Effect of Noise Stress on Pituitary Gonadal Axis in Albino Rats

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Abstract: Loud noise is an environmental stressor, not only affects the auditory apparatus but also other body functions. The effect of loud noise strss on sexual hormones and gonadal histology were reported in this study.
Male and female albino rats weighting 150–200 grams were exposed to 100 dB of noise for 6 hours daily for 30 days. The serum sexual hormones (testosterone, LH, FSH, progesterone, estradiol and prolactin) levels were measured and testicular and ovarian histological sections were taken for microscopic study. A significant reduction in sexual hormones levels with moderate abnormal histological changes in testes and ovaries were detected. Thus, the noise may be acts as severe deteriorative stress on other organs in the body.
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1. Introduction

Living organisms are exposed to potentially hazardous noise levels coming from the environment. Besides the direct effect on hearing, extra – auditory noise associated effects should be considered **(Uran *et al.,* 2010)**. Noise is partially responsible for reduced reproductivity and decrease in the number of fetuses of pregnant rats and had a lethal effect in mice embryos that were exposed to high frequencies of noise **(Archana and Namasivayam, 2000)**. Exposed of animals to loud noise stress restrict their movement and nutrition. The testosterone production was adversely affected by nutritional factors and water restriction, so noise stress, water stress, immobilization stress, nutritional stress, all affected on sex hormones and in turn produced change in the reproductive organs and glands **(Lue *et al.,* 2000).** The pituitary- gonadal response to nutriational stress would be a more sensitive index of abnormalities induced by protein calorie deficit in basal concentration of LH, FSH, or testosterone **(Faldikova *et al.,* 2001).** Glucocorticoid mediation of suppressed testosterone biosynthesis was also seen in male mice exposed to immobilization stress **(Dong *et al.,* 2004).** The influence of immobilization stress on testicular germ cell a poptosis was investigated in rats. Atransient increase in serum corticosterone and a transient decrease in serum testosterone were observed during each period of immobilization stress. Chronic immobilization stress provoked an incresse in serum corticosterone which caused the decline in testosterone concentration **(Sasagawa *et al.,* 2001).** Testosterone and follicular stimulating hormone suppression induced spermiation failure, this is may be due to the feedback action of testosterone on the hypothalamus **(Amanda and Beardsley, 2003).** In chronic noise exposed rats there was maturation arrest in the germ cells due to reduced testosaterone level and the epididymal sperms were agglutinated and the number of dead sperms was increased, also alterations in the normal testicular morphology associated with maturation arrest in the germinal cells **(Chandralekha, 2002).** The noise stress lead to accumulation of lipofuscin in mouse testes and subsequent decrease in testosterone production **(Ruffoli *et al.,* 2006).** A significant reduction in serum testosterone **levels** were noticed in noise exposed rats and the seminiferous tubules were shrunken so that there was a space between the septum and tubules. The maturation arrest in the germinal layers in some tubules and the basement membrane was broken and the germ cells sloughed into the interstitium and the sperms in the epididymis showed agglutination **(Chandralekha *et al.,* 2007)** Noise stress results in stimulation of adrenocorticotrophic hormone and increased corticosterone secreation with LH reduction and this may be one of pathophysiological mechanism involved in follicular cyst pathogenesis, thus, the stress disturb natural fertility through the inhibition of hypothalamic – pituitary-gonadal axis,so,decreased uterin receptivity through an ovarian - independent pathways **(Kondoh *et al.,* 2009).** Recent studies on reptiles have shown that a variety of stressors will induce a stress response with an increase in plasma corticosterone levels and this may affect on gonadal function, reproductive behavior pregnancy and egg – laying success **(Richard *et al.,* 2011*).***

2. Materials and methods

Mature albino rats (20 male and 20 female) weighting between 150 and 200 grams were obtained from the animal house of the faculty of Veterinary Medicine, Zagazig University. Animals were allowed

to acclimatize to laboratory conditions for 10 days before experimental manipulation, and fed ad libitum, during this time the female showed normal oestrus cycle phases by regular vaginal smears.

The animals were divided into 4 groups. The 1st and 2nd groups (10 male and 10 female respectively) were used as control groups and avoided any influence of noise stress. Whereas the 3rd and 4th groups (10 male and 10 female respectively) were exposed to noise stress 6 hours daily for 30 days.

