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Protective effect of montelukast against acute kidney injury in rats induced by diclofenac

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Abstract

Background: Acute kidney injury (AKI) is a syndrome encompassing much different etiology and is characterized by an acute deterioration of kidney function. Montelukast is work as an antagonist of the CysLT1 receptor which commonly used in medical treatment of asthma and allergic rhinitis.

Aim: This study was aimed to evaluate the protective effect of montelukast on acute kidney injury in male rats induced by diclofenac.

Materials and Methods: Thirty male rats were divided into five groups: Group1 received no treatment and served as a negative (-ve) control group. Group2 received ethanol and served as (vehicle group). Group3 (disc. Group) administrated diclofenac sodium (vulturine) at a dose (100 mg/kg, i.p.) for three days (20) and served as (diclofenac-treated group). Group 4 (disc. +mont.) received montelukast 30 min. The heart blood samples were taken from the heart; then it centrifuged for five minutes at 3000 rpm to prepare the serum. Creatinine and urea were measured using Chemistry Analyzer, while serum GSH and serum MDA concentrations were measured using ELISA technique. The histopathological changes of the kidney were evaluated by using a routine histopathological technique.

Results: Diclofenac plus montelukast treated group associated with significantly ($p < 0.05$) decreased serum urea and creatinine in comparison with the diclofenac-treated group. The results also revealed that diclofenac-treated group was significantly ($p < 0.05$) decreases serum GSH level when compared with –ve control group. Diclofenac plus montelukast treated group associated with significantly ($p < 0.05$) increased serum GSH level in comparison with the diclofenac-treated group. Diclofenac plus montelukast treated group was associated with significantly ($p < 0.05$) decreased serum MDA level in comparison with diclofenac. The histopathological results showed that montelukast treated group presented with mild Proteinaceous casts accumulation in kidney tubular lumen, mild congestion, and no tubular necrosis.

Conclusion: montelukast has a protective effect against diclofenac-induced acute kidney damage through its effect on kidney biochemical parameters and oxidative stress markers.

Keywords: montelukast; Acute kidney injury; diclofenac.

INTRODUCTION

Acute kidney injury (AKI) is a syndrome encompassing much different etiology and is characterized by an acute deterioration of kidney function [1]. AKI is resulted in decrease the physiological function of kidney and characterized by a reversible increment in nitrogenous waste products, and serum creatinine concentration with a decrease in kidney functions results in electrolyte disorders and decrease urine output [2]. Acute kidney injury recorded in many countries. Moreover, it is associated with increased mortality and morbidity in adults and children.

Moreover, it may be a development the diseases to chronic renal failure [3]. Acute kidney injury is causing deaths in people to reach two million years because the death occurs due to renal failure [4]. Acute necrosis in tubular of the kidney is acute kidney injury that occurs in patients that get in the hospital, and it usually leads to nephrotoxic or ischemic. One of secondary complication is acute interstitial nephritis that may be occurring, such as most common medication misuse [5]. Drugs such as NSAIDs are one of used medications classes in the USA [6]. Despite their several adverse side effects such as renal dysfunction and gastrointestinal bleeding and [7,8].

Diclofenac or called traditionally Voltaren is widely used as anti-inflammatory and analgesic. May studies founded renal dysfunction, or renal failure is detected in who take these drugs. Renal dysfunctions are usually associated with older peoples [9].

Acute renal failure has two form; two forms are occurring due to NSAID administration [10]. In rodents, Diclofenac may cause nephrotoxicity (11) and rising creatinine and urea level in serum that means a clear indicator for nephrotoxicity in rats [12,13]. Free radical (nitric oxide, hydroxyl radical, peroxynitrite, superoxide anion, singlet oxygen, hydrogen peroxide, etc.) are normally formed in the body and its deactivated by specific enzymes such as (catalase, superoxide dismutase and glutathione peroxidase) or by non-enzymatic methods such as (vitamin A, vitamin C and glutathione) [14]. Antioxidants and oxidants are in balance in the body. The oxidative stress is activated when free radicals are formed excessively or/, and the antioxidants are insufficient. However, the oxidative stress results in lipid peroxidation such as Malondialdehyde [15]. Montelukast is work as an antagonist of the CysLT1 receptor which commonly used in medical treatment of asthma and allergic rhinitis [16]. Montelukast has a gastroprotective effect on alendronate induced lesions and indomethacin-induced ulcerations of rat stomach that have a protective effect on oxidative damage activity [17]. Montelukast has ameliorated effect against sepsis and burns [18]. Also, the montelukast have a positive effect on acute lung injury in rats [19]. However, the effect of montelukast on AKI caused by diclofenac will be established in this research.

MATERIALS AND METHODS

Animals

The animals that used in our study are thirty of white male rats weight (200-250g) as average. The animals were housed and placed in auto control air-conditioned room wherever the animals exposed to (12 h light and 12h dark) continually at humidity (60–70%) and temperature (25±2◦C).

Sample collection and experimental design:

The experimental animals were divided into five groups: Group1 received no treatment and served as a negative (-ve) control group. Group2 received ethanol and served as (vehicle group). Group3 (disc. Group) administrated diclofenac sodium (vulturine) at a dose (100 mg/kg, i.p.) for three days (20) and served as (diclofenac-treated group). Group 4 (disc. +mont.) received montelukast 30 min. Before diclofenac administration (20mg p.o). At the end of the experiment (3 days) after (24) h from the last injection, thiopental sodium was used for anesthetizing the animals intraperitoneally at a dose (50 mg/kg). At the trial end, all rats were killed by using thiopental sodium as the dose (100 mg/kg). After opening rat abdominal cavity; Right kidneys were washed with distilled water then keep in formaldehyde (10%) for making histopathological testing. Direct heart puncture collected blood for assessment of serum urea, creatinine, GSH, and MDA concentrations.

The creatinine and urea and estimation

The heart blood samples were taken from the heart; then it centrifuged for five minutes at 3000 rpm to prepare the serum. Creatinine and urea are measured by using Chemistry Analyzer Cobas Mira plus CC (made in Switzerland).