Neurotoxic Effect of Paracetamol on Female Rats: Role of Antioxidant Treatment and Prevention

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ABSTRACT

Paracetamol (Acetaminophen) is the most common nonprescription analgesic and antipyretic drug used. It can be found in different pharmaceutical dosage forms such as syrup, capsule, suppositories and intravenous (I.V) infusion solution. Paracetamol is commonly taken by pregnant women. The intake frequency and the dose of paracetamol usually varied during pregnancy with a tendency toward higher doses in the last trimester. The effect of Paracetamol overdose was extensively studied on hepatocyte and nephrocyte of laboratory animals. However, the effect of paracetamol dose on the brain toxicity is the least studied after paracetamol overdose. The aim of this study is to focus on the effect of paracetamol overdose on Neurotoxicity (within Hippocampus, Cerebellum, and Olfactory Bulbs) of Paracetamol in the last trimester of pregnant rats. And this will be done through studying oxidative stress markers, the biochemical and antioxidant tests that indicate the presence of Hepatotoxicity and Nephrotoxicity, along

with the protective effect of Vitamin E as antioxidant in pre- and post-single toxic dose administration. Twenty female pregnant Wistar rats (average weight 200 gm ± 10) at gestational day 18 (GD_{18}) were used. The pregnant rats were divided into four groups; the first (control) group received a 0.5 ml p.o of corn oil. The second group (paracetamol) group received a 3000 mg/kg p.o paracetamol dissolved in corn oil. The third (E + paracetamol) group received a 3000 mg/kg paracetamol one hour after 300 mg/kg p.o vitamin E. The fourth (paracetamol + E) group received a 3000 mg/kg paracetamol one hour before 300 mg/kg p.o vitamin E dissolved in corn oil. Twenty-four hours After Paracetamol administration the rats were euthanized and the brain, the liver, the kidney, and the blood were collected. Various biochemical tests were performed to show the effect of paracetamol overdose on liver including Alanine aminotransferase (ALT), Aspartate aminotransferase (AST). Additionally, the effect of paracetamol on Blood urea nitrogen (BUN) and Creatinine levels were determined to detect nephrotoxicity, and the results showed significant elevation within the paracetamol treated group (148.7%, 451.89%, 287.7%, 170.8% increase respectively) and levels were restored to the normal levels with vitamin E treated groups (58.9%, 83.3%, 70.4% and 63.9% reduction for pre-treatment and 57.6%, 82.7%, 63% and 56.3% reduction for post-treatment). Uric acid (UA) and superoxide dismutase (SOD) were used to detect the oxidative stress within the Liver, the Kidney, the Hippocampus, the Cerebellum, and the Olfactory Bulbs. Results showed significant depletion in both Uric acid (UA) (23.8%, 26.3%, 10.3%, 8.1% and 22.3% reduction) and Superoxide dismutase SOD (69.5%, 72.6%, 61.4%, 68.6% and 70.8% depletion) in paracetamol treated group. On the other hand, vitamin E treated group showed significant restoration to their normal levels (29.1%, 34.4%, 6%, 6% and 20.9% elevation for pre-treatment and 34.4%, 38.7%, 4%, 6% and 27.4% elevation in post-treatment for UA, and 242%, 96.5%, 172.7%, 224.8% and 236% increase for pre-

treatment and 239.7%, 93.9%, 156.13%, 159.6% and 234.5% improvement for post-treatment). In conclusion results showed that paracetamol over dose in late pregnancy can cause oxidative stress in liver, kidney and various brain regions. Pre- and post-vitamin E treatment restores the damage caused by oxidative stress within those organs. These results suggest the effectiveness of using vitamin E for prevention and treatment as antioxidant in paracetamol over dose.