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Afr. J. Biomed. Res. Vol. 25 (January, 2022); 107 - 111

Research Article

Allium cepa Juice Ameliorate Maternal Dexamethasone-induced Alteration in Lipid Profile and Oxidative Stress in the Liver of Male Offspring of Wistar Rats

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ABSTRACT

Maternal glucocorticoid administration during lactation has an effect on metabolic imbalance. This study examines the effect of Allium cepa Lin on maternal dexamethasone-induced alteration in lipid profile and oxidative stress in the liver of the male offspring of Wistar rats. Twenty female Wistar rats were divided into four groups (n=5) during lactation. Group 1 was administered subcutaneously 0.05ml/kg/day normal saline from days 1-21. Group 2 was administered 30% onion mixed diet from lactation days 1-21. Group 3 was administered subcutaneously 100µg/kg/day dexamethasone from lactation days 1-21. Group 4 was administered subcutaneously 100µg/Kg/day dexamethasone (dex) for 21 days + 30% onion mixed diet throughout lactation. Results from this study showed that dexamethasone treatment during lactation significantly ($p<0.05$) reduced the body weight, HDL-cholesterol, hepatic catalase and SOD activities of the male offspring. There was also a significant ($p<0.05$) increase in hepatic MDA, total cholesterol, LDL-cholesterol and TAG when compared with the control. Meanwhile maternal exposure to dexamethasone and 30% onion mixed diet significantly ($p<0.05$) raised the serum HDl-cholesterol level, Hepatic SOD and catalase activities. The serum LDL-cholesterol, total cholesterol and TAG were reduced in the male offspring when compared with the dexamethasone-only treated group. Findings from this study suggest that maternal consumption of 30% onion mixed diet may ameliorate the metabolic alterations induced in the male offspring following maternal treatment with dexamethasone during lactation in Wistar rats

Keywords: *Dexamethasone, offspring, Lactation, Onion, Metabolic alteration*

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Received: March 2021; Revised version accepted: October, 2021

INTRODUCTION

Glucocorticoids are essential steroid hormones for human life. They regulate a series of important processes by binding with glucocorticoid receptors and activating genomic and non-genomic pathways (Irma et al., 2015).

Although Glucocorticoids are necessary for normative development, exposure to excessive levels of glucocorticoid may disrupt basic developmental processes and excessive exposures are associated with increased risk for affective problems (Davis and Sandman, 2012; Buss et al., 2012).

Exposure to dexamethasone in utero during the last week of pregnancy reduced birth weight and was associated with a permanent increase in hepatic PEPCK (phosphoenolpyruvate carboxykinase) activity in male offspring (Nyirenda et al., 1998). A key target appears to be the liver, where glucocorticoids regulate several important processes, including key enzymes regulating carbohydrate and fat metabolism, such as phosphoenolpyruvate carboxykinase, the rate-limiting enzymes in gluconeogenesis. There are indications that maternal treatment with dexamethasone during lactation may reduce the growth rate in the male offspring and also increased basal corticosterone levels in Wistar rats (Jeje and Raji, 2015). In addition, our data suggest that maternal dexamethasone administration during lactation may also induce metabolic imbalance that may be secondary to increase oxidative stress in the liver of a male offspring (Jeje and Raji, 2015).

In the liver, glucocorticoids increase the activities of enzymes involved in fatty acid synthesis and promote the secretion of lipoproteins (Wang, et al., 1995). The hepatic lipogenic effect of glucocorticoids is consistent with clinical findings that glucocorticoids therapy causes triglyceride accumulation within the liver (Dourakis et al., 2002). Since liver fat appears to be involved in the negative regulation of hepatic insulin sensitivity (Samuel et al., 2004) and is associated with certain features of the Metabolic Syndrome independent of visceral fat mass (Tiikkainen et al., 2002; Nguyen-Duy et al., 2003), hepatic fat accumulation promoted by glucocorticoids is likely to contribute to the programming of the metabolic alteration.

Onion (*Allium cepa* Linn) is a bulbous plant widely cultivated in almost every country of the world with leading

production in China, India and United States. It is rich in proteins, carbohydrates, sodium, potassium and phosphorus (Lampe, 1999).

