Section: Histology

Original Research Article

PERIPORTAL INLAMMATION OF LIVER OF ADULT ALBINO WISTAR RATS WITH ORAL FEBUXOSTAT

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Abstract

Background: The study aims to evaluate the microscopic changes in liver of adult Albino-Wistar rats administered with oral Febuxostat. **Materials and Methods:** 1. 12 adult male Albino-Wistar rats weighing 180-220 g. 2. Dimethyl Sulphoxide as solvent of the drug. 3. Drug Febuxostat 4. Orogastric tube 5. Distilled wate. Group A - Control group comprising of 6 rats were given 10% Dimethyl Sulphoxide for 60 days. Group B - Experimental group comprising of 6 rats were given 15 mg/kg Febuxostat orally for 60 days dissolved in 10% Dimethyl Sulphoxide. Group A and Group B animals were sacrificed after 60 days by cervical dislocation. The liver tissues were preserved in formalin, processed and stained with hemaetoxylin and eosin stain. The slides were examined under Olympus light microscope and the histological changes were seen. The slides were photographed using 6.1 Megapixel Nikon digital Camera. **Results:** The histological changes in the liver of rats administered with drug Febuxostat were periportal inflammation and hepatocyte degeneration. **Conclusions:** Hence the drug Febuxostat should be used carefully in those patients who have liver impairment before giving treatment for gout.

INTRODUCTION

Febuxostat is a new non-purine xanthine oxidase inhibitor indicated for chronic gout. The most common side effect is liver function abnormalities.[1] The pathogenesis of urate crystal deposition is reasonably well understood, and with appropriate urate-lowering therapy (ULT) and lifestyle advice, the objective of management is cure.[2] Nonetheless, many patients with gout continue to experience frequent and recurrent episodes of gout and progression of their disease. This is because the condition is often misdiagnosed, or diagnosed late, and treatment is frequently suboptimal.[3]

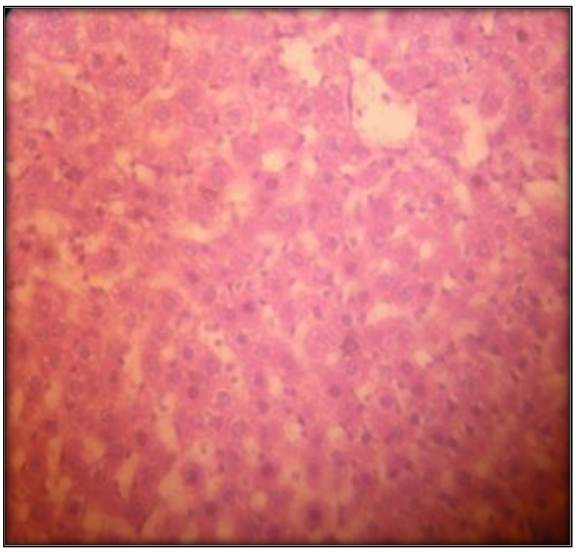
MATERIALS AND METHODS

Male albino rats (Rattus norvegicus albinus) (n=12) of the Wistar strain were used in this experiment. The animals, with weights between 65g and 190g and of the same age (180), were kept in individual plastic cages until the time determined for euthanasia. Animals were kept under natural light conditions, respecting day and night light cycles, at appropriate temperatures, noise and humidity conditions, receiving proper food with free access to food and water throughout the experiment. Animals were numbered, by simple drawing, and weighed before the procedures. The animals (n=12) were distributed in two groups. Group A experiment (n=6) and Group B control (n=6).

RESULTS

The histological changes in the liver of rats administered with drug Febuxostat periportal inflammation and hepatocyte degeneration.

Control Group



All the control group showed normal hepatocytes and no periportal inflammation.

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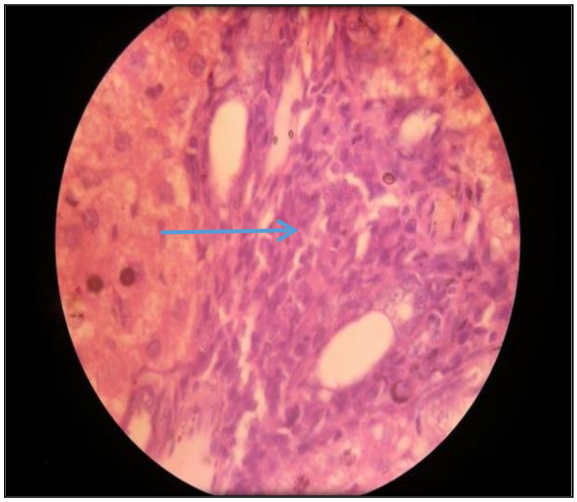
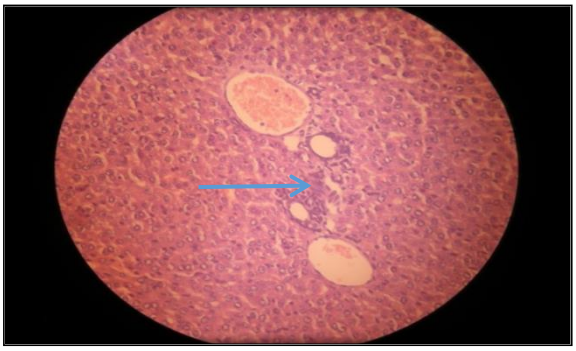


