



Research Article

## Dichlorvos Pesticide Inhalation affects Birth Weight but not Litter Number or Gestational Period of Pregnant Wistar Rats

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### Abstract

Reproductive outcomes of dichlorvos inhalation were determined in eight female wistar rats (unexposed control group and dichlorvos-exposed group). Dichlorvos was prepared in a dilution of 1:1 as for domestic use. Dichlorvos exposure was performed for four hours daily by placing freshly prepared mixture in a poorly-ventilated compartment into which rats were introduced. Exposed group of rats were exposed for one week before mating and continued until delivery. Number of litters delivered and birth weight were recorded. There was no significant difference in the mean number of litters delivered by exposed mother rats when compared to unexposed mother rats. A significant reduction in litter weight from exposed mother rats when compared with litters from unexposed mother rats was observed. It was concluded from this study that dichlorvos exposure adversely affect birth weight.

**Keywords:** Dichlorvos, Inhalation, Mating, Birth-weight

### Introduction

Dichlorvos is a synthetic organophosphate pesticide used to control household and agricultural pests (IARC, 1991). It is effective against flies, aphids, spider mites, caterpillars and white flies in greenhouse, outdoor fruits, and vegetable crops (Lotti, 2001). Dichlorvos has been used as a fumigant as well as in the treatment of parasitic worm infections in dogs, livestock and humans (Lotti, 2001). In Nigeria, dichlorvos is traded under different names and has been implicated as the major active ingredient in many local pesticide preparations (Umar et al, 2010) which are indiscriminately utilized in controlling household pests (Chedi and Aliyu, 2010).

Like other organophosphate pesticides, the major mechanism of dichlorvos toxicity is inhibition of neural acetylcholinesterase (AChE) leading to acetylcholine accumulation in the synapse. This results in increased firing of the postsynaptic neuron or neuroeffector activity. The consequences of this increase in cholinergic activity include; diarrhea, lacrimation, nausea, muscle fasciculation, cramps, depolarized type paralysis, mental confusion, fatigue, convulsions, impaired memory, anxiety, irritability, psychosis and coma. The non-cholinergic effects of dichlorvos exposure include leukemia, brain and prostrate cancers. Earlier studies on wistar rats exposed to dichlorvos reported adverse haematological effects (Edem et al, 2012a), altered pro-oxidant-antioxidant homeostasis (Edem et al, 2012b), and reduction of plasma Nitric oxide concentration (Akinyola et al, 2012) and significant disruption of liver histology (Owoeye et al, 2012).

A number of animal studies reported premature ovulation, endocrine disruption, and congenital abnormalities due to exposure to organophosphates (Akingbemi and Hardy, 2001; Garcia et al, 2003; Hanke and Jurewicz, 2004). Also, Tamura et al (2001) reported adverse estrogenic and antiandrogenic effects of organophosphates while other studies reported no adverse effect in animals (Chen et al, 2002). These previous studies did not consider the effects of pesticides on pregnancy outcomes. Our present study assessed the reproductive outcomes of inhaled dichlorvos by wistar rats..

### Materials and Methods

Eight (8) female and four (4) male Wistar rats aged 2 months were purchased from the animal house of Physiology Department, University of Ibadan and were quarantined for two weeks before the commencement of experiment. The animals were fed with standard fodder and water ad libitum.

The female rats were divided into two groups, dichlorvos exposed and unexposed rats. Female rats were each placed with two male rats in cages for mating. The male rats were separated from female rats during dichlorvos exposure in the exposed group. Exposed group of rats were exposed for one week before mating experiments and 4hours daily till delivery.

Dichlorvos (Hubei Sanonda Co. Ltd, China) was purchased from agrochemical shop and used at 1:1 dilution with clean water. This was placed in a poorly ventilated compartment in which animal cages were kept. Freshly prepared solution was used for exposure on daily basis. Litters were weighed on a sensitive scale and birth weights

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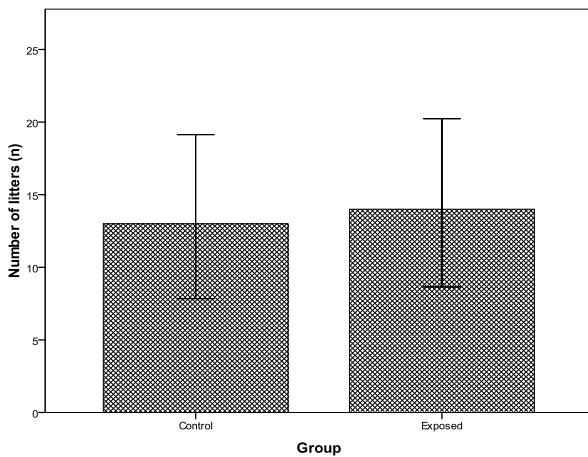
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recorded. Gestational age and litter numbers were also recorded.

