

Cortisone dose as combination treatment with antibiotic for liver infected by IP *E. coli* injection

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Abstract:

In acute liver failure, infections early treatment is necessary to reduce mortality. Antibiotics treatment causes Drug-induced liver injury. Corticosteroids are effective management of the obstructive and inflammatory disorders in many organs such as liver but have many side effects. The aim of this study is to evaluation of affectivity single cortisone dose with multiple antibiotic doses on antibiotic treatment of liver infection. 20 males Balb/c mice were used in this study. The mice aged about 2 months and weight about 24g. 15 mice were injected inter peritoneal (IP) with 200 μ l *E.coli* in final concentration (10^8 cell /ml). Five mice were injected with only normal saline (control group). Five mice from infected mice were injected ip after 48h with only normal saline (infected group) and 10 mice treated with Cefepime in final concentration 25mg/Kg daily for 3 days which divided to tow groups: 5 mice were treated with Cefepime only (treated Ab) and 5 mice were treated with the combination of cefepime 25mg/Kg multiple dose for 3 days with hydrocortisone 2.5mg/Kg single dose in the first treated day only (treated Ab+cort). All mice were killed by cervical distraction after 3 treated days. Blood was collected from the eye in dry sterile test tube to use in determination of serum glutamate pyruvate transaminase and glutamate oxaloacetate transaminase by the GOT and GPT kit from Bio system Reagents and instruments. Significantly higher serum GOT and GPT levels in infected group were detected, and it still higher tendency in treated with Ab compared to control and treated with Ab+Cort. While no significantly difference in serum GOT and GPT of infected mice treated with Ab was detected, significantly lower GOT and GPT levels in infected mice treated with Ab+Cort compared to infected mice group. Significantly positive correlations between GOT and GPT levels were established in control group, infected groups (with and without treatment), and all groups together. This suggested treatment way need to evaluate in different liver disease types and stages.

Key words: GOT, GPT, Cortisone, and Antibiotics.

INTRODUCTION:

The liver is a one of digestive organs that helps digestion and carries out many other essential functions include bile production to break food into energy, basic substances creating such as hormones, detoxification of blood from medication or alcohol and drugs, and control the storage of fat and produce of cholesterol and release them [1]

Liver infection is a reaction that occurs when the cells of liver are attacked by substance or pathogenic microbe [2]. Bacterial infection is a serious complication, and it is often fatal to patients with liver disease directly or through gastrointestinal bleeding, renal failure, or hepatic encephalopathy [3].

Serum Biochemical tests such as glutamic oxaloacetic transaminase [4] and glutamic pyruvic transaminase (GPT) plays an important role in increasing the detection of liver enzyme abnormalities in patients with symptoms [5] and they are very useful for liver damage or injury measures of different types of disease [6].

Corticosteroids are produced naturally by the adrenal gland in the body. They affect the performance of most of the body's systems (heart, immune, muscles and bones, endocrine and nervous system). They practice a wide range of effects including effects on metabolism of carbohydrates, protein, and fats. They help to maintain fluids and electrolytes balance [7]. Finally, corticosteroids have many biologic actions and the manner in which they influence cell destruction, phagocytosis, inflammation, cellular metabolism, and protein synthesis may also alter immune responsiveness in ways that are not yet well understood [8, 9]

Corticosteroids are effective management of the obstructive and inflammatory disorders in many organs such as liver in Chronic granulomatous disease (CGD) and well tolerated

with minimal infectious complications at low doses [10, 11]. In addition, multiple cases showed success indicate the use of concomitant corticosteroids with antimicrobials agents for pneumonia [12, 13], and in the syndrome of "mulch pneumonitis", which is acute inflammatory and necrotizing granulomatous lung disease. Mulch pneumonitis follows inhalation of organic matter such as mulch or hay. Steroids, used in mulch pneumonitis, are thought to reduce sever acute inflammatory response induced by fungal cell walls [14].

The aim of this study is to evaluation of effectivity single cortisone dose with multiple antibiotic dose on antibiotic treatment of liver infection.

MATERIAL AND METHOD:

E.coli was isolated from children, which have urinary infect. It was isolated and diagnosis in the medicine city/ Baghdad.

Experiment Animals

20 males Balb/c mice were used in this study, from preventive research center, Baghdad, Iraq. The mice aged about 2 months and weight about 24g. 15 mice were injected inter peritoneal (IP) with 200 μ l *E.coli* in final concentration (10^8 cell /ml). Five mice were injected with only normal saline (control group).

10 mice from infected mice after 48h were treated with Cefepime in final concentration 25mg/Kg daily by IP injection for 3 days. Five mice were injected with only normal saline (infected group).