Pronounced Periportal inflammation (line a←rrow shows) seen in 100x magnification



Periportal inflammation (thick arrow shows) with surrounding hepatocytes showing ballooning degeneration (line arrow shows) seen in 20x magnification stained with Haematoxylin and Eosin.

The tables 1 and 2 shows that the p value is not less than 0.05 and therefore the p value is not significant. The p value was calculated using Mann-Whitney test which is a non-parametric test.

Table 1: Arithmetic Mean, Standard Deviation and P Value of Liver Weight of Rats: And Test(T) Group

Rats	Individual Liver weight	Arithmetic Mean of control(C) group and test(T)group	Standard Deviation of control(C) group and test(T)group	P value
C1	4g	4.5	1.12	0.413
C2	3g			
C3	6g			
C4	2g			
C5	7g			
C6	4g			
T1	3g	5	1.53	
T2	5g			
T3	5g			
T4	5g			
T5	6g			
T6	6g			

Table 2: Arithmetic Mean, Standard Deviation and P Value of Body Weight of Rats

Rats	Individual body weight	Arithmetic Mean of control(C) and test(T) groups	Standard Deviation of control(C) and (T) test groups p value	P value
C1	160g	137.67	22.52	0.806
C2	110g			
C3	116g			
C4	120g			
C5	160g			
C6	160g			
T1	130g	135.8	37.91	
T2	140g			
T3	160g			
T4	170g			
T5	85g			
T6	130g			

DISCUSSION

Inflammation in the absence of pathogens occurs in all tissues in response to a wide range of stimuli that cause tissue stress and injury. Such sterile inflammation (SI) is a key process in drug-induced liver injury, nonalcoholic steatohepatitis, and alcoholic steatohepatitis and is a major determinant of fibrosis and carcinogenesis. In the liver, SI is particularly important because it is a major component of the pathology of a wide range of diseases, such as alcoholic steatohepatitis (ASH), nonalcoholic steatohepatitis (NASH), drug-induced liver injury, and ischemia/ reperfusion (I/R).[4] Gout is one of the rheumatic disorders for which complete cure is feasible. This can be achieved by reducing uric acid biosynthesis through inhibition of xanthine oxidase using allopurinol or febuxostat.[5] Febuxostat is, unlike allopurinol, a nonpurine xanthine oxidase

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inhibitor and received National Institute for Health and Clinical Excellence (NICE) approval in 2008 for the management of chronic hyperuricaemia in gout for people who are intolerant of allopurinol or for whom allopurinol is contraindicated.[6] It is used at a dose of 80 or 120mg daily. It is more effective at reducing serum urate than allopurinol but is more expensive, although it may be equally cost effective in the long term. The most common side-effects are diarrhoea, nausea, headache, liver dysfunction and a rash. Less commonly it may be associated with fatigue, oedema and dizziness.[7] Portal area showing inflammatory reaction in Allopurinol given patients.[8] The periportal lymphocytic infiltration is due to chronic hepatitis. And in previous literature they say that mononuclear infiltrate in the portal and periportal areas is the defining lesion of chronic hepatitis of any cause.[9]

Periductal location of inflammatory cells and ductules follow different principles. Throughout the portal tract system, hepatic arteries and bile ducts are paired and lies in close vicinity.[10]

Expression of proinflammtory cytokines by damaged bile duct epithelial cells can recruit mononuclear inflammatory cells depending on the inciting injury that is autoimmune or toxic in nature respectively.[11] Chronic hepatitis is characterized by necroinflammatory cells mainly in portal and periportal areas. This is composed of lymphocytes and macrophages.[12]

CONCLUSION

Hence, we the practitioners should use the drug Febuxostat carefully in those patients who have liver impairment before giving treatment for gout. Liver function tests serum AST (aspartate aminotransferase), ALT (alanine aminotransferase), PT (prothrombin time) and albumin should be done before treating the gout patients.

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