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Sperm abnormality and infertility in male mice treated with the recommended dose of dimethoate and its double

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Abstract

Background: Dimethoate (DM) is one of the most important organophosphate insecticides used for controlling many pests which affect vegetables, fruits, and agricultural crops, its persistence in soils and crops could cause a health hazard to humans as well as other non-target organisms.

Aim: This study was conducted to evaluate the effect of the recommended dose and its double of DM on sex hormones, sperm morphology, and fertility of adult male mice.

Methods: Twenty-seven Swiss albino adult male mice were divided into three groups of nine animals each: control group received distilled water only, while other groups received DM orally at doses (0.1 and 0.2 ml DM/100 ml distilled water) for 20 days, at the end of the treatment, six mice from each group were sacrificed. The sperm morphology was evaluated and sex hormones were measured. Three mice from each group were allowed to mate with untreated females (1:2).

Result: The results revealed a decrease in luteinizing hormone levels in mice treated with (0.2 ml DM/100 ml distilled water) compared with the control group while the levels of follicle-stimulating hormone and testosterone did not record any significant differences. Also, the results demonstrated a significant increase in abnormal sperm morphology such as head and tail. The fertility was reduced and the average number of dead embryos increased while the average number of live embryos decreased.

Conclusion: This current study confirmed that DM has detrimental effects on sperm morphology, fertility, and the embryos; therefore, more efforts should be exerted to protect ourselves and our environment from the harmful effects of this pesticide.

Keywords: Dimethoate, Male mice, Reproduction, Sex hormones.

Introduction

Pesticides are used in agriculture to enhance food production, especially in developing countries (Prakasam *et al*., 2001) and controlling insects and disease vectors (Farag *et al*., 2007). They can be harmful to humans and animals (Khogali *et al.*, 2005) and cause environmental contamination (Tuzmen *et al*., 2008). Organophosphate insecticides (OPI) constitute one of the most widely used classes of pesticides for pest control (Selimen *et al.*, 2014). They have toxic effects on many organs and systems such as the immune system, reproductive system, and nervous system (Yasin and Sharma, 2013), and can alter the genetic material particularly chromosomes in mammalian culture (Jamil *et al*., 2004). In addition, several physiological and behavioral dysfunctions occurred after exposure to light doses of OPI (Ambali *et al*., 2011; Ngoula *et al*., 2014).

Dimethoate (DM) is one of the most used OPI for controlling many pests as botflies in livestock (Abouamer *et al*., 2013), the insects affecting vegetables, fruits and agricultural crops (Mandal *et al*., 2002, 2008; Abouamer *et al*., 2013). It can affect humans and wildlife in their natural habitats (Ngoula *et al*., 2014). Moreover, DM products are moderately toxic to higher vertebrates by ingestion, inhalation, and dermal absorption (Verma and Mohanty, 2009). Several studies reported that DM has harmful effects on liver (Heikal *et al*., 2011; Saafi *et al*., 2011; Al-Ali *et al*., 2016), ovary (Farag *et al*., 2007), brain (Astiz *et al*., 2009), blood parameters (Yasin and Sharma, 2013), the embryos (Sasi *et al*., 2013) and also induce DNA damage in mice bone marrow (Ayed-Boussema

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et al., 2012). Many studies have shown that male mice treated with DM caused a decrease in sperm motility and an increase in the percentage of abnormal sperm (Jallouli *et al*., 2015; Sasi *et al*., 2018a, 2018b), as well as structural alterations in testicular tissues (Bakir *et al*., 2020; Sasi and ELGhoul, 2021). The main objective of this study was to investigate the effect of the recommended dose of DM and its double on sex hormones, sperm morphology, and fertility in adult male mice.

Materials and Methods

Chemicals

DM (40% EC, good quality, Germany) which was used in this study was bought from Soliman Khater Market (Tripoli-Libya) in the shape of a volumetric bottle (250ml). It was used to prepare the required doses. The working solution was prepared weekly and maintained in dark glass bottles at room temperature (25°C).

Experimental animals

Twenty-seven Swiss albino male mice weighing between (20 and 27 g), aging between 8 to 12 weeks and free of any pathogen or external parasites. The mice were bred in the animal house of the Department of Zoology, Faculty of Science, University of Tripoli, Libya. They were housed in plastic cages containing wooden flakes which were changed weekly and kept under controlled temperature conditions (22°C ± 3°C) and a normal photoperiod of 12 hours dark/12 hours light. They were given a standard diet and water *ad libitum*.

Experimental design

The animals were randomly divided into three groups of nine mice each and were put in separate cages and treated as follows: group I: control mice were orally given distilled water, while groups II and III received DM by gavage at the doses; dose I (0.1 ml DM/100 ml distilled water) and dose II (0.2 ml DM/100 ml distilled water), the experiments were continued for 20 days.