Treated mice were divided to tow groups:

1. First group (5 mice) treated with Cefepime only (treated Ab).
2. Second group (5 mice) treated with the the combination of cefepime 25mg/Kg multiple dose for 3 days

with hydrocortisone 2.5mg/Kg single dose in the first treated day only (treated Ab+cort). All mice were killed by cervical distraction after 3 treated days. Blood was collected from the eye in dry sterile test tube to use in determination of serum glutamate pyruvate transminase and glutamate oxaloacetate transminase by the GOT and GPT kit from Bio system Reagents and instruments. All the experiments were done in Biology department, Science collage, Al-Mustansiriyah University.

Statistic analysis

Results are expressed as mean \pm standard error (M \pm SE). Data were analyzed by one-way analysis of variance (ANOVA) followed by Fisher's test for multiple comparisons, using Statview version 5.0. Differences were considered significant when $p < 0.05$. Regression analysis was performed by analysis of covariance (ANCOVA) also using Stat view version 5.0.

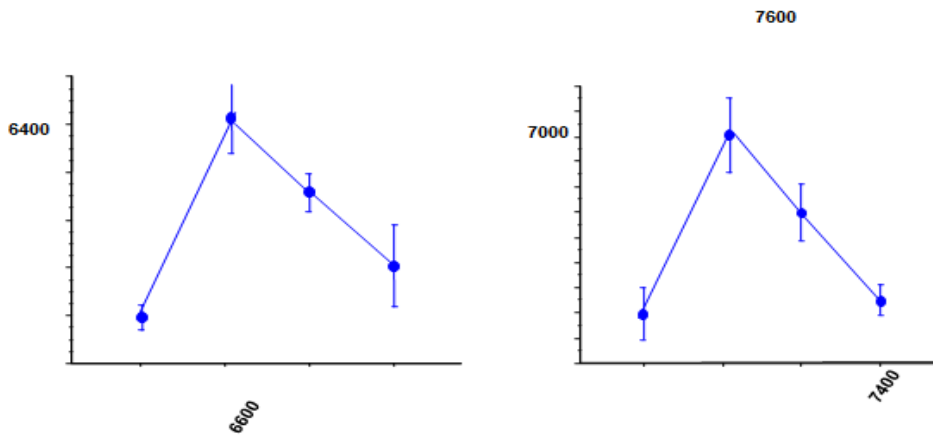


Figure 1: Serum GOT and GPT levels in control, infected groups, treated with Ab, and treated with Ab+Cort.. (A) GOT, and (B) GPT.

