Journal of Natural Product Research and Applications (JNPRA)

Home page : https://journals.univ-tlemcen.dz/JNPRA/index.php/JNPRA

Research Article

OPEN ACCESS

Effects of exposure of chlorpyrifos-ethyl on metabolism and oxidative damage in rats and their offspring

Khawla ABDERRAHIM [1], Meryem BENSALAH [1], Samira BOUANANE [1,*], Fatima Zohra BABA AHMED [1], Hafida MERZOUK [1]

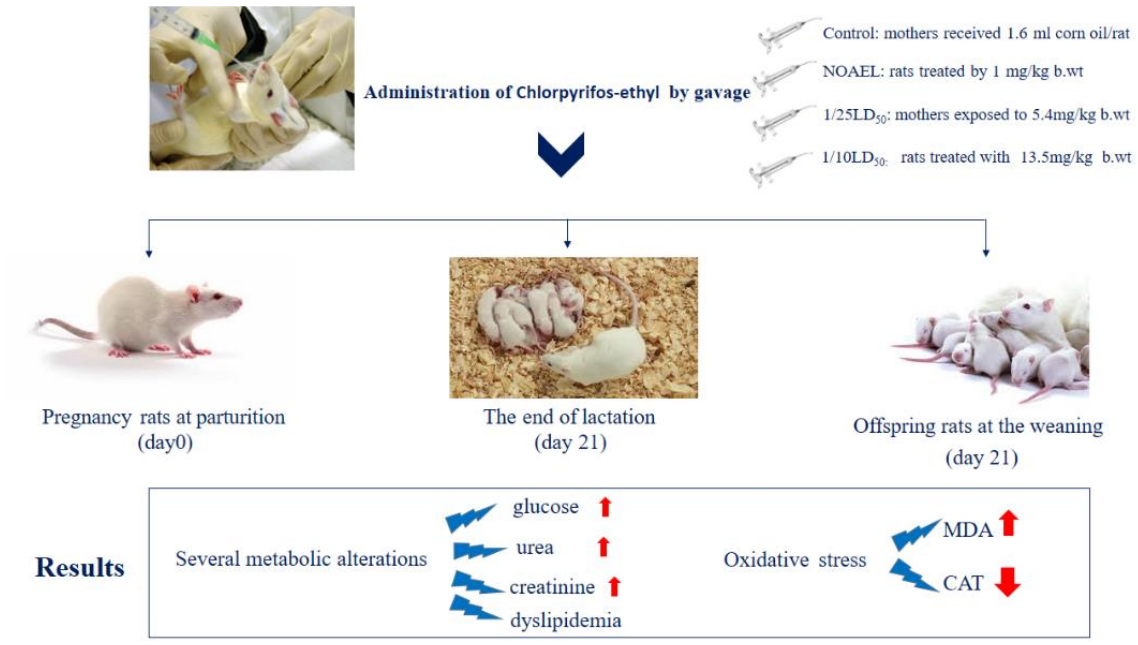
[1] Laboratory of Physiology Physiopathology and Biochemistry of Nutrition, Department of Biology, Faculty of Natural and Life Sciences, Earth and Universe, University Abou-Bekr Belkaïd, Tlemcen 13000, Algeria

*Corresponding author; sambouanane@hotmail.fr

Highlights

- Chlorpyrifos-ethyl exposure at different doses affects metabolism and induced oxidative stress in pregnant and lactating rats.
- Metabolic changes and oxidative stress caused by chlorpyrifos-ethyl were also observed in pups at weaning.
- Maternal chlorpyrifos-ethyl exposure during gestation and lactation induced the development of metabolic disorders and redox alterations in the offspring.

Graphical abstract



Abstract
Chlorpyrifos-ethyl (CE) is one of the most widely used organophosphorus insecticides for industrial, agricultural and public health purposes. The aim of the study was to evaluate the effect of CE exposure via gavage on metabolic and redox status in pregnant, lactating rats and their pups at weaning. The oral administration of this pesticide at doses of 1 mg/kg of body weight No Observed Adverse Effects Level (NOAEL), 5.4mg/kg b.wt (1/25LD50) and 13.5 mg/kg b.wt (1/10LD50) was given 1day/2 to female rats during the entire gestation and lactation period. Plasma biochemical parameters as well as lipid profiles and oxidative stress markers were determined. Oral CE exposure induced an increase in plasma glucose, urea, creatinine and lipid status levels in mothers at parturition (day 0) and at the end of lactation (day21) and in their offspring at weaning (day21). An altered oxidant/antioxidant status marked in mothers treated by the insecticide at day 0 and day 21 and these disturbances were also seen in their offspring. In conclusion, different doses CE exposure induced several metabolic and redox alterations leading to maternal physiological impairments and to offspring metabolic changes. CE should be used with caution especially during pregnancy and lactation period.

