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Assessing the Impact of Rifampicin on Some Hepatic Parameters of Albino Wistar Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author GDE designed the study, wrote the protocol and supervised the work. Authors EBE and KAO carried out all laboratories work and performed the statistical analysis. Authors EBE and KAO managed the analyses of the study. Author GDE wrote the first draft of the manuscript. Author EBE managed the literature searches and edited the manuscript. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

This study was aimed at investigating and evaluating the toxicity of Rifampicin on the liver of albino rats. The hepatoxicity of Rifampicin was determined by measuring the hepatic enzymes such as alanine amino transaminase (ALT) and alkaline phosphatase (ALP). Liver toxicity was induced by oral administration of Rifampicin per body weight for twenty one (21) consecutive days. The animals were divided into four groups with each group having six (6) animals. Group I rats served as control and were treated with distilled water while Groups II, III and IV received 3 mg/kg, 9 mg/kg and 18 mg/kg of Rifampicin orally respectively. After anesthesia with chloroform, they were sacrificed and blood sample was collected for biochemical analysis of hepatic enzymes. The results showed that Rifampicin treated rats in Group II and III showed no marked increase in ALP and ALT levels. Rifampicin treated rats in group four (IV) showed a marked increase in the serum enzymes levels. The results of this study suggest that Rifampicin is hepatotoxic at high doses.

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1. INTRODUCTION

Rifampicin and other first line drugs such as ethambutol, Isoniazid, streptomycin and pyrazinamide are considered drugs for the treatment of tuberculosis. Rifampicin has also been found to be effective against several other pathogens including mycobacterium and penicillin resistant pneumococci [1]. Rifampicin is an anti-mycobacterial drug that is a standard component of combination regimens for treating tuberculosis. It is a complex semisynthetic macrolytic antibiotic derived from streptomyces mediterranei. It is characterized as one of the first line antituberculosis agent [2]. It is almost completely absorbed and achieves a mean peak plasma levels within one to four hours [3]. It acts through the inhibition of DNA dependent RNA polymerase activity in susceptible cells. Rifampicin has a very broad spectrum of activity against most gram positive and gram negative organisms and specifically mycobacterium tuberculosis. It is metabolized in the liver and excreted in bile and to a much lesser extent in urine [4].

Adverse reactions occur more frequently when Rifampicin is used intermittently. A flu like syndrome may be seen in up to 20% to 50% of patients on high dose intermittent schedule. Hypersensivity reactions, rash, prutitus, urtacaria, pemphigoid reaction and flushing have been noted [5]. Rifampicin has been observed to increase the requirements for anticoagulant drugs of the coumarin type [6]. In patients receiving anticoagulants and Rifampicin concurrently, it has been recommended that prothrombin time be performed dailly or as frequently as necessary to establish and maintain the required dose of anticoagulant [7]. Fatal acute overdose in adults have been reported with doses ranging from 14 to 60gm. Alcohol or a history of alcohol abuse was involved in some of the fatal and non fatal reports. Non fatal overdose in pediatric patients of age 1 to 4 years old of 100 mg/kg for 1 to 2 doses have been reported [8]. This work was aimed at investigating the hepatotoxic effect of Rifampicin on some specific biochemical parameters of the liver.

2. METHODOLOGY

Adult albino rats of Wistar strain weighing (187.9-296.8 g) were used for the present investigation. They were housed in clean cages in a well ventilated room at the animal house of the Faculty of Basic Medical Sciences, University of Uyo, Uyo, Akwa Ibom State, Nigeria. The animals were fed with a standard balanced diet and clean drinking water ad libitum. All animals were handled according to the National Research Council (US) committee for the update of the guide for the care and use of laboratory animals. They were weighed using beam balance before administration of Rifampicin. The albino rats were divided into four (4) groups with each group having six (6) animals. Group one rat received normal saline orally and served as control. Group two (2) rats received 3mg/kg of Rifampicin orally. Group three (3) and four (4) received 9mg/kg and 18 mg/kg of Rifampicin orally respectively. After twenty-four (24) hours of the last dose schedule, the rats were anesthetized with chloroform and sacrificed. Blood sample was collected to measure the serum levels of two marker enzymes; alanine amino transaminase (ALT) and alkaline phosphatase (ALP).

2.1 Data Analysis

Data were analysed using analysis of variance (ANOVA) followed by posthoc test. All data were expressed as means ± standard error of means with a significant difference of $P< 0.001$ among groups. Data were analysed using window SPSS (version 15.0).

3. RESULTS

The result of the research is summarized in the Table 1.

From these findings, group I (control) rats showed no marked increase in the enzymes level. Group II rats administered with 3 mg/kg of Rifampicin showed a slight insignificant difference from the control. Group III rats administered with 9 mg/kg of Rifampicin indicated a slight insignificant difference from that of control. Group IV rats administered with 18 mg/kg of Rifampicin showed a marked significant difference from all the other groups ($P<0.001$) in both ALT and ALP enzyme levels.

4. DISCUSSION

The present results show that ALT and ALP toxicity was enhanced by administration of Rifampicin at certain doses with a marked shoot up of the levels of hepatic enzymes in animals administered with 18 mg/kg bd.wt.

Table 1. Relative body weights, serum levels of ALT and ALP in the control and groups administered with Rifampicin

Groups /Dosage	Mean weight (g)	ALT (µ/l)	ALP (µ/l)
Group I (control)	241.97 ± 11.90	3.9 ± 0.36	83.82 ± 5.30
Group II 3mg/kg	250.98 ± 9.31	5.15 ± 0.64	94.7 ±6.47
Group III 9mg/kg	231.62 ± 4.98	4.43 ± 0.83	108.23 ± 3.44
Group IV 18mg/kg	221.88 ± 8.56	$13.08 \pm 0.15^{a,b,c}$	$177.23 \pm 1.17^{a,b,c}$

All values are described as means ± SEM (Standard Error of Mean)
n = 6 for all values
a = Significantly different from Control (P< 0.001)
b = Significantly different from group II (P<0.001)
c = Significantly different from group III (P<0.001)
d = Significantly different from group IV (P<0.001)

The observed increases in the hepatic enzymes are in line with the reported toxic effects generally associated with Rifampicin [9]. This observation is in agreement with the earlier report of elevated serum alkaline phosphatase and alanine amino transaminase activities in this group of animals [10]. Results of this study are more in agreement with the findings of [11] who reported that ALT and ALP elevated activities are more specific for liver disease. Other than the liver, ALT has been reported to be slightly elevated in cardiac necrosis and the elevations of ALP, AST and LDH in nicotine treated animals. Another study [12] reported an increased levels of ALP (171.33 N/L) and ALT (67.57 N/L) in gossypol treated animals. Apart from increases in the serum levels of hepatic enzymes, a decrease in the total protein was reported in the liver tissue of rat treated with Rifampicin, heavy metals and other drugs [13]. Damage of the liver cells with or without necrosis caused acute release of intracellular constituents into the bloodstream [14]. Finally, these marker enzymes are important indexes for the diagnosis of liver disease and which could be used to indicate the damage of liver cells [15].

5. CONCLUSION

Rifampicin is an antibiotic with hepatotoxic effect. The results showed that the serum levels of ALP and ALT of Rifampicin treated rats were elevated in high doses.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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