Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i1.4076

COMPARATIVE STUDY OF EFFECTS OF IBUPROFEN AND DEXIBUPROFEN ON MOUSE LIVER

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Abstract

Introduction: Ibuprofen (2RS)-1[4-(2-methyl propyl) phenyl] propionic acid. Dexibuprofen [2-(4-isobutylphenyl) propionic acid] is also NSAID, and is an isomer derived from ibuprofen. Liver is main location for excretion, metabolism, maintenance, homoeostasis and body's performance. Increased concentrations of biochemical markers such as transaminases are indicators for liver damage.

Objective: The purpose of this study was to compare the Ibuprofen and Dexibuprofen to know their adverse effects on the liver.

Methodology: The mice were kept in the clean cages in the animal house of the Department of Zoology, Shah Abdul Latif University Khairpur. They were treated orally with Ibuprofen and Dexibuprofen for 14 days. At the end of experiment, blood samples were collected from control and experimental groups by anesthetizing animals with chloroform. Liver damage was checked by investigating the activity of biochemical marker enzymes by LFT (liver functioning test). The sections of tissues were cut in size of 4-5 micrometer with help of microtome machine at Department of Zoology of Shah Abdul Latif University, Khairpur. When treated groups were compared with the control group, all enzymes (AST, ALT, and ALP) increased in both drugs treated groups.

Results: Results were analyzed in excel and charts were created. According to the present study, the administration of both Drugs resulted in structural and functional alterations in the liver tissues and elevated levels of these enzymes in the circulation.

Key Words: Ibuprofen, Dexibuprofen, Liver, Enzyme, Mice

Introduction

Ibuprofen: Ibuprofen (2RS)-1[4-(2-methyl propyl) phenyl] propionic acid (Rabia and Nousheen 210) was discovered in the 1960s and first made available in tablet form in 1961 (Francesca *et al.*, 2019). It's a type of NSAID (Non-Steroidal Anti-Inflammatory Drug) that's prescribed to relieve agony and sickness of body.

Dexibuprofen: [2-(4-isobutylphenyl) propionic acid] Dexibuprofen (Muhammad Akhlaq *et al.,* 2016) is a nonsteroidal anti-inflammatory drug (NSAID) normally used for the treatment of painful conditions, osteoarthritis and rheumatoid arthritis. S (+) Ibuprofen is a nickname for dexibuprofen. Dexibuprofen is an ibuprofen isomer.

The liver is the primary site for maintenance, metabolism, excretion, physiological function and homoeostasis. It plays a vital role in all metabolic activities.The drugs used to treat liver problems are insufficient and can have negative consequences (Nasir *et al.,* 2013). The goal of my research was to examine the disadvantages of ibuprofen with dexibuprofen in terms of liver consequences. This work was aimed to find out how ibuprofen and dexibuprofen compare in terms of their effects, notably on the liver.

Materials and methods

Planning an experiment: Mice were arranged into three groups. Among them one group was kept as control group and they were not administered with drugs. While other two groups were treated as experimental groups and were treated with Ibuprofen (Group 2) and Dexibuprofen (Group 3).

Sampling and collection of Blood: Mice were kept at animal house of Department of Zoology, Shah Abdul Latif University Khairpur. The food and water were provided three times daily. Before the experiment they were kept for one week in cages for adjustment of the environment provided in cages. Tablets were purchased from local market Khairpur city. Both tablets were given by dissolving in water, to experimental groups for 15 days. On 16th day of experiment, they were dissected mercifully by anesthetizing with chloroform. For the liver function test, blood samples were taken from each animal through cardiac puncture with a separate sterile disposable syringe. The liver of dissected animal was separated and processed for Histopathological study. The separated serum was used to determine the level of biochemical marker enzymes in the blood such as ALP, AST and ALT (Mohsin*et al.,* 2013).

Biochemical parameters

The activity of AST ALP, and ALT was measured by colorimetric method using model: SBA-733PLUS Biochemistry Analyzer.

Liver Histopathological Assessment

Removed liver was cleaned in saline buffer before being sliced into little pieces, then were processed in 4% formalin for section cutting (Garba *et al.,* 2012). They were washed in buffer for 10 minutes two times. They were placed in 10% formalin (Talat*et al.,* 2017) for overnight. On next day they were washed in buffer for 5 minutes 3 times. In the next step tissues were passed through Ethanol series each for an hour, 25%, 50%, 70% and 85%. They were passed through 95% Ethanol+0.01% Eosin overnight. Next day passed through 100% Ethanol+0.01% Eosin for 60 minutes two times. After washing in buffer, they were passed through xylene series mixed with ethanol, 25%, 50% and 75% for 30 minutes each. Then they were passed through 100% xylene for two hours two times. The liver pieces were processed in paraffin wax for three days. Paraffin wax liquid was changed from samples in morning and evening time all three days. Three to four liver pieces were grouped and embedded on wooden blocks by pouring liquid wax on block. The blocks were carefully labelled and stored for microtomy.

