THE EFFECT OF RIFAMPICIN DRUG ON LIVER ENZYMES (ALT AND AST) IN RABBITS

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Abstract

The aim of this study was intend to study the effect of rifampicin drug on the level of liver enzymes in rabbits. Eight rabbits were used in this experiment and they were divided into two groups. The first group (control group) was administrated with 15 mg /ml/day normal saline for 35 days, while the second group (treated group) was administrated with 15 mg/ml/day for 35 days of rifampicin capsule (300 mg/kg). This study examined the influences of rifampicin drug on the concentration of Aspartate aminotransferase (ALT), Alanine aminotransferase (AST), total bilirubine and alkaline phosphates in rabbit sera. The results showed that there were a significant increase ($p<0.05$) in ALT concentration in rifampicin treated group compared with control group, and there were no significant differences in ALT and total bilirubine but there was a significant increase ($p<0.05$) in alkaline phosphates concentration. It was concluded that rifampicin produced a liver dysfunction .

تاثير عقار الريفامبسين على مستوى انزيمات الكبد (ALT و AST) في الارانب

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الخلاصة

هدفت الدراسة الحالية دراسة تاثير عقار الريفامبسين على مستوى انزيمات الكبد في الارانب حيث استخدامت ثمانية ارانب في هذه التجربة ، والتي قسمت الى مجموعتين. جرعت المجموعة الاولى (مجموعة السيطرة) ب(15 ملغم مل /يوم) محلولا فسيولوجيا ملحيا normal saline لمدة 35يوما، اما المجموعة الثانية (المجموعة المعاملة) تم تجريعها بـ(15ملغم/كغم/يوم) عقار الريفامبسين (كبسول 300 ملغم /كغم) ولمدة 35 يوما. اظهرت الدراسة ان لعقار الريفامبسين تاثير على تراكيز Aspartate aminotransferase و Alanine aminotransferae وصبغة البليروبين والفوسفاتيز القاعدي في مصل الارانب حيث اظهرت النتائج وجود زيادة معنوية ($p<0.05$) في تركيز الـAspartate aminotransferase في المجموعة المعاملة مقارنة مع مجموعة السيطرة, كما واظهرت النتائج عدم حدوث اي تغيرات معنوية في تركيز Alanine aminotransferase وتركيزصبغة البيليروبين الكلي، اما تركيز الفوسفاتيز القاعدي فقد لوحظ وجود زيادة معنوية ($p<0.05$) في تركيزه في المجموعة المعاملة مقارنة مع مجموعة السيطرة . يتضح من هذا أن لعقار الريفامبسين تاثير سلبي يودي الى حدوث اختلال في وظائف الكبد.

Introduction

The liver is an important organ concerned with the biological functions in the human body and it represents the largest organ in the vertebrate body (1), (2). The liver has a central role in drug metabolism and detoxification and it is affected by the drugs; therefore a damage to the liver caused by hepatotoxic agents is a serious matter (1).

The aminotransferase include Aspartate aminotransferase AST (SGOT) and Alanine aminotransferase ALT (SGPT) that are excellent markers of liver function (3) and hepatocellular injury (1). Functions of the liver are: storage organ, synthesis, bile secretion, formation and distraction of red cells, detoxification, function and metabolism (4). Liver function enzymes which represent markers for its function, are aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and total bilirubine (3), (4), (5).

Rifampicin drug is a semisynthetic derivative of rifamycin. It is an antibiotic that is active against some Gram-negative, Grame-positive, some enteric bacteria and mycobacteria (6). Rifampicin binds strongly to DNA - dependent RNA polymerase and thus inhibits RNA synthesis in bacteria and chlamydiac. It is also used as a drug for anti-tuberculosis (7), (8), (9).

