A STUDY OF LIVER FUNCTION TESTS IN PATIENTS RECEIVING FOUR DRUGS REGIMEN IN INITIAL TWO MONTHS AS ANTITUBERCULAR DRUGS

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Summary

Biochemical monitoring of liver function is essential because Anti Tubercular Therapy (ATT) induced hepatotoxicity can cause permanent injury to liver and death. This cross-sectional comparative study was conducted in department of Biochemistry of Chittagong Medical College during the period of July 2009- Jun 2010 to determine the association of Anti-TB treatment to alter the liver function in patients of intensive phase of tuberculosis taking Four Fixed Dose Combination of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. A total of 100 subjects were enrolled in this study. They were divided into two groups. Group A (case) was diagnosed case of tuberculosis and had taken anti TB drugs (four Fixed dose combination) at least for fifteen days and group B (control) was consisting of normal subjects. Serum ALT, AST, Bilirubin and prothrombin time were measured. After finishing my work I found, out of 70 subjects 20% had increased level of serum ALT, 17.1% had increased level of serum AST, 20% had increased level of serum bilirubin and only 2.9% had increased level of prothrombin time in case group. Finally, determination of liver functions in patients receiving Anti TB therapy (in intensive phase) should be done irrespective of presence or absence of established risk factors, to minimize not only the incidence but also the morbidity and mortality.

Key words

Anti tubercular therapy (ATT); liver function test; hepatotoxicity

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Introduction

Drugs are an important cause of liver injury. Approximately 75% of the idiosyncratic drug reaction results in liver transplantation and death [1]. Drug induced hepatic injury is the most common reason cited for withdrawal of an approved drug The manifestations of drug induced hepatotoxicity are highly variable, ranging from asymptomatic elevation of liver enzymes to fulminent hepatic failure [2]. Knowledge of the commonly implicated agents and a high index of suspicion are essential in diagnosis [3].

The current recommended treatment regimens for tuberculosis involve drugs which are potentially hepatotoxic [4]. Certain genetic and environmental factors are attributed to coincide to produce sufficient quantity of toxic metabolites that then cause varied alterations in liver functions [5].

WHO has declared that Tuberculosis is a global emergency. An effective control has been achieved by the widespread use of anti tubercular drugs. Again the ATT (anti-Tubercular therapy) has adverse effects that they cause hepatotoxicity [4,6]. Early recognition of ATT (Anti-tubercular therapy) induced hepatotxicity with immediate withdrawal of offending agent is very important to arrest its development. British Thoracic Society suggests that if there is a rise in ALT (Alanine amino transferase) and/or AST (Aspertate amino transferase) to greater than 3 times normal, or a rise in bilirubin, or if the patient showed clinical symptoms of hepatitis then drugs should be stopped and reintroduced sequentially when these parameters falls to previous levels [7]. Patients of Tuberculosis usually belong to poor socioeconomic status and they cannot afford regular LFTs (Liver function tests). Close monitoring of the patient's physical condition can be done in such situations. Physician must be vigilant in identifying drug related liver injury because early detection can decrease the severity of hepatotoxicity if the drug is discontinued [8].

The patients need to follow them up more closely, to identify hepatotoxicity at the earliest possible time to design new drug regimen [9].

Materials and methods

The cross-sectional comparative study was carried out from July 2009 to June 2010 in the Department of Biochemistry, Chittagong Medical College. A total of 100 subjects were enrolled in the study. Among the subjects 70 were in case group and 30 were in control group.

Patients of Tuberculosis, who had pre-treatment normal liver function (ALT, AST, Serum Bilirubin and Prothrombin time) and were negative for HBsAg, anti-HCV Ab, and HIV, age ranging from 15 to 49 years, coming in the DOT center of Chittagong Medical College Hospital, Chittagong General Hospital and Chittagong Infectious Disease Hospital were case group (Total 70 subjects).

Patients receiving other drugs in addition to anti-TB drugs , relapsed cases of tuberculosis and who were positive for HBsAg, Anti - HCV Ab and HIV were excluded from the study.