Microtomy

Microtomy was done at the Endocrinology Laboratory of Zoology department, Shah Abdul Latif University, Khairpur. Microtome machine was set on 4-6 micro meter for cutting tissue sections. The tissue ribbons were handled with forceps and brush and were placed for two to five minutes on distilled water on hot plate. The stretched ribbons were taken on clean glass slide. The tissue on slides were dried on hot plate. They were passed through ethanol 25%, 50%, 75%, 100%, and xylene 100%, series for five minutes each. Finally permanent slides were prepared for observation under

microscope. The slides were observed under microscope (Model B.S-2035DA1) connected with laptop and photographs were captured. The tissues images were edited with Image Scope software provided with microscope.

Results and Discussion

Histological Findings

Histopathological abnormalities in the liver of Ibuprofen-treated mice included necrosis of vascular connective tissues, wide-spread regions of vacuolar degeneration, and severe dilation of blood vessels. In Ibuprofen-treated animals' liver sections, there was vascular congestion within the central venula, along with minimal portal tract irritation.

Hepatic abnormalities are evidenced histologically by vascular congestion inside the central venula and minor portal tract inflammation that is persistent in the Dexibuprofen-treated group, also concentration of serum, which reflects major changes in mice's biochemical indicator parameters revealed that administration of Dexibuprofen may cause hepatotoxicity. In the present study, the alterations in histopathology which occurred in the liver included of significant congestion, degeneration with hepatocyte necrosis. These results agree with (Tyagi *et al.*, 2005). In dxibuprofen-treated mice, blood vessel dilation and severe congestion were found. Clarifying vascular congestion within the central venula associated with modest chronic portal tract inflammation in the Dexibuprofen-treated group was observed.

Central vein, Hepatic arteries and bile ducts were clearly seen in control group's liver slices. The sinusoids extending from the central vein were neatly arranged in branching plates with the hepatocytes. When comparing with both drugs treated (stained with eosin) to the liver tissue of the control group, histopathological evaluation revealed a normal histological appearance of hepatocytes structure.

Discussion

Hepatotoxins are chemicals that cause liver damage. More than 900 medications have been linked to liver damage, which is a justification for a drug's withdrawal from the market (Ostapowicz *et al.*, 2002). The evaluation of liver enzymes in the blood is a useful tool for determining the kind and severity of liver impairment. Previous research has shown that an increase of these enzymes in the blood after taking ibuprofen indicates liver cellular damage (Aprioku, *et al.*, 2014). Hepatic toxicity was found to be increased with greater doses and longer durations of ibuprofen exposure in previous investigations. The current findings revealed that ALT and AST levels in the liver of IBU-treated rats reduced. The decline in liver function AST and ALT are important in detecting the presence of liver disorders because these enzymes are abundant in the liver and increase in plasma while decreasing in the liver when cellular damage or degeneration occurs (Hassoun and Stohs 1995).

Our research found that taking of ibuprofen for 10 to 15days resulted in a significant increase in serum levels of liver function indicators such as ALT, AST, and ALP were evidence of hepatotoxicity as compared to the control group. In the current investigation, serum enzyme concentration in the treated groups Ibuprofen and Dexibuprofen increased, this could occur as a result of hepatotoxicity (Baravalia *et al.*, 2011; Tan *et al.*, 2013). The rise of these enzymes in blood is an indicative of IBU toxicity and indication of possible hepatocellular damage that could exert through alterations in the liver functions. These findings corroborate the conclusions of the previous study by (Garba *et al.*, 2012) in which plasma ALT and AST activities showed significant increase in the ibuprofen (100mg/kg) treated rats. Aprioku *et al.*, (2014) reported in their investigation, ibuprofen caused rise in serum concentrations of, alanine transaminase (ALT) and alkaline phosphatase (ALP) which showed cellular impairment to the liver.

Histological results revealed that IBU induced several histopathological alterations in liver of experimental mice. Similarly, Senthilkumar *et al., (*2013) reported that Ibuprofen (500 mg/kg B.W.) caused severe alterations in normal liver cells, including vacuolization, hepatomegaly and centrilobular necrosis. Ibuprofen has been shown to alter permeability, hepatic cell architecture. Because of cellular leakage and loss of functional integrity of the cell membrane in the liver, ibuprofen-induced hepatic necrosis is frequently linked with higher levels of liver marker enzymes. According to the findings of this study, both Ibuprofen and Dexibuprofen administration resulted in the production of biochemical and histological abnormalities in the mice's hepatic tissues. Hepatic disturbances can be seen histologically by vascular blockage within the central venula and minor portal tract swelling, which are common in both treated groups. In present both ibuprofen and dexibuprofen treatment result in histological changes in liver tissues and biochemical marker enzyme levels, as shown in this study.