Sperm suspension preparation

After 24 hours of the last day of the treatment, six mice from each group were weighed prior to sacrifice. The mice were sacrificed by rapid cervical dislocation. Sperm samples were collected by squeezing vas deferens into 1 ml of physiological normal saline (0.9% NaCl) in a small dish. The sperm suspension was incubated for 10 minutes at 37°C to prevent sperm adherence, while the rest number of the mice from each group were used for a fertility test.

Determination of sperm morphology

Sperm morphology observation was done by making smears from sperm suspension. One drop of sperm suspension was placed on a clean slide and smears were made and allowed to dry in air. Smears were stained with 1% eosin for 10 minutes. Sperm morphology was observed at 400× magnification using a light microscope, and then the normal and abnormal percentages of sperm were determined. Sperm with normal morphology and abnormalities in the head, mid-piece, and tail were assessed according to Otitoloju *et al*. (2010).

Hormones measurement

Blood samples were collected from the facial vein of control and treated animals. The samples were introduced into EDTA-containing tubes and were labeled and then sent for analysis. Luteinizing hormone (LH), follicle stimulating hormone (FSH), and testosterone were assayed using an ELISA hormone test kit.

Fertility test

After 24 hours of the last day of the treatment, each male treated with DM was mated with two untreated females overnight. Once the vaginal plug was observed, each female was caged separately. On 18 days of gestation, pregnant mice were killed by cervical dislocation, and the embryos were removed from the uterus. The number of live and dead embryos was determined and their body length was recorded.

Table 1. Effect of DM on the level of sex hormones in adult male mice.

Parameters	Control	Mice treated with dose I	Mice treated with dose II
FSH (IU/l)	1.50 ± 0.57	1.26 ± 0.20	0.66 ± 0.35
LH (IU/l)	2.58 ± 0.37	2.38 ± 0.22	1.70 ± 0.84*
Testosterone (ng/ml)	5.43 ± 2.31	3.99 ± 1.82	3.65 ± 1.31

*$p < 0.05$ significant difference from the control group, values were expressed as (mean ± SD).

Table 2. Effect of different doses of DM on sperm morphology.

Treatment	Abnormal head	Abnormal tail	Abnormal mid-piece	Normal sperm
Control	0.104 ± 0.36	0.173 ± 0.03	0.043 ± 0.02	0.679 ± 0.045
Dose I	0.165 ± 0.06	0.412 ± 0.12*	0.077 ± 0.06	0.347 ± 0.190*
Dose II	0.290 ± 0.07*	0.420 ± 0.12*	0.019 ± 0.02	0.269 ± 0.160*

*($p < 0.05$) significantly different from the control group, values were expressed as (mean ± SD).

Statistical analysis

All data were analyzed using SPSS (version 20) by one-way analysis of variance (ANOVA) followed by *post-hoc* Duncan, s test for multiple comparisons. ANOVA was used to determine the level of significance between the control and the treated groups, $p < 0.05$ was considered statistically significant. The data were expressed here as mean ± standard deviation (mean ± SD).

Ethical approval

Ethical approval for the experimental protocol of the study was obtained from the Ethics Committee of University of Tripoli (Ref No; SREC 17-2022).

Results

Effect of different doses of DM on the level of sex hormones

No animals died during the experimental period. The results in (Table 1) showed a significant decrease ($p < 0.05$) in LH level in the mice treated with dose II of DM in comparison with the control and dose I treated group. Levels of FSH and testosterone hormone declined but this reduction was not significant ($p > 0.05$) among the treated groups and the control group.

Effect of different doses of DM on sperm morphology

Morphological analysis of sperm in this study revealed a significant decrease ($p < 0.05$) in the percentage of spermatozoa with normal morphology in all treated groups compared to the control group. A significant increase ($p > 0.05$) of sperm with abnormal heads was recorded in the dose II treated group as compared to the control and dose I treated groups. A significant increase ($p < 0.05$) in the percentage of sperm with abnormal tails was observed in all treated groups compared to control (Table 2). DM had no effect on the percentage of sperm with abnormal mid-piece ($p > 0.05$) (Table 2). The types of abnormal sperm in this study included sperm with abnormal tails and sperm with abnormal heads compared to normal morphology of sperm (Figs. 1–3).

Effect of different doses of DM on the fertility

The results showed that fertility reduced significantly with treated males when mated with normal virgin females (Table 3).

