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Adverse effects of cefotaxime sodium in comparison with ceftiofur sodium in male rats

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Abstract

The present work was designed to assess the adverse effect of two members of third generation cephalospoines; cefotaxime sodium and ceftiofur sodium in comparison with each other on the male fertility, some biochemical, haematological and histopathological findings in male albino rats. Forty five mature male albino rats (140-160 g wt, 16-18weeks age) were divided into 3 equal groups (15 rats each). Control group was injected intramuscularly with saline 2 ml /kg b.wt. . The second group was injected intramuscularly with cefotaxime sodium at a dose of (90 mg/kg b.wt.) twice daily for 10 days. The third group was injected intramuscularly with ceftiofur sodium at a dose of (7.5mg/kg b.wt.) once daily for 10 days. The experiment was conducted for 8 consecutive weeks. Cefotaxime sodium induced a significant reduction in reproductive organs weights, sperm count, sperm motility percent, alive sperm percent and serum testosterone level and significant increase in sperm abnormalities percentage. Moreover, some of the liver and kidney functions testes and some haematological parameters were significantly affected at 2nd & 4th week of experiment. Histopathologically, Cefotaxime sodium caused impairment in testes, epididymes, accessory sex glands, liver and kidney tissues. Conversely, administration of ceftiofur sodium did not induce any significant changes in reproductive system, liver ,kidney functions and haematological parameters in rats. Histopathologically all tested organs appeared normal allover the experimental period. Thus it could be concluded that ceftiofur sodium can be used safely at therapeutic dose but caution is required when using cefotaxime sodium due to its adverse effect on sperm characters and blood as well as liver and kidney functions. Despite, it effects on biochemical and blood analysis were reversible.

Key-Words: Cefotaxime sodium, Ceftiofur sodium, Reproductive toxicity, Liver, Kidney, Blood

Introduction

The cephalosporins are semisynthetic antibiotics derived from cephalosporin C, a natural antibiotic produced by the mould *Cephalosporium acremonium.* They are structurally and pharmacologically related to the penicillins. Like the penicillins, cephalosporins have a beta-lactam ring structure that interferes with synthesis of the bacterial cell wall and so are bactericidal. They are grouped into "generations" based on their spectrum of antimicrobial activity. Each generation has a broader spectrum of activity than the one before **(Sweetman 2009).** The third-generation cephalosporins have extended potency against gram negative bacteria but are generally less active against susceptible staphylococci **(Kathleen, 2004)**.

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Third Generation Parenteral Cephalosporins are distinguished by their high antibacterial activity and their broad resistance to beta-lactamases; they have particularly good activity against most *Enterobacteriaceae* .Exceptions include *Enterobacter* and *Serratia*, *Streptococci* are highly susceptible, *staphyloccci* moderately susceptible, and *enterococci* are resistant .They include Cefmenoxime, Cefotaxime, Cefovecin, Ceftizoxime, Ceftriaxone, Ceftiofur, and Latamoxef **(Giguère et al., 2013)**.

Cefotaxime is a third-generation cephalosporin antibiotic with a broad spectrum of activity against Gram-positive and Gram-negative aerobic and anaerobic bacteria. It is generally more active against Gram-negative bacteria than the first and second generation cephalosporins. Cefotaxime is highly stable in the presence of beta-lactamases produced by certain Gram-negative and Gram-positive bacteria **(Plosker et al., 1998).** It is used in the treatment of infections due to susceptible organisms, especially serious and life

threatening infection including: brain abscess, endocarditis, gonorrhea, intensive care, Lyme disease, meningitis, peritonitis, pneumonia, septicemia, preoperative prophylaxis and typhoid fever **(Van zanten et al.,2007; Sweetman, 2009).**

Ceftiofur sodium is a late third generation, β-lactamase resistant, broad spectrum and bactericidal antibiotic. It is characterized by its aminothiazol structure which accounts for its antimicrobial activity against Gram negative, Gram positive bacteria and its resistance to many β-lactamase enzymes. Ceftiofur is more effective than other cephalosporins and more active than ampicillin against *E.coli, Haemophilus pleuropneumonia, H.somnus, Pasteurella haemolytica, P. multocida, Salmonella typhimurium or Staphylococcus aureus.* **(Yancey et al., 1987**; **1990).** It has larger spectrum of activity against Gram-negative bacteria than either first or second generations **(Webber and Wheeler, 1982; Neu, 1982; Thornsberry,1985) .** Ceftiofur sodium and its primary metabolites, desfuroylceftiofur, are highly active against (539) isolated veterinary pathogens including *Actinobacillus, Pleuropneumonia, Pasteurella spp., Haemophilus sommus, Salmonella spp., Escherichia coli., Staphylococci and streptococci* **(Salmon et al., 1996)** . It has worldwide approvals for respiratory disease in swine, ruminants, horses, foot rot , metritis infections in cattle and early mortality infections in day-old chicks and turkey pouts **.** Also, it is used for treatment of various system infection as respiratory, gastrointestinal and urinary infections **(Hornish and Kotarski, 2002 ; Brander et al., 2005)**.