Onion (Allium cepa Linn), a very commonly used vegetable, and ranks third, (Mitra et al., 2011) in food preparations especially in the tropical countries. Besides adding a delicious taste and flavour, onion serves as a good medicinal compound for cataract, cardiovascular disease and cancer due to its hypocholesterolemic, thrombolitic and antioxidant effects (Nuutila et al., 2003; Vidyavati et al., 2010). Onions are used in the treatment of anaemia, urinary disorders, bleeding piles and teeth disorders, Anti tumor and anti-cancer effect (Kamel and Saleh, 2000; Miron et al., 2003), platelet-anti-aggregating agent (Mochizuki and Nakazawa 1995), anti-ulcer and anti-gastric cancer agent (Canizares et al., 2004; Elsom et al., 2000,), antimicrobial (Whitemore and Naidu 2000), antiasthmatic (Dorsch and Wagner, 1991). anti-inflammatory, antiallergenic, and vasodilatory (Corzo-Martínez, et al., 2007), as well as antioxidant capacities (Santas, et al., 2010; Škerget, et al., 2009).

The anti-oxidative effects of consumption of onions have been associated with a reduced risk of metabolic disorders, many forms of cancer, cataract formation, ulcer development and prevention of cardiovascular diseases by inhibition of lipid peroxidation and lowering of low-density lipoprotein (LDL) cholesterol levels.

Therefore, in this study, the protective role of Allium cepa Linn against the maternal dexamethasone-induced metabolic alterations in the male offspring of Wistar rat was investigated.

MATERIALS AND METHODS

Drugs: Dexamethasone 21-Phosphate disodium salt purchased from Sigma Aldrich Chemical UK was used for this study. A dose of100 µg/Kg/day of dexamethasone was administered to the drug-treated groups

Preparation of Allium cepa Mixed Feed: Allium cepa bulb juice was prepared according to the method described by Ola-Mudathir et al. (2008). The Red variety of fresh Allium cepa bulbs was purchased from Okuku market in Cross River State. It was identified at the Department of Botany, Cross River University of Technology, Calabar. The fresh bulbs were washed, cut into small pieces and homogenized in a blender. The resultant slurry was squeezed and filtered through a fine cloth. The juice is then mixed with grower feed in the ratio of 30/70 v/w respectively. Fresh feed was prepared daily in the morning.

Experimental animal: Twenty Female Wistar rats weighing 150-180g were purchased from the Cross River University of Technology, Okuku Campus, Yala Local Government Area, Cross River State Central Animal House. The animals were housed in the department of Physiology Animal House, Cross River University of Technology, Okuku Campus, Yala Local Government Area, Cross River State. After one week of acclimatization the rats were divided into four (4) groups of five rats in each cage. The female rats were exposed to proven males breeder at proestrous and the presence of sperm in their vaginal smear the next morning marked gestation day 1 (GD1). The rats were thereafter left until delivery. Immediately after delivery the animals were group into four groups. Administration was between 7am and 8am daily. 0.05ml/kg bwt normal saline was administered to the control groups, 100µg/kg bwt dexamethasone was administered to the drug treated groups, 30% onion mixed diet (30ml of onion juice + 70g of grower feed) was administered to the onion groups, and 100µg/kg bwt dexamethasone + onion mixed diet (30ml of onion juice + 70g of grower feed) was administered to the onion + dex group throughout lactation. All administration were done subcutaneously. The male offspring were allowed to grow to adulthood (12 weeks of age).
All experiment were conducted in accordance with the Animal Scientific Procedure acceptable at the Faculty of Basic Medical Sciences, Cross River University of Technology, Okuku Campus.

Evaluation of body weight: Body weight at birth was determined by using a digital weighing balance.

Blood and tissue collection: Blood was collected from the heart by cardiac puncture under sodium thiopental anaesthesia (50 mg/kg, i.p.) into plane tubes. Tissues (liver) was also collected, the weight measured and recorded. The tissues were homogenised in 0.25M sucrose solution. The homogenate was centrifuge in cold centrifuge at 10000g for 10minute and the supernatant was used for the bioassay. The blood sample was centrifuge at 3000rpm for 5minute to produce the serum for the determination of lipid profile

RESULTS

Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on body weight: The weight at weaning was significantly reduced ($p<0.05$) in the group that was administered dexamethasone alone when compared with the control and other treatment groups. The mean weight at postnatal day 12 weeks was significantly ($p<0.05$) reduced in the groups administered dexamethasone alone and the group administered dexamethasone and fed with 30% onion feed (Table 1). The relative weight of the liver was significantly increased in the group that was administered dexamethasone only when compared with the control (Table 1).

