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HISTOLOGICAL STUDY OF PANCREAS TISSUE OF ALBINO RATS WHICH THE TREATED WITH FLUTAMIDE

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Abstract:
This study's objective was to ascertain the effect غلا the anti-androgen drug flutamide in the tissue of the pancreas in adult male rats. flutamide widely used for the treatments of prostatic cancer, acne and hirsutism in women. In this study 15 male white rats were divided into three groups of groups treated with two concentrations of flutamide 12.5 mg / kg / day and 8 mg/kg and control group (distilled water) for 28 days. The results showed that flutamide had an effect on pancreatic tissue include edema, necrosis fat by lipase also there is destruction wall in blood stream with hemorrhage.

Keywords: Flutamide, Pancreas, Rats

INTRODUCTION

Flutamide is anti-inflammatory nonsteroidal which make competitive inhibition the link between the androgens and the androgen receptor [1]. The Flutamide structure and kinetic is similar to bicalutamide and nilutamide. [2]

Flutamide was used to treated the hirsutism, prostate cancer and acne, during this uses lead to interim raise of transaminases and, in some patient, sharp hepatic dysfunction [3,5]. Although the appliance not clear it association of cytochrome P450 is suggested [4,6,7]. Probably response to its cytotoxicity is the bioactivation of flutamide and subsequent covalent attachment to proteins in cells. [8]. Hepatitis is the commonest documented type of hepatotoxicity related with anti-androgens. The cummins period of hepatitis is between two half and nine months for flutamide with a little rehabilitation period of three weeks to four months [9]. In this study, we description the report of a patient in austere flutamide- lead to hepatotoxicity and long-lasting liver sickness. The onset of thrombocytopenia in this study was a novel element. After quitting flutamide and receiving ursodeoxycholic acid (UDCA) therapy, he made a full recovery. [10]

A probable, irregular, twice-blind, placebo-controlled trial with 49 patients who had been clinically diagnosed with pancreatic carcinoma was conducted [11] to determine if flutamide, a pure androgen receptor blocker, prolongs survival in individuals with pancreatic cancer and, consequently, whether testosterone is a major growth factor for this tumor. A placebo was given to 25 patients while flutamide was given to 24, respectively. Analysis In the flutamide group, there were 14 and 8 living patients at 6 months and 1 year, compared to 10 and 1 in the control group, respectively. The comparison with results were fourteen (88%) and eight (50%) active in the flutamide cluster paralleled with ten (50%) and one (5%) in the control group after eliminating those patients in each cluster who were treated for less than six weeks due to worsening illness and prompt death. In the flutamide cluster, eight months was the median survival time for all patients. compared to four months in the control group. With the 6-week rejections, the median lifespan increased to 12 months from 5 months[12]. The data, according to the author, supports the idea that testosterone acts as a growth factor for pancreatic cancer and that blocking androgen receptors is a suitable new therapeutic strategy [13].

In a tiny Indian trial, the impact of flutamide on pancreatic cancer patients' survival was assessed. Flutamide 250 mg three times a day (n = 23) was compared to a placebo (n = 23) in a dose-controlled study of individuals with histologically problematic, untreatable pancreatic adenocarcinoma that had not yet been treated. Whole-life survival was the primary outcome, followed by six-month and one-year survival rates, concert status, and reaction rates. With reference to demographic, disease-related, and treatment-related characteristics, both clusters were tightly bound.
This smaller body of research data was unable to establish flutamide's persistent adverse effects. The difference between the median overall survival on flutamide medication and placebo treatment (136 days) was not statistically significant. The study's combined

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six-month survival rate was 39%, while the study's combined one-year survival rate was 4% compared to 13% for the flutamide group. There was no discernible difference in the amount of time it took for patients' performance to degrade (flutamide 90 days versus control 68 days) or for them to pass away entirely due to tumor development [14].

Experimental design

The study include the effect different concentration from flutamide (12.5 ,8 mg /kgm/day) on the pancreas tissue .

The experimental animals divided in to three groups each group cincluded five animals as the following :

1- group (1) it given distal water orally 28 day as control group.
2- Group2 was administered at 8 mg / kg / day orally with flutamide for 28 days.
3- group3 was administered at 12.5 mg / kg / day orally with flutamide for 28 days.

MATERIAL AND METHODS

Drug preparation

The anti-androgen-flutamide was obtained 250 mg by trade name Eulexin and prepared by Schering-ploughlaboN.V. Belgium, sub of schering -plough\USA and it dissolved in a water and calculate the doss according to human dose .

Experimental animals

This study was reported in the Animal House of the Faculty of Science / University of Babylon, where the study used 15 male white male, which was purchased from the Animal House of the Center of Embryology and Infertility / University of Baghdad. The average weight was 200-300 g and was 2.5-3 months old and was putting in metal cages for breeding rats. Experimental animals were subjected to appropriate laboratory conditions with temperature 20-25 m, 12 hours day and twelve hours of darkness. Animals were provided free access to food and water on a daily basis for ten days so they could get used to the lab environment.

