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Research article

Allium cepa Linn juice protect against alterations in reproductive functions induced by maternal dexamethsone treatment during lactation in male offspring of Wistar rats

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ABSTRACT

Treatment with dams with dexamethasone during lactation has been reported to induce oxidative stress in the testis of the offspring. *Allium cepa L* (Red Onion) is known to be a potent free radical scavenger. The protective role of *Allium cepa* against oxidative stress induced in testis following treatment with dexamehasone during lactation in Wistar rats was assessed. Twenty female rats were assigned into four groups (n = 5) during lactation and they were treated as follows: Group 1 serve as Control (distilled water), Group 2, 3, and four were admistered dexamethasone (60 μg/kg), *Allium cepa* (5 ml/kg) and dexamethasone + *Allium cepa* respectively. Testicular descent, pubertal age, sperm quality indices, and serum hormonal profile were assessed as indices of reproductive function. Testicular malondialdehyde (MDA) reduced glutathione (GSH) as well as superoxide dismutase (SOD) and catalase activities were assessed as measures of oxidative stress. Results obtained showed that dexamethasone caused significant ($P < 0.05$) reduction in testes weights, indices of sperm quality, serum testosterone, FSH, LH levels and testicular antioxidant enzyme activities. There was significant delay ($P < 0.05$) in days of testes descent, preputial separation and increase in testicular MDA. However, maternal treatment with *Allium cepa Linn* juice significantly ($P < 0.05$) improved both indices of reproductive function and testicular antioxidant enzymes. These findings suggest that *Allium cepa Linn* has a protective effect against testicular oxidative stress and reproductive dysfunction following treatment of dams with dexamethasone during lactation.

1. Introduction

Epidemiological reports in humans and experimental results from laboratory animals show that adverse intrauterine and early postnatal life conditions alter adult phenotypes and predispose the exposed individuals to lifelong development of cardiovascular, metabolic and reproductive disorders (Drake et al., 2005, 2007; Jeje et al., 2016).

The aetiology of many cases of reproductive dysfunction has been traced to adverse maternal environment (Barker, 2004). Available information points to a significant role of glucocorticoids in tissue programming. Glucocorticoids are growth inhibitory and they affect the development of all tissues and organ systems most at risk of postnatal alteration due to impairment in fetal growth (Fowden and Forhead, 2004). Normally, glucocorticoid levels are maintained within physiological range by a number of factors including the acitivities of 11β hydroxysteroid dehydrogenase type 2 (11βHSD-2). However, maternal glucocorticoid levels may rise due to; increased maternal stress, impaired activity of 11βHSD-2 and administration of dexamethasone or other synthetic glucocorticoids to achieve organ maturation in threatening preterm delivery and for treatment of medical conditions that are not specific to pregnancy such as asthma (Singh et al., 2012).

Dexamethasone is a common synthetic glucocorticoid drug with about 25 folds more glucocorticoid activity than endogenous cortisol produced by the adrenal glands (Tegethoff et al., 2009). Reports have shown that in rodents and other mammals including non-human primates, glucocorticoid overexposure resulting from maternal stress, impaired activity of 11βHSD-2 or treatment with dexamehasone during lactation may reduce growth rate and affect the development of reproductive structures (Jeje et al., 2016). It has been suggested that maternal treatment with dexamethasone during lactation may increase the susceptibility of testicular and epididymal tissues to oxidative stress (Jeje et al., 2017). Excess glucocorticoids reduce the activities of the

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antioxidant enzymes: superoxide dismutase, catalase, and glutathione peroxidase; both *in vivo* and *in vitro* (Zafir and Banu, 2009). The presence of high level of testicular reactive oxygen s may be linked with lipid peroxidation of the spermatozoa outer membrane which may lead to loss of motility (Urata et al., 2001), decrease sperm-oocyte fusion capacity (Aitken et al., 1993) and increased chromatin damage (Aitken and Krausz, 2001). It is therefore crucial for the male reproductive system to be well guarded against oxidative injury (Zubkova and Robaire, 2004).

Allium cepa L (Red Onion) is a natural plant commonly used as a food condiment and spice in cooking. *Allium cepa Linn* contains antioxidants such as glutathione, selenium and vitamin C. It also contains flavonoids such as quercetin and isorhamnetin (Markham, 1982). These antioxidant properties enable *Allium cepa Linn* to act as a free radical scavenger (Khaki et al., 2009; Lee et al., 2012). Studies have elucidated the beneficial effect of *Allium cepa Linn* on the reproductive function. Previous works have reported a decrease in epididymal malondialdehyde (MDA) level in rats treated with *Allium cepa L* juice (Ige and Akhigbe, 2012; Khaki et al., 2012). Ola-Mudathir et al. (2008) also suggests that the protective role of *Allium cepa L* in cadmium-induced testicular oxidative damage and sperm toxicity is possibly by reducing lipid peroxidation and improving the antioxidant status in rats.