Keywords: Chlorpyrifos Ethyl; Pregnancy; Oxidative damage; Metabolism.

1. Introduction

Pesticides are ubiquitous in the environment and have significant economic, environmental and public health impact. Their usage helps to improve human nutrition through greater availability, longer storage life and lower costs of Food (El-Demerdash and Nasr, 2014). Organophosphorus insecticides (OPIs) are one of the largely used classes of compounds for pest control in various scenarios. Use of OPIs has increased owing to their low toxicity and low persistence in mammalian system. OPIs act via inhibition of acetylcholinesterase (AChE; EC 3.1.1.7), an enzyme involved in regulation of neurotransmission by hydrolysis of the neurotransmitter, acetylcholine (ACh) (Joshi and Rajini, 2009). OPIs exposures have been associated with metabolic disorders (Reygner et al., 2016) and oxidative stress characterized by increased lipid peroxidation and alterations in the status of enzymatic antioxidant defense mechanisms in humans (Ranibar et al., 2005). Chlorpyrifos (CFP) and its derivatives are used organophosphorus compounds to control a variety of insects and pests in agricultural practices (Galloway and Handy, 2003). They are among the most used insecticides in the world, that is why they have been the subject of numerous toxicity studies (Kenfack et al., 2007). CPF (0,0-diethyl 0-3,5,6-trichloro-2- pyridyl phosphorothionate) ($C_9H_{11}Cl_3NO_3PS$) is classified as a moderately hazardous, class insecticide by the world health organization (WHO, 1997). Its acute toxicity varies according to the species and route of exposure, acute oral LD50 for females' rats is estimated to be 135 mg/kg body weight (Mc Collister et al., 1974). Chlorpyrifos-ethyl (CE) is one of the most recent derivatives of CPF. In addition, CE is widely used in the agricultural production in Algeria (Agricultural Ministry, Algeria 'Alphyte Spa: Algérienne des phytosanitaires'). Increasing evidence indicates that CPF is involved in metabolic perturbations (Joshi and Rajini, 2009) and oxidative stress in the body by enhanced levels of Malondialdehyde (MDA) accompanied by a concomitant decrease in the activity of catalase (CAT). Available reports indicate that CPF alter the activities associated with antioxidant defense mechanisms (Attia et al., 2012). The aim of this study was to investigate the effect of oral CE exposure at different doses on metabolic parameters and oxidative stress biomarkers in pregnant rats at parturition (day 0) and at the end of lactation (day 21) and their offspring at weaning (day 21).

2. Materiel and methods

2.1 Chemicals

CE is a synthetic organophosphate insecticide [O, O-diethyl-O-(3, 5, 6-trichloro-2-pyridyl) phosphorothioate], which is being widely used as an insecticide in Algeria. The commercial formulation of CE, namely Dursban 4® (Dow agrosciences) containing 480 g CE perliter, was used in this study and all other chemical products were obtained on 2013 from National Institute of Agronomic Research of Algeria (INRAA).

2.2 Animals and experimental design

A total of 24 female Wistar rats (weighing 200g) were obtained from the Pasteur Institute (Algiers, Algeria). Animals were housed in wood-chip-bedded plastic cages, with a 12 h light/dark cycle, room temperature of 23 °C, air humidity of 60 ± 5%. The rats had free access to water and a standard diet (O.N.A.B). The female rats were randomized into four groups of six animals for each group. Control group (C/oil): Rats were received only corn oil (1.6 ml/ 200g of rat). CE was prepared by corn oil. In Group 1, the rats were given CE at a dose of 1 mg/kg body weight [NOAEL: no observable adverse effects level; low dose (Mansour and Mossa, 2011)]. Group 2 received CE at a dose of 5.4mg/kg b.wt [median dose; equivalent to 1/25 LD_{50} (Tanvir et al., 2015)], whereas rats in Group 3 treated by CE at 13.5 mg/kg body weight (highest dose 1/10LD_{50}) according to the protocol (Goel et al., 2007).The route of administration selected for the study was oral gavage (every two days) for all female rats during one month before matin. After this period, the female rats were mated. The presence of sperm on the vaginal smear was used to determine the first day of pregnancy, the male rats were removed and gavage was continued for the pregnant rats of the four groups by the same doses of CE during pregnancy and lactation. The experimental procedures were carried out according to the National Institute of Health Guidelines for animal care and approved by the Regional Ethical Committee.