Histosectioning preparation the luna method (1986) is dependent .

RESULT :

Histological examination

The study explained some histological changes with concentration 8, 12.5 mg/kg/day when compared with control , where observed acute pancreatitis include focal pancreatic parenchymal necrosis with edema in group 2 fig(2), and necrosis fat by lipase also there is destruction and proteolytic breakdown of pancreatic parenchyma of artery and vein with bleeding in group 3 fig(3) .

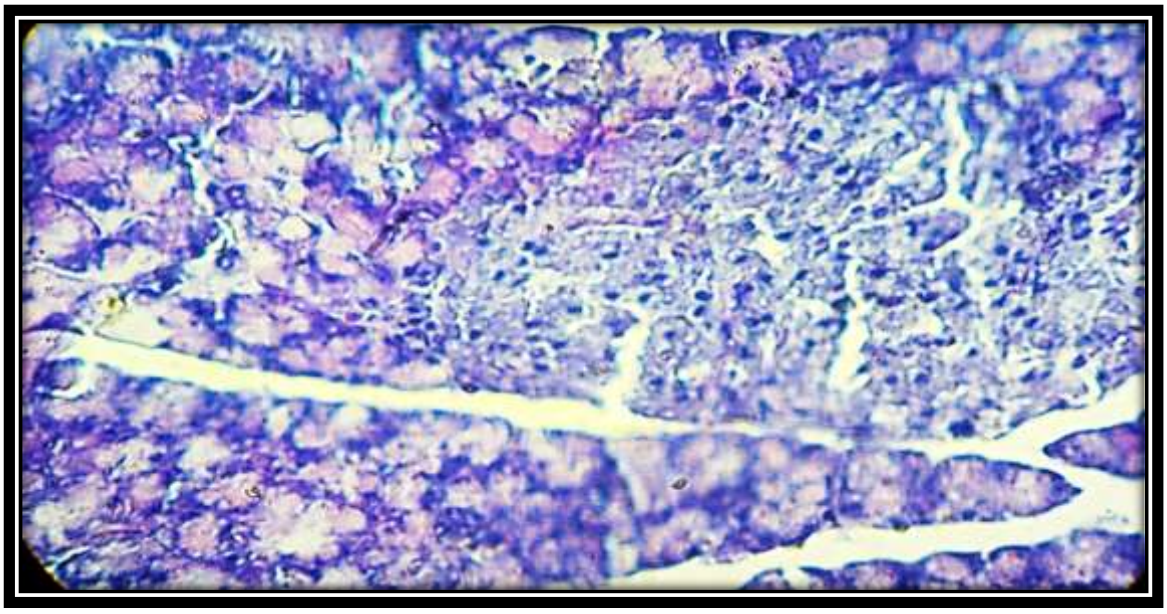

Fig (1) cross section of pancreatic tissue explain don't be found any effect of tissue.

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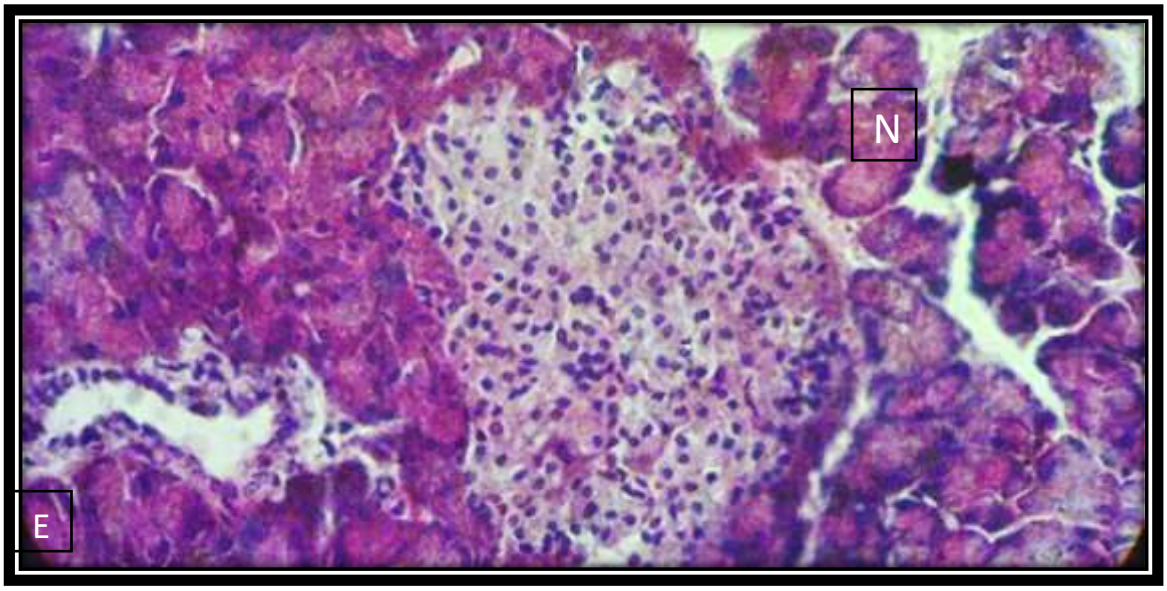

