Vol.1 No.1 (Apr 2012)

Indian Journal of Medicine and Healthcare

Alterations in some biochemical indices of hepatic function in tuberculosis patients on antituberclosis therapy

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Abstract

This study was to investigate the hepatic pathophysiology and biochemical changes during antituberclosis therapy. Among the intake 200 patients: 60 were on therapy, another 60 were not on therapy, while 80 were non tuberculosis patient. A comparative decrease in the level of total protein and albumin in tuberculosis patients were recorded while increase in Asparate Aminotransfarace (AST),Alanine Aminotransferace (ALT), and Alkaline Phosphatase (ALP) were observed in comparison with the control. On treatment with antituberclosis therapy, the hepatic involvements are transient.

Keywords: Biochemical indices, Hepatic pathophysiology, Antituberculosis therapy

Introduction

Tuberculosis caused by Mycobacterium tuberculosis is a major socio-economic and public health problem in developing countries (Nnodim *et al.,* 2011). Tuberculosis mainly affects the lungs and also extra pulmonary like lymph nodes, bones & joints, skin, meninges, eyes, kidneys and gastro-intestinal tract, where an insidious disease develops without any pathognomonic clinical evidence (Hardy & Schumidek,1968) can also present as congenital tuberculosis -by transmission of Mycobacterium tuberculosis from the mother through amniotic fluid to fetus (Cantwell *et al.,*1994)The initial symptoms such as loss of appetite, productive cough, night sweats and loss of energy or loss of weight are not pathognomonic of Tuberculosis (Akiibinu *et al.,* 2009).

The presence of co-existent hepatic disease poses a challenge in treatment of tuberculosis. Though impairment of hepatic functions is quite rare, involvement of hepatic dysfunction has been observed in tuberculosis (Hill & Premkumar,1991;Essop *et al.,*1984) Pre-existent chronic liver disease or hepatotoxicity developed during treatment for tuberculosis may result in acute viral hepatitis.

Hepatic dysfunction interferes with the absorption and distribution of drugs that are metabolized or excreted by the liver. During severe liver diseases to extend the period of treatment, advisable to administer fewer

hepatotoxic drugs .Since many of the drugs are hepatotoxic, regimens may need modification by limiting their use or discontinuation accordingly.

Previous studies showed transient elevations of the serum enzymes: Alanine Aminotranferase (ALT) and Aspartate Aminotransferase (AST) in approximately 10% of patients who received standard chemotherapy combinations which included isoniazid and rifampicin 1-2% of these patients were withdrawn from the treatment because of severe hepatotoxicity which ultimately led to fulminant hepatitis. Certain patients showed higher risk to develop hepatotoxicity during the course of anti-tuberculosis chemotherapy, though prediction was difficult (Kimmoun & Samuel, 2002). This study aims to evaluate the extent of hepatotoxicity among Owerrian's by therapy with anti-tubercular drugs.

Materials and methods

Among the intake 200 patients (120 were diagnosed as Tuberculosis): 60 were on therapy, another 60 were not on therapy, while 80 were non tuberculosis patient (Control). Patients with complication such as renal disease and HIV – positive were excluded from the study. Consent was obtained from all the subjects selected for the study. Treatment was planned as recommended under National Tuberculosis and Leprosy Control Programme (NTBLCP).. Patients were given Directly Observed Treatment, Short course (DOTS) for a period of 8 months at the clinic - doses of drug regimen regulated on the basis of pretreatment body weight.

Blood sample

5ml of venous blood was collected using anticoagulant (EDTA) from all the subjects. The plasma was separated by centrifugation, wistefuge (model 684) at 2500g for 10 minutes and used for the estimation of ALT, AST, ALP, albumin and total protein test using Randox kits.

Statistical analysis

The values were expressed as mean ± standard deviation. The student t-test (P<0.05).was used for significance among the values.

Results

Table 1 shows the mean values of Total Protein (6.94 ± 0.31), Albumin (3.22 ± 0.25) and Body weight (58.46± 9.43) were significantly lower (P<0.05) in male Pulmonary TB subjects on therapy when compared with the control group I.

Table 1. Mean value of total protein (T.B), albumin (alb) and body weight (wt) of pulmonary T.B subjects on therapy and control group according to sex.

Parameters	Control (N=80)	Pulmonary TB + therapy (N=60)	P-value
Total Protein(g/dl)			
Male	8.42± 0.90	6.94± 0.31	P<0.05
Female	8.34± 0.78	6.25± 0.34	P<0.05
Albumin(g/dl)			
Male	5.35 ± 0.51	3.22 ± 0.25	P<0.05
Female	4.57± 0.77	3.04 ± 0.25	P<0.05
Weight(Kg)			
Male	66.30 ± 9.13	58.46 ± 9.43	P<0.05
Female	66.50 ± 8.61	57.11 ± 8.22	P<0.05

*P<0.05= Statistically Significant

While the Total Protein (6.25 ± 0.34), Albumin (3.04 ± 0.25) and Body weight (57.11 ± 8.22) were significantly reduced (P<0.05) in female Pulmonary TB subjects when compared with the control group.