Material and Methods

Eight mature rabbits weighing about 1300─1600 grams were used in the present experiment. Animals were kept under standard laboratory conditions and were given food and water. Animals were divided into two groups and were subjected to experimental schedule as follows: first group was administrated daily with 15mg/ml/day normal saline for 35 days and used as control group, while the second group was administrated daily with 15mg/kg/day for 35 days of rifampicin (capsule 300mg/kg), (Mumbai, Ajanta). Twenty four hours after the last injection, peripheral blood was collected and serum samples were separated out and were frozen until assayed. Aspartate aminotransferase, Alanin amino-trance ferase, were total bilirubine and alkaline phosphates was measured by using spectrophotometer.

AST and ALT were measured by using kit of (Spinreact). The same procedure was used for both, but it differs in the buffer which was used. At first we took two tubes (test and blank). We put 0.5 ml from the DL_Aspartate ,α_ketoglutarate, to measur AST concentration, and when we measured ALT concentration, we used (DL_Alanine, α–ketoglutarate) after that put 0.1 ml from serum in each tubes mixed it and left for 30 minuets at 37 ^{o}C after that we added 0.5 ml from 2,4 dinitrophenylhydrine and 20 ml frome NaoH mixed it and left it at room temperature ,after that read the absorption of tubes in spectrophotometer (ALT in 550 nm,AST in 520 nm). Bilirubine concentration was measured by using kit from (Bio Elite). We took two tubes (test and blank), put in blank tube 0.05ml from serum and 1 ml from total bilirubine, and in test tube we put 1 ml from water reagent and 0.05ml.from serum mixwd and put them in water bath for 5 minuets at 37 after that read the absorption of tubes in apectrophotometer on 550 nm.

Alkaline phosphates was measured by using kit from (BioMerieux) we took three tubes (test,standared and blank) in each tubes we put 0.5 ml from alkaline substrate plus 0.05 ml serum then mixed it at 37 for 10 minuets at room temperature after that read the absorption in spectrophotometer in 580 nm.

Results and Discussion

The results of statistics analysis showed significant increase ($p<0.05$) in AST concentration in the treated group (39±6.53 U/L) compared with control group (18.5±7.85 U/L) and there was no significant increase ($p>0.05$) in the mean concentration of ALT in treated group (13.25±5.5 U/L) compared with the concentration of alt in treated group (13.25±5.5 U/L) compared with the concentration of control group.

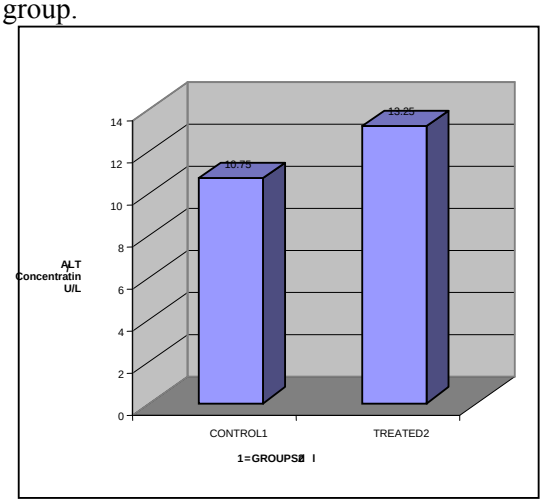

Figure 1: Effect of rifampicin (15mg/kg/day) on serum ALT concentration.

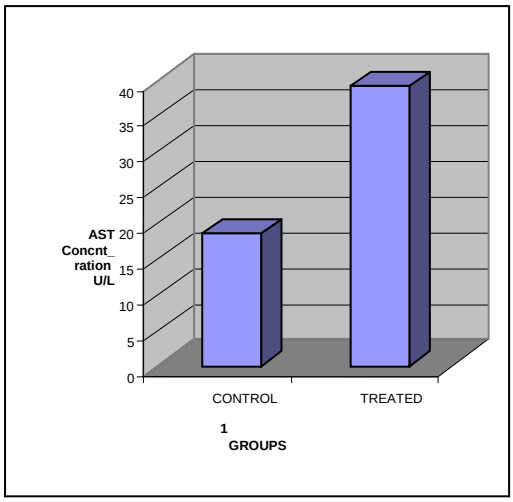

Figure 2: Effect of rifampicin (15mg/kg/day) on serum AST concentration.

