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Perinatal exposure to energy drink induces oxidative damage in the liver, kidney and brain, and behavioral alterations in mice offspring

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ABSTRACT

The worldwide consumption of energy drinks (EDs) has increased in recent years. EDs have several side effects and can be linked to liver injury, kidney damage and risk-seeking behavior. The impact of perinatal consumption of EDs on the newborns has not been previously investigated. In this study, we evaluated the effects of perinatal exposure to a caffeinated ED on the liver, kidney, brain, locomotor activity and anxiety in mice newborns. Pregnant mice received 2.5 or 5 ml ED by oral gavage from the first day of pregnancy until day 15 after birth. Perinatal exposure to the ED induced a significant increase in lipid peroxidation and declined antioxidant defenses in the liver, kidney, cerebrum, cerebellum and medulla oblongata of the newborns at days 21 and 35 after birth. ED induced several histological alterations, including vacuolations and lipid infiltration of hepatocytes, developing and degenerated glomeruli and dilated urinary spaces in the renal cortex, pyknosis and chromatolysis of the cerebral and medullary neurons, and degenerated and abnormal Purkinje cells in the cerebellum. In addition, ED increased the locomotion and induced anxiety-like behavior in mice newborns. In conclusion, perinatal exposure to EDs induces oxidative stress, tissue injury and behavioral alterations in the mice newborns. Therefore, the consumption of EDs during pregnancy and lactation has a negative impact on the newborns and should be treated as a significant health problem that warrants attention.

1. Introduction

Energy drinks (EDs) are carbonated beverages that contain high concentrations of metabolic stimulants [1]. These drinks were advertised to boost alertness, endurance and energy; therefore, their consumption has increased dramatically over the past years [2]. EDs were launched in the 1960s and achieved worldwide recognition in 1997 once the Red Bull® brand reached the market in USA. In 2006, the number of EDs around the world reached 500 different brands [3] and are now available in more than 140 countries [2]. Despite the vast array of EDs, most of them contain similar ingredients, including caffeine, taurine, glucuronolactone, inositol, carbohydrates, minerals and B complex vitamins [1,4]. Several studies have supported the temporary health benefits of EDs in improving alertness, and physical and mental stamina, and restoring fatigue among adolescents and adults [1,5]. Recently, Souza et al. have shown improved muscle strength and endurance, performance on endurance exercise, and sport-specific actions following consumption of EDs [6].

In contrast, many studies have reported the negative health effects of short- and long-term consumption of EDs, such as, aggressive behavior, substance abuse [7], depressive symptoms, stress, anxiety [8], low academic achievement [7], increased heart rate, increased systolic and diastolic blood pressure [9], overweight, type 2 diabetes and obesity risk [10], accelerated progression of chronic kidney disease, renal microvascular damage [11], dental decay [12], headaches, stomachaches, irritation, tiredness/fatigue and sleep dissatisfaction [7]. Recent evidences have suggested the role of EDs in inducing oxidative stress in different organs [13,14]. Increased production of reactive oxygen species (ROS) and declined antioxidant defenses can damage proteins, lipid and nucleic acids, or even cell death [15]. Most of the literature propose that the high levels of caffeine and sugar are responsible for the health disadvantages of EDs [16]. To our knowledge, nothing has yet been reported on the effects of perinatal consumption of EDs on the newborns. Therefore, we investigated the effect of perinatal exposure to an energy drink (Red Bull®) on the liver, kidney, brain, locomotor activity and anxiety-like behavior of mice newborns.