2.3 Experimental procedures

At days 0 and 21 for mothers and days 21 for pups, six rats from each group were anesthetized with intraperitoneal injection of sodium pentobarbital (60 mg/kg of body weight). The blood was collected from the abdominal aorta puncture into EDTA tube. Blood samples were centrifuged to obtain the plasma for determination of biochemical and some oxidative stress parameters. After removal of plasma, the remaining erythrocytes were washed three times in isotonic saline, hemolysed by the addition of ice- cold distilled water (1/4) and stored at 4 °C for 15 min. The cell debris was removed by centrifugation (2000g for 15 min). The erythrocyte lysates were assayed for catalase activity and MDA.

2.4 Biochemical analyses

Plasma glucose, triglycerides, total cholesterol, urea, creatinine levels were measured using commercial kits obtained from Spinreact (by colorimetric enzymatic assays). Triglycerides and total cholesterol were determined in different lipoprotein fractions after separation by precipitation according to the method of Burstein et al. (1989).

2.5 Oxidant/antioxidant marker determination

MDA levels, a marker of lipid peroxidation, were estimated by the procedure of Draper and Hadley, (1990) using thiobarbituric acid (TBA).

Erythrocyte CAT (EC.1.11.1.6) activity was assayed by measuring the rate of hydrogen peroxide (H_2O_2) decomposition according the kinetic method described by Aebi (1984). The reaction was initiated by additional of hemolysate to the reaction mixture containing

phosphate buffer (0.05 M, pH 7.2) and H_2O_2. Change in absorbance was recorded spectrophotometrically at 240 nm. Enzyme activity was expressed as U/g of hemoglobin (Hb).

2.6 Statistical analysis

Results are expressed as means ± standard deviation (SD). Significant differences among the groups were analysed by one-way analysis of variance (ANOVA) test followed by Tukey's multiple comparison tests. p-Value < 0.05 was considered statistically significant. All data were done with the Statistical Package for Social Sciences (IBM SPSS, 20.0 for windows).

3. Results

3.1 Clinical signs of toxicity

No signs of toxicity and deaths were observed in any of the treatment groups during the experimental period. But a decrease of the number for newborns of rats exposed to the high dose of CE (13.5mg/kg b.wt; $1/10LD_{50}$) during gestation compared with other doses and control, are noted in this study.

3.2 Effect of treatment on plasma and lipoproteins biochemical parameters

3.2.1 Effect of treatment on Mother rats

The administration of CE resulted in the increase in plasma glucose, urea and creatinine levels in mothers rats at parturition and at the end of lactation for all doses Table 1) compared to the control mothers, with the highest effective concentrations being $1/25LD_{50}$.

The oral exposure of CE at all of the applied dose levels induced a general but dose-dependent elevation of the total cholesterol level in the plasma, LDL and VLDL of mothers rats tested with three doses of this pesticide during gestation and lactation compared with control mothers at day0 and day21 (**Table 1**). The pronounced effect being with the $1/25LD_{50}$ and $1/10LD_{50}$ dose levels while, HDL cholesterol was very low in experimental mother rats exposure to CE $1/10L\ D_{50}$ compared with both doses of CE and control values at parturition and at the end of lactation (Table 1).

Plasma, LDL and VLDL triglycerides contents were significantly higher (p 0.000) in rats' mothers treated by CE at different doses than in control mothers' rats at day0 (Table1), with the highest effective concentrations being $1/25LD_{50}$ and $1/10LD_{50}$ of CE. At day 21, A high significant decreases (p 0.000) in HDL triglycerides contents were noted in experimental mothers rats treated with CE $1/10LD_{50}$ compared to other doses of CE and control mothers rats at parturition and at the end of lactation (Table1).

3.2.2 Effect of treatment on Offspring

Palsma glucose, urea and creatinine levels were significantly enhanced in pups, at weaning, from mothers given CE at different doses (low, median and high) during gestation and lactation had higher significant increase (p 0.000) compared with control pups (Table 1), with the highest effective concentrations being $1/25LD_{50}$ and $1/10LD_{50}$ doses of this pesticide.

The results of the present study showed that CE gavage to the mother rats at dose of NOAEL, 1/25 LD_{50} and $1/10LD_{50}$ throughout gestation and lactation, produced a general significant increase (p 0.000) in plasma total cholesterol, VLDL-C and LDL-C levels from their offspring at weaning day 21 compared with control pups. The highest increase values was recorded in pups that mothers treated with the $1/25LD_{50}$ and $1/10LD_{50}$

doses levels. On the other hand, there were a significant decreases in HDL-C levels in pups of different treated groups compared to pups of control group (Table 1) and this reduction was more pronounced with 1/25LD_{50} dose level.

The gavage of 1/25LD_{50} of CE to pregnant/lactating female rats caused a significant elevation in plasma, LDL and VLDL triglycerides levels of their pups at weaning compared with pups of other treated groups NOAEL, 1/10LD_{50} and pups of control group (Table 1). A slight but not significant decrease of HDL triglycerides contents in plasma of pups from dams treated with NOAEL dose level. However, the treated group with 1/25LD_{50} dose level had a significant decrease in plasma HDL-TG concentrations of offspring from mothers given this dose level during gestation and lactation than offspring from mothers tested by CE at 1/10LD_{50} dose level (Table 1).

