Original Article

Hepatoprotective Effect of Alpha Tocopherol in Rats

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Abstract

Introduction: The liver is the largest exocrine gland in our body. It is the vital organ undertaking wide range of functions, such as detoxification, metabolism, storage of iron and vitamins. It is very much important to protect liver in spite of continuous hepatotoxicity. The present study has been carried out with the aim to investigate the hepatoprotective effect of alpha tocopherol in paracetamol induced acute toxicity in rat. **Materials and methods:** This study was conducted at the department of Pharmacology, Dhaka Medical College from July 2014 to June 2015. Seven rats were taken as control while 7 rats were given hepatotoxic dose of paracetamol and 7 were given hepatotoxic dose of paracetamol along with alpha tocopherol. Serum level of bilirubin, ALT and AST were compared to find out any hepatoprotective effect alpha tocopherol. **Results:** Serum bilirubin level were 0.55 ± 0.09 mg/dl, 3.31 ± 0.53 mg/dl and 0.92 ± 0.20 mg/dl in control group, pretreated paracetamol and pretreated paracetamol with alpha tocopherol group respectively, serum ALT were 18.51 ± 2.00 U/L, 76.74 ± 17.69 U/L and 24.59 ± 5.08 U/L in control group, pretreated paracetamol and pretreated paracetamol with alpha tocopherol group respectively and serum AST were 24.75 ± 3.27 U/L, 69.23 ± 15.18 U/L and 29.00±3.97 U/L in control group, pretreated paracetamol and pretreated paracetamol with alpha tocopherol group respectively which were statistically significant. **Conclusion:** Compiling all results of this study it can be concluded that alpha tocopherol have hepatoprotective activity. These results provide a rationale for the use of alpha tocopherol in the development of new herbal medicine, much needed for the treatment of various liver ailments.

Keywords: Alpha tocopherol

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Introduction

The liver is the largest exocrine gland in our body. It is the vital organ undertaking wide range of functions, such as detoxification, protein-fat-carbohydrate metabolism, storage of iron and vitamins. The liver also plays major role in decomposition of RBCs, hormone production, plasma protein synthesis, glycogen storage and synthesis of urea. The organ liver is inevitable for survival and one cannot live without it for long period [1]. Liver is the key organ for detoxification of toxic substance and disposition of endogenous substances [2]. It is continuously and widely exposed to toxins and chemotherapeutic agents that lead to impairment of its functions. All types of injuries to the liver (e.g. circulatory, traumatic, toxic or microbiological) lead to damage of hepatocytes which results in its malfunctioning [3]. Therefore, the disruption of the integrity of liver function leads to fatal cases or even irreversible organic death. In liver injury, it is supposed that the intervention of free radicals in normal metabolic process is responsible for the patho-

logical changes. Free radicals attack biomolecules and induce lipid peroxidation, enzyme inactivation, and finally cell necrosis [4].

Hepatotoxicity is a growing concern of today's modern society. The World Health Organization (WHO) estimates that 140 million people worldwide suffer from alcohol dependency [5]. The increasing incidence of alcoholism, cigarette smoking, abusing substance and other unhealthy lifestyle options, like eating fatty foods, have contributed to the morbidity and mortality due to liver disease [6]. More than 900 drugs have been implicated in causing liver injury. Chemicals often cause subclinical injury to the liver, which manifests only as abnormal liver enzyme tests. Drug-induced liver injury is responsible for 5% of all hospital admissions and 50% of all acute liver failures [7].

Paracetamol or acetaminophen, chemically named N-acetyl-p-aminophenol (APAP) is generally safe for use at recommended doses [8]. The initial symptoms of overdose are nausea, vomiting, diarrhea and abdominal pain. Acute overdoses of paracetamol can cause potentially fatal kidney, brain and liver damage and, in rare individuals, a normal dose can do the same [9]. In cases of paracetamol overdose, the sulfate and glucuronide pathways become saturated, and more paracetamol is shunted to the cytochrome P450 system to produce NAPQI. As a result, hepatocellular supplies of glutathione become depleted, as the demand for glutathione is higher than its regeneration [10]. NAPQI therefore remains in its toxic form in the liver and reacts with cellular membrane molecules, resulting in widespread hepatocyte damage and death, leading to acute hepatic necrosis [11].

Antioxidant vitamins are important elements in protecting many cellular damages, for example vitamin C and E which protect against oxidant-mediated inflammation and inflammatory tissue damage. Vitamin E protects against liver damage and prevents fibrosis and cirrhosis progression in metal overload states. Alpha-tocopherol, a form of vitamin E, is an important lipid-soluble antioxidant. It performs its functions as antioxidant in the glutathione peroxidase pathway [12] (Wefers and Sies, 1988). As an antioxidant, vitamin E acts as a peroxyl radical scavenger, preventing the propagation of free radicals in tissues, by reacting with them to form a tocopheryl radical, which will then be reduced by a hydrogen donor and thus return to its reduced state (Traber and Stevens, 2011) [13].