Effect of different doses of DM on embryos of untreated females impregnated by DM-treated males

The results revealed a significant increase ($p < 0.05$) in the average number of dead embryos of females impregnated by treated males with dose II of DM and a significant decrease ($p < 0.05$) in the average number of live embryos of females impregnated by treated males. The body length of embryos of females impregnated by males received DM did not record any significant differences ($p > 0.05$) when compared to embryos of females impregnated by males of the control group (Table 4).

Discussion

This study was conducted to assess the effects of oral administration of DM on sperm morphology, sex hormones, fertility, and embryos. Our results demonstrated that administration of the recommended dose and the double recommended dose of DM pesticide to male mice caused a significant decline in LH level in the group treated with dose II and non-significant changes in the levels of FSH and testosterone in the treated groups as compared to the control. Similar results were done by Choudhary *et al*. (2008) and Joshi *et al.* (2007) revealed that DM led to a decrease in LH level. Ali and Ibrahim (2018) reported that exposure of

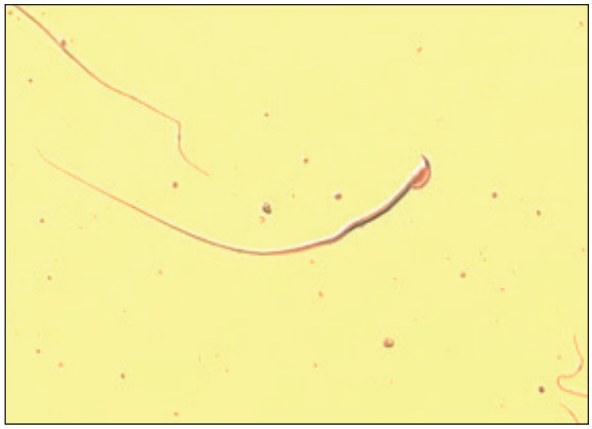

Fig. 1. Normal sperm with a hook (400×).

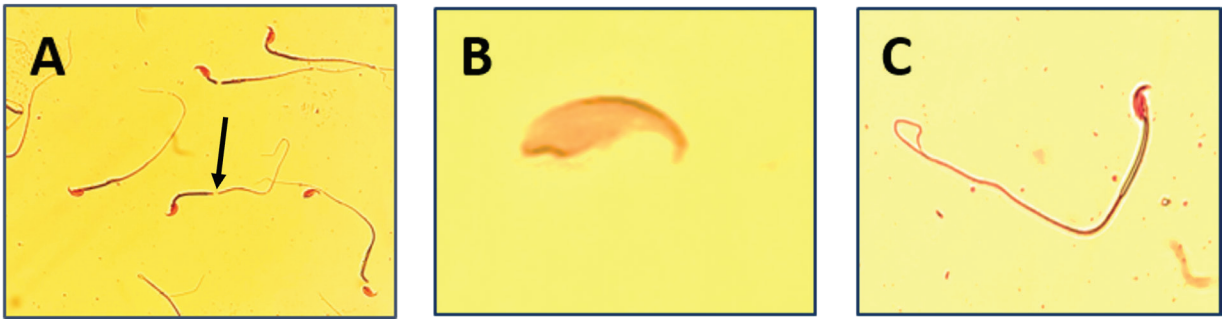

Fig. 2. Microscopic observation of sperm tail abnormalities (400×). (A) Irregular tail; (B) tailless head; and (C) coiled tail.

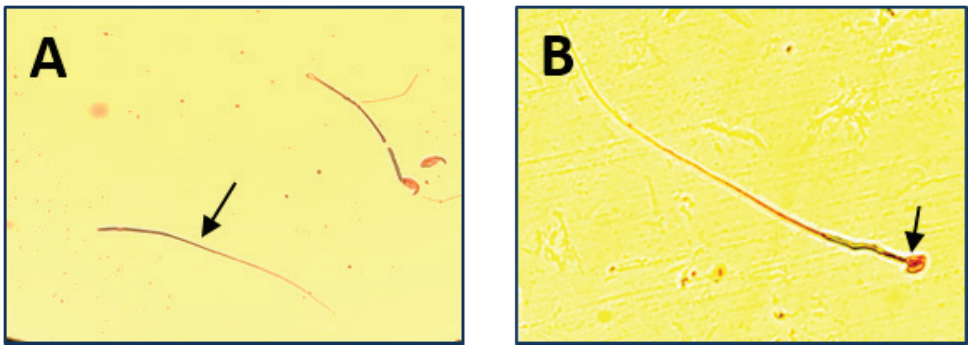

Fig. 3. Microscope observation of sperm head abnormalities (400×). (A) Headless tail and (B) amorphous head.

Table 3. Effect of different doses of DM on fertility.