The most common adverse effects associated with cefotaxime and other cephalosporins are hypersensitivity reaction including skin rashes, urticaria, eosinophilia, and anaphylaxis **(Fujiwaki et al., 2008)**. Other side effects may include diarrhea, vomiting, nausea, pseudomembranous colitis and transient elevation in liver enzymes **(O'Connor et al., 2004; Rivkin, 2005)** induction of chromosomal aberrations in spermatocytes and sperm abnormalities in mouse germ cells **(Fahmy and Diab , 2010)**. There are some side effects may accompany ceftiofur use as mild skeletal muscle irritation at the site injection of horses given ceftiofur sodium. Prevalence and severity of the muscle irritation tended to increase with increasing concentration of the dosing solution. Hair loss and pruritis were observed in cow after 8 and 12 days of treatment, respectively. Clinical signs and laboratory test results normalized after ceftiofur administration was stopped .Long term exposure to high dosage of ceftiofur sodium during post-fertilization culture adversely affects embryo development *in vitro* thus it may act as potential teratogen **(Mahrt ,1992;Tyler, et al.,1998). Moreover Shaheen, et al. (2000)** reported that ceftiofur sodium induced a variety of fertility troubles in male albino rat's male albino rats.

There are little studies concerning the effect of the 3rd generation cephalosporins on male fertility. Consequently, the present work was designed to study the pharmacodynamic effects of cefotaxime sodium in comparison with ceftiofur sodium on fertility, some biochemical, haematological and histopathological findings in male albino rats.

Material and Methods

1-Drugs:

a-Cefotaxime sodium: (Cefotax®, sterile powder)was obtained from Egyptian International Pharmaceutical Industries campany (EPICO).

b-Ceftiofur sodium: (Excenel®, sterile powder) was obtained from Upjohn Company, kalamazoo, USA .

2- Experimental design:

Forty five mature male albino rats (140-160 g wt, 16-18 weeks age) were obtained from a closed random bred colony at the Medical Research Institute of Alexandria University, Egypt. Rats were housed in plastic cages with free access to the commercial basal food and water. The standard laboratory diet was purchased from Damanhur Feed Co. (Behera, Egypt). Rats were acclimatized 2 weeks prior to the experiment and received humane care in compliance with the guidelines of the National Institutes of Health (NIH) of Animal Care and the local committee approved this work. Rats were divided into 3 equal groups (15 rats each) as follow:-

a-The First group: Rats were injected intramuscularly with saline 2 ml /kg b.wt. (Control rats) .

b- The second group: Rats were injected intramuscularly with cefotaxime sodium (90 mg/kg b.wt.) twice daily for 10 days.

c-The third group: Rats were injected intramuscularly with ceftiofur sodium (7.5mg/kg b.wt.) once daily for 10 days. The rat doses of both drugs were calculated according to **Paget and Barnes (1964).**

3- Blood sampling:

Blood samples were taken from five rats from each group at the end of 2 nd,4th and 8th week since beginning of drug administration . Two blood samples were collected from each rat from retero-orbital plexus under light ether anesthesia. The first sample was collected on disodium salt of ethylene diamine tetra-acetic acid (EDTA) for hematological studies. The second one was collected without anticoagulant to

obtain serum and kept frozen at –20°C until used for biochemical and hormonal analysis.

4-Fertility studies:

4.1.Reproductive organs weight:

At the specific killing time, the animals were weight and sacrificed, the testes, epididymis and accessory sex organs were dissected out, grossly examined and weighed. The index Weight (I.W) of each organ was calculated as described by **Matousek (1969). Index weight (I.W) = organ weight / body weight x 100**

4.2. Epididymal sperm count:

Epididymal spermatozoa were counted by a modified method of **Yokoi et al., (2003).** Briefly, the epididymis was minced in 5ml of saline, placed in a rocker for 10 min and incubated at room temperature for 2min. The supernatant fluid was diluted 1:100 with a solution containing 5 g NaHCO3, 1ml formalin (35%) and 25mg eosin per 100ml distilled water. About 10µl of the diluted semen was transferred to each counting chamber of the improved Neubaur haemocytometer (Deep 1/10mm, LABART, Munich, Germany) and was allowed to stand for 5min for counting under a light microscope at ×200 magnification.

4.3. Epididymal alive sperm percent

A drop of epididymal contents of each rat was mixed with an equal drop of eosin–nigrosin stain. The semen was carefully mixed with the stain and thin film was spread on a clean slide. Two hundred sperms were randomly examined per slide at ×400 magnification according to **Bearden and Fuquay (1980).**

4.4. Sperm motility

Sperm progressive motility was evaluated microscopically within 2–4 min of their isolation from the cauda epididymis as described by **Sönmez et al., (2005).** Fluid was obtained from the cauda epididymis with a pipette and diluted to 2ml with tris buffer saline. The percentage of motility was evaluated at ×400 magnification.

4.5. Sperm abnormalities

A total of 300 sperm was counted on each slide under light microscope at ×400 magnification and the percentages of morphologically abnormal spermatozoa (detached head and coiled tail) were recorded according to **Evans and Maxwell (1987).**

4.6. Determination of serum testosterone levels

The total serum testosterone was assessed according to **Demetrious (1987)** using solid phase radioimmunoassay (RIA) kits. This assay based on testosterone-specific antibody immobilized to the wall of a poly propylene tube.