Therefore, this study was carried out to investigate the possible protective role of *Allium cepa Linn* on testicular oxidative stress and reproductive toxicity in male offspring of lactating Wistar rat dams treated with dexamethasone.

2. Materials and methods

2.1. Drug

Dexamethasone-BP (DEX) tablets (Xasthen®, Jiangsu Penyao Pharmaceuticals Ltd, China) was suspended in distilled water in a dose of 60 μg/kg.

2.2. Collection and preparation of Allium cepa Linn. juice

Allium cepa Linn. juice was prepared according to the method of Ola-Mudathir et al. (2008). The Kano Red Creole variety of fresh *Allium cepa* bulbs was obtained. It was identified at the herbarium of Botany Department, University of Ibadan and National Institute of Horticultural Studies (NIHORT), Ibadan. The fresh (100 g) *Allium cepa* bulbs were washed, cut into small pieces and homogenized in a blender. The resultant slurry was filtered and the filtrate was used. The *Allium cepa* bulb extract was administered to the rats with the aid of a flexible oral gavage tube throughout the course of the study. Fresh juice was prepared daily every morning.

2.3. Experimental animal

Twenty virgin female (180–200 g) and ten male Wistar rats (200–250 g) (12 weeks of age) were obtained from the Central Animal House, College of medicine, University of Ibadan. The animals were housed in well ventilated cages with access to adequate rodent's feed and water *ad libitum*. Acclimatization took place for two weeks. Female rats were mated overnight during their proestrous phase with proven male breeders in ratio 2:1 (female to male). After mating had been established, female rats were randomly divided into four groups of five animals each and were treated during lactation (Table 1). Parturition was allowed to occur naturally and maternal dexamethasone administration commenced on Postnatal Day (PND) 1. Litter size was standardized to six pups per litter. All animal experiments were conducted in accordance with the International Ethical Norms on Animal Care and Use as contained in NIH publication/85-23, revised in 1985. The study was approved by Ethical committee on the use of laboratory animals, Department of Physiology, Cross River University of Technology, Calabar, Nigeria.

Table 1. Experimental groups.

Group	Treatment
Control	Distilled water (5 ml/kg body weight)
Allium cepa L only	5 ml/kg Allium cepa L juice (Lee et al., 2012).
Dex only	60 μg/kg Dexamethasone
Dex + *Allium cepa L*	60 μg/kg Dexamethasone +5 ml/kg *Allium cepa L* juice.

n=5.

2.4. Experimental design

Treatment lasted for 21 days PND 1–21. The male pups were weaned on PND 28. Testis descent and preputial separation were monitored starting from PND 21 and PND 42 respectively. Body weight was measured at PND 56 (8 weeks) and PND 84 (12 weeks) to examine the progression in growth rate. The animals were sacrificed under Sodium thiopentone anesthesia (50 mg/kg, i. p.) at the end of PND 96 (14 weeks) (Pereda et al., 2006). Blood samples were collected via cardiac puncture and serum was obtained for hormonal analysis. The testis was harvested, weighed and placed in phosphate buffer solution for oxidative status analysis.

2.5. Serum preparation and evaluation of serum testosterone, FSH, LH and corticosterone

Blood was obtained via cardiac puncture (PND 96) into polythene tubes and allowed to clot for 1 h. The blood samples were centrifuged at 3000 rpm for 10 min. Serum was aspirated and stored at 4 °C. Serum testosterone, FSH, LH and corticosterone were assayed using enzyme-linked immunosorbent assay (ELISA) kits (Fortress Diagnostics, UK) according to the protocol in respective manufacturer's manual.

2.6. Evaluation of markers of oxidative stress

The testis was harvested, weighed and homogenized in phosphate buffer solution for oxidative status analysis. The homogenate was centrifuge at 10,000 rpm in a cold centrifuge. The supernatant was aspirated into a plane tube, stored at 4 °C until use. The assays were done within 48 h of collecting the sample. Level of Lipid peroxidation was evaluated by method of Buege and Aust (1978). Catalase activity was evaluated by method of Sinha (1972). The SOD activity was evaluated by method of Misra and Fridovich (1972). The GST activity was evaluated by the method of Habig et al. (1974). Protein estimation was done by method of Lowrey et al. (1951). GSH content was evaluated by the method of Beutler et al. (1963).