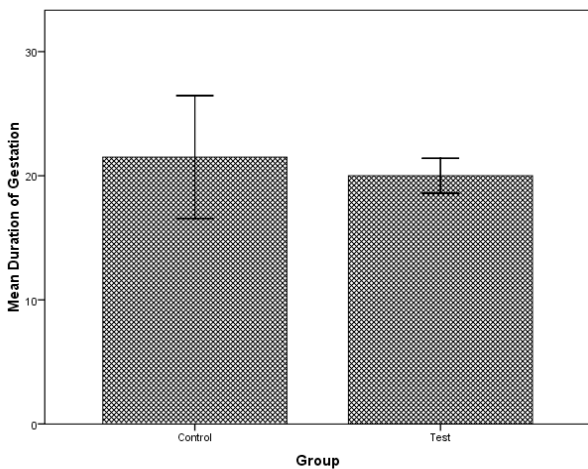
The data was analyzed using statistical package for social sciences (SPSS) version 17.0. The Student's *t*-test was used to compare mean values of birth weights and gestational ages between exposed and unexposed groups. Also, the numbers of litters delivered by exposed and unexposed mother rats were compared using the Binomial test. The criterion for significance was set at  $p < 0.05$ .

## Results

All rats in both groups (exposed and unexposed) were able to achieve pregnancy and carried to term (delivery). Figure 1 shows the number of litters delivered by exposed and unexposed mother rats. All litters were delivered alive and no physical malformations were observed in litters delivered by exposed and unexposed mothers. There were no significant differences in litter number (Figure 1) and duration of gestation (Figure 2) of exposed and unexposed mother rats.



**Figure 1:**  
Number of litters in control and dichlorvos-exposed mother rats



**Figure 2:**  
Mean duration of gestation in control and dichlorvos-exposed mother rats

The mean birth weight of litters delivered by exposed mother rats was significantly reduced when compared to litters delivered by unexposed mothers (Figure 3).

## Discussion

Pesticides like other chemicals were reported to be toxic to reproductive system and may lead to varieties of adverse outcomes. The impact of exposures to these toxic chemicals on reproductive health includes impaired gametogenesis, defective sperm maturation, decreased semen quality, miscarriages, ovulation and menstrual disturbances, subfertility, still births, developmental anomalies, cryptorchidism, hypospadias and cancer (Stavros et al, 2011; Peiris-John and Wickremasinghe, 2008; Weselak et al, 2007; Garcia, 2003). They may also act like hormones in the endocrine system and disrupt the function of the natural endogenous hormones, therefore classified as endocrine disruptors (EDs) (Diamanti-Kandarakis et al, 2009; Lathers, 2002). Substantial amounts of research have been conducted to associate exposure to pesticides with fertility problems in men (Bretveld et al, 2006). However, there is paucity of information on effect of dichlorvos exposure to reproductive outcomes.

The mechanism by which organophosphate pesticides affect female reproductive function includes; decreased compensatory weight gain of the ovaries in hemi-castrated rats, decreased healthy follicles (Dhondup and Kaliwal, 1997), decreased number of oestrus cycles and duration of each phase, biochemical changes in ovaries and placenta (Kaur and Dhanju, 2005; Levario-Carrillo et al, 2004), and disruption of endogenous endocrine function (Bretveld et al, 2006). However, the present study observed no effect on fertility and fecundability in dichlorvos exposed female rats, as exposed rats were able to achieve pregnancy and carry pregnancy to term. Furthermore, the number of offsprings was also not affected by dichlorvos inhalation in our study. This supports previous animal studies which demonstrated no adverse effect on female fertility in dichlorvos exposed experimental animals (NITE, 2004; ASTDR, 1997), despite detrimental effects of dichlorvos exposure on male fertility (USEPA, 1994; WHO, 1989).

Fetal growth is generally assessed at delivery by surrogate measures such as, length of gestation, fetal size and most commonly, birth weight (Windham and Fenster, 2008). Fetal birth weight is of public health importance because of the strong relationship between low birth weight and infant morbidity and mortality, risk of neurological disorders such as cerebral palsy and seizure disorders, severe mental retardation, lower respiratory tract conditions, and learning disabilities later in life (Kiely et al, 1995). Previous reports demonstrated that most low birth weight in developing countries is related to intrauterine growth retardation (IUGR) whereas in developed countries it is related to preterm birth (Perez-Escamilla and Pollitt, 1992; Villar and Belizan, 1982). Dichlorvos exposure was implicated as causative of low birth weight in the present study. Significant decrease in birth weight of pups from mothers exposed to dichlorvos compared with birth weight of pups from unexposed mothers (control) could be due to fetal developmental toxicity of maternal dichlorvos inhalation. Furthermore, several human reproductive and developmental toxicity studies have associated pesticide exposure to decreased birth weight (Chevrier, 2011; Barr,

2010; Ochoa-Acuna, 2009; Whyatt, 2004; Levario-Carrillo, 2004).