5- Serum Biochemical Parameters:

Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were measured colourimetrically according to **Reitman and Frankel(1957)**. Alkaline phosphatase (ALP) was estimated colourimetrically according to **Kind and King (1954)**. Serum urea was measured using colorimetric method as described by **Coulomb** and **Farreau (1963**). Serum creatinine was measured by colorimetric kinetic method according to **Husdan and Rapoport (1968).** Serum total proteins were measured using modified Biuret method as described by **Weichselbunm , 1946**. Serum albumin was measured using colorimetric method as described by **Doumas et al., (1971).** Serum globulin level was estimated by subtracting the albumin value from total protein value of the same sample as described by **Coles (1974**).

6- Haematological studies:

Hemoglobin concentration (Hb) was determined by the method described by Drabkin and Austin (1932) using commercially available diagnostic kits. Packed cell volume (PCV) percent was determined by microhematocrite technique according to Dacie and Lewis (1984). Erythrocytic (RBCs) and total leukocytic (WBCs) counts were estimated using Double improved Neubauer haemocytometer according to Dacie and Lewis (1984). Differential leukocytic counts were determined by using Battlement method and the percentages of various leukocytes were recorded (Dacie and Lewis, 1984).

7-Histopathological examination:

Five rats from each control and treated groups were scarified after 2, 4 and 8 weeks from beginning of drug administration. Macroscopic examination was performed then fresh specimens from liver, kidney, testes, epididymis and accessory genital glands were removed and preserved in 10% buffered formalin solution. The fixed specimens were dehydrated in ascending grades of ethyl alcohol 70, 86, 96, 100% cleared in chloroform and embedded in paraffin wax at 60^{o}C . The paraffin blocks were sectioned by microtome into 5 microns thick sections and stained with hematoxyllin and eosin as described by **Culling (1974).**

8-Statistical analysis:

Statistical analysis was performed using the SAS computer program **(SAS, 2002)**. The data were analyzed using analysis of variance (One way ANOVA) with Duncan's multiple range test to compare treatment means. All data were expressed as the mean ± standard error (SE).

Results and Discussion

Reproductive organs weights:

It was found that intramuscular administration of cefotaxime sodium induced a significant ($P \leq 0.05$) reduction in index weight of testes, epididymis and

accessory genital glands after 2,4 and 8 weeks as compared to control. While administration of ceftiofur sodium did not induce significant changes in index weight of testes, epididymis and accessory genital glands allover experimental periods compared to control (Table 1).

Sperm characteristics and testosterone level:

Administration of cefotaxime sodium induced a significant ($P \leq 0.05$) decrease in the progressive sperm motility percent, alive sperm percent, sperm cell concentration and testosterone level as well as a significant ($P \leq 0.05$) increase in sperm abnormalities at all experimental periods compared to control group . On the other hand administration of ceftiofur sodium induced insignificant changes in sperm count, percentages of sperm motility percent, livability & abnormalities and testosterone level at different periods of experiment compared to control group (Table 2).

Biochemical studies

Intramuscular administration of cefotaxime sodium induced a significant ($P \leq 0.05$) increase in ALT, AST, ALP ,urea and creatinine levels and a significant($P \leq 0.05$) decrease in serum total protein and albumin levelsat 2nd & 4th week of experiment but returned to normal values at 8th weeks compared to control group. Otherwise, There was insignificant changes in all previous parameters in rats treated with ceftiofur sodium compared to control group (Tables 3&4).

Hematological Parameters

The obtained results showed that there was a significant reduction in Hb g%, PCV%, RBCs and WBCs counts and lymphocytes percent and a significant increase in neutrophils percent in rats treated with cefotaxime sodium at 2nd & 4th week of experiment but returned to normal values at 8th weeks compared to control rats. While, there was insignificant changes in all previous parameters in rats treated with ceftiofur sodium compared to control group (Tables 5&6).

Histopathological findings:

Cefotaxime sodium treated rats:

The microscopical examination of the parenchymatous organs of cefotaxime sodium treated rats revealed mild to moderate histopathological alterations in the liver, kidneys and male genital organs.

The testes of cefotaxime treated rats revealed a congestion of the interstitial blood vessels, edema in the interstitium at 2ndweek of experiment. Moreover, at 4th and 8th week of experiment the seminiferous tubules were lined by few layers of degenerated germ cells .Occasionally, some degenerated tubules showed necrotic debris or exfoliated epithelial cells in their lumen (Fig. 1). Also, the basement membranes of some degenerated tubules were bended or corrugated (Fig. 2).

The epididymis showed normal histological appearance of their tubules at all experimental periods.

The seminal vesicles showed congested blood vessels and interstitial lymohocytic cellular infiltration at 2nd week of experiment. At 4th and 8th weeks, hyperplasia of the lining epithelial cells of seminal glands (Fig. 3) accompanied by multifocal exfoliation of some cells in the lumen were detected.

T**he prostate gland** showed congested blood vessels and interstitial edema admixed with few numbers of inflammatory cells (Fig. 4) at all experimental period .

The livers of cefotaxime sodium treated rats showed congestion of the portal blood vessels at 2nd week of the experiment and the degenerative changes of the hepatocytes in the form of hydropic degeneration of the hepatocytes particularly in the periportal areas were commonly seen at 4th week of experiment (Fig. 5). Also, small focal areas of lymphocytic cellular aggregates were occasionally seen in between the degenerated hepatocytes. The portal areas were expanded by moderate numbers of mononuclear inflammatory cells mainly lymphocytes and fewer macrophages. At 8th week the lesions were mild.