2.7. Evaluation of sperm characteristics

Sperm analysis was done by microscopy as previously described (Raji and Bolarinwa, 1997; Raji et al., 2003). Epididymal spermatozoa were obtained by mincing the epididymis with anatomical scissors in 5ml of pre-warmed physiological saline and incubated for 2 min. An aliquot of this solution was placed in improved Neubauer counting hemocytometer and motile sperm were counted by using microscope at 400× magnification. Non-motile sperm numbers were first determined, followed by counting of total sperm. Sperm motility was expressed as a percentage of motile sperm of the total sperm counted. Percentage of morphologically abnormal spermatozoa was determined by preparing two slides with Hemaoxylin and Eosin stains for morphological examination of live–dead ratio. A total of 400 sperm cells were counted on each slide under light microscope at 400× magnifications. Sperms with abnormal head and/or tail were considered abnormal. Sperm motility, viability and count were done immediately and quickly. A sperm viability test was done using eosin/negrosin stain (containing 1 g of Eosin and 4 g of Negrosin in 100

ml phosphate buffer). A drop of the epididymal fluid was placed on the slide and two drops of the stain was added. A thick smear was made from this and dried. After this, the slide was studied under light microscope using 40x objective lens. The unstained spermatic cells were considered as live sperms while the stained ones was considered as dead sperm. A minimum of 100 spermatic cells (both stained and unstained) was counted and an average was taken for the percentage live sperm.

2.8. Statistical analysis

Data were presented as mean ± SEM and Anova was used for comparison of results, followed by Tukey's post-hoc test to compare the differences in means of the different treatment groups. $P < 0.05$ was considered significant. The data analysis was done with the use of Graphpad Prism Version 7.0 for Windows.

3. Results

3.1. Effects of maternal administration of dexamethasone and Allium cepa L juice during lactation on the progressive body weights in the male offspring of Wistar rats

The result shows that at postnatal week (PNW) 1, there were no significant differences in the body weights of the male pups in all the groups compared with the control. At PNW 4 and PNW 8, the Dex group had significantly ($P < 0.05$) lower weights than control but there were no significant differences in the body weights of the *A. cepa L* and Dex + *A. cepa L* groups compared with the control. At PNW12, the body weights of the Dex and Dex + *A. cepa L* groups significantly ($P < 0.05$) increased compared with the control group but there was no significant difference in the body weight of *A. cepa L* group when compared with the control (Figure 1).

3.2. Effects of maternal administration of dexamethasone and Allium cepa L juice during lactation on the caudal epididymal sperm characteristics in the male offspring of Wistar rats

The results show that sperm motility in the Dex group was significantly ($P < 0.05$) lower compared with the control. There were no significant differences in sperm motility in the *A. cepa L* and Dex + *A. cepa L* groups compared with the control. The sperm motility in the *A. cepa L* and Dex + *A. cepa L* groups were significantly ($P < 0.05$) higher when compared with the Dex group (Figure 2a).

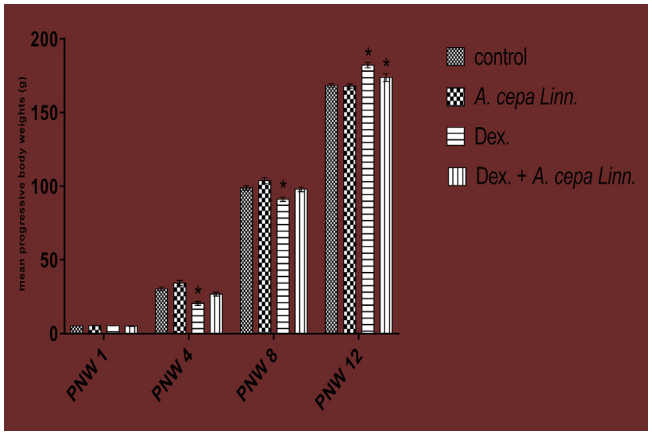

Figure 1. Progressive body weight of male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* PNW: Postnatal week, Dex: Dexamethasone, *A. cepa L: Allium cepa L.* *$P < 0.05$ when compared with the control group.

Sperm viability in the Dex group was significantly ($P < 0.05$) lower compared with the control. There were no significant differences in sperm viability in the *A. cepa L* and Dex + *A. cepa L* groups compared with the control. The sperm viability in the *A. cepa L* and Dex + *A. cepa L* groups were significantly ($P < 0.05$) higher when compared with the Dex Group (Figure 2b).

Pups from the mothers treated with Dex had significantly ($P < 0.05$) lower sperm count compared with the control. There were no significant differences in sperm count in the *A. cepa L* and Dex + *A. cepa L* groups compared with the control. The sperm count in the *A. cepa L* and Dex + *A. cepa L*groups were significantly ($P < 0.05$) higher when compared with the Dex Group (Figure 2c).

3.3. Effects of maternal administration of dexamethasone and Allium cepa L juice during lactation on pubertal timing in the male offspring of Wistar rats

The results show that there was no significant difference in the day of testes descent in pups from the *A. cepa L* group compared with the control. The day of testes descent in pups from the Dex group and Dex + *A. cepa L* groups were significantly ($P < 0.05$) delayed compared with the control. The day of testes descent in pups from the *A. cepa L*, and Dex + *A. cepa L* groups were significantly earlier compared with the the Dex group (Figure 3a).

In addidion, preputial separation occurred significantly earlier ($P < 0.05$) in pups from the *A. cepa L* group compared with the control while it was significantly later ($P < 0.05$) in pups from Dex group and Dex + *A. cepa L* group compared with the control. Preputial separation occurred significantly earlier in pups from the *A. cepa L*, and Dex + *A. cepa L* group when compared with the Dex group (Figure 3b).

