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Acetaminophen induced nephrotoxicity in experimental albino rats - Histopathological study

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ABSTRACT

Acetaminophen in overdose cause Nephrotoxicity (Acute Renal Failure) which exert toxic effects by one or more common mechanisms such as interglomerular hemodynamic tubular cell toxicity, inflammation, or decreased cellularity by proximal tubules, which lead to acute renal failure. Blood samples were collected by cardiac puncture for biochemical investigations like estimation of blood urea, creatinine, uric acid, total protein, albumin sodium and potassium. By using one way ANOVA, the results are significant at 0.001. Wister albino rats weighing 125- 150 gms were used for the present study. The present study finds few of the proximal tubules with hyaline degeneration and interstitium with hemorrhage in thick-walled vessels. The glomerular basement shows edema with histiocytes. Most of the tubules show acute tubular necrosis with ghost structures of tubules with intraluminal casts. The interstitium shows increased inflammation. The hilar fat shows up in the ureter with inflammation of the wall. Hyaline cast formation is observed with cellular degeneration in PCT with atrophic glomeruli. It is concluded that more than 1 gms/bw for a day should not be taken because it causes harmful effects on renal function test. Also suggested that acetaminophen must be given in the lowest effective therapeutic doses along with antioxidant administration to prevent early acute renal failure.

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INTRODUCTION

Most drugs found to cause nephrotoxicity which exerts the toxic effect by one or more common pathogenic mechanism such as altered glomerular hemodynamics, tubular cell toxicity, inflammation, and decreased cellularity causing acute renal failure (Nagai and Takamo, 2004). In Acetaminophen overdose induction study, Depletion of Cytochrome P- 450 pathway and inhibition of prostaglandin synthetase were the major causes for acute renal failure in the proximal tubular cell damage. Free radicals such as Superoxide anion radical (O_2) Hydrogen peroxide (H_2O_2) and Hydroxyl ions (OH) play an important role in acetaminophen nephrotoxicity. Acetaminophen causes ischemia, suppressing Na^+-K^+ ATPase, accumulation of intracellular calcium, inducing apoptotic cell death. Renal cortical mitochondria are the source of reactive oxygen metabolites inducing renal injury (Nagai and Takamo, 2004).

Very few studies on histopathology were reported in acetaminophen induced acute renal failure in albino rats. So, the present study is taken to measure the Nephrotoxicity by biochemical investigations

and to correlate it with histopathological damage in the structure of rat kidney.

MATERIALS AND METHODS

Wister albino rats weighing 150gms were used for the present study. Experiments were performed with the approval of the Institutional animal ethical committee (IAEC).

Group – I: Normal Control rats (received 1 mL of 5% CMC solution for 15 days) 6 animals in each group.

Group – II: Induction group (received Acetaminophen 1 gms/ kg bw) as a single dose for 15 days

Animals used in the present study were obtained from the animals breeding station. They were housed in polypropylene cages (38 X 23 X 10 cm) with not more than six animals per cage and maintained under standard environmental conditions (14 hours of dark/10 hours of light cycles) and were fed with standard pellet diet and fresh water ad libitum. The animals were acclimatized to the environment for two weeks before experiments. Animals fasted overnight before the experimental schedule, but have free access to water *ad libitum*.

Blood sampling

At the end of the experimental regime, all the animals were anesthetized with ether; cardiac puncture and animals collected blood samples are decapitated. The serum was separated by centrifugation at 2500 rpm and analyzed for biochemical parameters.

Biochemical investigations like blood Urea, Creatinine, Uric acid, Sodium and Potassium determination were carried out. Right and left kidneys were removed quickly, weighed and preserved in 10% formalin.

Determination of serum Electrolytes

Sodium and Potassium were accomplished by Excel diagnostics kit method according to the method of (Terri and Sesin, 1958).

Histopathological examination

Kidneys were immediately removed and fixed with 10 % neutral buffered formalin and processed to 5 micron sections and were stained with Hematoxylin and Eosin, Masson's trichrome, and periodic acid Schiff and are examined under a light microscope at 100 and 400 magnification.

RESULTS

Histopathological observations

Group – I: Treated with 5% CMC solution:

The untreated control rats (5% CMC solution) revealed the renal parenchyma with mild interstitial inflammation and congestion with few glomeruli with increased cellularity. The tubules appeared normal with few of them showing hyaline change (Fig. 1 a, b, c).