The kidneys revealed a congestion of the renal blood vessels and intertubular capillaries at 2nd week of experiment. At 4th week, vacuolar and hydropic degeneration of the lining epithelial cells of some renal tubules particularly the proximal and distal convoluted ones were prevalent (Fig. 6). Occasionally, coagulative necrosis of few renal tubules characterized by pyknosis of the nuclei and hypereosinophilic cytoplasm was observed. At 8th week all these lesions were mild.

Ceftiofur treated rats:

The microscopical examination of the parenchymatous organs of ceftiofur sodium treated rats revealed no histopathological changes in the liver, kidneys and male genital organs and they were normal similar to the control group.

Studies concerning the effect of ceftiofur sodium on the reproductive organs and fertility of male rats are limited. Hence, this study was conducted to evaluate the effect of 3rd generation cephalosporines; cefotaxime sodium and ceftiofur sodium in comparison with each other on male reproductive organs weight, sperm characteristics, serum testosterone level, blood, liver &kidney functions tests and histopathology.

The duration of the present study lasted for 8 weeks to cover complete spermatogenic cycle in rats which

ranges from 48 – 56 days **(Clermont and Harvey, 1965).**

Genital organ weight is a fundamental benchmark for the adverse effects studies of the drugs and chemicals **(Yavasoglu et al., 2008).** In our study administration of cefotaxime sodium to male rats showed a significant reduction in index weight of testes, epididymis and accessory genital glands all over the experimental periods. The reduction in the reproductive organs weights may be due to the decrease in serum testosterone levels reported in that study. The reported findings are in agreement with those recorded by **El-Homosany et al. (2012)** who mentioned that administration of cefotaxime sodium induced significant decrease in the weight of testes, epididymis and accessory sex glands in male albino rats. On the other hand administration of ceftiofur sodium in male rats induced insignificant changes in index weight of testes, epididymis and accessory genital glands as well as testosterone level allover the experimental periods. These findings are similar to those of **Mwafy (2010)** who reported that injection of ceftiofur sodium in male rats for 5 successive days produced insignificant changes in testicular and seminal vesicle weights. But our results are in disagreement with findings of **Shaheen et al. (2000)** who found that administration of ceftiofur sodium in male rats evoked a significant decrease in seminal vesicle weight. The weight of the testis is dependent on the mass of the differentiated spermatogenic cells; hence the reduction in the weight of the testis may be due to decreased number of germ cells, inhibition of spermatogenesis and steroidogenic enzyme activity **(Takahashi and Oishi, 2001).**

Our study revealed that rats treated with cefotaxime sodium had markedly impaired sperm quality. Since, it was significantly lowered sperm count, sperm motility and alive sperm percent and significantly increased sperm abnormalities, as well as it reduced testosterone level. The reduction in sperm count may be due to an adverse effect of cefotaxime sodium on spermatogenesis. The harmful effect of cefotaxime sodium on spermatogenesis could be ascribed to the reduction in serum testosterone levels. The reduction in sperm count was consistent with changes in epididymal weights. Testosterone is essential to maintain the structure and function of the male accessory sex gland. Moreover, a lack of testosterone disrupts spermatogenesis **(Broockfor and Blake, 1997).** Impaired sperm motility in treated rats is indicatives to a defect in the acquisition or maintenance of motility. Cefotaxime sodium may alter the epididymal secretory products or has a direct action on sperm motility or morphology. The reported findings are in agreement with those recorded by **Manson et al. (1987)** ; **Akaike et al. (1990)** who found that cephalosporins induced toxic effects on testicular tissue and decrease sperm production in rats as well as findings of **El-Homosany et al. (2012)** who reported significant decrease in sperm count and motility in cefotaxime sodium treated rats. The significant increase of sperm abnormalities in cefotaxime sodium treated rats are supported by results of **Fahmy and Diab (2010)** who found that cefotaxime induced different types of head and tail sperm abnormalities and increase the percentage of morphological sperm abnormalities with dose-dependent relationship . Such effect may be explained by the fact that the chemical penetrated the blood testis barrier and affected the process of spermatogenesis **(Wong and Cheng 2005).** These alterations in the fertility were confirmed by our histopathological findings in reproductive organs represented by congestion, degenerative changes, also showed incomplete spermatogenesis and absence of spermatozoa in testes of cefotaxime sodium treated rats.

On the other hand, injection of ceftiofur sodium induced insignificant changes in percentages of progressive sperm motility, abnormalities and a live sperm, sperm count, testosterone level and histopathological findings in genital organ of male rats allover the experimental period. These findings are in agreement with those of **Mwafy (2010)**. But our results are disagree with findings of **Shaheen et al.(2000)** who reported that ceftiofur sodium induced a significant decrease in sperm cell concentration, motility &alive sperm percentages and a great elevation in sperm abnormalities percent in male albino rats. Moreover, the histopathological findings of testes revealed intertubular oedema, most of seminiferous tubules showing immature spermatozoa and vacuoles in the spermatogonial cells male albino rats**.**

The present results showed that administration of cefotaxime sodium induced significant increase in serum ALT, AST and ALP levels in male rats at 2nd &4th week of the experiment. Activities of AST and ALT are most commonly used biochemical markers for monitoring chemically induced liver damage (**Sturgill and Lambart, 1997).** These findings are coincident with those of **El-Homosany et al. (2012**) who reported that administration of cefotaxime induced liver and kidney damages in treated rats . Also, mild transient elevations in hepatic transaminases levels reported with cephalosporin use **(Oakes et al., 1984, Balant et al., 1985 and Reddy and Schiff, 1995).**

Moreover intramuscular administration of cefotaxime sodium induced a significant decrease in serum total

protein and albumen after 2,4 weeks of the experiment. These results are confirmed by our histopathological findings of liver (congestion of the portal blood vessels and hydropic degeneration in hepatocytes) that support the liver damage and subsequently increased liver enzymes serum level.