3.4. Effects of maternal administration of dexamethasone and Allium cepa L juice during lactation on the serum hormone level in the male offspring of Wistar rat

The results show that there was a significant ($P < 0.05$) decrease in the serum FSH level in the pups of Dex and Dex + *A. cepa L* groups when compared with the control. There was a significant ($P < 0.05$) increase in the serum level of FSH in the pups of *A. cepa L* when compared with the Dex group (Figure 4a). There was also a significant ($P < 0.05$) decrease in the serum level of LH in the Dex group compared with the control (Figure 4b).

There was a significant ($P < 0.05$) decrease in the serum level of testosterone in the pups of Dex and Dex + *A. cepa L* groups when compared with the control group. In addition, there was also a significant ($P < 0.05$) increase in the serum level of testosterone in the pups of *A. cepa L* group compared with the control group. There was also a significant ($P < 0.05$) increase in the serum testosterone level in the pups of *A. cepa L* and Dex + *A. cepa L* groups when compared with the Dex group (Figure 4c).

Serum corticosterone level in the pups of Dex group was significantly ($P < 0.05$) increased when compared with the control group. The serum corticosterone level in the pups of *A. cepa L* group significantly ($P < 0.05$) decreased when compared with the Dex group (Figure 4d).

3.5. Effects of maternal administration of dexamethasone and Allium cepa L juice during lactation on testicular makers of oxidative stress in the male offspring of Wistar rats

The result shows that there were significant ($P < 0.05$) decrease in the testicular SOD activities in the Dex group when compared with the control. Administration of Alllium cepa L. juice significantly ($P < 0.05$) increases the SOD level when compared with the control and Dex groups (Figure 5a).

There was a significant ($P < 0.05$) decrease in the testicular catalase activity in the Dex group compared with the control. Also, the testicular

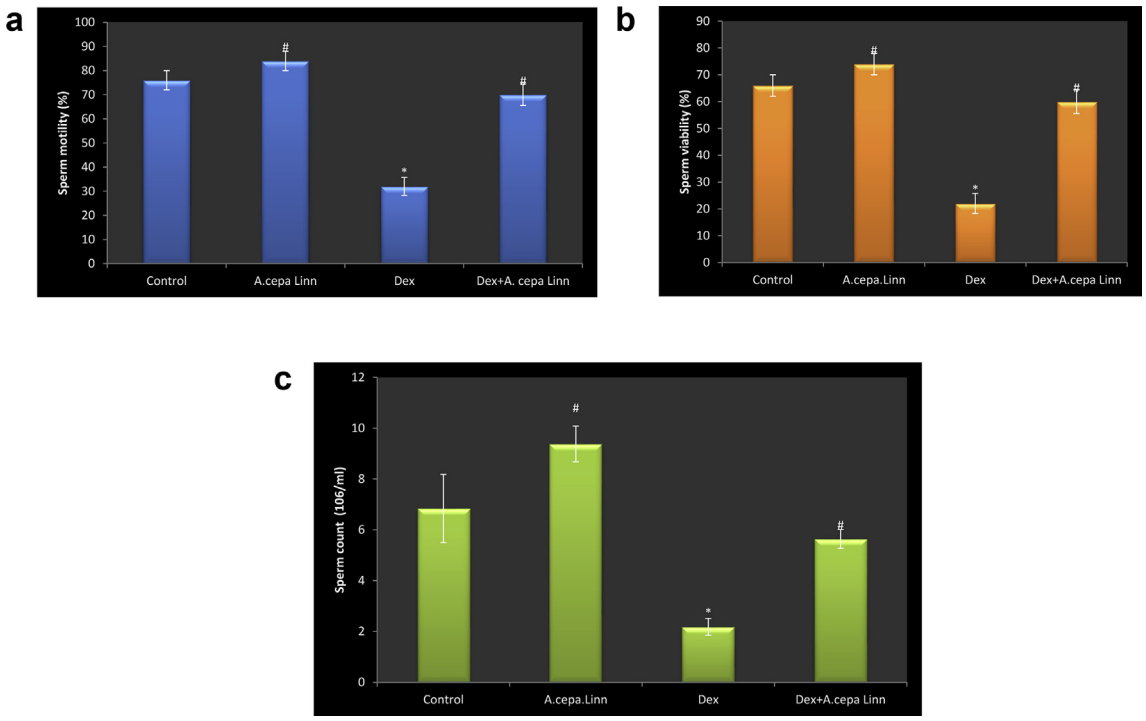

Figure 2. a: Caudal epididymal sperm motility of adult male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* b: Caudal epididymal sperm viability of adult male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* c: Caudal epididymal sperm count of adult male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* *P < 0.05 when compared with the control group. #P < 0.05 when compared with the Dex group.