Table 1:
Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on body weight

	Weight at weaning (3 weeks of Age) (g)	Weight at 12 weeks of Age (g)	Relative weight of the liver (%)
Control	26.36±0.55	203.00±8.40	3.55±0.05
Onion	24.86±1.50	198.00±3.21	3.39±0.09
Dex	18.09±0.83*	175.43±4.21*	4.08±0.04*
Dex+Onion	23.06±1.27	179.00±2.74	3.42±0.06

*$p<0.05$ significantly different from control, n=5

Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on Tissue protein, Malondialdehyde (MDA) levels and catalase enzyme activity of a male offspring of Wistar rats: The mean Tissue protein level and Malondialdehyde level were significantly increased ($p<0.05$) in the group administered dexamethasone only when compared with control (fig 1 and 2). However, the mean catalase and SOD activities was significantly reduced ($p<0.05$) (fig 3 and 4). In addition the mean MDA level was significantly raised ($p<0.05$) in the group fed with onion mixed feed and administered dexamethasone when compared with control (fig 2). But the mean catalase and SOD activities were not significantly different from control (fig 3 and 4).

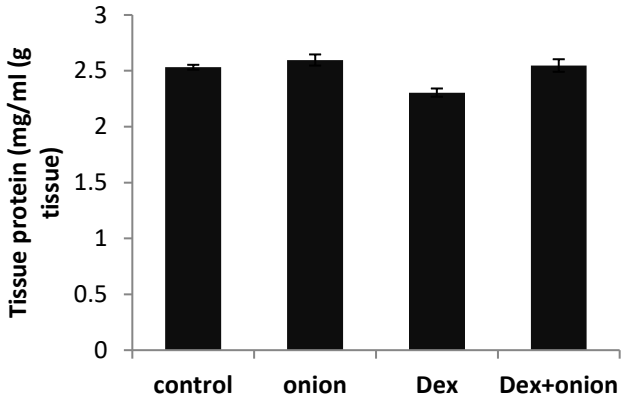

Figure 1:
Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on liver protein level of a male offspring of Wistar rats. n=5

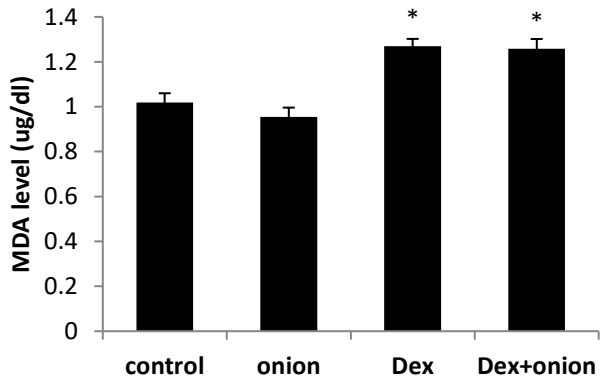

Figure 2:
Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on liver malondialdhyde (MDA) level of a male offspring of Wistar rats.
*p<0.05 significantly different from control, n=5

Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on serum Lipid profile of a male offspring of Wistar rats: The mean total cholesterol, TAG and LDL cholesterol were significantly higher ($p<0.05$) in the group administered dexamethasone only when compared with the control. However, the serum HDL-cholesterol level was significantly ($p<0.05$) lower when compared with the control. In the 30% onion fed +dexamethasone group, there was a significant reduction in serum HDL-cholesterol level with an increase in the LDL-cholesterol level when compared with the control (Table 2).

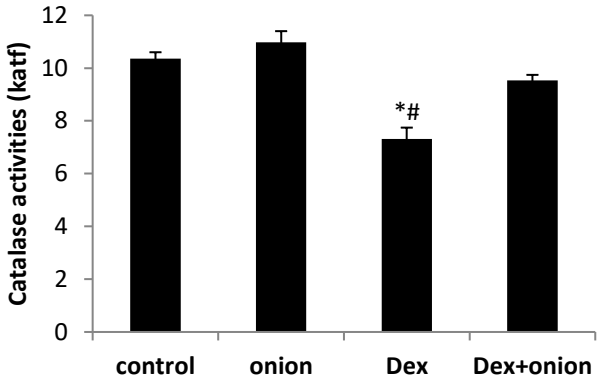

Figure 3:
Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on liver catalase enzyme activity of a male offspring of Wistar rats
*p<0.05 significantly different from control, #p<0.05 significantly different from Dex+onion group n=5

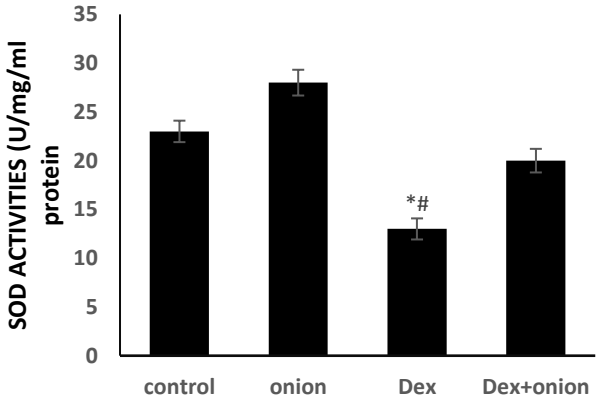

Figure 4:
Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on liver Superoxide dismutase (SOD) enzyme activity of a male offspring of Wistar rats
*p<0.05 significantly different from control, #p<0.05 significantly different from Dex+onion group n=5