Group – II

Induction group (received Acetaminophen 3 gms/ kg bw) as a single dose on day 3.

Table 1: Effect of acetaminophen on biochemical parameters in rats when compared to controls

Parameters	Units	Controls	Acetaminophen
Body weight	Gm	120-150	120
Urea	Mg/dL	3.35 ± 0.36	15.35 ± 1.70
Creatinine	Mg/dL	0.70 ± 0.03	1.83 ± 0.19
Uric acid	Mg/dL	1.66 ± 0.15	3.22 ± 0.19
Total protein	g/dL	3.41 ± 0.06	2.6 ± 0.18
Albumin	g/dL	77.31 ± 2.15	66.92 ± 3.19
Sodium	Meq/dL	128.48 ± 2.13	120.21 ± 0.08
Potassium	Meq/dL	4.15 ± 0.09	4.94 ± 0.31

Values are expressed as mean ± S.E.M. (n=6)

In group II, a section of renal cortex showed massive proximal tubular distortion with the wide lumen. Signs of necrosis in the form of epithelial degeneration and vacuolization of luminal brush border were observed. Hyaline casts and necrotic cell debris were seen in the Lumina of some tubules (Fig.2 a, b, c). Extravasation of RBC and congested blood vessels in the interstitium of the renal cortex were seen. The glomerular basement shows edema with histiocytes. Most of the tubules show acute tubular necrosis with ghost structures of tubules with intraluminal casts. The hilar fat shows ureter with inflammation of the wall (Fig.3 a, b, c).

DISCUSSION

Acetaminophen in large doses causes renal necrosis in human and experimental animals. Its administration into rats induced impairment of renal function through the liberation of oxygen free radical (Heibashy and Abdel, 1999). In the present

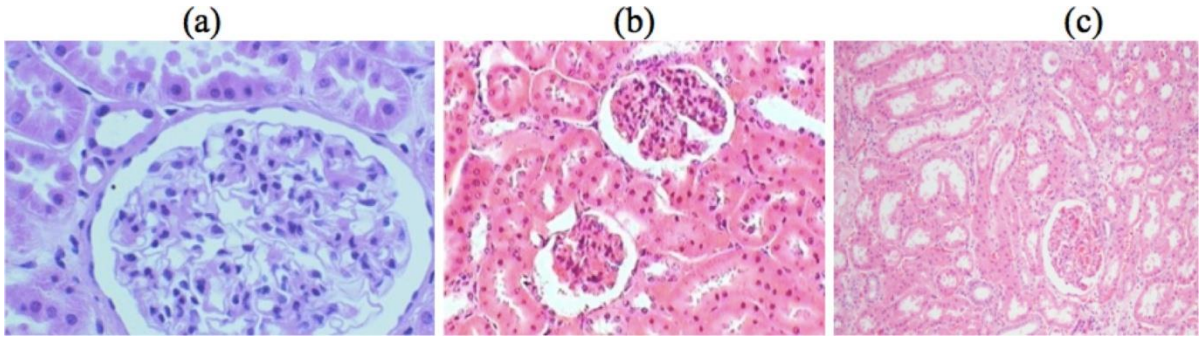

Figure 1: Normal control rats treated with 5% CMC solution
(a). Control rats – showing normal tubules and Glomerulus. (b). Control rats – showing mild glomerular congestion. (c). Control rats – showing a mild hyaline change of the tubules.

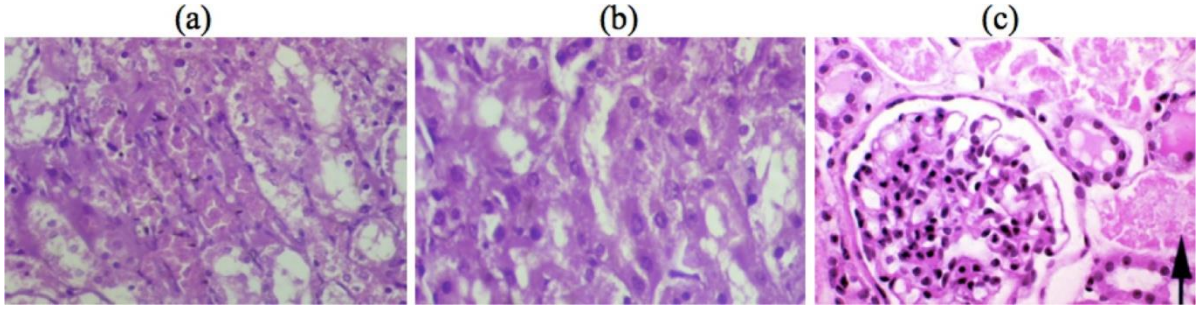

Figure 2: Nephrotic rats treated with acetaminophen
(a). Proximal tubules with RBC (b). Hyalinisation of tubules (c). Rats show Acute tubular necrosis