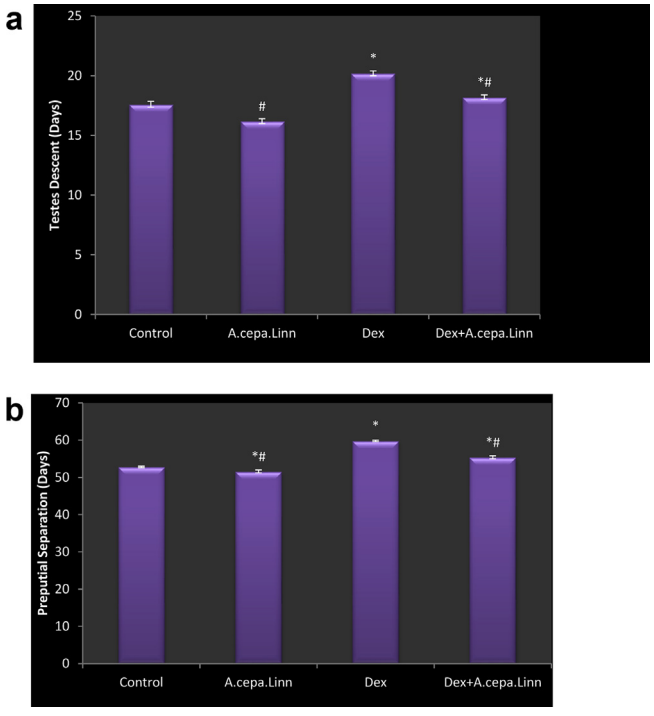

Figure 3. a: Day of testes decent in adult male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* b: Day of preputial separation in adult male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.**P < 0.05 when compared with the control group. #P < 0.05 when compared with the Dex group.

catalsae activity in the pups of *A. cepa L* group was significantly (P < 0.05) increased when compared with the Dex group (Figure 5b).

There were significant (P < 0.05) increases in the testicular GPx activity in all the treated groups compared with the control. The testicular GPx activities in the pups of *A. cepa L* and Dex + *A. cepa L* groups were significantly (P < 0.05) raised when compared with the Dex group (Figure 5c).

There was a significant (P < 0.05) increase in the testicular GSH activity in the pups of *Allium cepa L* group compared with the control and Dex groups (Figure 5d).

Moreover, there were significant (P < 0.05) increase in the testicular level of MDA in the Dex and Dex + *A. cepa L* groups when compared with the control. This was significantly (P < 0.05) decreased in following administration of *A. cepa L* when compared with the control group.

3.6. Effects of maternal administration of dexamethasone and Allium cepa Linn. juice during lactation on testes weight per 100g body weight in the male offspring of Wistar rats

The result shows that there was a significant decrease in the relative testes weight of pups in the Dex. + *Allium cepa Linn* group compared with the control. There were no significant differences in the relative testes weight of pups in the *Allium cepa Linn.* and Dex groups compared with the control (Figure 6a). Meanwhile in the epididymis, the relative weight of the epididymis was not significantly different (Figure 6b).

4. Discussion

Manipulation of hormonal status through administration of glucocorticoids is known to have a significant impact on redox physiology; notably generating oxidative stress. Several studies in experimental animals have reported that oxidative stress and interference with the reproductive axis occur following prolonged exposure to glucocorticoids (Iuchi et al., 2003; Dong et al., 2004; Hardy et al., 2005; Kapoor et al.,

