

Toxic Effect of Isoniazid Hydrochloride on Liver and Reversal of it by *Curcuma Longa*

Isoniazid
Hydrochloride &
Reversal by
Curcuma Longa

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ABSTRACT

Objective: Isoniazid Hydrochloride is a drug used for prophylaxis and treatment of tuberculosis with the combination of other drugs.

Study Design: Experimental study.

Place and Duration of Study: This study was conducted at the at Shahida Islam Medical College, Lodhran, during July 2017 to December 2017.

Materials and Methods: The present study was conducted on 30 rabbits which were group from A to C consisting of 10 rabbits in each group with the weight of 2500-3500 grams. The first control group A was fed on fresh alfa alfa and water, the second group B was given 50 mg per kilogram body-weight of INH dissolved in water twice a day and the third group C was given INH with curcuma longa 100 mg twice a day dissolved in water in powder form. The blood samples were taken on day 01, 10 and 20.

Results: The AST level has non-significant changes in group A where P value was 0.21. The changes in group B and C are significant where P value in both were 0.01. In group B the AST level raised high during initial ten days where as AST level came down on day 20 probably due to addition of curcuma longa. The level of AST has remained close to normal in group C due to addition of high dose of curcuma longa. The liver paranchymal damage was observed on treatment with INH in group B. The restoration of hepatocytes architecture and minimum fibrosis was observed in group C.

Conclusion: Curcuma longa has protective effect against all the toxic agents of the liver. Curcumin has several group which function as antioxidant²⁰. It has been proved practically that curcuma longa is very effective against the Hepatotoxic agents.

Key Words: Carcuma longa, hepatotoxic, Isoniazid hydrochlorid.

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INTRODUCTION

Since 1952, isoniazid is used for the treatment of tuberculosis¹. It does not allow the the cell membrane of the bacteria to be formed. So, the proliferation of the Mycobacterium Tubreculae is stopped. Isoniazid is not only used for the treatment of tuberculosis but also used for its prophylaxis². The membrane of the mitochondria has the same configuration, as the cell membrane has, so the wall of the mitochondria is disrupted, damaging the heptocytes and produced the heptotoxicity³, 10-20%

of the people on INH can raise their ALT, in the beginning of the use of the drug. Neither only ALT but also AST also raised in first two months of the start of the drug. After 3-6 months, the enzymes become normal if the use of the drug is stopped⁴. Many infections can cause damage in the form of viruses, bacteria and helmanthiasis. Multiple other factors are available, can cause damage to liver, such as antibiotics, anticonvulsants, psycotropic drugs and abuse of alcohol⁵. Non alcoholic fatty liver disease (NAFLD) is also a big cause of chronic liver failure⁶. Liver can be injured at the level of hepatocytes, Kupffer cells, bile canaliculi and sinusoidal epithelial cells. All these injuries bringing the result as liver dysfunction⁷. These liver injuries are more common in old people and females than young people and males respectively⁸. There are different species of *Curcuma Longa*. *Curcuma* is the commonest one used in daily diet. The most active ingredient present in curcuma longa is Curcumin⁹. Turmeric or curcuma longa is a herbaceous plant which has protective effect against liver hepatotoxicity, cardiovascular diseases, rheumatoid artheritis, diabetes, Alzheimer's disease and cancer¹⁰.

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Curcuma longa has a common name as HALDI. South Asia is a place where it is commonly found. It grows in twenty to thirty degree centigrade temperature and in abundant rain fall areas¹¹. Curcuma longa has polyphenols with yellow colour. It is quickly decomposed if exposed to high temperature, bright light and oxidative condition¹². It has an anti-inflammatory, anti oxidant and protective effect for liver against hepato toxic agent¹³

MATERIALS AND METHODS

Thirty healthy rabbits were taken weighing between 2500-3500 grams. The animals were divided in to three groups. Each group, the blood samples were taken up, was divided in to ten animals (N=10). Group A was taken as control. It was on fresh Alfalf and tape water. Experimental Group B was given INH dissolved in fresh water morning and evening till twenty days while 10 mg of curcuma longa was added in last ten days. Group C was given Curcuma longa powder 100 mg with INH 50 mg per kilogram of body weight twice a day.