Table 2:
Effects of maternal dexamethasone administration and consumption of onion mixed feed during lactation on lipid profile

	Total Cholesterol (mg/dl)	Triacylglyrol (md/dl)	HDL-Cholesterol (mg/dl)	LDL-Cholesterol (mg/dl)
Control	79.67±6.78	71.28±7.33	34.28±3.36	30.14±3.70
Onion	76.97±5.78	79.28±6.43	33.19±4.38	27.98±3.72
Dex	130.0±5.01*#	130.71±5.88*#	5.36±2.039*#	98.49±7.42*#
Dex+Onion	91.33±2.055	94.37±3.68	17.19±3.65*	52.74±5.38*

*p<0.05 significantly different from control, #p<0.05 significantly different from Dex+onion group n=5

DISCUSSION

This study examined the effects of consumption of onion mixed feed on lipid profile and oxidative stress-induced in the liver of a male offspring by maternal dexamethasone administration during lactation in Wistar rats.

The results showed that exposure to 100µg/kg body weight dexamethasone early in postnatal life significantly increase the serum total cholesterol level in rats. In addition, serum TAG follows a similar pattern. Administration of dexamethasone significantly raised the serum level of LDL-C. It has been previously shown that glucocorticoids decrease the concentration of LDL-C receptors on hepatocytes (Rainey et al., 1992) leading to higher LDL-C levels. Glucocorticoid administration leads to hypertriglyceridemia through increased production and secretion of very-low-density lipoprotein (VLDL) from the liver (Brindley, 1995). However, HDL-C was significantly reduced by maternal dexamethasone treatment during lactation.

This result is in line with epidemiology report in human population that prenatal exposure to glucocorticoids can lead to subsequent development of hyperlipidemia and other cardiometabolic diseases (Drake et al., 2005). According to Drake et al., 2005, this association appears to be independent of the adult lifestyle risk factors. In explaining this, it has been proposed that a stimulus or insults acting during critical periods of growth and development permanently alters tissues structure and function, a phenomenon termed "fetal programming" (Drake et al., 2005). Indeed, evidence from both human and animal studies suggests that adult pathophysiology can be induced by manipulating the environment during development (Barker, 1998). Consumption of 30 % onion mixed diet significantly reduced the serum total cholesterol and TAG when compared with control. Meanwhile it increased the HDL-choleterol level when compared with dexamethasone administered group. These results are in agreement with the findings of Hussein et al. (2007), who reported that onion and garlic oils reduced cholesterol and triglyceride level in rats. In a clinical study of alimentary hyperlipidemia, onion and onion essential oil prevented fat-induced increases in serum cholesterol (Beier et al., 1990).

Results from this study show that maternal dexamethasone administration during lactation significantly reduced the antioxidant enzyme catalase and SOD in the liver and raised the level of lipid peroxidation. Increase lipid peroxidation with reduced antioxidant enzymes level are indicators of oxidative stress (Schafer and Buettner, 2001). In humans, oxidative stress is thought to be involved in the development of many diseases or may exacerbate their symptoms (Peter, 1989). Consistent with these findings, is the report that oxidative stress may be especially pronounced with prolonged glucocorticoids exposure (Whitworth et al., 2001). Patients with Cushing syndrome may have increased nitrotyrosine levels (a measure of increased oxidative stress) in vascular tissue and decreased brachial artery reactivity (Iuchi et al., 2003).

It is therefore possible that the increase in metabolic imbalances observed in these rats is secondary to increase oxidative stress in the liver since the liver is the major metabolic organ. However, consumption of 30% onion mixed diet significantly increase the level of the antioxidant enzyme catalase, although lipid peroxidation was still higher compared to control. Several studies have demonstrated that dietary quercetin (a major constituent of Onion) enhanced the antioxidant defense system by upregulating antioxidant enzymes (Nagata et al., 1999; Javadzadeh et al., 2009).

In conclusion, findings from this study suggest that maternal consumption of 30% onion mixed diet may ameliorate the metabolic alteration as a result of maternal dexamethasone exposure during lactation in the male offspring of Wistar rats.

Acknowledgment:
The author acknowledged the support of the technical staff of the Department of Physiology, Cross River University of Technology, Okuku campus.

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