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Hematological and Biochemical Changes in Blood, Liver and Kidney Tissues under the Effect of Tramadol Treatment

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Abstract

This study aimed to investigate the effects of tramadol administration on some haematological and biochemical indices in rats. Tramadol was administered orally to rats for 28 days at a dose of 10 mg/kg body weight/day, 50 mg/kg body weight/day and 100 mg/kg body weight/day. Twenty-four hours after the last tramadol, blood, liver and kidney were removed from the animals after an overnight fast and analysed for their haematological and biochemical parameters. Results obtained revealed that tramadol administration significantly reduced the levels of white blood cells (WBC), red blood cell (RBC), haemoglobin and platelet count (PLT) while its resulted in non-significant changes in other haematological parameters examined when compared with control rats. Tramadol intake significantly increased plasma levels of alkaline phosphatase (ALP), aspartate aminotransferase (AST), creatinine and urea while its reduced total protein levels. Hepatic and renal thiobarbituric acid reactive substances (TBARS) levels were significantly increased by tramadol administration while levels of endogenous antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) were reduced. This study confirmed the risk of increased oxidative stress, hepatotoxicity and nephrotoxicity due to tramadol administration. Although tramadol is reported to be effective in pain management, its toxicity should be kept in mind.

Introduction

Tramadol is a synthetic centrally acting analgesic with e ects similar to those of codeine and 10 times less than morphine. Tramadol has a wide range of applications mostly in the treatment of moderate to severe, acute or chronic pain. It is an e ective analgesic in acute ureteric spasm, postoperative, musculoskeletal and cancer pain. He analgesic e ect of tramadol is mediated by three mechanisms: mu opioid binding, nor-epinephrine and serotonin reuptake inhibition.

Tramadol is metabolized mainly in the liver by cytochrome P450 (CYP2D6), cytochrome P4503A (CYP3A4) and cytochrome P450 isozyme (CYP2B6), being O-and N-demethylated to five di erent metabolites, followed by conjugation with glucuronic acid and sulphate. Tramadol is responsible for life-threatening poisonings, resulting in consciousness impairment, seizures, agitation and respiratory depression. Like other opioids, central apnea has been attributed to the ingestion of elevated doses of tramadol. Herefore, tramadol toxic e ects should be kept in mind during long term therapy especially in large doses.

Similarly, in Nigeria, the rate of tramadol abuse has been on the increase among Nigerian youths in recent time. He main factor responsible for this could be link to o -label use of tramadol as ondemand treatment for premature ejaculation (PE). However, wide-spread use of tramadol is associated with toxicity and a recent study showed that tramadol cause brain, heart and lung toxicity . Herefore, there is need to conduct a study that would examine the toxicity of tramadol in the liver where tramadol is metabolized and, in the kidney, where tramadol metabolites are excreted, thus making liver and kidney the primary toxicity targets for tramadol. Herefore, in the present work, we performed an in vivo study, using male Wistar rats, to analyse oxidative stress, biochemical and haematological alterations, at the liver and kidney levels, deriving from exposure to a broad range of tramadol.

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Materials and Methods

Reagents

Thiobarbituric acid (TBA), nicotinamide adenine dinucleotide reduced (NADH) and tramadol hydrochloride were obtained from Sigma–Aldrich Chemical Co. Ltd. (England). Nitrobluetetrazolium (NBT), 5,5′-Dithiobis (2-nitrobenzoic acid) (DTNB) are product of Fluka (Buchs, Switzerland). All other chemicals used were analytical grade.

Determination of urea, creatinine, total protein and ALP, AST activities in plasma: Plasma concentrations of alkaline phosphatase (ALP), aspartate aminotransferase (AST), urea, creatinine and total protein were determined using enzymatic kits (CYPRESS® Diagnostics, Langdorp, Belgium) according to the manufacturer's instructions.

Preparation of liver and kidney homogenates: Prior to biochemical analyses, the liver and kidney samples were cut into small pieces and homogenized in Phosphate buffer saline (PBS) with a homogenizer to give a 10% (w/v) liver and kidney homogenate. He homogenates were then centrifuged at 12,000 rpm for 15 min. He supernatant obtained was used for the assay of superoxide dismutase, catalase, gluthathione, thiobarbituric acid reactive substances (TBARS) content, and protein estimation.

Haematological study

Freshly collected blood samples in EDTA bottles were analysed for haematological assay using an automatic haematological assay analyser (ERMA PCE 210, ERMA, Japan). Different tested haematological parameters were as follows: White Blood Cell (WBC), Red Blood Cells (RBC), Haemoglobin (HGB), Haematocrit (HCT), Red cells (RDW%), Red cells Distribution Width (RDW), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Platelet (PLT), Mean Platelet Volume (MPV), Mean Corpuscular Volume (MCV), Platelet crit (PCT), Platelet distribution width (PDW).

Conclusion

Our results evidence that tramadol administration may cause hepatotoxicity, nephrotoxicity and haematoxicity, its use should therefore be limited to prescription only. Our findings underlined the need to avoid indiscriminately and prolong use of tramadol, since prolonged daily use of the drug either at a therapeutic dose or the extreme dose may lead to damage accumulation

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