Table 1. Influence of different doses of chlorpyrifos-ethyl on metabolic parameters in pregnancy rats at parturition (day 0), at the end of lactation (day 21) and offspring rats at the weaning (day 21).

	Parameter	Control	NOAEL	1/25LD_{50}	1/10LD_{50}	*P*(ANOVA)
Mothers	**Glucose (g/L)**					
	Day 0	0.86±0.04^{d}	0.98±0.02^{c}	1.12±0.03^{a}	1.04±0.02^{b}	0.000
	Day 21	0.89±0.02^{d}	1.72±0.01^{c}	1.95±0.01^{a}	1.90±0.01^{b}	0.000
	Total cholesterol (g/L)					
	Day 0	1.20±0.04^{c}	1.39±0.02^{b}	1.69±0.03^{a}	1.67±0.02^{a}	0.000
	Day 21	1.24±0.02^{c}	1.62±0.02^{b}	1.86±0.02^{a}	1.80±0.02^{a}	0.000
	Triglycerides (g/L)					
	Day 0	0.95±0.12^{c}	1.29±0.11^{b}	1.50±0.17^{a}	1.52±0.04^{a}	0.000
	Day 21	1.03±0.02^{d}	1.38±0.02^{c}	1.72±0.02^{a}	1.65±0.02^{b}	0.000
	Urea(mg/dL)					
	Day 0	40.08±0.76^{c}	35.22±1.15^{d}	95.11±2.01^{a}	88.55±0.54^{b}	0.000
	Day 21	42.01±0.9^{c}	37.94±0.3^{d}	100.88±0.75^{a}	90.09±0.4^{b}	0.000
	Creatinine (mg/dL)					
	Day 0	0.40±0.10^{c}	0.62±0.07^{b}	0.73±0.05^{b}	1.07±0.13^{a}	0.000
	Day 21	0.49±0.02^{d}	0.63±0.07^{c}	0.77±0.03^{b}	1.11±0.10^{a}	0.000
	LDL-TG (g/L)					
	Day 0	0.30±0.02^{c}	0.47±0.02^{b}	0.65±0.05^{a}	0.66±0.08^{a}	0.000
	Day 21	0.26±0.02^{c}	0.52±0.03^{b}	0.77±0.01^{a}	0.76±0.02^{a}	0.000
	LDL-C (g/L)					
	Day 0	0.40±0.02^{c}	0.60±0.02^{b}	0.75±0.02^{a}	0.70±0.02^{a}	0.000
	Day 21	0.41±0.03^{b}	0.80±0.03^{a}	0.90±0.02^{a}	0.86±0.04^{a}	0.000
	HDL-TG (g/L)					
	Day 0	0.22±0.01^{a}	0.17±0.01^{b}	0.19±0.01^{b}	0.16±0.01^{b}	0.000
	Day 21	0.22±0.03^{a}	0.13±0.02^{b}	0.13±0.04^{b}	0.11±0.02^{b}	0.000
	HDL- C (g/L)					
	Day 0	0.47±0.02^{a}	0.35±0.01^{b}	0.37±0.02^{b}	0.30±0.02^{c}	0.000
	Day 21	0.47±0.02^{a}	0.27±0.02^{b}	0.27±0.02^{b}	0.25±0.02^{c}	0.000
	VLDL-TG (g/L)					
	Day 0	0.45±0.01^{c}	0.63±0.01^{b}	0.68±0.01^{a}	0.70±0.01^{a}	0.000
	Day 21	0.55±0.01^{c}	0.73±0.03^{b}	0.86±0.03^{a}	0.78±0.03^{b}	0.000
	VLDL-C (g/L)					
	Day 0	0.33±0.01^{c}	0.54±0.01^{b}	0.66±0.01^{a}	0.65±0.02^{a}	0.000
	Day 21	0.36±0.01^{c}	0.45±0.02^{b}	0.69±0.01^{a}	0.66±0.01^{a}	0.000
Offspring	**Glucose (g/L)**	0.65±0.07^{c}	1.01±0.01^{b}	1.25±0.06^{a}	1.23±0.08^{a}	0.000

