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Pathological Changes Of Phenobarbital Injection In Local goats

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Abstract: The effect to phenobarbital pathological pre treatment in the *Calotropisprocera* local male goats was examined. The goats receiving phenobarbital sodiumat daily injection doses of 65mg/kg/day for 90 days , exhibited marked depression, lateral deviation of the head and neck, dyspnea and frequent urination and histopathological, they showed centri lobular hepato cellular necrosis and fatty cytoplasmic vacuolation of the hepatocytes with central vein with fibrosis in liver ,lung showed emphysema of alveoli and dilated of blood vessels and hyperplasia of bronchiole ,kidney showed degeneration of epithelial cells lining of renal tubules ,while rumen undergo vacuolated of mucosal layer , degenerative changes in spleen and thickening in the capsule of testis with suppression of seminiferous tubules.

Key word:- Pathology ,phenobarbital, ,liver ,spleen, , rumen, lung, testis



1 Introduction

The Phenobarbital is a barbiturate and it is the most widely used anticonvulsant worldwide [1]. It is also used to control epilepsy (seizures) and as a sedative to relieve anxiety. It is used for short-term treatment of insomnia to help to sleep, [2] It was used to treat neonatal jaundice by increasing liver metabolism and thus lowering bilirubin levels.[3]. Phenobarbital has an oral bioavailability of about 90%. Peak plasma concentrations are reached eight to 12 hours after oral administration. It is one of the longest-acting barbiturates available – it remains in the body for a very long time (half-life of two to seven days) and has very low protein binding (20 to 45%). Phenobarbital is metabolized by the liver.

Phenobarbital is a known inducer of microsomal enzymes (Cytochrome P-450 (CYP), NADPH-cytochrome P-450 reductase, NADPH oxidase, glutathione S-transferase) which are responsible for the metabolic breakdown of a large number of endogenous and exogenous chemical compounds [4,5,6]. It is reported that Phenobarbital decreases the toxicity of some organophosphates as a result of an increase in paraoxonase activity. In addition, a number of xenobiotics increase serum AST and ALT activities and are used as markers of liver toxicity and it is reported that Phenobarbital treatment increased these activities and protein levels in the liver [7]. Phenobarbitone (BAN) is a long-acting barbiturate and the most widely used anti-seizure medication globally [8]. It has sedative properties, but as with other barbiturates, benzodiazepines are more commonly used for this purpose.[9].

Phenobarbital is removed from the body by the liver and should be used with extreme caution in animals with liver disease at higher dose, also Phenobarbital decreases the ability of the lung to function properly. and should be used very carefully in animals who have lung disease or lung condition. such as dogs and cats use panting from the lungs to cool themselves as they cannot sweat. Depressing breathing cannot only cause oxygen shortage, but can cause animal to overheat [3].

1.1 Veterinary uses:

Phenobarbital is one of the initial drugs of choice to treat epilepsy in dogs, and is the initial drug of choice to treat epilepsy in cats. ^[10] It is also used to treat feline hyperesthesia syndrome in cats when anti-obsessional therapies prove ineffective. ^[11] It may also be used to treat seizures in horses when benzodiazepine treatment has failed or is contraindicated. ^[12]



2 MATERIALS AND METHODS

2.1 Animals:

Sixteen healthy adult local male goats were selected from a herd animals, aged between nine months to one year and weight ranged between 25-35 Kg.. All goats were treated against internal and external parasites by using Ivermectin (Kela-Belgium) at dose of 200 µg/Kg B.W. subcutaneously with Rafoxind 3% at a dose 1.25 mg /kg B.W. The animals were fasted for 36 hours of food and 12 hours water with held preoperatively. (Ehasanetal,2015). were given by the oral route phenobarbital only at 65mg/kg/day for 90 days

2.2 Histopathological Technique

The specimen were taken from animals after necropsy on the 45 and 90 days, these include , (testis, spleen, lung, rumen, and liver). Then fixing in natural buffered formalin (10%) , dehydration was done by passing the specimens in increasing concentration of ethanol, infiltrated 3 times with xylene or chloroform and embedded in paraffin. 5-6 microns and stained with Hematoxyline – Eosin. and finally examined under light microscope.

3. Results:

3.1 Clinical finding:

Goats receiving phenobarbital sodium at daily oral doses of 65mg/kg/day for 90 days , exhibited marked depression, lateral deviation of the head and neck, dyspnea and frequent urination.

3.2 Necropsy finding:

Necropsy revealed varying degrees of jaundice of the subcutaneous, omental and mesenteric fat including serous and mucous membranes. The livers were enlarged and firm, mottled and icteric with distended gall bladders.