Length of gestation and maintenance of pregnancy have been linked with a cascade of genetic and non-genetic mechanisms (Hoque et al, 2002) with no one fundamental mechanism being solely responsible (Jenkin and Young, 2004). Our study found no significant differences in the lengths of gestation in both exposed and unexposed mother rats. Though, Eskenazi et al (2004) reported an association between reduced gestational age and increased levels of maternal urinary dimethyl phosphate (an organophosphate metabolite) as well as decreased umbilical cord cholinesterase in a cohort of Latina women living in an agricultural area. This difference may be as a result of longer pesticide exposure or exposure to a mixture of pesticides as is obtainable in agricultural areas.

In conclusion, our study demonstrates adverse effects of dichlorvos exposure on birth weight; hence users of dichlorvos should be appropriately advised. Selected reproductive hormones and histology of certain reproductive organs should be considered in future study.

## References

- Akingbemi BT, Hardy MP (2001). Oestrogenic and antiandrogenic chemicals in the environment: effects on male reproductive health. *Ann. Med.* 33(6): 391-403.
- ATSDR, Agency for Toxic Substances and Disease Registry (1997). Toxicological profile for dichlorvos. Atlanta, GA.
- Barr DB, Ananth CV, Yan X, Lashley S, Smulian JC, Ledoux TA et al. (2010). Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey. *Sci Total Environ* 408(4):790- 795.
- Bretveld RW, Thomas CMG, Scheepers PTJ, Zielhuis GA, Roeleveld N (2006). Pesticide exposure: the hormonal function of the female reproductive system disrupted? *Reproductive Biol. Endocrinology* 4(30): 1-14.
- Chedi B.A.Z. and Aliyu M. (2010). Effect and management of Acute Dichlorvos poisoning in wistar rats. *Bayero Journ. of Pure and Appl. Sc.* 3(2):1-3.
- Chen H, Xiao J, Hu G, Zhou J, Xiao H, Wang X (2002). Estrogenicity of organophosphorus and pyrethroid pesticides. *J. Toxicol. Environ. Health* A65(19):1419-1435
- Chevrier C, Limon G, Monfort C, Rouget F, Garlantezec R, Petit C et al.(2011). Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort. *Environ Health Perspect* 119(7):1034-1041
- Dhondup P and Kaliwal BB (1997) Inhibition of ovarian compensatory hypertrophy by the administration of methyl parathion in hemicastrated albino rats. *Reprod Toxicol* 11: 77-84.
- Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, Hauser R, Prins GS, Soto AM, et al (2009). Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocr. Rev.* 30:293-342.
- Edem VF, Akinyoola SB, Olaniyi JA, Rahamon SK, Owwoye O, Arinola OG (2012). Haematological parameters of Wistar rats exposed to 2,2 Dichlorovinyl Dimethyl Phosphate Chemical. *Asian J. Exp. Biol. Sci.* 3(4): 838-841.
- Edem VF, Kosoko A, Akinyoola SB, Owwoye O, Rahamon SK, Arinola OG (2012b). Plasma antioxidant enzymes, lipid peroxidation and hydrogen peroxide in wistar rats exposed to Dichlorvos insecticide. *Arch. Appl. Sci. Res.* 4(4): 1778-1781.
- Eskenazi B, Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, et al (2004). Association of in utero organophosphate pesticide exposure and fetal growth and length of gestation in an agricultural population. *Environ. Health Perspect.* 112:1116-24.
- García AM (2003). Pesticide exposure and women's health. *Am. J. Ind. Med.* 44:584-94.
- Garcia SJ, bu-Qare AW, Meeker-O'Connell WA, Borton AJ, Boudonia MB (2003). Methyl parathion: a review of health effects. *J. Toxicol. Environ. Health B. Crit. Rev.* 6(2): 185-210.
- Hanke W, Jurewicz J (2004). The risk of adverse reproductive and developmental disorders due to occupational pesticide exposure: an overview of current epidemiological evidence. *Int. J. Occup. Med. Environ. Health* 17(2): 223-243.
- Hoque MA, Amin MR, Biak DH (2002). Genetic and non-genetic causes of variation in gestation length, litter size and litter weight in goats. *Asian-Aust. J. Anim. Sci.* 15(6): 772-776.