Total cholesterol (g/L)	0.57±0.03^{c}	0.71±0.02^{b}	0.84±0.04^{a}	0.82±0.02^{a}	0.000
Triglycerides (g/L)	0.60±0.08^{d}	0.95±0.08 ^{c}	1.33±0.05^{a}	1.23±0.03^{b}	0.000
Urea(mg/dL)	38.99±0.31^{c}	35.85±0.35^{d}	87.92±0.40^{a}	85.18±0.43^{b}	0.000
Creatinine (mg/dL)	0.40±0.03^{d}	0.57±0.03^{c}	0.68±0.02^{b}	0.98±0.05^{a}	0.000
LDL-TG (g/L)	0.10±0.02^{c}	0.27±0.02^{b}	0.45±0.03^{a}	0.42±0.02^{a}	0.000
LDL-C (g/L)	0.12±0.01^{c}	0.29±0.01^{b}	0.40±0.01^{a}	0.36±0.01^{a}	0.000
HDL-TG (g/L)	0.20±0.02^{a}	0.18±0.02^{a}	0.10±0.01^{c}	0.16±0.01^{b}	0.000
HDL- C (g/L)	0.29±0.02^{a}	0.22±0.02^{b}	0.10±0.01^{d}	0.13±0.01^{c}	0.000
VLDL-TG (g/L)	0.30±0.01^{d}	0.50±0.01^{c}	0.75±0.02^{a}	0.65±0.01^{b}	0.000
VLDL-C (g/L)	0.19±0.01^{c}	0.22±0.01^{b}	0.34±0.01^{a}	0.33±0.01^{a}	0.000

Values are means ± S.E.M. n= 6 rats in each group. Control: mothers received 1.6 mL corn oil/rat; NOAEL: rats treated by 1 mg/kg b.wt of CE; 1/25LD$_{50}$: mothers exposed to 5.4mg/kg b.wt; 1/10LD$_{50:}$ rats treated with 13.5mg/kg b.wt. LDL-TG: low-density lipoprotein triglycerides; LDL-C: low- density lipoprotein cholesterol; HDL-TG: high-density lipoprotein triglycerides; HDL-C: high-density lipoprotein cholesterol; VLDL-TG very low-density lipoprotein triglycerides; VLDL-C: very low-density lipoprotein cholesterol. Values with different superscript letters (a, b, c, d) are significantly different at $p < 0.05$.

3.3 Effect of treatment on oxidative stress markers

3.3.1 Mothers

Oral exposure of CE during gestation and lactation to the rats at different doses, caused induction of oxidative stress as evidenced by higher increase in the levels of MDA ; the major end product of lipid peroxidation, in plasma and erythrocyte compared to mothers rats of the control group at day0 and at day21 (Figure 1). The highest increase values were recorded in rats that were treated with the 1/25LD$_{50}$ dose level.

In comparison to the control group, the erythrocyte catalase activity CAT was significantly lowered in mothers treated by CE at dose level of 1/25LD$_{50}$ at day0 and day 21; no significant difference was marked in mothers exposed to other doses of CE (NOAEL, 1/10LD$_{50}$) at parturition, but the decreased CAT activity was found in lactating rats tested with 1/10LD$_{50}$ dose level, which was significantly different from the control dams (Figure 1).

3.3.2 Offspring

A higher significantly increase in the MDA level was found in the plasma and erythrocyte of pups from pregnant rat mothers given CE at all of the applied dose levels during gestation and lactation compared with pups of control group, with the highest effective concentrations being 1/25LD$_{50}$ dose level (Figure 2). In other hand, there were significant alterations in erythrocyte antioxidant status in pups from pregnant/lactating rats exposed to CE in comparison to pups from control exposed to CE in comparison to pups from control group as indicated by a high decreases of erythrocyte CAT activity level at day21 (Figure 2). The highest decrease values were observed in pups of 1/25LD$_{50}$ of CE group.

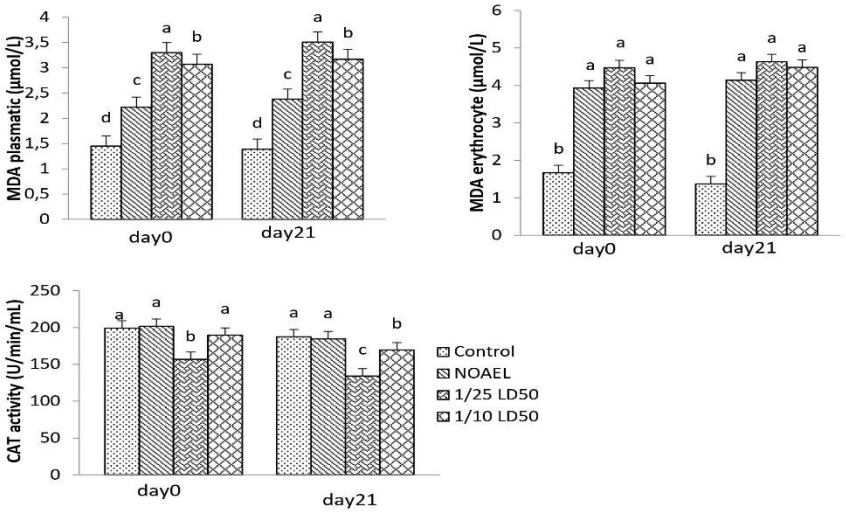


Figure 1. Oxidative stress markers in control and experimental rats at parturition (day0), at the end of lactation (day 21).