Cefotaxime sodium induced a significant increase in serum urea and creatinine levels of treated rats at 2nd &4th week of the experiment. This elevation is reflecting the state of glomerular filtration and indicates kidney damage. These results are in agreement with findings of **El-Homosany et al. (2012**) who support the evidence of renal function impairment by cefotaxime sodium as the drugs was increased serum urea and creatinine levels in rats .These results are compatible with our histopathological findings of the kidneys (congestion of the renal blood vessels, Vacuolar and hydropic degeneration of the lining epithelial cells of some renal tubules and coagulative necrosis of few renal tubules).These histopathological findings are in accordance with those recorded by **Harada, et al. (1982)** who recorded sever renal cortical necrosis in rabbits received cefazolin, cefotiam and cefotaxime.

On the contrast, our results showed the safety effects of ceftiofur sodium on liver and kidney of rats, as the drug did not induce any significant changes in liver and kidney functions testes. These results are in agreement with those of **Mwafy (2000; 2010)** who recorded insignificant changes in serum urea, creatinine, AST, ALT, ALP, total protein, albumen, and globulin levels at different experimental periods in chickens and rats, respectively .These results are confirmed with normal histopathological findings of hepatic and renal tissues in ceftiofur sodium treated rats.

Intramuscular administration of cefotaxime sodium (90 mg/kg.bwt). twice daily for 10 days induced a significant reduction in haemoglobin, packed cell volume, RBCs, total leucocytic and differential leucocytic counts after 2,4 weeks and return to normal after 8 weeks . These hematological alterations could be explained on basis that cefotaxime may cause some sort of bone marrow depression which are compatible with findings of **Fekety (1990)** who reviewed that leucopenia may be occurred secondary to reversible suppression of the bone marrow has been reported after two to three weeks of high-dose therapy with cephalosporins. Characteristic features include depletion of bone marrow precursors, marrow cell proliferation.

On the other hand, our observed results showed that ceftiofur sodium did not induce any significant alterations in tested haematological parameters in treated rats at different periods of experiment. These results are agree with those recorded by **Mwafy (2000 ;2010)** who found that ceftiofur sodium treated healthy chickens and rats, respectively displayed no significant changes in RBCs count, Hb value, PCV%, mean corpuscular volume and mean corpuscualr haemoglobin concentrations.

Conclusion

On basis of the present study, it could be concluded that ceftiofur sodium can be used safely at therapeutic dose but cefotaxime sodium must be used with caution because of its potential adverse effect on sperm characters, liver and kidneys functions as well as blood picture. However, it effects on biochemical and blood analysis was reversible.

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Table 1: Effect of cefotaxime sodium in comparison with ceftiofur sodium on the reproductive organs weights and testosterone hormone level in male albino rats

Parameters	Duration	Groups		
		Control	Cefotaxime sodium	Ceftiofur sodium
Index weight of testes	2Wk	1.81±0.04 [a]	1.05±0.09 [b]	1.78±0.03 [a]
	4Wk	1.79±0.03[a]	1.18±0.01[b]	1.77±0.06[a]
	8Wk	1.74±0.02[a]	1.16±0.02 [b]	1.75±0.04 [a]
Index weight of epididymis	2Wk	0.79±0.06 [a]	0.58±0.02[b]	0.82±0.05 [a]
	4Wk	0.74±0.01[a]	0.46±0.01[b]	0.77±0.03[a]
	8Wk	0.84±0.06[a]	0.48±0.00[b]	0.82±0.03[a]
Index weight of accessory genital glands	2Wk	1.07±0.04 [a]	0.66±0.03[b]	1.02±0.06[a]
	4Wk	0.97±0.03[a]	0.58±0.01[b]	0.97±0.02[a]
	8Wk	0.96±0.06[a]	0.51±0.01[b]	0.95±0.04[a]
Testosterone hormone level (ng/ml)	2Wk	2.29±0.05[a]	1.04±0.01[b]	2.27±0.02[a]
	4Wk	2.32±0.02[a]	1.08±0.03 [b]	2.28±0.04 [a]
	8Wk	2.24±0.04[a]	1.11±0.04 [b]	2.22±0.02 [a]

Values are expressed as mean±SE. N= 5. Values with different letters at the same raw are significantly different at $P \leq 0.05$ (ANOVA with Duncan's multiple range test). I.W. = organ weight (g)/100×body weight (g)(

Table 2: Effect of cefotaxime sodium in comparison with ceftiofur sodium on sperm characteristics in male albino rats