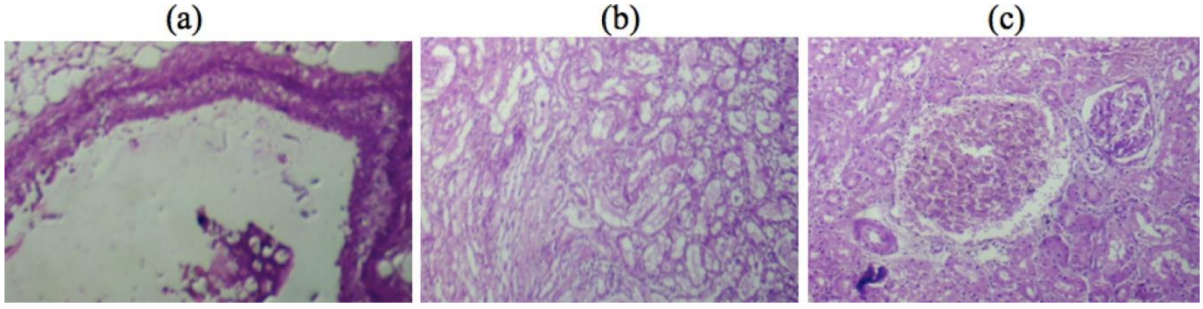

Figure 3: Acute tubular necrosis of glomeruli
(a) Shows Hilar Fat with thick wall vessels. (b) Shows cloudy swelling tubules. (c) Shows vessel wall necrosis.

study increased lipid peroxidation, BUN and Creatinine indicates oxidative stress, including tissue damage, enzyme inactivation and changes in glutathione status and cellular non-enzymatic and enzymatic antioxidant defence system. The oxidative stress precedes cell necrosis and is involved in the propagation of cell injury. The production of reactive oxygen species (ROS), O_2^- and nitric oxide induce oxidative damage to all cellular macromolecules.

The lower level of serum sodium indicates the inability of the kidney to conserve sodium and chloride. An increase of potassium is due to reduced excretion of K^+ aggravated by leakage of intracellular potassium into the bloodstream. These results confirmed acetaminophen produced acute tubular injury as previously reported by (Seham and Awaty, 2008) and ischemic renal atrophy (Gobe and Axelsen, 1987). Acetaminophen treated rats show tubular epithelial damage with intense granular degeneration involving 50 % of the renal cortex. Thus, apoptosis is involved

CONCLUSION

It is concluded that more than 3 gms/bw for a day should not be taken because it causes harmful effects on renal function test. Also, suggested that acetaminophen must be given in the lowest effective therapeutic doses along with antioxidant administration to prevent early acute renal failure.

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Nil

Conflict of Interest

No conflict to disclose.

REFERENCES

Nagai J. Takamo M. Molecular aspects of the renal handling of aminoglycosides and strategies for preventing the nephrotoxicity. Drug Metab pharmacokino., 2004: 19 (3)1159-70.

Heibashy, M. I. A. and Abdel Moneim, A. E. Kidney and liver function tests after late Dimethyl sulfoxide (DMSO) administration in rats with gentamicin-induced acute renal failure. J. Egypt. Ger. Soc. Zool., 1999: 30(A): 35-48.

Terri AE, Sesin PG. Colorimetric determination of potassium in human Serum and plasma using sodium tetraphenyl boron. Am. J. Clin. Path 1958; 29: 86-89.

Seham H. Refaat and Awaty A. Mady. Vitamin A against the Acetaminophen induces toxicity in the renal cortex of albino rats. Egypt. J of hist., 2008: Vol 31: 321-331

Gobe G C, Axelsen R A. Genesis of renal tubular atrophy in experimental hydronephrosis in the rat. Role of apoptosis. Lab Investing. 1987: 56:273–282.