Values are means ± S.E.M. n = 6 rats in each group. Control: mothers received 1.6 mL corn oil/rat; NOAEL: rats treated by 1 mg/kg b.wt of CE; 1/25LD_{50}: mothers exposed to 5.4mg/kg b.wt; 1/10$LD_{50:}$ rats treated with 13.5mg/kg b.wt. Values with different superscript letters (a, b, c, d) are significantly different at $p < 0.05$. CAT: catalase, MDA: malondialdehyde.

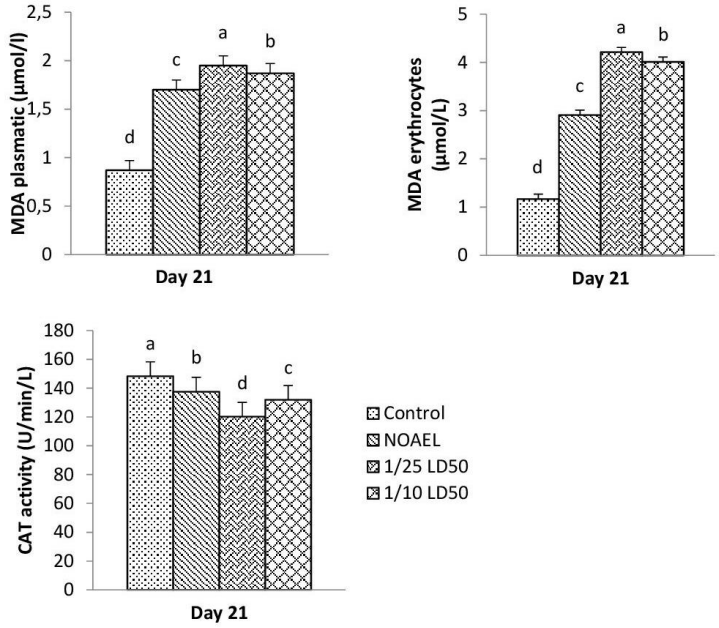


Figure 2. Oxidative stress markers in control and experimental offspring.

Values are means ± S.E.M. n = 6 rats in each group. Control: mothers received 1.6 mL corn oil/rat; NOAEL: rats treated by 1 mg/kg b.wt of CE; 1/25LD_{50}: mothers exposed to 5.4mg/kg b.wt; 1/10$LD_{50:}$ rats treated with 13.5mg/kg b.wt. Values with different superscript letters (a, b, c, d) are significantly different at $p < 0.05$. CAT: catalase, MDA: malondialdehyde.

4. Discussion

The present study, suggested that gestation and lactation exposures to CE may be affect the metabolism and the balance oxidant/antioxidant in dams at parturition and the end of lactation as well as their offspring at weaning.

The exposition of dams to CE at low, median and high doses during these periods induced several biochemical changes. Our data showed increased plasma glucose levels at day 0 and day 21 in dams and in their pups at weaning; this increase was more pronounced in 1/25LD_{50} dose, similar results have been found by Reygner et al. (2016). In contrast, Zama et al. (2005) reported a hypoglycemia in pregnant rats exposed to CE from 6th to 15th day of pregnancy than dissected on 19th day. The majority of experimental studies designed to evaluate the effects of OPI on glucose homeostasis have revealed a pronounced hyperglycemia, as an immediate consequence of OPI administration (Lasram et al., 2014). Previous studies indicated that CE exposure at different doses causes an increase in blood glucose in adult male rats (Acker and Nogueira, 2012; Orabi et al., 2013), which was explained by stimulation of glycogenolysis in several organs (Rezg et al., 2007) and of gluconeogenesis in liver, provoking glucose release into the blood (Acker and Nogueira, 2012).

The current results indicate that CE exposure during gestation and lactation resulted in the increase in plasma urea and creatinine levels in both dams and their pups at weaning. While the opposite are noted concerning plasma urea levels in group of dams treated by NOAEL dose and their offspring compared to the control group. The exposure indicates reduced glomerular function (Ali and Ismail, 2012), because these metabolic parameters are the waste products of protein metabolism requiring excretion through the kidney (Al-Attar and Al- Tisan, 2010). These findings corroborated with previous investigations in pregnancy rats (Zama et al., 2005), lactating rats (Mansour and Mossa, 2011) and in adult male and female rats (Mansour and Mossa, 2010; Nisar et al., 2013) treated by CPF.