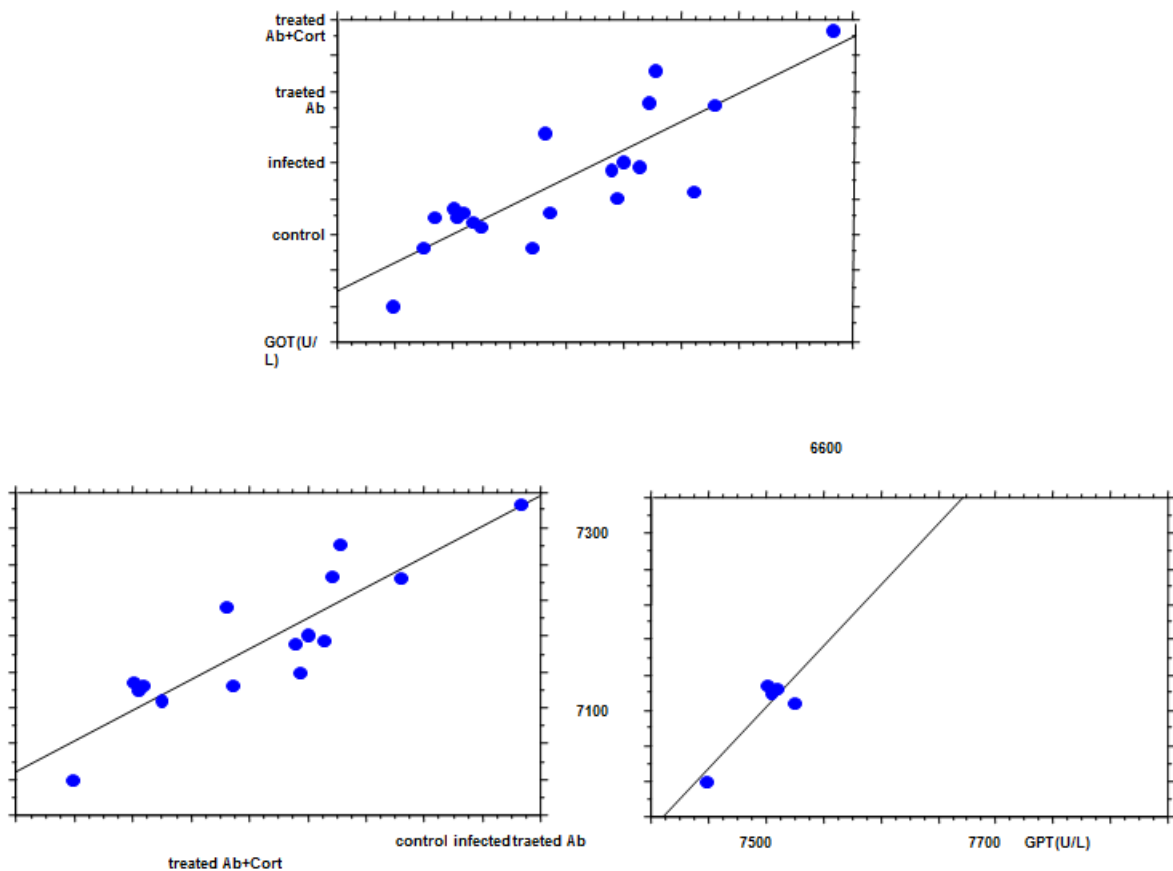


Figure 2: the correlation between GOT and GPT in the infected, control, and all groups together

RESULTS:

The GOT and GPT levels were determined in the serum of control, infected, treated with Ab, and treated with Ab+Cort mice groups. Significantly higher ($p < 0.05$) serum GOT and GPT levels in infected group were detected, and it still higher tendency in treated with Ab compared to control and treated with Ab+Cort. While no significantly difference in serum GOT and GPT of infected mice treated with Ab was detected, significantly lower GOT and GPT levels in infected mice treated with Ab+Cort compared to infected mice group (Figure 1)

Serum GOT was (6591.1 ± 51.9 U/L) in control group, while it was (7424.4 ± 141.8 U/L) in infected group. This alteration was abrogated in the treated mice with Ab+Cort more than Ab and (6806.8 ± 172.1 U/L, and 7115.9 ± 78.3 U/L, respectively).

Serum GPT was (6795.5 ± 75.7 U/L) in control group, and it became (7503.5 ± 147.8 U/L) in infected group. This alteration was abrogated in the treated mice with Ab+Cort more than treated mice with Ab (6842.6 ± 58.1 U/L, and 7197.2 ± 112.7 U/L, respectively) (Figure 1).

Significantly positive correlations between GOT and GPT levels ($p < 0.05$) were established in control group ($R^2 = 0.778$), infected groups (with and without treatment) ($R^2 = 0.791$), and all groups together ($R^2 = 0.771$) (Figure 2)

DISCUSSION:

The blood reached to liver by both systemic and portal circulations [15]. If there is exposure to the bacteria flow with the blood, Kupffer cells, lining the hepatic sinusoids, swallow bacteria so efficiently [16, 17], which due to increase hepatic abscesses [18] and damage [19]. Hepatic abscess and damage causes hepatic failure [20], Which releases GPT and GOT into the bloodstream [21] by increase the permeability of the hepatocyte membrane [22]. These evidences can explain the elevated in the serum GOT and GPT levels in the infected mice which agreement with Jouda, *et al* (2016) results [23].

In acute liver failure, infections early treatment is necessary to reduce mortality. Thinking about antibiotics only after creating positive culture reports leads to the loss of vital time [24]. Drug-induced liver injury commonly was caused by Antibiotics [25]. However, after regulatory bodies' actions targeting specific antibiotics, public awareness of antibiotic-induced hepatotoxicity has increased in recent years [26]. In our results, the levels of GOT and GPT was decreased but not normalized after treatment with antibiotic for 3 days.

It is well establishes Corticosteroids can quickly inhibit excessive immune response and inflammatory response [27, 28]. Zhangs research group reported that the corticosteroids are effective in pre-acute and chronic liver failure treatment [29, 30]. Therefore, treatment of acute and sever acute liver failure and with corticosteroids is a reasonable treatment regimen. Some previous studies have shown that corticosteroids has been effective in treating acute liver failure- associated viral infections and drug-induced acute liver failure [30-32]. Karkhanis *et al* (2015) reported that corticosteroids were not effective in improving the diagnosis of patients with acute liver failure

[33]. Corticosteroids has a limited effect on the regenerative capacity of liver cells over a short time period [34] so corticosteroids is not able to improve the diagnosis of patients with extensive confluent cellular necrosis develops in acute liver failure. However, the administration of corticosteroids in patients with ALF and SALF remains controversial [35]. In our work, single ip injection hydrocortisone with multiple ip injection Cefepime antibiotic normalized the levels of GOT and GPT in infected groups. This suggested treatment way need to evaluate in different liver disease types and stages.

Both serums GOT and GPT, types of serum aminotransferase enzymes, are produced from its sources under the same condition and have a same functions [36]. So acute and chronic liver disease are diagnosed using these enzymes as indicators [5]. These evidences explain the positive correlation between them in control and infected groups this study which matched to Jouda (2016) results [23].

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