Fresh Alfalfa was given to all groups with fresh water. A male and female rabbit were together and was ad libitum. On day one, ten and twenty, the blood samples were taken from venous puncture of ear lobule of each animal.

The blood taken from ear lobule of rabbit is shifted to the centrifuge machine and centrifuged at the rate of 3000 rpm for twenty minutes. The Aspartate Amino Transferase (AST) in the serum was estimated by the Kits from Randox USA. Samples of liver were sent for histopathological evaluation.

RESULTS

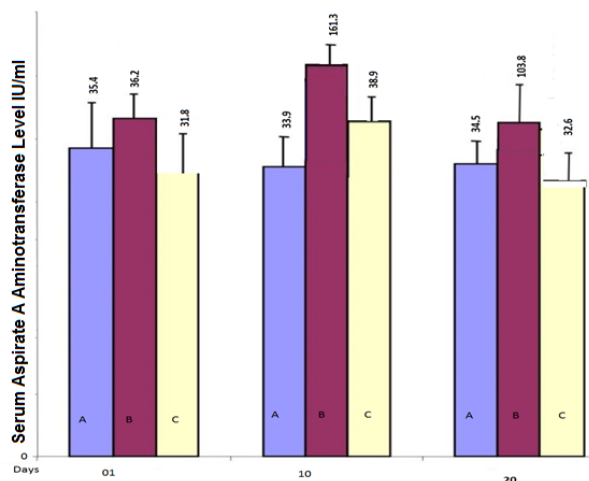
The liver enzymes were measured, which showed the liver toxicity was produced successfully by giving isoniazid 50mg/Kg of body weight twice a day. Aspartate aminotransferase in serum of first group A was 35.4±8.09IU/ml on day one, 33.9± 5.09 IU/ml on day ten and 34.5±4.98 IU/ml on day 20.

Table No: 1 Changes in the Serum aspartate aminotransferase level

Serum aspartate aminotransferase level (AST) (normal range=14-113 IU/ml)				
Animal Groups	Day 1	Day 10	Day 20	P Value
Group A	35.4 ± 8.09	33.9 ± 5.09	34.5 ± 4.98	0.21
Group B	36.2 ± 7.57	161.3 ± 39.87	103.8 ± 25.71	0.01
Group C	31.8 ± 9.01	39.9 ± 8.73	32.6 ± 3.09	0.01

Group B has aspartate aminotransferase in serum as 36.2±757 IU/ml on day 1, after giving INH the aspartate

amino-transferase level raised to 161.3±39.87 IU/ml and on day 20 aspartate aminotransferase level was 103.8±25.7 IU/ml, (10 mg of curcuma longa added in last ten days).



Graph No.1: Variations in AST Level in Rabbits after giving the INH in Group B and INH – Curcuma Longa Group C/ Group A is control on Alfa Alfa with fresh water.

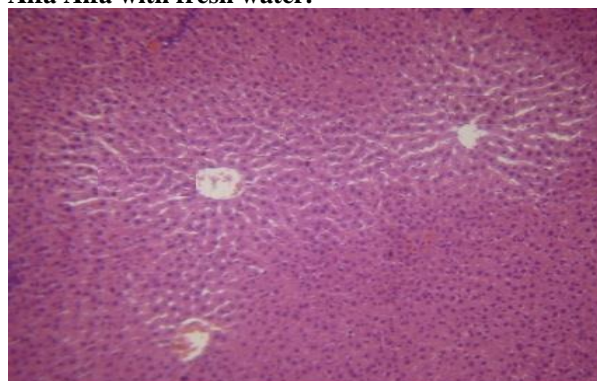


Figure No.1: Histology Pictures of normal lobes of liver of group A rabbits when they are on alfalfa and fresh water H&E X 100.

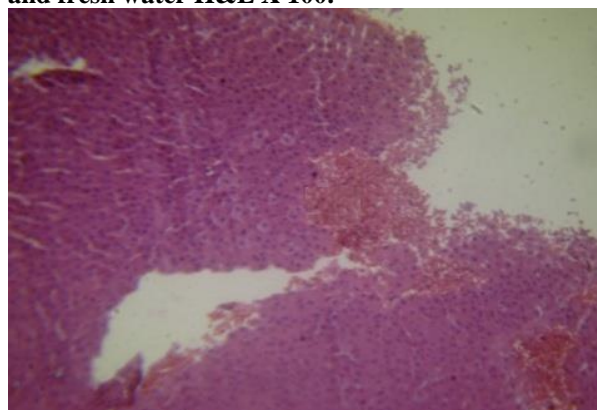


Figure No.2: Histological picture of liver hepatocytes disarrangement in group: B rabbits when given INH 50 mg/ kg/bw H&E X 100.

