Potentiation of Hepatotoxic Effects of Methotrexate by Isoniazid in Mice; an Explorative Study

Aamna Khokhar1, Sadia Shaukat2, Aisha Qayyum3, Jawaria Iftikhar4, Rukhsana Munawar5

1Department of Pharmacology, Islamabad Medical and Dental college, Islamabad. 2Anatomy Department, Rehman Medical College, Peshawar. 3Department of Pharmacology, Fazaia Medical College, Islamabad. 4Department of Pharmacology, WATIM Medical and Dental College, Rawalpindi. 5Depmartment of Pharmacology, Islamic International Medical College, Rawalpindi.

ABSTRACT Objective: To evaluate the effect of isoniazid on methotrexate induced hepatotoxicity.

Study design: Laboratory-based experimental study

Place and Duration of Study: Department of Pharmacology Army Medical College, from November 2015 to November 2016.

Material and Methods: Thirty mice were randomly divided into five groups (n=6). Group ? was given 0.2 ml normal saline by intraperitoneal injection. Group ? received 0.2 ml of distilled water by oral gavage for 5 days a week for 4 weeks. Group ? received single intraperitoneal injection of methotrexate 20 mg/kg. Group ? received Isoniazid 25 mg/kg oral for 5 days a week for 4 weeks. Group ? received Isoniazid 25 mg/kg oral for 5 days a week for 4 weeks and methotrexate 20 mg/kg i.p after two weeks. Blood samples for measuring serum ALT, AST and ALP along with liver samples for hepatic histological H&E examination were taken after 24 hours of last dose.

Results: Serum ALT, AST, ALP levels were significantly raised in group V (MTX + INH) higher than all other groups exhibiting significant potentiation of MTX induced hepatotoxicity by INH. Histologically group III (MTX) and group IV (INH) showed mild to moderate inflammatory changes whereas group V (MTX + INH) were graded as severe hepatotoxicity with Central vein ischemic changes

Conclusion: It was concluded from results that Isoniazid Potentiates Hepatotoxic effects of Methotrexate in mice as evidenced by histological changes and elevated hepatic enzymes.