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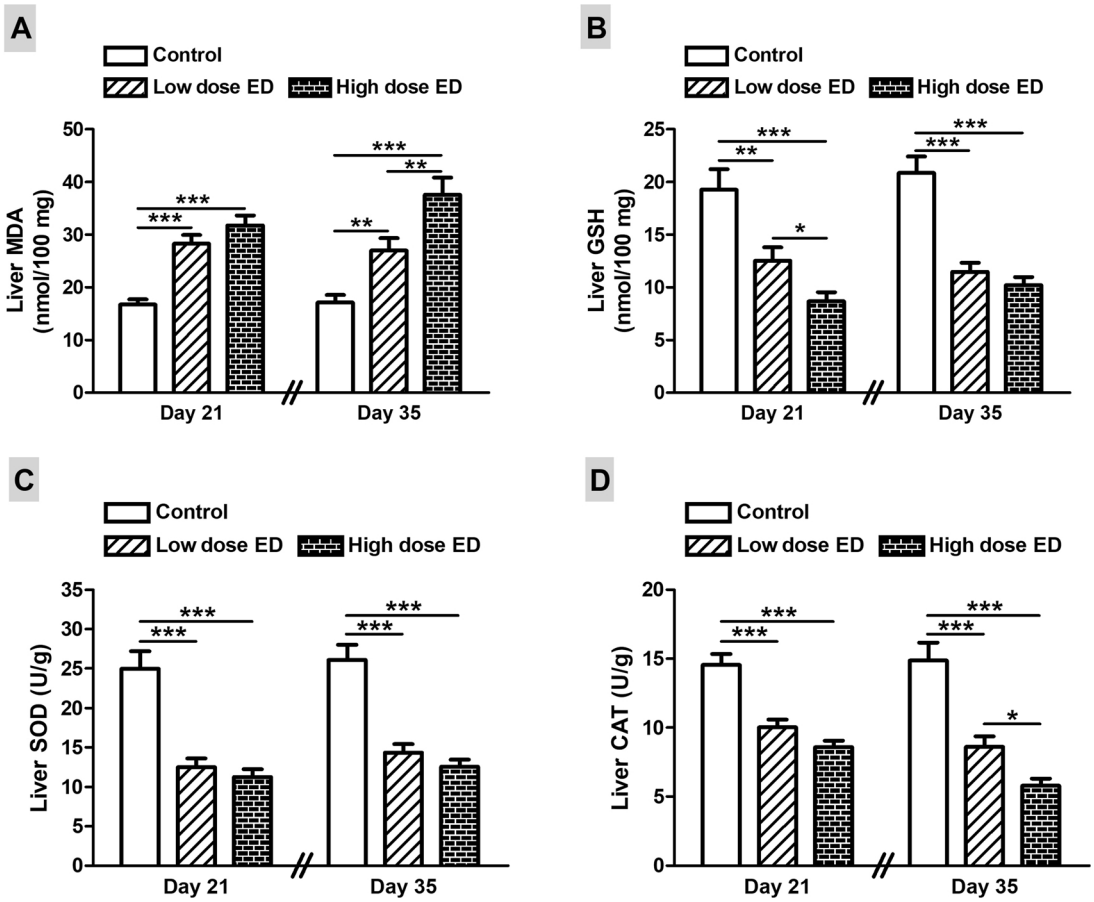

Fig. 1. Effects of low- and high-dose energy drink administration on (A) lipid peroxidation, (B) GSH, (C) SOD and (D) CAT in the liver of newborn mice at D21 and D35 after birth. Data are Mean ± SEM, (N = 6). $^{*}P < 0.05$, $^{**}P < 0.01$ and $^{***}P < 0.001$. ED, energy drink; MDA, malondialdehyde; GSH, reduced glutathione; SOD, superoxide dismutase; CAT, catalase.

2. Materials and methods

2.1. Experimental animals

Male and female Swiss Webster mice (*Mus musculus*) of 10–12 weeks and weighing 20–25 g were used in the present study. The animals were obtained from the animal house of the Faculty of Pharmacy, King Saud University (Saudi Arabia) and housed in standard cages at normal temperature (23 ± 1 °C) and 12 h light/dark cycle. The mice were given a standard diet and water *ad libitum*. All experiments and protocols were approved by the Ethics Committee for Animal Experimentation at King Saud University which complied with the *Guide for Care and Use of Laboratory Animals* published by the US National Institutes of Health (NIH Publication No. 85–23, revised 2011).

2.2. Experimental design and treatments

The female mice were investigated, and each three pro-estrous female mice were housed with a male for 12 h in a mating cage. The vaginal plug was monitored, and its appearance was considered the first day of pregnancy and each pregnant mouse was isolated until delivery. The pregnant mice were randomly divided into 3 groups (N = 4–5) as following:

Group I (Control): received distilled water by oral gavage from the first day of pregnancy until the 15th day after birth.

Group II (Low-dose ED): received 2.5 ml/kg body weight Red Bull® by oral gavage from first day of pregnancy until the 15th day after birth.

Group III (High-dose ED): received 5 ml/kg body weight Red Bull® by oral gavage from first day of pregnancy until the 15th day after birth.

In previous experimental studies, EDs such as Red Bull® have been administered at doses range between 5–15 ml/kg body weight [17,18]. In our investigation, we selected the 5 ml/kg body weight dose and a lower dose of 2.5 ml/kg body weight Red Bull®. We used Red Bull® which contains (per 100 ml) 400 mg of taurine, 32 mg of caffeine, 240 mg of gluconolactone, 20 mg inositol, 8 mg of niacin, 11.3 g of sucrose and glucose, 2.4 mg of pantothenic acid, vitamins B2/B6/B12, citric acid, flavorings, colors.

Six male newborn mice from each group were sacrificed under ketamine/xylazine anesthesia at day 21 (D21) and day 35 (D35) after