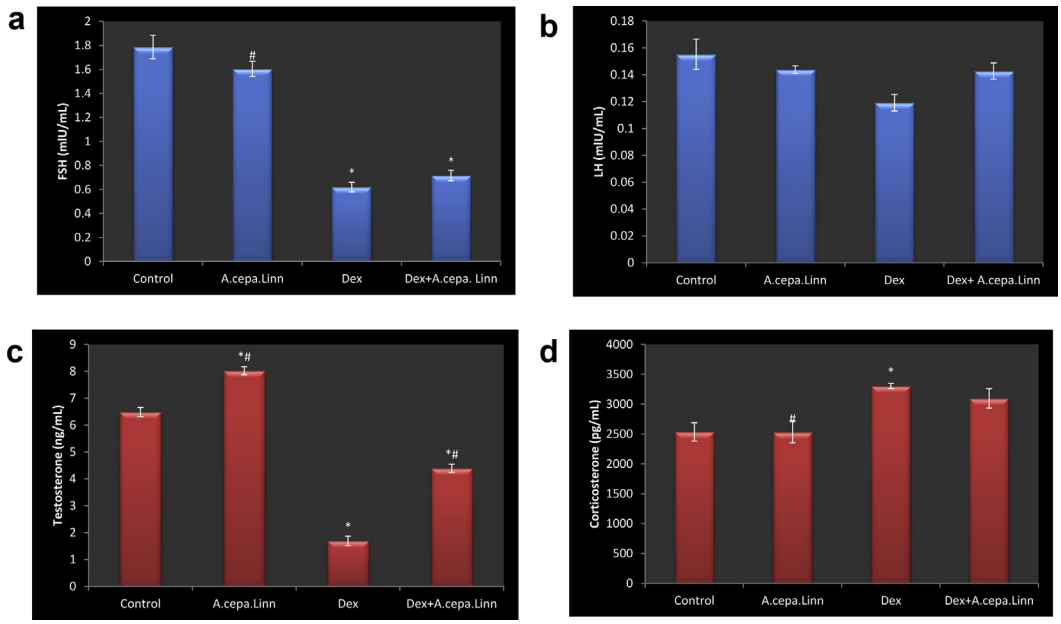

Figure 4. a: Follicle Stimulating Hormone (FSH) levels of adult male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* b: Luteinizing Hormone (LH) level of adult male offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* c: Testosterone levels of adult offspring of lactating Wistar rats treated with dexamethasone and *Allium cepa L.* d: Corticosterone level of adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* *P < 0.05 when compared with the control group. #P < 0.05 when compared with the Dex group.

2006; Jeje et al., 2017). This study was designed to examine the effects of maternal treatment with *Allium cepa L.* juice on maternal dexamethasone-induced testicular oxidative status and the reproductive axis in the male offspring of Wistar rats.

Body weight assessment is among the initial observations in the examination of systemic toxicity induced by any chemical or drug (Mukherjee et al., 2014). The result of this study showed that there were no significant differences in the body weights of the male pups in all the groups compared with the control at postnatal day one (PND1); that is, baseline body weights prior to maternal administration was not significantly different. Dex group had the slowest progressive body weight at PNW 4 and PNW 8 until after 12th week of postnatal life when their body weight outshot those of other groups. This was in accordance with previous reports that early life dexamethasone exposure negatively affects somatic growth (Wang et al., 2010). Similarly, Jeje et al. (2016) reported that maternal treatment with dexamethasone during the first two weeks of postnatal life and throughout lactation significantly reduced body weight of offspring at puberty. It was suggested that retardation of body weight may be linked to increased corticosterone level in offspring of dams treated with dexamethasone during lactation. Because corticosterone is a catabolic hormone, excessive corticosterone increases the breakdown of protein in tissues except liver (Aron et al., 2007). This may leads to rise in tissue catabolism or excess breakdown of protein (Leitch et al., 1999; Neal et al., 2004). Consequently, leading to muscle wasting and muscle mass reduction, hence a loss of weight.

As the testes develop, they move within the abdominal cavity and gradually descend into the *scrotum.* The temperature of the scrotum is maintained at about 35 ° C— about 2 °C below normal body temperature. This cooler temperature is needed for spermatogenesis. When testes fail to descend, they remain within the abdomen where the temperature does not favour spermatogenesis, thus leading to severely altered sperm characteristics and ultimately, infertility. The process of testes descent is androgen dependent. Preputial separation which is the separation of the prepuce from the glans penis, has been shown to be androgen dependent also and it occurs around the time of puberty in rats. It is an easily determined external sign of sexual development in male rats and may be used as an index of change in peripubertal androgen secretion. Maternal dexamethasone administration significantly delayed testes descent and preputial separation; however, administration of *A. cepa L* to lactating dams enhanced testes descent and preputial separation.

The result from this study also showed a significant decrease in all sperm characteristics in the Dex group compared with the control group. It was observed from the results that pups from mothers treated with dexamethasone had lower epididymal sperm count. Lower epididymal sperm count may be an index of infertility in male. The significant decrease recorded was in accordance with a previous study (Jeje et al., 2016). The significant reduction in sperm profile observed may be due to testicular oxidative damage caused by the increased ROS generation due to the prolonged exposure to dexamethasone (Jeje et al., 2017). Lipid peroxidation (LPO) is a marker of oxidative damage, which plays an important role in the toxicity of many xenobiotics. MDA is a stable end product of LPO and can be used as an indirect assessment of the cumulative LPO. Mammalian spermatozoa are susceptible to LPO due to the rich polyunsaturated fatty acids in the plasma membrane and a very low concentration of cytoplasmic antioxidants (Aitken et al., 1993). High level of LPO can results to reduction in the sperm motility, probably by a rapid loss of intracellular ATP leading to axonemal damage, decreased sperm viability, and increased midpiece abnormal morphology with deleterious effects on sperm capacitation and acrosome reaction (Lenzi et al., 1993). This consequently affects testicular steroidogenesis and spermatogenesis. The *A. cepa L* group had the highest sperm motility, sperm viability and sperm count followed by the control group. The increased sperm motility, sperm viability and sperm count in the *A. cepa L* group can be attributed to the antioxidant property ascribed to *A. cepa Linn* (Ola-Mudathir et al., 2008). Consumption of *A. cepa L* juice significantly improved the sperm characteristics in the Dex administered group. The *A. cepa L* was able to attenuate the deleterious effect of Dex probably due to its antioxidant property and metal chelating activity on the free radicals generated from the oxidative stress induced by dexamethasone.