In last group C, aspartate aminotransferase in serum was 31.8 ± 9.01 IU/ml on day one, on tenth day, the level was 38.9 ± 8.73 IU/ml and on 20th day the level of the enzyme was 32.6 ± 3.09 IU/ml. The same results have been shown in Graph 1.

In group A, the arrangement of the hepatocytes are normal as is shown in figure 1. The dis-arrangement of the normal architecture of hepatocytes was observed in group B when INH 50mg/Kg has been given. The congestion of hepatocytes and hepatic necrosis can be observed in figure 2. The normal arrangement of the hepatocytes is regained when curcuma longa has been added to the rabbits in group C with INH, as has been given by figure 3.

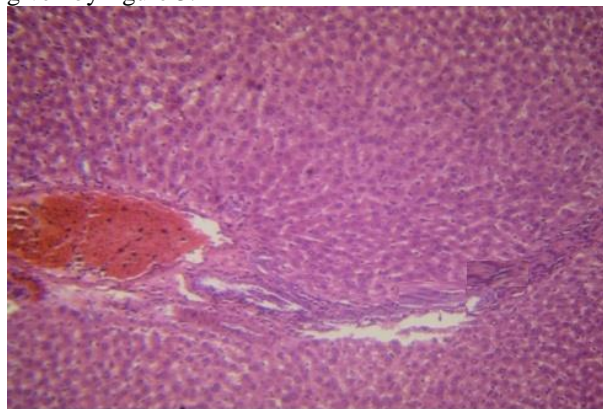


Figure No.3: In group C hepatocytes are arranged normally with INH + curcuma longa H&E X 100.

DISCUSSION

Liver, the largest gland of the body, has many chemical and important functions. It metabolized and detoxified many toxic substances coming in the body through our food. It is a store house for fat and certain vitamins¹⁴. Many drugs are capable to cause injury to liver others can lead to liver failure¹⁵. The idiosyncrasy of a drug to liver can lead to neither only hepatotoxicity but also to liver failure¹⁶. Liver is the place where all metabolism of all the drugs occurs¹⁷. The paranchyma of the liver can be damaged directly or inflammation may be there in the liver. Certain genetic and environmental factors can change the response of the liver¹⁴. In liver toxicity, the enzyme P 450 is released which is toxic for liver, then damage to the mitochondria is observed in hepatocytes. Now the deficiency of ATP is there and the different species of reactive oxygen accumulate in liver cells, causing more damage¹⁸. INH can damage the membrane of mitochondria, which can increase the permeability of mitochondria, releasing the cytochrome C, leading to cellular necrosis¹⁹.

Curcuma longa has protective effect against all the toxic agents of the liver. Curcumin has several group which function as antioxidant²⁰. It has been proved practically that curcuma longa is very effective against the Hepatotoxic agents.

CONCLUSION

The AST level has non significant changes in group A where P value was 0.21. The changes in group B and C are significant where P value in both were 0.01. In group B the AST level raised high during initial ten days where as AST level came down on day 20 probably due to addition of curcuma longa. The level of AST has remained close to normal in group C due to addition of high dose of curcuma longa. It does show the protective role of curcuma longa in Hepatotoxic drugs. The histopathological changes are visible in diagram after giving the INH and the reversal of it after giving the high doses curcuma longa. The damage of the liver paranchyma caused by isoniazid is reversed by adding the high dosage of curcuma longa.

Author's Contribution:

Concept & Design of Study: Mujahid Akbar Mamoun
 Drafting: Jawad Sodhar
 Data Analysis: Sama-ul-Haq, Mazhar ul Haque
 Revisiting Critically: Mujahid Akbar Mamoun, Jawad Sodhar
 Final Approval of version: Mujahid Akbar Mamoun

Conflict of Interest: The study has no conflict of interest to declare by any author.

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