Vaginal smears:

Vaginal smears taken from the female rats by vaginal washing were examined daily under light microscope for relative abundance of nucleated epithelial cells, cornified cells and leukocytes. Cycle with duration of 4-5 days were considered regular. The oestrus phase of the oestrus cycle was detected by the presence of cornified epithelial cells which increase in number and eventually predominat as the oestrus progress. The observation of cornified cells in the smears during a minimum of 10 serial days was defined as persistent vaginal cornification and considered to be an indication of follicular cystic development.

Noise-stress induction procedure:

When noise stress of any kined exceeds 90 dB, noise becomes a stressor **(Ramsey and Flanagan, 1982).** Noise was produced by two loud speakers mounted 40 cm a part on opposite sides of the cage (15 w) and driven by a white noise generator (range 0-26 KHz) installed (suspended) 30 cm above the cage. The noise level was set at an intensity of 100 dB uniformly throughout the cage and monitored by a sound level meter (RAT-M Model RE-120, Germany).

Sampling of blood:

After the end of the last exposure, the animals were sacrificed and about 5 ml of blood was collected from each rat and then centrifuged for 5 minutes at 5000 rmp. The collected sera were liquated and stored at–20ºC until used for estimating the hormonal levels.

The technique of Enzyme-Linked Immunosorbent Assay (ELISA) was used to determine the levels of testosterone, estradiol, progesterone, LH, FSH and prolactine hormone in serum specimens. The ELISA kits were supplied from Biocheck, Inc 323 Vintage Park Dr. Foster City, CA 94404. The ELISA test was detected in the Advanced Medical Laboratory in Veterinary Medicine, Zagazig University.

The obtained data were statistically analyzed by student's t-test for comparison according to **Selvin (1996).**

On the stipulated day after the collection of blood for hormonal assay, sections from testes and ovaries were taken for histopathological investigation according to the method of Raghavendra ***et al.*, (2003).**

3. Results

There was a high significant ($P < 0.01$) reduction in both serum LH and FSH levels and very high significant ($P < 0.001$) reduction in serum testosterone levels in noise exposed male albino rats (table 1), moreover, the testicular sections from these males showed a moderate reduction in the size of seminiferous tubules with focal degenerative and decrease of spermatogenic cells and diffuse hyperplasia of Leydig cells in the interstitium (photo 2 and 3), whereas, the serum of noise exposed female albino rats showed a high significant ($P < 0.01$) decrease in both LH and FSH levels and very high significant ($P < 0.001$) decrease in serum estradiol and progestrone levels (table 2), while, the ovarian sections from these females showed cystic follicles formed of cystically dilated follicles lined by granulose cells separated by normal ovarian stroma (photo 5 and 6).

Table (1): Effect of noise stress on serum testosterone, LH, FSH and prolactine hormones in male albino rats.

Groups	Hormones / Parameters	Testosterone (ng/ml)	LH (mlu/ml)	FSH (mlu/ml)	Prolactine (ng/ml)
Control	Mean ± SE	0.732 ± 0.03	6.01 ± 0.53	8.32 ± 0.52	4.95 ± 0.41
Treated	Mean ± SE	0.434 ± 0.024	4.63 ± 0.043	5.92 ± 0.59	5.06 ± 0.31
	% of change	- 40.7	- 22.96	- 28.8	+ 2.22
	P value	< 0.001**	< 0.01*	< 0.01*	> 0.05

* High significant

** Very high significant

Table (2): Effect of noise stress on serum estradiol, progesterone, LH, FSH and prolactine hormones in female albino rats.