- IARC Working Group (1991). *Dichlorvos*. IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. 53: 267-307.
- Jenkin G and Young IR (2004). Mechanism responsible for parturition; the use of experimental models. *Animal Repro. Sc.* 82-83: 567-581.
- Kaur S and Dhanju CK (2005) Biochemical effects of some organophosphorus pesticides on the ovaries of albino rats. *Indian J Physiol Pharmacol* 49: 148-152.
- Kiely JL, Brett KM, Yu S, Rowley DL (1995). Low birth weight and intrauterine growth retardation. *J. Preventive Med. Suppl* 9:1-122.
- Lathers CM (2002). Endocrine disruptors: a new scientific role for clinical pharmacologists? Impact on human health, wildlife, and the environment. *J. Clin. Pharmacol.* 42:7-23.
- Levario-Carrillo M, Amato D, Ostrosky-Wegman P, Gonzalez-Horta C, Corona Y, Sanin LH (2004). Relation between pesticide exposure and intrauterine growth retardation. *Chemosphere* 55(10):1421-1427.
- Levario-Carrillo M, Olave ME, Corral DC, Alderete JG, Gagiotti SM, Bevilacqua E (2004). Placental morphology of rats prenatally exposed to methyl parathion. *Exp Toxicol Pathol* 55: 489-496.
- Lotti M (2001). Clinical toxicology of anticholinesterase agents in humans. In: Krieger R, (ed). Handbook of pesticide toxicology. Volume 2. Agents. 2nd ed. Academic Press; San Diego: pp. 1043-1085.
- NITE/Japan, National Institute of Technology and Evaluation, Japan (2004) Project for Development of Chemical Substance Risk Assessment Technology and Risk Assessment Methods (2003 Report), NEDO Project.
- Ochoa-Acuna H, Frankenberger J, Hahn L, Carbajo C (2009). Drinking-water herbicide exposure in Indiana and prevalence of small-for-gestational-age and preterm delivery. *Environ Health Perspect* 117(10):1619-1624.
- Owoeye O, Edem VF, Akinyoola SB, Rahaman S, Akang EE, Arinola OG (2012). Histological changes in liver and lungs of rats exposed to dichlorvos before and after vitamin supplementation. *Eur J Anat.* 16 (3): 190- 198.
- Peiris-John RJ and Wickremasinghe R (2008). Impact of low-level exposure to organophosphates on human reproduction and survival. *Trans. R. Soc. Trop. Med. Hyg.* 102:239-45.
- Pérez-Escamilla R and Pollitt E (1992). Causes and consequences of intrauterine growth retardation in Latin America. *Bull Pan Am Health Organ* 26: 128-47.
- Stavros Sifakis, Mihalis Mparmpas, Offie P. Soldin and Aristides Tsatsakis (2011). Pesticide Exposure and Health Related Issues in Male and Female Reproductive System, Pesticides - Formulations, Effects, Fate, Prof. Margarita Stoytcheva (Ed.), ISBN: 978-953-307-532-7.
- Tamura H, Maness SC, Reischmann K, Dorman DC, Gray LE, Gaido KW (2001). Androgen receptor antagonism by the organophosphate insecticide fenitrothion. *Toxicol. Sci.* 60(1): 56-62.
- U.S. EPA (U. S. Environmental Protection Agency). 1994. Integrated Risk Information System (IRIS). Washington, DC.

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- Umar M, Stephen SH, Abdullahi M, Garba M (2010). Dichlorvos concentrations in locally formulated pesticide (Ota-piapia) utilized in northeastern Nigeria. *Scientific Research and Essay*. 5(1):049-054.
- Villar J and Belizan JM (1982). The relative contribution of prematurity and fetal growth retardation to low birth weight in developing and developed societies. *Am J Obstet Gynecol* 143:793-8.
- Weselak M, Arbuckle TE, Foster W (2007). Pesticide exposures and developmental outcomes: The epidemiological evidence. *J. Toxicol. Environ. Health B Crit. Rev.* 10:41-80.
- WHO (1989). Environmental Health Criteria 79: *Dichlorvos*. World Health Organization, Switzerland: Geneva.
- Whyatt RM, Rauh V, Barr DB, Camann DE, Andrews HF, Garfinkel R et al. (2004). Prenatal insecticide exposures and birth weight and length among an urban minority cohort. *Environ Health Perspect* 112(10):1125-1132.
- Windham G and Fenster L (2008). Environmental contaminants and pregnancy. *Fertility and Sterility* 89(1): e111-e115.