Parameters	Duration		Groups	
		Control	Cefotaxime sodium	Ceftiofur sodium
Sperm cell concentration (10^6 / ml)	2Wk	343.50±8.50 [a]	221.33±6.81[b]	328.00±8.31[a]
	4Wk	348.17±6.37[a]	233.17±8.64[b]	346.33±3.12[a]
	8Wk	355.00±6.03[a]	226.67±9.13[b]	363.17±7.82[a]
Sperm motility (%)	2Wk	87.67±0.95[a]	55.63±3.96[b]	85.00±1.39[a]
	4Wk	90.83±0.73[a]	59.17±2.01 [b]	85.00±2.58[a]
	8Wk	91.17±2.01[a]	55.67±1.05 [b]	84.50±1.71[a]
Sperm abnormalities (%)	2Wk	8.83±0.88[b]	28.00±1.07[a]	10.17±0.46[b]
	4Wk	12.50±0.92[b]	33.33±1.13[a]	13.27±0.73[b]
	8Wk	11.63±1.22[b]	38.00±0.58[a]	11.18±0.44[b]
Sperm live (%)	2Wk	95.00±0.58[a]	79.17±1.28[b]	92.00±0.83[a]
	4Wk	94.00±0.77[a]	78.00±0.57[b]	89.00±1.03[a]
	8Wk	93.50±0.65[a]	79.17±1.37[b]	88.17±0.83[a]

All values are expressed as mean ± S.E. Number of rats in each group is five. Values with different letters at the same raw are significantly different at $P \leq 0.05$ (ANOVA with Duncan's multiple range test).

Table 3: Effect of cefotaxime sodium in comparison with ceftiofur sodium on some liver and kidney function tests in male albino rats

Parameters	Duration	Groups		
		Control	Cefotaxime sodium	Ceftiofur sodium
Serum ALT activity (U/L)	2Wk	45.80 ±2.72 [b]	89.20±2.33 [a]	41.00±2.49 [b]
	4Wk	42.40±2.13[b]	84.4±2.11[a]	43.00±1.65[b]
	8Wk	44.00±1.13[a]	43.20±1.35[a]	44.00±1.85[a]
Serum AST activity (U/L)	2Wk	137.40±5.83 [b]	198.40±5.28 [a]	134.00±6.13[b]
	4Wk	134.00±7.40[b]	210.00±5.42[a]	142.00±6.26[b]
	8Wk	138.40±6.48[a]	139.00±8.84[a]	139.40±6.37[a]
Serum ALP activity (U/L)	2Wk	75.5±8.24 [b]	198.52±8.24 [a]	85.5±2.24 [b]
	4Wk	84.8±4.84 [b]	200.1±9.24[a]	74.6±5.24 [b]
	8Wk	80.22±6.23 [a]	85.5±3.90 [a]	88.2±4.13 [a]
Serum urea level (mg / dl)	2Wk	27.14 ±0.17 [b]	40.00±1.00 [a]	29.17 ±0.86 [b]
	4Wk	28.86±0.29 [b]	41.12±1.53 [a]	30.90 ±0.740 [b]
	8Wk	28.23 ±0.68 [a]	28.52±1.13[a]	30.65 ±1.12[a]
Serum creatinine level (mg / dl)	2Wk	0.86±0.01 [b]	1.3±0.02[a]	0.83 ±0.02 [b]
	4Wk	0.87 ±0.02 [b]	1.32±0.04[a]	0.87 ±0.03 [b]
	8Wk	0.89 ±0.01 [a]	0.94±0.02[a]	0.90 ±0.02 [a]

All values are expressed as mean ± S.E. Number of rats in each group is five. Values with different letters at the same raw are significantly different at $P \leq 0.05$ (ANOVA with Duncan's multiple range test).

Table 4: Effect of cefotaxime sodium in comparison with ceftiofur sodium on serum total protein, albumin and globulin levels in male albino rats

Parameters	Duration	Groups		
		Control	Cefotaxime sodium	Ceftiofur sodium
Serum total protein level (g /dl)	2Wk	7.21 ±0.06 [a]	6.26±0.03 [b]	7.23±0.08 [a]
	4Wk	7.27±0.03[a]	6.20±0.06[b]	7.20±0.06[a]
	8Wk	7.30±0.02[a]	7.15±0.09[a]	7.16±0.04[a]
Serum albumin level (g / dl)	2Wk	3.08 ±0.04 [a]	2.03±0.02 [b]	3.20 ±0.01 [a]
	4Wk	3.04 ±0.03 [a]	2.12±0.01 [b]	3.10±0.04 [a]
	8Wk	3.08 ±0.01 [a]	3.20±0.01[a]	3.05±0.03 [a]
Serum globulin level (g / dl)	2Wk	4.13 ±0.05 [a]	4.23±0.09 [a]	4.03 ±0.06 [a]
	4Wk	4.23 ±0.06 [a]	4.08±0.05 [a]	4.10 ±0.08 [a]
	8Wk	4.22 ±0.01 [a]	3.95±0.02 [a]	4.11 ±0.06 [a]

All values are expressed as mean ± S.E. Number of rats in each group is five. Values with different letters at the same raw are significantly different at $P \leq 0.05$ (ANOVA with Duncan's multiple range test).