The activities of SOD, Catalase, GPx, GSH and MDA were evaluated to assess level of induction of oxidative stress in the testis of the offspring following treatment with dexamethasone and the *A. cepa L* during lactation. The testicular activities of SOD, Catalase and GPx were significantly decreased in the pups of mothers treated with Dexamethasone when compared with the control. There is also a reduction in the

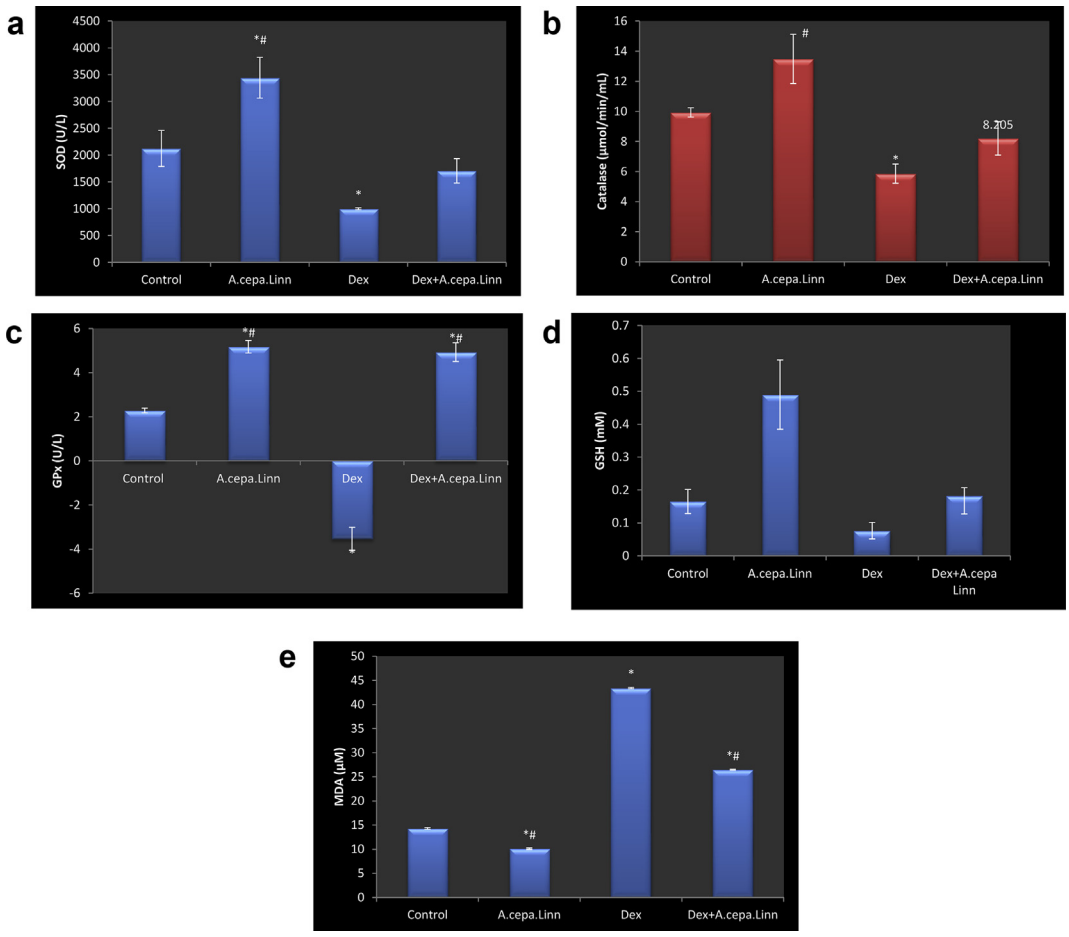

Figure 5. a: Testicular superoxide dismutase (SOD) activity in adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* b: Testicuar catalase activity in adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* c: Testicular glutathione peroxidase (GPx) activity in adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* d: Testicular glutathione (GSH) activity in adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* e: Testicuar malondihaldehyde (MDA) level in adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* *P < 0.05 when compared with the control group. #P < 0.05 when compared with the Dex group.