Fig(2) histological cross section of pancreas with 8 mg observed acute pancreatitis include edema(E) , and necrosis of fat by lipase(N)

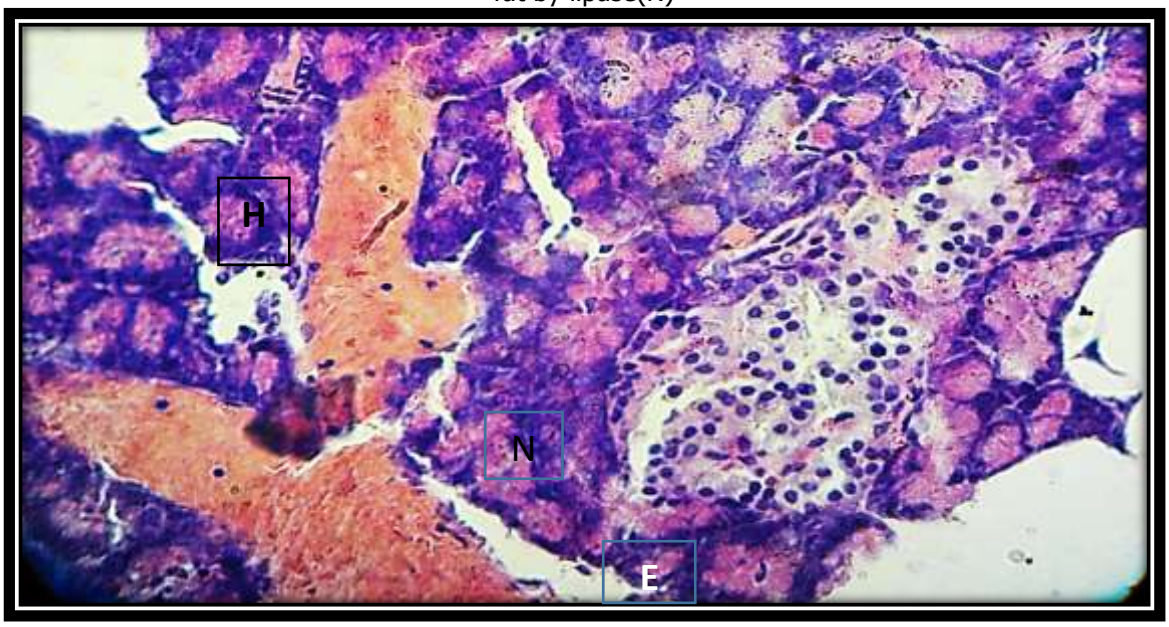

Fig (3) cross segment of pancreas tissue with 12.5 mg explain effect cutionof tissue observed edema(E) , and necrosis fat by lipase (N) destruction the vessels of blood and cause hemorrhage (H)

DISCUSSION:

Gomez et al. reported two patients with severe liver damage who presented with jaundice, ascites, impaired coagulation, and hepatic coma after receiving flutamide[15]. This was the first case of flutamide-related pancreas failure.

Flutamide is frequently used in clinical settings to treat PC [16,17].Systemic therapy is known to be quite ineffective against pancreatic cancer. The nucleoside antimetabolite gemcitabine has a significant effect that has been validated in randomized dosing for treating established disease, although the benefits to patients during treatment are extremely minimal.

In this group of patients with severe symptoms, an endocrine therapy that is well tolerated would appear to be an appealing option. Flutamide, however, can harm the liver, as shown by transaminitis, cholestatic jaundice, liver necrosis, encephalopathy, and, very infrequently, liver failure that results in death[18]. Since many pancreatic cancer illnesses are linked to hepatic disorders, there is a larger risk that patients who enter this trial would experience flutamide-induced liver

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damage. Flutamide was administered at a usual dose of 250 mg three times daily in the randomised placebo-controlled trial for the development of human pancreatic cancer, and no incidences of liver damage were reported.

Furthermore, flutamide was administered as a single drug for the treatment of a group of 26 patients in our own institution who had radiological signs of advanced pancreatic cancer but no histological or cytological proof of the disease. No hepatic-related adverse effects were reported in the current group [19]. The findings of the present study demonstrate that gemcitabine and flutamide can be safely combined in individuals with advanced pancreatic cancer. There were not many grade 3 and none grade 4 toxicity reported.

In an infected man who became jaundiced while receiving the combined therapy, leaving out the flutamide necessitates hepatic blood testing, but the patient may still be able to get gemcitabine alone. 60% of patients were able to withstand the full dose of the medication without experiencing any serious side effects. The majority of patients whose treatment was altered required a dose reduction of gemcitabine for reasons expected by the drug's known side effect profile.

This and the median duration of 6 months are consistent with other phase II research data for gemcitabine-based combination regimens that have recently been available [20], even though many of these cytotoxic regimens are linked to higher levels of drug-related toxicity than those reported in this study.

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