Parameters Groups	No of untreated females	No of treated males	No of fertilized females	Fertilized females %
Control	6	3	6	100
dose I treated group	6	3	5	83.33
dose II treated group	6	3	2	33.33*

*($p < 0.05$) significantly different from the control group, values were expressed as (mean ± SD).

Table 4. Effect of different doses of DM on embryos of untreated females mated with treated males.

Treatments	No of live embryos	No of dead embryos	Body length (cm)
Control	10.2 ± 0.18	0.3 ± 0.82	1.9 ± 0.11
Dose I	5.33 ± 0.78*	1.17 ± 0.41*	1.8 ± 0.11
Dose II	5.17 ± 1.51*	1.67 ± 0.87*	1.6 ± 0.10

*($p < 0.05$) significantly different from the control group, values were expressed as (mean ± SD).

male mice to pesticide malathion resulted in a significant decline in LH hormone. The reduction in LH level may be attributed to the effect of organophosphorus pesticides including DM on the pituitary-testicular axis (Tarmura *et al*., 2001; Verma and Mohanty, 2009), or by disrupting the central nervous system (Colborn, 2006) via suppression of releasing of brain' hormones which stimulate FSH and LH secretion (Tarmura *et al.*, 2001). Our study contradicted previous studies indicating that exposure of male rats to malathion pesticides (Ali and Ibrahim, 2018) and dichlorvos pesticide (Ezeji *et al*., 2015) caused a drop in testosterone levels. Zidan (2009) stated that treatment of male rats with mixed pesticides (chlorpyrifos, diazinon, and profenofos) added to powdered food at concentrations of 5 and 50 ppm of each pesticide for 65 days, led to a decrease in the serum testosterone in all treated groups and FSH level decreased with the highest concentration of the tested pesticides. This controversy in results among different studies may be attributed to the type of pesticide, the period of treatment, route of administration.

Treatment of male mice with DM for 20 days caused an increase in the percentage of abnormal spermatozoa compared with the control group, this was in concord with previous studies (Trivedi *et al*., 2010; Sasi *et al*., 2018a, 2018b). The results of the present study also support previous findings obtained by many other researchers. Kata (2018) stated that dichlorvos pesticide-induced a significant increase in sperm abnormalities in male mice treated intraperitoneal for 15 days. Akinwande *et al*. (2019) have reported that rats treated with chlorpyrifos pesticide for 3 weeks have a higher frequency of sperm abnormalities, especially at the tail and neck regions. Gaber *et al*. (2023) illustrated that long-term administration of malathion to male rats (3 times/week) for 60 days led to a significant increase in sperm abnormalities. These abnormalities in sperm may be attributed to the abnormal structure of microtubules in sperm that causes morphological abnormalities in the tail and to sperm DNA damage that causes morphological abnormalities in the head (Creasy, 2001; Trivedi *et al*., 2010), or a result of abnormal chromosomes (Narayana *et al.*, 2002), or minor alteration in testicular DNA (Giri *et al*., 2002). Agunbiade *et al.* (2012) reported that abnormalities may be caused by errors in the spermatozoa differentiation process during spermatogenesis. Bruce and Heddle (1979) found that the chromosomal aberrations which occur during the packaging of genetic materials in sperm heads or point mutations in testicular DNA led to sperm abnormalities.

Our results also revealed a decline in fertility. Similar results were also reported by Ngoula *et al.* (2014) and Petrelli *et al.* (2003). This reduction in fertility may be due to a decrease in sperm motility or an increase in sperm abnormalities (Jallouli *et al*., 2015; Sasi *et al*., 2018a, 2018b) or an increase in the level of malondialdehyde which affects fertility (Vasudeva *et al*., 2008). The current study demonstrated that untreated females impregnated by DM-treated males gave fewer number of viable embryos. The same result was obtained by Sasi *et al.* (2018b) and Sasi and EL-Ghoul (2021). The possible reason for the effect of DM on the embryos may be attributed to alterations in sperm DNA of male mice treated with DM by overproduction of free radicals (Navarro and Bustos, 2014; Bakir *et al*., 2020).

Conclusion

In conclusion, the results of the present study have shown that administration of DM orally to adult male mice during 20 days affected sperm morphology, sex hormones, fertility, and also on the embryos. Therefore, it is better to avoid the increased risk of pesticide use and the application of an integrated control program that contributes significantly to reducing the number of different insect pests.

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Conflict of interest

All authors declare that there is no conflict of interest.

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None.

Authors contribution

SMS and NMA designed, organized, and conducted the study; SMS and NMA wrote the manuscript and performed the analysis of data; all other authors revised and approved the final manuscript.

Availability of data

All data supporting the findings of this study are available within the paper.

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