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The effect of albumin administration on renal dysfunction after experimental surgical obstructive jaundice in male rats

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Abstract

The aim was to study the influence of albumin supplementation on the changes of the kidney function and structure in cirrhotic rats induced by common bile duct ligation (BDL). Twenty-four male albino rats weighing 200–250 g were divided into *Group I*: 6 rats underwent laparotomy alone, and the bile duct was only dissected from the surrounding tissue; *Group II*: 6 rats underwent a sham operation and received 2% albumin in their drinking water; *Group III*: 6 rats were subjected to bile duct ligation only; and *Group IV:* 6 rats were subjected to bile duct ligation and received a daily albumin 2% in drinking water. All rats were sacrificed after 4 weeks. We measured the liver and kidney functions and oxidative stress markers in the renal tissue and conducted a histological evaluation of the liver and kidney. The liver enzymes were decreased, but there was no significant difference in the bilirubin levels in group IV compared to group III. There was a significant elevation of serum creatinine in group III compared to group II, and serum creatinine was attenuated in group IV. The renal tissue catalase activity and reduced glutathione, as well as the nitric oxide levels, were significantly increased in group IV and were elevated in group III. Histologically, the livers of group IV showed degeneration and inflammatory cell infiltration with regeneration areas in which normal hepatocytes appeared. The kidneys of group IV showed recovery as well as areas of inflammatory cell infiltration. Some tubules appeared with normal epithelial lining. In conclusion, the results suggest that albumin partially improves the renal functions and structures after their disturbances as a result of BDL.

Keywords: Albumin; Bile duct ligation; Liver; Kidney; Rats; Hepatorenal syndrome

1. Introduction

Cholestatic (Obstructive) jaundice occurred within 2 weeks of common bile duct ligation (BDL) and progressed to cirrhosis within 4 to 6 weeks [1]. The patients with cholestatic jaundice may have a higher incidence of renal dysfunction, and approximately 6–8% of the patients suffer from acute renal injury,

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with mortality over 68% [2]. Renal dysfunction secondary to liver cirrhosis, which was experimentally induced by BDL, is known as hepatorenal syndrome (HRS) [3].

The oxidative stress and generation of reactive oxygen species (ROS) secondary to cholestasis could give rise to the involvement of remote organs other than the liver, such as the kidney with alterations in its function [4]; antioxidant administration improves these alterations [5]. Experimentally, the in vitro addition of excess bile acids or bilirubin to a mixture of reactive enzymes inhibited mitochondrial oxidative enzymes. Thus, high concentrations of these substances in the blood may explain the development of renal failure during cholestatic liver disorders [6]. The blockage of the biliary pathway in cholestasis may cause an overload on the kidney with a consequent disturbance of the kidney function, which may progress to renal failure [7].

Albumin is a liver protein; its production depends on food intake and the integrity of liver cells. The main function of albumin is the maintenance of the colloidal osmotic pressure of the plasma and interstitial fluid [8]. Moreover, albumin plays a significant antioxidant role because of its ability to reduce the production of free radicals by leukocytes [9]. Patients with a reduced serum albumin level are more liable to the dangers of oxidative stress and excess free radicals [10]. Recently, albumin infusion was shown to improve renal function in decompensated cirrhotic patients with acute kidney injury by impacting on the renal blood flow autoregulation [11].

This study was designed with the aim of evaluating the renal function parameters and renal histological changes in rats subjected to a ligation of the extrahepatic bile duct and the influence of albumin supplementation in these animals.

2. Materials and methods

2.1. Animals

The present study was performed on adult male albino rats weighing 200–250 g. The rats were purchased from *Vacsera Animal House (Helwan)* and were maintained in the Physiology Department Animal House under standard conditions of boarding and feeding. The given diet consisted of bread, milk and green vegetables, and the diet and water were provided ad libitum. All surgical procedures were performed with diethyl ether inhalation.

2.2. Experimental protocol

2.2.1. Animal groups

Twenty-four male albino rats were divided into four groups:

- *Group I: sham/untreated* ($n=6$) rats underwent laparotomy with handling of the bile ducts, but without ligation of the bile duct and were sacrificed *4 weeks* after the manipulation.
- *Group II: sham/treated* ($n=6$) rats underwent a sham operation and received 2% albumin (aqueous solution) ad libitum and were sacrificed *4 weeks* after manipulation.
- *Group III: BDL/untreated* ($n=6$) rats underwent laparotomy with ligation of the common bile duct and were sacrificed *4 weeks* after the common bile duct ligation.
- *Group IV: BDL/treated* ($n=6$) rats underwent laparotomy with ligation of the common bile duct, were treated with 2% (albumin aqueous solution) ad libitum [12], and were sacrificed ***4 weeks*** after the common bile duct ligation.

Rats in the sham-operated group were subjected to a 1.5-cm upper midline abdominal incision, and the common bile duct was isolated from the surrounding tissues. The rats in the BDL group underwent the same procedure and the common bile duct was doubly ligated with a 4–0 silk suture and transected between the two ligatures. The rats were subjected to either bile duct ligation (BDL) or the sham operation using aseptic techniques, as previously described by [13].

During the period of the study, the animals were kept at room temperature and were subjected to a light/dark cycle of 12 h each. All animals received rat chow and water ad libitum, whereas in the case of the animals in the treated groups (groups II and IV), the water contained 2% albumin.

After the end of the experimental period, animals were anaesthetized by an overdose of diethyl ether and were sacrificed, blood was collected, and the liver and kidney were excised and weighed immediately and preserved in parafilm and 10% formalin for biochemical and histological analyses, respectively.

2.2.2. Blood samples collection

Initially, a few drops of blood were collected in a heparinized capillary tube that was centrifuged by microcentrifuge to determine the haematocrit value. Most of the blood collected was then centrifuged to separate the serum, which was stored at −20 °C for

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