatic cholestasis was higher significantly than that in intrahepatic cholestasis.

Impaired bile flow in cholestasis results in the accumulation of conjugated bilirubin in intra- and extrahepatic bile ducts. The accumulation of conjugated bilirubin will increase its level in the blood as well; its level can be more than 2 mg/dl or more than 20% of total bilirubin.[1,3,5,6,12] We found that the total bilirubin level in the extrahepatic was higer than that in intrahepatic cholestasis. Similarly, the conjugated bilirubin level in extrahepatic was higher than that in intrahepatic cholestasis, though the difference was not statistically significant.

Conclusions

Our series of patients with cholestasis shows us that the means of the transaminase enzymes (SGOT, SGPT) were higher significantly in intrahepatic than those in extrahepatic cholestasis); conversely the means of alkaline phospatase and GGT were higher significantly in extrahepatic cholestasis than those in intrahepatic cholestasis ($p < 0.05$). The mean levels of total and conjugated bilirubin were higer in extrahepatic than those in intrahepatic cholestasis, but the differences were not statistically significant.

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