Effect of rifampicin on certain biochemical parameter in the liver of albino rats

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Abstract

The aim of this study was to evaluate the toxicity of rifampicin in the liver of albino rat. The hepatotoxicity of rifampicin was determined by measuring the marker enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total protein in the liver. The study was designed to evaluate the toxicity of rifampicin in albino rats. Liver toxicity was induced by oral administration of rifampicin at a dose of 10 mg/kg of body weight (21 consecutive days) the rifampicin treated rats showed a significant decrease in the Protein and marked increase in the marker enzymes such as AST, ALT and ALP. The results of the present study suggest that rifampicin showed hepatotoxic effects.

INTRODUCTION

First line drugs such as isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin are considered drugs for the treatment of tuberculosis [1]. Rifampicin has also been found to be effective against several other pathogens including mycobacterium and penicillin resistant Pneumococci [2345].

Tuberculosis treatment regimens that contain rifampicin are generally more effective than non-rifampicin containing regimens. Rifampicin is an antimycobacterial drug that is a standard component of combination regimens for treating tuberculosis [6]. A number of tablets that contain rifampicin in combination with other antituberculosis drugs are used to treat the tuberculosis disease. Rifampicin has been recently approved by Food and Drug Administration (FDA) for the treatment of pulmonary TB in HIV non infected adults. Rifampicin is semi synthetic derivative of the rifampicins, a class of antibiotics that are fermentation products of Nocardia mediteranei [7] a species from a soil sample collected in France.

Liver is the most important among the organs concerned with the metabolic activities. The intracellular enzymes of the parenchyma of liver cells have an amazing capacity to perform diverse and complicated biochemical functions.

An elevation in the levels of serum marker enzymes is generally regarded as one of the most sensitive index of hepatic damage [8]. The present study has been undertaken to study the effect of rifampicin on certain biochemical parameters such as Protein, AST, ALT and ALP enzyme activities in the liver tissue of albino rat.

MATERIALS AND METHODS

Healthy adult albino rats of Wistar strain weighing (150 – 250 gm) were used for the present investigation, and his work approved by the Animal ethical committee of Bharathiar University (Reg.No. 722/02/9/CPCSEA). They were housed in clean cages in a well ventilated room with 12 ± 1 light and 12 ± 1 hour dark schedules. They were fed with a standard balanced diet and clean drinking water ad libitum.

All the chemical and reagents used in the experiments were of analytical grade and were obtained from CR-Cinese, Lubin Laboratories, Auraugabad, India. Glaxo Smithkline Pharmaceuticals (Mumbai), E-Merck (Germany and India). Sigma Aldrich (USA) Sharabhai M. Chemicals (India) Labachemi (Indo-Austranol India), Himedia Laboratories, India.

The albino rats were divided into two groups. Group 1. The rats received saline orally and treated as controls. Group 2. Rifampicin treated group. The rats were received rifampicin (10 mg/kg body wt.) orally for 21 consecutive days.

After 24 hours of the last dose schedule, the rats were sacrificed by cervical decapitation. The liver was dissected out and washed in 0.9% saline, freed from the adhering connective tissue mass and blotted on a filter paper. The tissue was stored at 4°C until used for further biochemical

analysis.

Alanine amino transaminase (ALT) and aspartate amino transaminase (AST) enzyme activity levels in the tissue homogenate was estimated by the method of [9]. Alkaline phosphatase (ALP) was assayed by the method of [10]. Protein was estimated by the method of [11].

RESULT AND DISCUSSION

Albino rat treated with rifampicin (10 mg/kg body wt.) orally for 21 consecutive days) showed a marked increase in all parameters such as AST, ALT and ALP except Protein. A significant decrease in protein was observed in the liver tissue of albino rat treated with rifampicin (Table 1).

Table 1: Effect of rifampicin on total protein, (aspartate and alanine amino transaminase and alkaline phosphatase concentrations in the liver of albino rats .

Protein is the most important and abundant biochemical constituent present in the animal body. Proteins are important in all biological system. It plays a major role in the synthesis of microsomal detoxifying enzymes and helps to detoxify the toxicants which enter in to the animal body [12]. In the present investigation the total protein was decreased in the liver tissue of rat treated with rifampicin. Many investigators have reported that the decreased levels of protein in rat treated with different heavy metals and drugs [13] add other authors.

[14] has reported a decrease in protein synthesis in the liver tissue of acetaminophen treated rat. Similar trend of a decrease in protein synthesis has been reported in the liver cells of rat [15]. Oral administration of rifampicin showed on increase in the liver AST, ALT and ALP enzyme activity levels when compared to control rat.

The transaminases are enzymes that are involved in the transfer of amino group from an alpha-amino acid to an oxaloaceticacid. ALT (alanine amino transferase) is more abundant in the liver than the other tissues whereas AST (Aspartate amino transferase) is widely distributed, with high concentration in cytosol as well as mitochondria of heart, liver, skeletal muscle, kidney and erythrocytes. Liver damage may range from areas of focal necrosis to extensive destruction caused by infections, toxins or drugs. Damage to liver cells with or without necrosis caused acute release of intra-cellular constituents into the blood stream [16].

ALT is more abundant in the liver cells than in any other cells in the body and primarily used a specific markers of hepatic damage. ALT and AST enzymes are regarded as markers of liver injury since liver is the major site of metabolism [17].

Liver tissue is rich in alanine aminotransaminase and aspartate aminotransaminase. Though both transaminases are elevated in sera of patients with acute hepatic disease, ALT which is only slightly elevated by cardiac necrosis, is a more specific for liver disease [181920]. Elevation in the level of ALT, AST and ALP has been reported in the rat treated with CCl4 [21].

Alkaline phosphatase enzymes are zinc containing metal enzymes which catalyses the hydrolysis of number of phosphate esters. It is an enzyme produced in the liver bone and placenta that is released into the blood during injury or during normal activities such as bone growth or pregnancy [2223].

Rifampicin is a complex semisynthetic macrocyclic antibiotic derived from streptomyces mediterranei [24]. It is a member of the rifamycin class of antibiotics which is used for the treatment of tuberculosis and other infectious diseases [2526242728].

It is categarized as one of the first line anti tuberculosis agents, however various side effects such as hepatotoxins allergic rashes, lack of appetite nausea or immunological disturbances have been reported associated with the administration of the drug [293028].

The impact of isoniazed and rifampicin on the levels of protein, bilirubin and in hepatocyte of experimental rats has been reported [31]. Urea has observed an alterations in protein metabolism have been considered for decades to be one of the conditions associated with the hepatic dysfunction.

Decreased level of protein in the serum and the liver of isoniazid and rifampicin administered rats as compared to control group has been reported. He further suggested that the disaggregation of polyribosomal profiles induced by antitubular drugs is also associated with the inhibition of protein synthesis which may be parallely responsible for the fatty liver, probably not necrosis although it contributes to disabling of the cell. [32] have reported the elevations of marker enzymes namely ALP, ALT, AST and LDH in the nicotine treated animals. These markers enzymes are important indexes for the diagnosis of liver disease and indicate the damage of cells in liver [33].

In conclusion, the antituberculosis drug, rifampicin induced alterations in the level of protein, AST, ALT and ALP enzymes activities in the albino rat when orally administered for 21 consecutive days.

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