Table 5: Effect of cefotaxime sodium in comparison with ceftiofur sodium on hemoglobin (Hb g%), packed cell volume (PCV %), red blood corpuscles (RBCs) and white blood cells (WBCs) counts in male albino rats

Parameters	Duration	Groups		
		Control	Cefotaxime sodium	Ceftiofur sodium
Hb g%	2Wk	12.84 ±0.22[a]	10.40±1.24 [b]	12.62 ±0.34[a]
	4Wk	12.68±0.24 [a]	10.20±0.84 [b]	12.44 ±0.34 [a]
	8Wk	12.60±0.19 [a]	12.00±0.24[a]	12.40±0.19 [a]
PCV %	2Wk	41.01 ±1.32 [a]	35.40±1.74 [b]	41.50±1.02 [a]
	4Wk	39.00 ±1.54 [a]	35.60±1.66[b]	41.00 ±0.94[a]
	8Wk	41.20 ±0.26 [a]	43.42 ±1.23[a]	41.60 ±0.08[a]
RBCs (10^6 / cmm)	2Wk	6.80 ±0.46 [a]	5.33±0.88 [b]	6.90 ±0.21[a]
	4Wk	6.68 ±0.18 [a]	5.20±0.18[b]	6. 74 ±0.20[a]
	8Wk	6.44 ±0.34[a]	6.30 ±0.40[a]	6.24 ±0.38 [a]
WBCs (10^3 / cmm)	2Wk	11.90 ±0.95 [a]	8.42±1.22[b]	11.82 ±0.84 [a]
	4Wk	11.70±0.40 [a]	8.10±1.34[b]	11.74 ±0.22[a]
	8Wk	12.34±0.24[a]	11.82±0.38[a]	11.90±0.64[a]

All values are expressed as mean ± S.E. Number of rats in each group is five. Values with different letters at the same raw are significantly different at $P \leq 0.05$ (ANOVA with Duncan's multiple range test).

Table 6: Effect of cefotaxime sodium in comparison with ceftiofur sodium on differential leucocytic counts in male albino rats

Parameters	Duration	Groups		
		Control	Cefotaxime sodium	Ceftiofur sodium
Lymphocyte (%)	2Wk	66.20 ± 4.54[b]	51.80 ± 4.71[a]	66.80 ± 4.11[b]
	4Wk	66.60 ± 3.86[b]	49.80 ± 4.25[a]	65.80 ± 3.20[b]
	8Wk	65.60 ± 5.15[a]	62.40± 5.24[a]	64.20 ± 3.16[a]
Neuterophile(%)	2Wk	25.40 ± 4.21[b]	36.80 ± 2.58[a]	24.40 ± 4.86[b]
	4Wk	24.40 ± 2.30[b]	38.80 ± 4.73[a]	23.60 ± 2.14[b]
	8Wk	25.20 ± 2.6[a]	28.8 ± 1.58[a]	27.20 ± 2.30[a]
Basophile (%)	2Wk	0.60 ± 0.1[a]	1.40 ± 0.24[a]	0.80 ± 0.0[a]
	4Wk	0.40 ± 0.24[a]	0.80 ± 0.24[a]	0.60 ± 0.24[a]
	8Wk	0.80 ± 0.20[a]	0.80 ± 0.24[a]	0.60 ± 0.24[a]
Eosinophile(%)	2Wk	1.60 ± 0.41[b]	1.60 ± 0.51[a]	1.20 ± 0.58[b]
	4Wk	1.40 ± 0.51[a]	1.80 ± 0.66[a]	1.0 ± 0.32[a]
	8Wk	1.20 ± 0.20[a]	1.80 ± 0.37[a]	1.60 ± 0.51[a]
Monocyte (%)	2Wk	6.40 ± 1.36[a]	8.40 ± 0.40[a]	6.80 ± 1.12[a]
	4Wk	7.20 ± 0.37[a]	8.80 ± 1.16[a]	7.00 ± 0.37[a]
	8Wk	7.20 ± 1.00[a]	6.20 ± 1.16[a]	6.40 ± 0.86[a]

All values are expressed as mean ± S.E. (n=5), Values with different letters at the same raw are significantly different at $P \leq 0.05$. (ANOVA with Duncan's multiple range test).

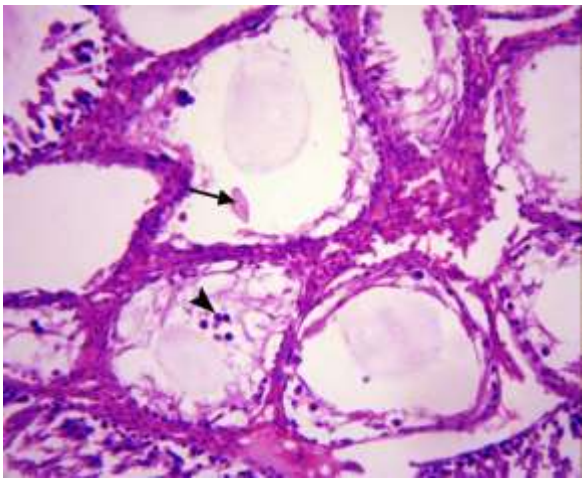

Fig. 1: Testis of rat administered cefotaxime sodium (90 mg/ kg b.wt) and killed at 4th weeks post administration: ecrotic debris (arrow) and exfoliated epithelial cells (arrow head) in the lumen of some degenerated tubules. H&E stain x 400.