The analysis of blood yields information about the predominant metabolic pathways in the body. Our results showed alteration in plasma lipid and lipoproteins levels, these dyslipidemia manifested as high plasma, LDL, VLDL triglycerides and cholesterol levels and low total cholesterol and triglycerides HDL concentrations in experimental dams treated by CE in all group during gestation and lactation at parturition and at the end of lactation compared with control group. These results are in agreement with previous studies (Uchendu et al., 2013; El-Demerdash and Nasr, 2014; Tanvir et al., 2015; Akande et al., 2016). The same observation has mentioned concerning their nursing pups at day 21, suggested by Bonvallot et al. (2018), who reported that a modification observed in offspring may be a consequence of the altered metabolism in dams. On the other hand, Reygner et al. (2016) recommended a low plasma triglycerides levels and insignificant change in plasma, LDL and HDL cholesterol contents in pregnancy/lactating rats treated by CPF and their pups. Also, the decrease in plasma triglycerides and VLDL cholesterol in adult male Wistar rats exposed to CPF reported by the study of Ambali et al. (2011).

In this study, lipid changes observed in treated rats seemed to be acquired through permanent modulation of lipid and lipoproteins metabolism in dams during gestation and lactation and their pups in early development (fetal life), it is not mentioned in this present study and postnatal exposure through milk; who is an important route of elimination from the mammalian body (Syed et al., 2016). Currently, oxidative stress isthe second aspect of organophosphates toxicity after cholinesterase inhibition, and remains today under investigation. Induction of free radicals, lipid peroxidation and impaired antioxidant status by organophosphates has been widely studied in humans and animals (Sidhu et al., 2014; Zhang et al., 2014). The preliminary results arising from the current investigation

reveal that exposure of CE during gestation and lactation affect the balance between reactive oxygen species (ROS) generation and the activity of scavenging systems, resulting in the formation of further oxidative stress (Hussien et al., 2013). In our work, oxidative stress was marked by high oxidative markers MDA in plasma and in erythrocyte and low antioxidant defense CAT activity . The decrease in antioxidants might be due to their increased utilization in response of oxidative stress in treated dams. Our research found that dams exposed to CE during gestation and lactation and their pups at weaning had an enhanced increase in the levels of MDA; the major product of lipid peroxidation, in plasma and erythrocytes at parturition and at the end of lactation. These results are parallel to the results of many authors (Mansour and Mossa, 2010; Ambali et al., 2011; Ma et al., 2013; Uchendu et al., 2013). The high MDA concentrations in the CE group demonstrates the role of lipid peroxidation in the CE induced alteration in lipid profiles in this study cholesterol and triglycerides component of lipoprotein fraction can be oxidized by toxic radicals and can lose their chemical structures and cellular function (El-Banna et al., 2009).

Antioxidant enzyme namely catalase CAT is the first line of defense against oxidative stress. CAT soluble protein in erythrocytes plays a role in the decomposition of hydrogen peroxide to give water. CAT activity decreased in the erythrocyte after CE exposure in all dams treated by different doses of this pesticide during gestation and lactation at day0 and at day21 and their offspring at day21. Low CAT activity could also be attributed to enzyme inactivation by ROS induced damage to proteins (Nelson et al., 2006). On balance, our results are in accordance with other investigations (Mansour and Moussa, 2009) in the erythrocyte and in different tissues (El-Demerdash, 2011). CAT seems to be maximally susceptible to inhibition by CE, it is one of the most active enzymes and its levels change first following induction of oxidative stress.

5. Conclusion

In summary, we concluded that CE induced metabolic disorders and oxidative stress in pregnant and lactating mother rats These abnormalities were also observed in their offspring at weaning, but the precise mechanism of transmission of CE in prenatal/postnatal exposure of pups cannot be ascertained from the results of this research and thus remains to be explored in future.

Conflict of interest

The authors declare that they have no conflicts of interest.

Acknowledgments

Abou Bekr Belkaid University supported this work. The authors thank INRAA (Sidi Bel Abbes, Algeria) for providing pesticides (chlorpyrifos-ethyl).

ORCID

ABDERRAHIM Khawla: 0000-0002-3646-8794

References

Acker, C.I., & Nogueira, C.W. (2012). Chlorpyrifos acute exposure induces hyperglycemia and hyperlipidemia in rats. *Chemosphere*, 89, 602–608.

Aebi, H. (1984)). Catalase in vitro. *Methods Enzymology*, 105, 121–126. .

Akande, M.G., Aliu, A.Y., Ambali, S.F., & Ayo, G.O. (2016). Co-treatment of chlorpyrifos and lead induce serum lipid disorders in rats: Alleviation by taurine. *Toxicol Ind Health* 32, 1328-34.

