البحث الثاني

Effects of Valproate Sodium on Liver and Kidneys of Albino Rats and the Role of Metformin as Adjuvant Therapy

Authors: Heba H. Rohym, 1Ghada M. El Gallad, 1Manar M. Bayoumi, 2Reham Sh. El Nemr and 1Amal R. Saleh

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ABSTRACT

Background: Valproate (VPA) which usually prescribed as its sodium salt, was approved for treatment of epilepsy either as monotherapy or in combination with other anticonvulsant drugs. It is also used in the treatment of a variety of neuropsychiatric illnesses. It was reported that it has sever toxic effects on different organs of body. Metformin is one of the most widely used oral antidiabetic drugs for the treatment of type 2 diabetes. Aim of the study was to assess the effect of the administration of valproate sodium on liver and kidneys of albino rats as and compare effect of its administration alone and with administration of metformin to study metformin possible protective effect**. Methods**: Four groups of 80 rats formed of a control group, Valproate sodium - treated group that received Valproate sodium dissolved in water for 12 weeks, Metformin -treated group that received Metformin dissolved in water for 12 weeks and Valproate sodium plus metformin -treated group that received Valproate sodium plus Metformin for 12 weeks. For all, liver and kidneys function tests and hepatic, kidneys histopathologic examinations were done **Results:** There was a statistically significant difference ($P < 0.05$) among rats' liver function tests in different study groups, with high mean of liver enzymes (ALT, AST and ALP) levels in Valproate sodium group. Also, among the valproate sodium about 40% of liver tissues showed Grade 2 hepatic necrosis. There was liver fibrosis in Valproate sodium group, about 50% of liver tissues of valproate sodium shows Grade 2 hepatic fibrosis, 50% showed Grade 1. There was a statistically significant difference ($P < 0.05$) among rats' kidneys function tests(urea and creatinine) in different study groups, with high mean of urea and creatinine levels in Valproate sodium group. Also, among the valproate sodium kidneys tissues revealed moderate vascular congestion dense inflammation, fibrosis and vacuolar degeneration

(ballooning) of some of the tubular cells with marked tubular dilatation and intratubular casts. Adding metformin to Valproate sodium was found to produce significant improvement in liver, kidneys function, liver and kidneys histopathological findings.

Conclusion: Long term use of Valproate sodium in albino rats produces hepatotoxicity and nephrotoxicity and metformin restored the altered liver and kidneys function and possessed hepatoprotection and nephroprotection against Valproate sodium induced hepatotoxicity and nephrotoxicity.