Groups	Hormones / Parameters	Estradiol (pg/ml)	Progesterone (pg/ml)	LH (mlu/ml)	FSH (mlu/ml)	Prolactine (ng/ml)
Treated	Mean ± SE	16.15 ± 0.63	4.8 ± 0.049	9.566 ± 0.31	10.383 ± 0.35	18.00 ± 0.66
	% of change	- 41.73	- 44.33	- 28.93	- 26.29	+ 6.00
	P value	< 0.001**	< 0.001**	< 0.01*	< 0.01*	> 0.05

* High significant
** Very high significant

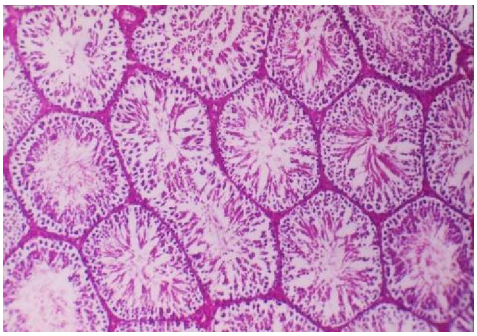

Photo (1): Normal testis
(Stained by H/E × 100)

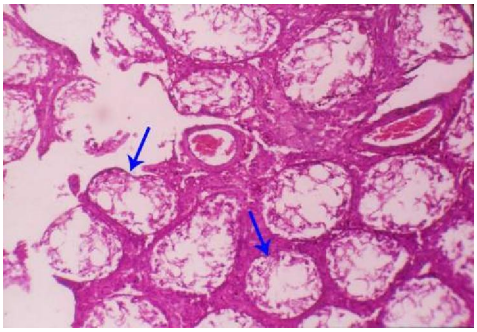

Photo (2): Noise exposed testis
(Stained by H/E × 100)

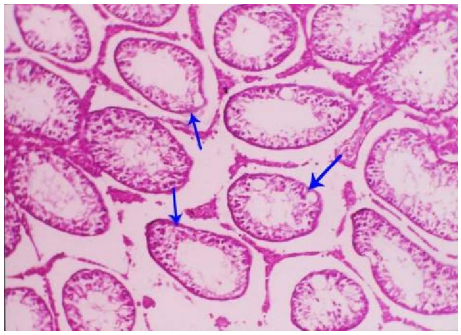

Photo (3):Noise exposed testis
(Stained by H/E × 100)

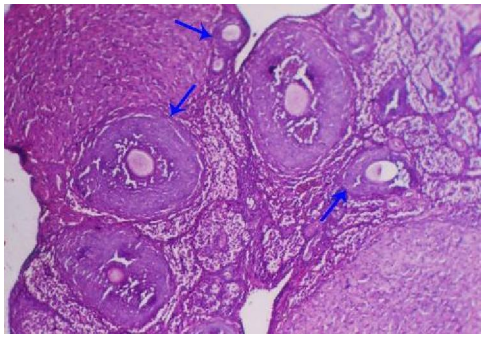

Photo (4): Normal ovary
(Stained by H/E × 100)

Photo (5):Noise exposed ovary
(Stained by H/E × 100)

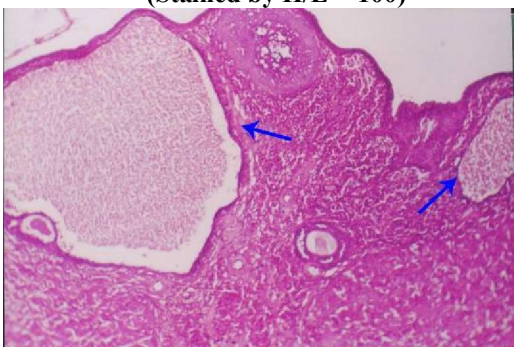

Photo (6):Noise exposed ovary
(Stained by H/E × 100)

4. Discussion

Of all types of environmental pollutants, noise is the most prevalent and insidious natural pollutant which causes deleterious physiological and structural effect. the present study revealed avery high significant (P <0.001) decrease in serum testosterone and a high significant (P < 0.01) decrease in LH and FSH levels after chronic exposure of adult male albino rats to noise stress, moreover, a testicular histoligocal changes were observed in the form of a moderate reduction in the size of semimiferous tubules with focal degeneration and decrease of spermatogenic cells and diffuse hyperplasia of Leydig cells in the interstitium. These results coincide with those of **Amanda *et al.,* (2003),** who reported that, leutinizing hormone acts on the testes and increases the plasma testosterone level. The follicular stimulating hormone controls the secreation of androgen- binding protein by Sertoli cells. The protein increases the concentration of testosterone in the seminiferous tubules for proper spermatogenesis. Testosterone and follicular stimulating hormone suppression induced spermiation failure. Moreover, the noise stress is thought to influence pituitary luteinizing hormone secreation indirectly through central neural pathways that regulate hypothalamic gonadotropin-releasing hormone release, as well as by direct effects of circulating adrenal glucocorticoids hormones on pituitary gonadotropes.