Liver pathology was further confirmed by presence of necropsy where evidence of liver changes was shown. The livers were consistently slightly enlarged and containing marked thickened bile duct, and the kidneys were darker than normal. Cholangitis and mild bile retention were also observed.

3.3 Histopathological findings:

After examined the slides under the microscope we observed histological changes in some organs. In goats, testis showed degeneration of the seminiferous tubules with thickening of capsule and suppression of spermatogenesis (Fig.1,2). Lung showed emphysema of alveoli and dilated of blood vessels and hyperplasia of bronchiole (fig.3,4). In liver showed dilation of sinusoid sub capsular fatty degeneration hypertrophy of hepatic cells , excessive fibrosis in portal area with narrowing the lumen of portal duct (fig.5,6).

rumen showed degenerative changes of epithelial cells ,)and edematous fluid with infiltration of inflammatory cells (fig.7,8). spleen showed hemorrhagic area degenerative of epithelial cells, also hemosiderosis and fibrosis(fig.9,10).



Figure
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Figure (2): Testis, vacuolation of somniferous tubules cells(V), interstitial edema(E), congestion of blood vessels (C), and suppression of somniferous tubules cells (S). H&E. 10x .

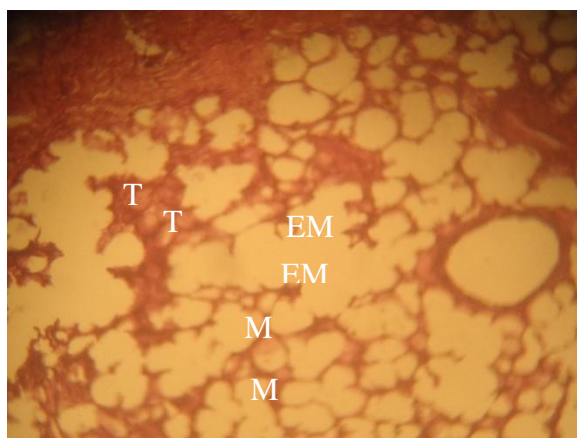
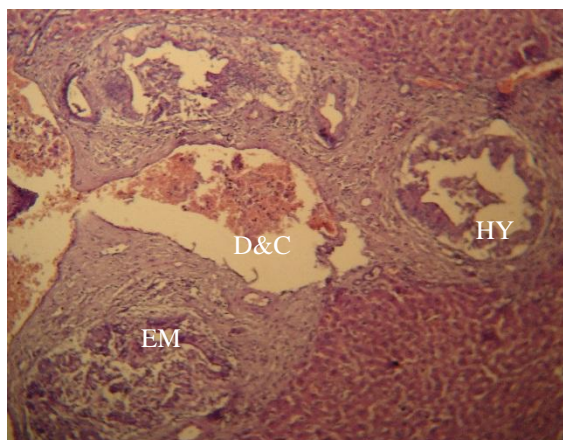


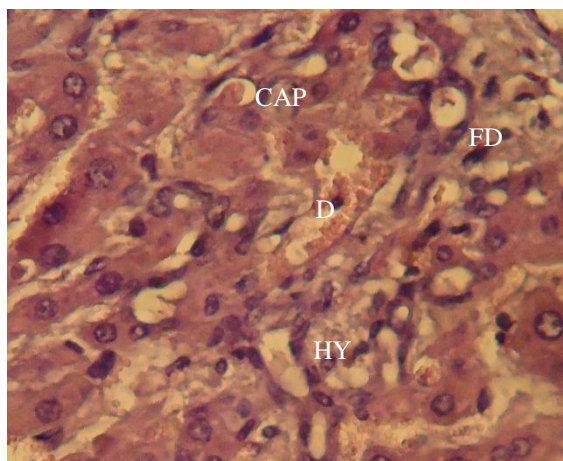
Figure (3): lung showed emphysema of alveoli(EM) thickening of alveolar wall (T) with mucinous exudates(M).H&E stain.10x



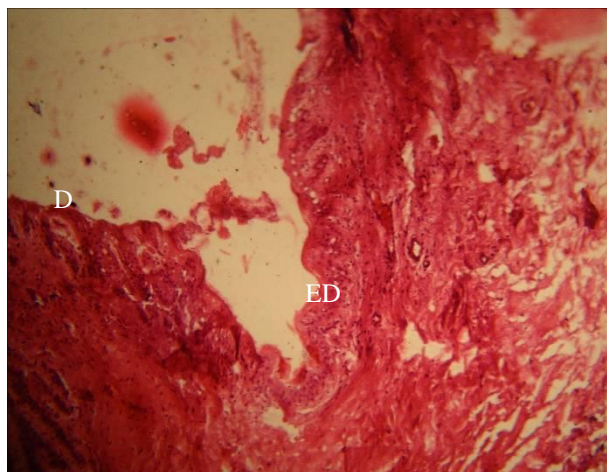
Figure (4): lung showed fibrosis in alveolar wall (F) and bronchus wall and hyperplasia of bronchus epithelial cells (HY) .H&E stain.10x.