So, we have done an experiment in rats with the research question of whether there is any difference in hepatoprotective effect of alpha tocopherol in paracetamol induced acute toxicity in rat? Our aim was to find out the hepatoprotective effect of alpha tocopherol in animals.

Materials and Methods

This study was conducted at the department of Pharmacology, Dhaka Medical College from July 2014 to June 2015. Seven rats were taken as control while 7 rats were given hepatotoxic dose of paracetamol and 7 were given both paracetamol and alpha tocopherol. Serum level of bilirubin, ALT and AST were compared to find out any hepatoprotective effect of alpha.

The experiment was carried out on 21 Long Evan Norwegian rats of either sex weighing between 150-200 grams which were collected from icddr,b, Dhaka. The rats were kept in animal house of the Department of Pharmacology, Dhaka Medical College. Rats of different batches of different groups were kept in different metallic cages. Male and female rats were also kept in different metallic cages and were allowed to feed on standard laboratory diet and to drink ad libitum. These rats were acclimatized five days at room temperature and humidity.

The rats were grouped in

Group A: This group consisted of 7 rats, were served as control. They received normal pelleted diet with water adlibitum for 15 days. On the 16th day 2cc of distilled water was feed orally to each rat through nasogastric tube.

Group B: This group consisted of 7 rats, were fed on normal diet with water adlibitum for 15

days. On the 16th day all the rats were treated with powdered Paracetamol orally at the dose of 2gm/kg body weight dissolved in 2cc distilled water.

Group C: This group consisted of 7 rats, received normal diet with adlibitum along with alpha tocopherol at a dose of 250 mg/kg body weight for 15 days. Then on the 16th day, all the rats were treated with powdered paracetamol orally at a dose of 2 gm/kg body weight dissolved in 2cc distilled water.

At the end of the scheduled treatment and after overnight fasting on the 18th day, blood sample was collected from all groups of rat by cardiac puncture and was collected in plain test tube for estimation of serum bilirubin, serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST).

Results

We have taken serum bilirubin, ALT and AST as marker of hepatotoxicity. We have compared these markers with control group (Group A), the group given toxic dose of paracetamol (Group B) and the group given alpha tocopherol (Group C).

The comparison of serum bilirubin, ALT and AST between group A and group B is shown in table 1 which shows significant hepatotoxic effect of paracetamol on rats. Table 2 shows the markers of hepatotoxicity is significantly normal after given toxic dose of paracetamol as well as alpha tocopherol.

Table 1: Comparison of serum bilirubin, ALT and AST between group A (control) and group B (pretreated paracetamol).

Variable	Group	Mean ± SD	*p* value*
Serum bilirubin (mg/dl)	A (Control)	0.55 ± 0.09	<0.001
	B (Paracetamol)	3.31 ± 0.53	
Serum ALT (IU/L)	A (Control)	18.51 ± 2.00	<0.001
	B (Paracetamol)	76.74 ± 17.69	
Serum AST (IU/L)	A (Control)	24.75 ± 3.27	<0.001
	B (Paracetamol)	69.23±15.18	

*Unpaired t-test was done

Table 2: Comparison of serum bilirubin, ALT and AST between group B (pretreated paracetamol) and group C (pretreated paracetamol + pretreated α-tocopherol).

Variable	Group	Mean ± SD	*p* value*
Serum bilirubin (mg/dl)	B (Paracetamol)	3.31 ± 0.53	<0.001
	C (Pretreated α-tocopherol)	0.92 ± 0.20	
Serum ALT (IU/L)	B (Paracetamol)	76.74 ± 17.69	<0.001
	C (Pretreated α-tocopherol)	24.59 ± 5.08	
Serum AST (IU/L)	B (Paracetamol)	69.23 ± 15.18	<0.001
	C (Pretreated α-tocopherol)	29.00 ± 3.97	

*Unpaired t-test was done

Discussion

In this study, hepatotoxicity was induced by single oral administration of paracetamol at the dose of 2gm/kg body weight. Hepatic damage was assessed by significant rise of serum bilirubin, ALT and AST, which were compared to that of the control group. The elevation of the enzyme levels was found by several studies [15, 16].

In the present study alpha tocopherol was used to compare the hepatoprotective activity with A. paniculata and N. sativa. It was used at a dose of 250 mg/kg body weight according to the review of Adikwu and Nelson et al [17].

IIn the present study, comparison of hepato-

protective effects of alpha tocopherol was evaluated by estimating the levels of serum bilirubin, ALT and AST. There was evidence of significant prevention in rise of the biochemical parameters pretreated with alpha tocopherol. Same observations were found by most of the studies reviewed so far [12, 14 and 17].

Comparing the biochemical findings in different groups of experimental animals, it is obvious that toxic effects in the liver produced by paracetamol can be prevented by pretreated alpha tocopherol.

Conclusion

Compiling all results of this study it can be concluded that alpha tocopherol have hepatoprotective activity. These results provide a rationale for the use of alpha tocopherol in the development of new herbal medicine, much needed for the treatment of various liver ailments.

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