

Effect of adrenergic blockers, carvedilol, prazosin, metoprolol and combination of prazosin and metoprolol on paracetamol-induced hepatotoxicity in rabbits

Maysaa B. Zubairi, Jawad H. Ahmed, and Sawsan S. Al-Haroon

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Abstract

Objectives:

To evaluate hepatoprotective potential of carvedilol, prazosin, metoprolol and prazosin plus metoprolol in paracetamol-induced hepatotoxicity.

Materials and Methods:

Thirty-six male rabbits were divided into six groups, six in each, group 1 received distilled water, group 2 were treated with paracetamol (1 g/kg/day, orally), group 3, 4,5 and 6 were treated at a dose in (mg/kg/day) of the following: Carvedilol (10 mg), prazosin (0.5 mg), metoprolol (10 mg), and a combination of metoprolol (10 mg) and prazosin (0.5 mg) respectively 1 h before paracetamol treatment. All treatments were given for 9 days; animals were sacrificed at day 10. Liver function tests, malondialdehyde (MDA) and glutathione (GSH) in serum and liver homogenates were estimated. Histopathological examinations of liver were performed.

Results:

Histopathological changes of hepatotoxicity were found in all paracetamol-treated rabbits. The histopathological findings of paracetamol toxicity disappeared in five rabbits on prazosin, very mild in one. In carvedilol group paracetamol toxicity completely disappeared in three, while mild in three rabbits. Paracetamol hepatotoxicity was not changed by metoprolol. In

metoprolol plus prazosin treated rabbits, moderate histopathological changes were observed. Serum liver function tests and MDA in serum and in liver homogenate were elevated; GSH was depleted after paracetamol treatment and returned back to the control value on prior treatment with prazosin. MDA in serum and liver homogenate, alkaline phosphatase, total bilirubin were significantly decreased after carvedilol and prazosin plus metoprolol treatments.

Conclusion:

Carvedilol and prazosin are hepatoprotective in paracetamol hepatotoxicity, combination of prazosin and metoprolol have moderate, and metoprolol has a little hepatoprotection.

KEY WORDS: Antioxidant, carvedilol, liver toxicity, metoprolol, paracetamol, prazosin