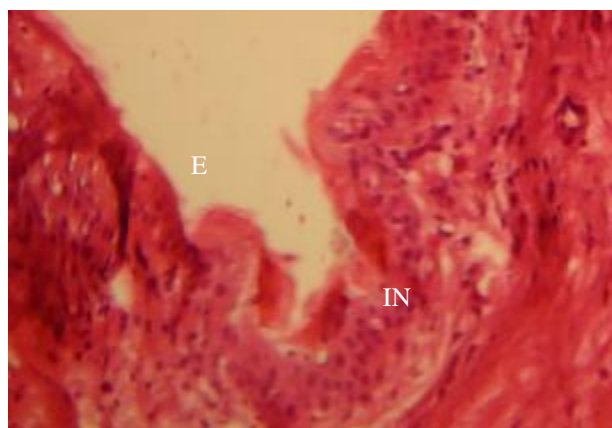
Figure(5): section of liver showed dilation (D) and congestion (C) of hepatic duct, excessive fibrosis in portal area, narrowing the lumen of portal duct (N), hyperplasia of epithelial lining (HY). H&E.40x



Figure(6): section of liver showed dilated sinusoid (D), sub capsular fatty degeneration (FD), hypertrophy of hepatic cells (HY), new capillaries formation (CAP). H&E.40x



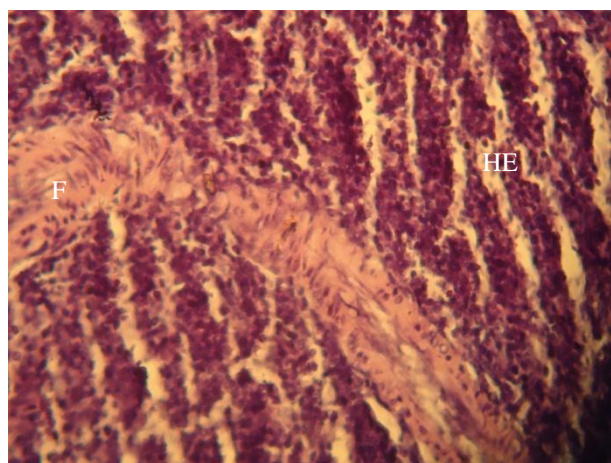
Figure(7): section of rumen showed degenerative changes of epithelial cells D , and edematous fluid (ED). H&E stain.10x



Figure(8): section of rumen showed erosion of epithelial cells (E) , infiltration of inflammatory cells(IN), H&E stain.40x



Figure(9): section of spleen showed hemorrhagic area degenerative of epithelial cells, H&E stain.10x



Figure(10): section of spleen showed hemosiderosis (HE) and fibrosis (F).H&E stain.40x



4. Discussion:

In the present study goats were given by the oral route phenobarbital only at 65mg/kg/day for 90 days. It showed liver enlargement and increased its weights indicating the presence of hepatomegaly. The increased weights were consistent with data from microscopic examination of the liver showing edema and compound related Centro lobular hepatocyte hypertrophy in deranged goats. These observations are in agreement with the findings were described by other researches [14&15].

This study tested several hypotheses about the effects of Phenobarbital on liver regeneration, testes and pancreas due to the androgen sensitive. Reproductive organs of treated animals suffering from suppression of spermatogenesis through the effect of Phenobarbital such as necrosis of the testicular cells that agree with [16]. vacuolated in testes and pancreas which are well supported with biochemical and enzymatical studies that provide the effect of phenobarbital that agree with [17]. there were seen acute passive congestion is seen in spleen due to distention of red pulp by blood, the lymphoid tissues (periarteriolar lymphoid sheathes and splenic follicles are widely separated and replacement by fat tissue or connective tissues, various exogenous and endogenous stimuli lead to activate acute inflammation and then chronic inflammation in the body in which the tissue response consists of the leakage or accumulation of fluid into epithelial cells as response in intestine, rumen and pancreas [18&19].

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