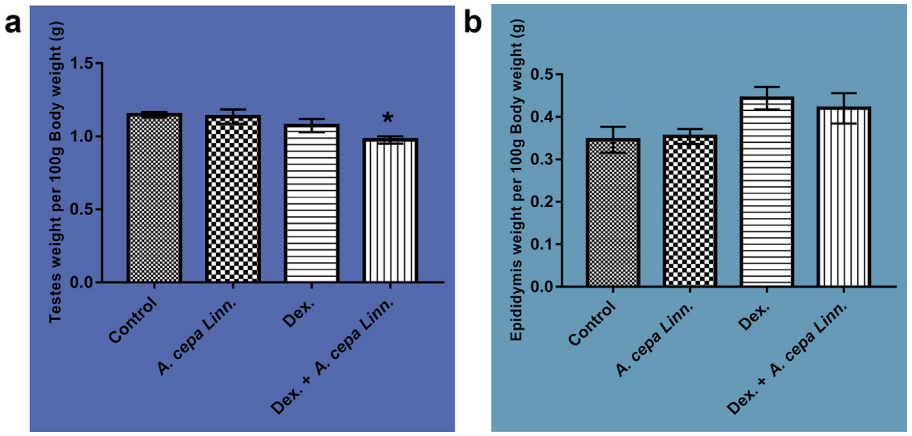

Figure 6. a: Testicular weight per 100g body weight in adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* b: Epididymal weight per 100g body weight of adult male offspring of lactating Wistar rat treated with dexamethasone and *Allium cepa L.* *P < 0.05 when compared with the control group.

testicular activity of GSH in the pups of Dex treated group but the decrease was not significant when compared with the control. The reduction in the testicular activities of SOD, Catalase, GPx and GSH are in agreement with the findings of Mukherjee et al. (2014).

The key mechanism by which ROS induced sperm damage is considered to be through lipid peroxidation of the sperm membrane which may lead to infertility (Agarwal et al., 1994). This phenomenon leads to cell death through damage on the cellular plasma membrane. Malondialdehyde is a stable end product of lipid peroxidation. Elevation in testicular MDA level is a sign of lipid peroxidation. Therefore, an increase in MDA levels has deleterious effects on sperm function and leads to infertility (Hsieh et al., 2006). The result of this study shows a

significant increase in the testicular level of MDA in the pups of mothers treated with dexamethasone when compared with the control. This rise in the testicular MDA level may be attributed to the prolonged exposure to dexamethasone, enhancing excess production of ROS in the testes. This causes more lipid peroxidation of the testicular cell membranes and thus, increases the level of MDA. Treatment of dams with *A. cepa L* significantly reduced the testicular MDA level in the pups. This suggests the potency of *A. cepa L* in attenuating the oxidative damage caused by dexamethasone.

Delayed puberty may occur due to either alteration in the androgenic system or disruption of the hypothalamic-pituitary-gonadal system. Studies have shown that glucocorticoids treatment delays the first spermatogenic cycle which are associated with the onset of puberty (Consten et al., 2001). These disorders may remain throughout the lifespan after period of apparent normality is restored (Seck, 2001; O'Brien et al., 2008). In this study, the result showed that serum FSH concentrations in the Dex and Dex + *A. cepa L* groups were significantly lower when compared with the control. Similarly, there was reduction in LH concentration in the Dex group compared with the control. The reduction in FSH and LH levels observed in these groups may be as a result of Dexamethasone-induced generation of ROS in the pituitary as previous study have shown the presence of glucocorticoids receptor in the pituitary gland (Banjanin et al.,2004; Sloboda et al., 2007). There were no significant differences in the LH concentration in male offspring of mothers treated with *A. cepa L* and Dex + *A. cepa L* when compared with the control. The serum LH concentration observed in the Dex + *A. cepa L* demonstrates the ameliorative potency of *A. cepa L* on the deleterious effect of the Dexamethasone. One of the indicators of reproductive toxicity due to exposure to chemicals is reduction in the level of testosterone (Yoshida et al., 2002). Testosterone is essential for the maturation and maintenance of the structure and function of the male accessory sex glands. Moreover, insufficiency of this hormone hinders spermatogenic function (Brookfor and Blake, 1997). The present result showed a significant reduction in the serum concentration of testosterone in the Dex group when compared with the control group. This was in agreement with previous findings by Sadi-Guettaf and Hadj-Bekkouche (2014) and Jeje et al. (2016) who demonstrated the reduction in serum testosterone in the male rats following maternal exposure to Dex. Results from this study also showed a significant increase in the serum testosterone concentration of male offspring from mothers treated with *A. cepa L* when compared with the control. This was in accordance with studies by Khaki et al. (2009, 2012). The serum testosterone concentration of male offspring from mothers treated with *A. cepa L* and Dex + *A. cepa L* group significantly increased when compared with the Dex group. The result of this study shows higher concentration of serum corticosterone in the pups of Dex group when compared with the control. This may be attributed to the altered HPA activity in the dams which might have probably programmed stress-like secretion of corticosterone by the adrenal glands of the offspring. In addition, the serum corticosterone level in the Dex + *A. cepa L* is lower compared with the Dex group.

The findings from this study suggest that *Allium cepa Linn* juice has a protective effect against testicular oxidative stress and reproductive dysfunction following treatment of dams with dexamethasone during lactation.

Declarations

Author contribution statement

Jeje S.O: Conceived and designed the experiments; Analyzed and interpreted the data; Perform the experiments; Wrote the paper.

Adegbite L.O: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Akindele O.O, Kunle-Alabi O.T: Performed the experiments; Contributed reagents, materials, analysis tools or data.

Raji Y: Conceived and designed the experiments; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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