Conclusion

According to the findings of this study, all enzymes (ALP, AST and ALT) elevated in both drug-treated groups as compared to the control group.This study discovered the Ibuprofen and Dexibuprofen caused liver toxicity in both drugs treated mice. This study will help to uncover the side effects of both drugs on liver.The present study showed a larger rise in biochemical marker enzyme activity (ALT, AST) is evident that Ibuprofen induced more hepatic damage than Dexibuprofen suggested that Ibuprofen is more toxic than Dexibuprofen.

Recommendation

As it is seen that due to use of Ibuprofen and Dexibuprofen the levels of LFT enzymes were abnormal. So, the unnecessary use of these drugs should be avoided and also avoided without the prescription of physician.

Figures

Fig.1 A. The Blue line bars indicate the level of ALT, Orange line bar shows the AST and grey line bar shows the ALP level of drug treated and controlled Group.
Fig. 1 B. Blue line shows the level of ALT, Orange color line shows the AST and Dark line shows the ALP level of Ibuprofen Dexibuprofen treated and controlled Group.
Fig. 1 C. light blue line shows the level of ALT, Dark color line shows the AST and Blue line shows the ALP level of Ibuprofen Dexibuprofen treated and controlled Group.
Fig. 2. Shows histogram of Ibuprofen treated group animal.
Fig. 3. Shows histogram of Dexibuprofen treated group animal.
Fig. 4. Shows histogram of control group animal.

Fig. 1. A

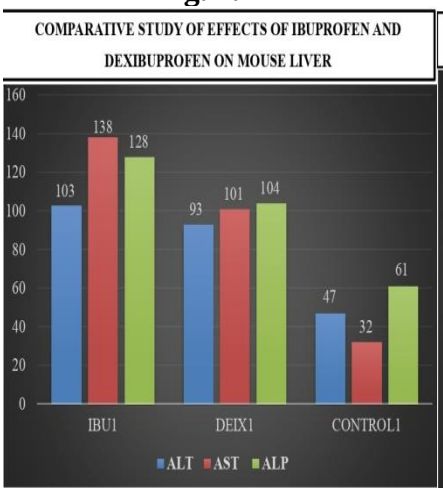


Fig. 1. B

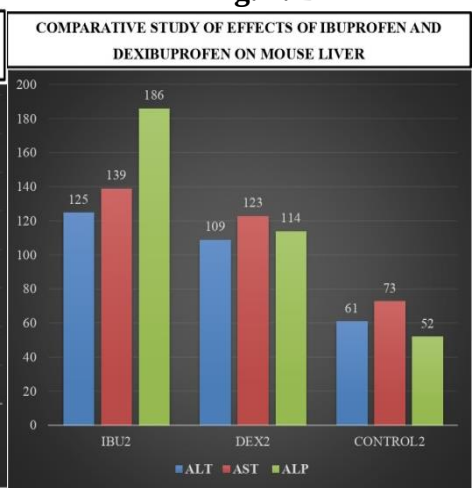


Fig. 1. C

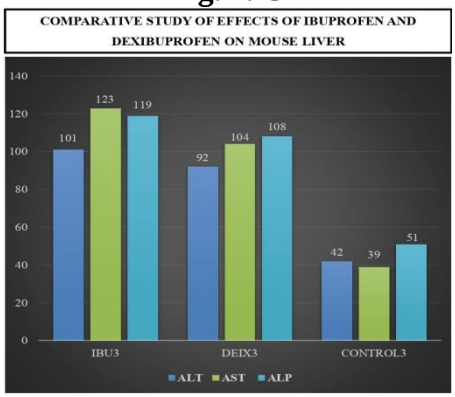


Fig 2. Ibuprofen

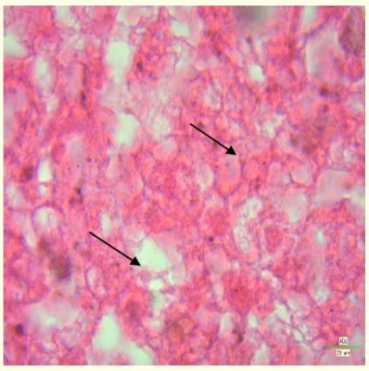


Fig 3. Dexibuprofen

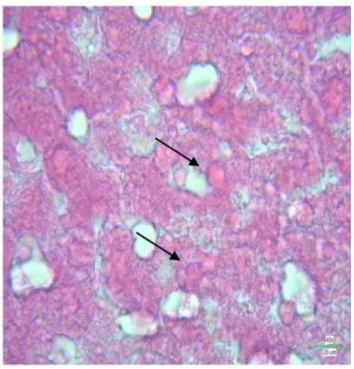
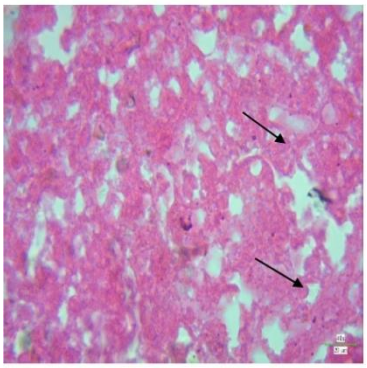


Fig 4. Control



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