During stress, the hypothalamic-pituitary-adrenal axis is activated, the glucocorticoid secreation increases and consequently, circulating testosterone level are decreased via glucocorticoid receptors in leydig cell. There was maturation arrest in the germ cells due to reduced testosterone level. The leydig cell proliferation is likely to be a compensatory mechanism to increase testicular steroidogenesis trigged by testosterone insufficiency. The low testosterone production adversely affects the quality of ejaculates and subsequent fertility. The decrease in testosterone level is also associated with the marked reduction in epididymal sperm number **(Mylchreest *et al.,* 2002).**

The epididymal sperms were agglutinated in chronic noise exposure and the number of dead sperms was increased, so, alterations in the normal testicular morphology associated with maturation arrest in the germinal cells were found **(Chandralekha, 2002; Oakes *et al.,* 2002 and Ozguner *et al.,* 2005).** This was in support of previously established finding that administration of corticosterone cause production of free radical formation in the mitochondria of leydig cells and free radical generation is known to stimulate lipfuscin formation. Therefore, lifestyle and work environment involuing high level of noise exposure may be cause detrimental to testicular function **(Terman and Brunke, 2004 and Agarwal *et al.,* 2008).** Excessive glucocorticoid exposure have various adverse effects on testosterone production in testis, such as apoptosis of leydig cells, which are the site of testosterone production, by inhibiting the expression of steroidogenic enzyme glucocorticoid may be a regulator of spermatogenesis because glucocorticoid receptors are expressed in spermatogonia in boar testes and glucocorticoids initiate apoptosis **(Gao. *et al.,* 2003 and Claus *et al.,* 2005).** Glucocorticoids have adverse effects on steroidogenesis in testis, there is a need for a cortisol inactivation system in order to maintain normal androgen production in leydig cells **(Anderson *et al.,* 2011** and **Grissom and Bhatnagar 2011).** A variety of stressors will induce a stress response with an increase in plasma corticosterone levels and that this increase in corticosterone may affect gonadal function, reproductive behavior, pregnancy and egg- laying success, survival and other aspects of fitness **(DU *et al.*, (2010)** and **Richard *et al*., 2011)**.

As regard the effect of chronic noise stress on the pituitary-ovarian axis of the adult female albino rats, the present study showed a very high significant (P < 0.001) decrease in serum stradiol and progesterone and a high significant (P < 0.01) decrease in serum LH and FSH, moreover, an ovarian histological changes were detected in the form of cystically dilated follicles lined by granulose cells separated by normal ovarian stroma this indicate failure of ovulation and are similar to those of polycystic ovarian syndrome, which may be attributed to adrenocorticotrophic hormone–stimulated secretion of dehydro- epiandrosterone from the adrenal cortex. Dehydro - epiandrosterone was used for the induction of an experimental model to assess polycystic ovarian syndrome ***(*salvetti *et al.,* 2003 and 2004).** The noise stress results in stimulation of adrenocorticotrophic hormone, adrenal hyperactivity and increased corticosterone secretion with LH reduction and this may be one of pathophysiological mechanism involued in follicular cyst pathogenesis ***(kondoh et al., 2009)***, who concluded that the intermittent sonic stress can cause decreased uterine receptivity through an ovarian-independent pathway and may be attributed to stress - induced increase in the secretion of cortico-releasing hormone, adreno-corticotrophic hormone, glucocorticoids, urocortins, endorphins and orexin. Chronic noise stress – induced hypoinsulinemia may lead to upregulation of the expression of 11β-HSD enzyme, which may cause alteration in cortisol metabolism, which may be one of the etiologies of polycystic ovary encountered in the present study **Uran *et al*., (2010)**.

In conclusion, continuous exposure to noise stress may have many adverse effects on some of vital physiologic functions in which the alteration in the levels of these hormones may play a significant contributory role, i.e. chronic exposure to high level of noise may be detrimental to testicular and ovarian function.

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