Table 2 .Mean values of AST, ALT and ALP in pulmonary T.B.subjects on therapy and control group according to sex

Parameters	Control N=10	Pulmonary TB +Therapy N=9	P-value
AST (IU/L)			
Male	11.42 ± 0.95	13.74 ± 0.66	P<0.05
Female	12.06 ± 0.90	13.82 ± 0.44	P<0.05
ALT (IU/L)			
Male	1.32 ± 1.24	13.22 ± 0.45	P<0.05
Female	10.20 ± 0.98	13.24 ± 0.55	P<0.05
ALP (IU/L)			
Male	4.79 ± 2.49	27.00 ± 0.83	P<0.05
Female	24.76 ± 2.14	27.40 ± 2.15	P<0.05

*P<0.05=Statistically Significant

Table 2, there was significant increase (P<0.05) in AST (13.74 ± 0.66), ALT (13.22 ±

0.45) and ALP (27.00 ± 0.83) in Male Pulmonary TB Subjects on therapy when compared with the control group; AST (11.42 ± 0.95), ALT (11.32 ± 1.24) and ALP (24.79 ± 2.49) while the Female Pulmonary TB Subjects on therapy shows a significant rise (P<0.05) AST (13.82 ± 0.44), ALT (13.24 ± 0.55) and ALP (27.40 ± 2.15) when compared with in the control group; AST (12.06 ± 0.90), ALT (10.20 ± 0.98) and ALP (24.76 ± 2.14).

In Table 3, shows the mean levels of Total Protein (6.60 ± 0.47), Albumin (3.13 ± 0.26) and Body Weight (57.78 ± 8.61) were significantly increased (P< 0.05) in Pulmonary TB Subjects on anti tubercular therapy while the level of AST (13.78 ± 0.55), ALT (13.23 ± 0.50) and ALP (27.20 ± 1.60) was significantly reduced as compared with those not on therapy (Total Protein=5.81 ± 0.68; Albumin=2.60 ± 0.26; Body Weight=47.18 ± 6.37; AST=21.80 ± 1.00; ALT=15.80 ± 0.62; ALP= 32.84 ± 1.80 respectively).

Table 3 .Biochemical parameters of pulmonary TB subjects on therapy and pulmonary tb subjects not on therapy

Parameters	Pulmonary TB +Therapy	Pulmonary TB -Therapy	P-value
Total Protein(g/dl)	6.60 ± 0.47	5.81 ± 0.68	P<0.05
Albumin(g/dl)	3.13 ± 0.26	2.60 ± 0.26	P<0.05
AST(IU/L)	13.78 ± 0.55	21.80 ± 1.00	P<0.05
ALT(IU/L)	13.23 ± 0.50	15.80 ± 0.62	P<0.05
ALP(IU/L)	27.20 ± 1.60	32.84 ± 1.80	P<0.05
Weight(Kg)	57.78 ± 8.61	47.18 ± 6.37	P<0.05

*P<0.05=Statistically Significant

Discussion

The present study shows significantly lower levels of total protein and albumin in subjects with pulmonary tuberculosis comparable with similar report was given by Sasaki *et al*.,1999 & Yamanaka *et al*.,2001 reported that the total protein and albumin were significantly lower in nomads when compared with domiciled tuberculosis patients and healthy men. Aily *et al*.,1999 also observed lower levels of albumin which might have been caused by anorexia, malnutrition and mal-absorption commonly observed in tuberculosis.

Significantly decrease in body weight has been commonly found in patients with active TB and is most likely the result of a combination associated with the inflammatory and immune response (Paton *et al.,* 2004). More is known about nutritional status at the time of diagnosis than of the wasting process which precedes diagnosis per se (Macallan, 1999).

Newly diagnosed pulmonary TB subjects on hepatotoxic first line drugs were associated with increase in AST, ALT and ALP. In animal experiments oral administration of rifampicin showed an increase in the liver AST, ALT and ALP enzyme activity levels when compared to control (Pessayre *et al.,*1977).

The impact of isoniazid and rifampicin has shown in animal studies affects the levels of protein, bilirubin and in hepatocyte, while increased liver enzymes due to endogenous Reactive Oxygen Species (ROS); similar to phagocytes in mycobacterium tuberculosis of patients (Niwa *et al.,1984*).High levels of free radicals are produced in the lungs by activated inflammatory cells, i.e. neutrophils, eosinophils and alveolar macrophages. If not detoxified, cause cellular damage, affecting the hepatocytes and leading to increased liver enzymes in pulmonary TB patients (Arun Kulkarni & Narayan A Madrasi, 2008).

Recent researches suggest that in pulmonary tuberculosis there is increase in several circulating markers of free radical activity, indicating ongoing oxidative stress and decrease in the antioxidant activity contributing to development of liver function abnormalities (Ragunath R Rai & Madhavi S Phadke, 2006; Sardesai,1995).

Hepatotoxicity is the most common adverse effect of anti-tubercular treatment leading to interruption of therapy. Parameters of liver function monitored at regular intervals prevent this condition by withdrawal of hepatotoxic drugs when values of liver enzymes reach critical levels. Hepatotoxicity risk factors if accessed before starting

antitubercular treatment may help to determine the frequency of monitoring required. Screening for chronic viral hepatitis in endemic areas of hepatitis B virus and hepatitis C infection prevents drug induced liver disease in risk groups on antitubercular treatment.

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