Data were taken in a pre-designed data collection sheet. Samples were collected from patients who had been taking anti-TB therapy at least for fifteen days (in intensive phase).

The samples were tested within 4 hours of collection. Following tests

i. Serum alanine aminotransferase

ii. Serum aspartate aminotransferas

iii. Serum bilirubin (Total)

iv. Prothrombin time had been done by proper method.

Results

The findings obtained from data analysis were presented below.

Table I : Distribution of study subjects by type of tests

Tests	Frequency	Percentage
AST	12	17.1%
ALT	14	20%
Serum Bilirubin	14	20%
Prothrombin Time	02	2.9%

The table-I shows the distribution of serum AST, serum ALT, serum Bilirubin and Prothrombin time in study subjects. Among the subjects serum AST level were found higher in 17.1% subjects, serum ALT level were found higher in 20% subjects, serum bilirubin were higher in 20% subjects and Prothrombin time were higher in 2.9% subjects.

Table II : Descriptive Statistics

Statistics	Range		Mean ± SD	
	Group-A	Group- B	Group-A	Group- B
AST	14-142	12-70	96 ± 30.11	26.80 ± 11.85
ALT	11-191	17-90	46.44 ± 52.25	30.53 ± 13.74
Serum Bilirubin	0.3-5.2	0.4-3.2	1.13 ± 1.14	0.83 ± 0.52
Prothrombin Time	11-17	11-15	13.56 ± 1.19	13.10 ± 1.27

In the table-II, the mean serum AST was 96 ± 30.11 in group- A and 26.80 ± 11.85 in group- B. The mean difference between two groups was statistically significant.

The mean serum ALT was 46.44 ± 52.25 in group- A and 30.53 ± 13.74 in group- B. The mean difference between two groups was statistically significant.

The mean serum Bilirubin was 1.13 ± 1.14 in group-A and 0.83 ± 0.52 in group- B. The mean difference between two groups was not statistically significant.

Comparison of Prothrombin time of group-A (13.56 ± 1.19) with that of group – B (13.10 ± 1.27) was statistically insignificant.

Discussion

In the present study 75.7% subjects were male and 24.3% subjects were female in group A (case) and 50% subjects were male and 50% were female in group B (control). Most of the participants were in 21-30 yrs of age group (43%) .

Majority of the study subjects were from urban area, of average socioeconomic status, married, service holder and had the educational status below SSC level.

Serum ALT levels were found higher in 20% subjects in group A (case) and no such in group B (control). This result is consistent with study of that where 19% patients had increased level of serum ALT [10]. Another study showed that 19.8% patients taking anti-TB drugs developed increased level of serum ALT [11]. In both studies anti-TB treatment has significant association with increased level of serum ALT . This is also consistent with my study [10,11].

Among the subjects of group A serum AST levels were found higher in 17.1% subjects and no such in group B (control). Our findings were also supported by N. P Thompson et al. They found anti tubercular treatment had significant association with increased level of serum AST in 25% patients [12].

In our study the mean serum bilirubin was higher in 20% subjects of group-A. In study serum bilirubin levels increased in 9.4% patients and in the study showed elevation of serum bilirubin in 19% patients [10,11].

In our study among 70 subjects of group A, only two subjects (2.9%) developed increased level of prothrombin time . The result was not statistically significant but there was trend of increase in prothrombin time [12].

Conclusion

We found in this study that anti tubercular therapy was associated with hepatotoxicity .So patients on anti tubercular therapy should be counseled thoroughly for the early detection of hepatotoxicity and on occurrence of hepatotoxicity the patients should be managed appropriately.

So, we can conclude that monitoring of liver function tests in patients receiving anti-TB drugs (four Fixed Dose Combination) in intensive phase should be done to detect drug induced hepatotoxicity as early as possible and to treat accordingly to minimize not only the incidence but also the morbidity and mortality.

This study will sensitize the health service providers about the necessity of monitoring liver function and delivering the best skilled care to patients of tuberculosis.

Disclosure

All the authors declared no competing interestes.

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