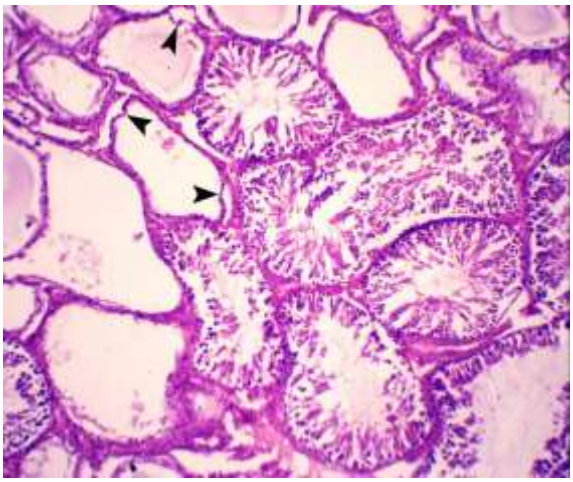

Fig. 2: Testis of rat administered cefotaxime sodium (90 mg/ kg b.wt) and killed at 8th weeks post administration: Bending or corrugation (arrow head) of the basement membranes of some degenerated tubules. H&E stain x 200.

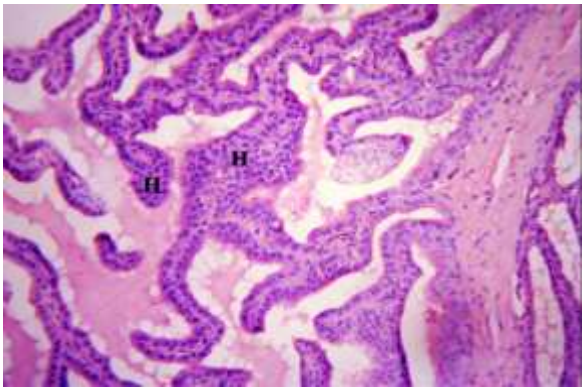

Fig. 3: Seminal vesicle of rat administered cefotaxime sodium (90 mg/ kg b.wt) and killed at 8th weeks post administration: Hyperplasia (H) of the lining epithelial cells. H&E stain x 400

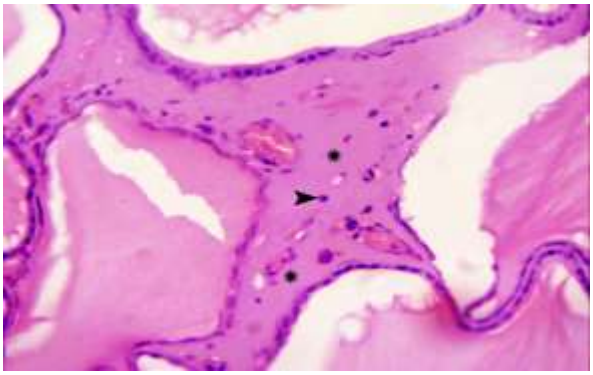

Fig. 4: Prostate gland of rat administered administered post administration: Marked interstitial edema (asterisk) admixed with few numbers of inflammatory cells (arrow head). H&E stain x 400.cefotaxime sodium (90 mg/ kg b.wt) and killed at 4th weeks

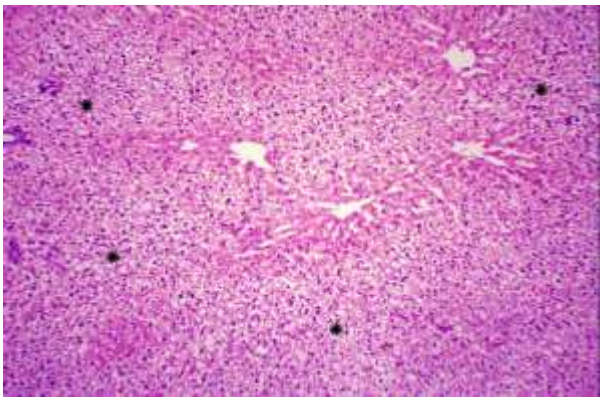

Fig. 5: Liver of rat administered cefotaxime sodium (90 mg/ kg b.wt) and killed at 4th weeks post administration: Periportal hydropic degeneration (asterisk) of the hepatocytes. H&E stain x 100.

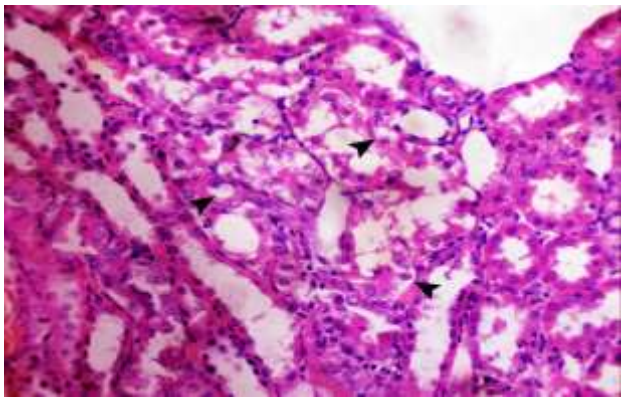

Fig. 6: Kidney of rat administered cefotaxime sodium (90 mg/ kg b.wt) and killed at 4th weeks post administration: Vacuolar and hydropic degeneration (arrow head) of the lining epithelial cells of some proximal and distal convoluted tubules. H&E stain x 400.

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