The increasing in AST and ALT concentrations due to the effect of rifampicin drug, which caused diminishes in the activity of transaminease (10) with a necrosis, inflammation in liver cells and also caused liver injury (11) that lead to increasing in AST and ALT concentration in blood serum (1) ,(4),(12).

Rifampicin was found to produse liver dysfunction (6) with acute liver failure (11) and when the cells of the liver damage livers enzymes leak into the blood and AST, ALT levels procid an indicator of the degree of inflammation as well as the possible cause of hepatocellular damage (13).

The risk of hepatotoxicity increased significantly after treatment by rifampicin in patients with tuberculosis (14) therefore rifampicin considered as a hepatoxic agents (15).

Also the result showed that there was no significant increase ($p>0.05$) in the concentration of total bilirubine mean concentration in treated group 0.75±0.1 mg/dl where in control group was 0.65±0.1 mg/dl Figure (4). This low difference in the change may due to the short period of the treatment with rifampicin, because other researches found that rifampicin produced competition for elimination of bile and bromylphatein by the liver and also caused increasing of excreting on bile (15).

Rifampicin effect on concentration of total bilirubine caused injury for liver especially when administred for along period (1), especially when it used in the treatment of tuberculosis for 9 monthes (3), also rifampicin found to be inducer and enhance formation of reactive metabolites which impair the uptake of bilirubine and cause acute cellular necrosis (1) that all cause elevation of total bilirubine in blood.

The results revealed that there was a significant increase ($p<0.05$) in alkaline phosphatase concentration in treated group (18.65±2.05 U/L) compared with concentration in control group (6.48±0.23 U/L) (Figure 3). This difference due to the effect of rifampicin on liver which was found to cause increasing in the level of alkaline phosphatase (1), (6), (8).

Rifampicin was found to cause an increasing in the rate of T3, T4 metabolism (17), anemia (9), (13), thrombocytopenia and lukopenia (6), (18), also rifampicin reduced the level of glutathione (19) and the level of lipids (20).

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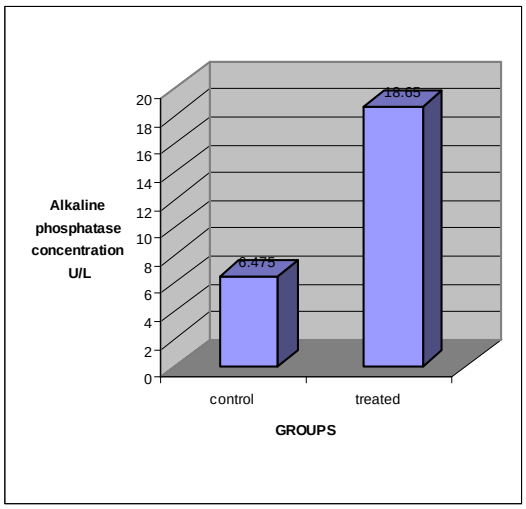

Figure 3: Effect of rifampicin (15mg/kg/day) on serum alkaline phophatase concentration.

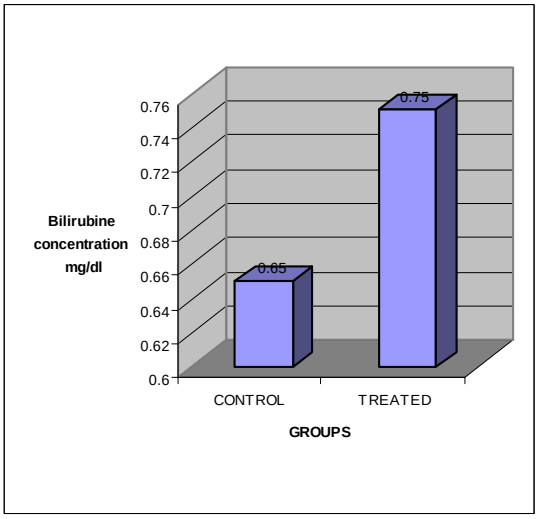

Figure 4: Effect of rifampicin (15mg/kg/day) on serum bilirubine concentration.

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