Al-Attar, A.M., & Al-Taisan, W.A. (2010). Preventive effects of black seed (*Nigella sativa*) extract on Sprague Dawley rats exposed to diazinon. *Aust. Journal of Basic & Applied Sciences* , 4, 957–68.

Ali, A.R.A., & Ismail, S.H. (2012). Protective effect of honey against amikacin-induced nephrotoxicity in rats. *Iraqi Journal of Pharmaceutical Sciences*, 21, 85–93.

Ambali, S.F., Shittu, M., Ayo, J.O., Esievo, K.A.N., & Ojo, S.A. (2011). Vitamin C Alleviates Chronic Chlorpyrifos Induced Alterations in serum Lipids and Oxidative Parameters in Male Wistar Rats. *Americain Journal of Pharmacology and Toxicology*, 6, 109–118.

Attia, A.A., El Mazoudy, H.R., & El-Shenawy, N.S. (2012). Antioxidantt role of propolis extract against oxidative damage of testicular tissue induced by insecticide chlorpyrifos in rats. *Pesticide Biochemistry and Physiology*, 103, 87–93.

Bonvallot, N., Canlet, C.A., Estrada, F.B., Gautier, R., Tremblay-Franco, M., Chevolleau, S., Cordier, S., & Cravedi, J.P. (2018). Metabolome disruption of pregnant rats and their offspring resulting from repeated exposure to a pesticide mixture representative of environmental contamination in Brittany. *PLoS. One* , 13(6), e0198448.

Burstein, M., Fine, A., & Atger, V. (1989). Rapid method for the isolation of two purified subfractions of high-density lipoproteins by differential dextran sulfate magnesium chloride precipitation. *Biochemistry*, *7*1, 741–746.

Draper, H., & Hadley, M. (1990). Malondialdehyde determination as index of lipid peroxidation. *Methods in Enzymology,* 186, 421–31.

El-Banna, S.G., Attia, A.M., Hafez, A.M., & El-Kazaz, S.M. (2009). Effect of Garlic Consumption of Blood Lipid and Antioxidant Parameters in Rats Males Exposed to Chlorpyrifos. *Slovak Journal of Animal Science,* 42, 111–117.

El-Demerdash F.M. (2011). Lipid peroxidation, oxidative stress and acetylcholinesterase in rat brain exposed to organophosphate and pyrethroid insecticides. *Food and Chemical Toxicology,* 49, 1346–1352.

El-Demerdash, F.M., & Nasr, M.H. (2014). Antioxidant effect of selenium on lipid peroxidation, hyperlipidemia and biochemical parameters in rats exposed to diazinon. *Journl Trace Element Medicine Biology,* 28, 89–93.

Goel, A., Dani, V., & Dhawan, D.K. (2007). Zinc mediates normalization of hepatic drug metabolizing enzymes in chlorpyrifos- induced toxicity. *Toxicology Letters*, 169, 26–33.

Hussein, H.M., Abdou, H.M., & Yousef, M.I. (2013). Cypermethrin induced damage in genomic DNA and histopathological changes in brain and haematotoxicity in rats: the protective effect of sesame oil. *Brain Research Bulletin*, 92, 76–83.

Joshi Apurva Kumarh, R., & Rajini, P.S. (2009). Reversible hyperglycemia in rats following acute exposure to acephate, an organophosphorus insecticide: role of gluconeogenesis.
Toxicology, 257, 40–45.

Kenfack, A., Watcho, P., Ngouba, F., Tchoumdoue, J., & Kamtchouing, P. (2007). Influence du chlorpyriphos-éthyl sur quelques paramètres de reproduction chez le rat male albinos exposé pendant le développement post natal. *International Journal of Biological and Chemical Sciences*, 3, 237–243.

Lasram, M.M., Bini Dhouib, I., Annabi, A., El Fazaa, S., & Gharbi, N. (2014). A review on the molecular mechanisms involved in insulin resistance induced by organophosphorus pesticides. *Toxicology*, 232, 1–13.

Ma, P., Wu, Y., Zeng, Q., Gan, Y., Chen, J., Ye, X., & Yang, X. (2013). Oxidative damage induced by chlorpyrifos in the hepatic and renal tissue of Kunming mice and the antioxidant role of vitamin E. *Food and Chemical Toxicology*, 58, 177–183.

Mansour, S.A., & Mossa, A.H. (2009). Lipid peroxidation and oxidative stress in rat erythrocytes induced by chlorpyrifos and the protective effect of Zinc. *Pesticide Biochemistry and Physiology*, 93, 34– 39.

Mansour, S.A., & Mossa, H.A. (2010). Oxidative damage, biochemical and histopathological alterations in rats exposed to chlorpyrifos and the antioxidant role of zinc. *Pesticide Biochemistry and Physiology*, 96, 14–23.

Mansour, S.A., & Mossa, H.A. (2011). Adverse effects of exposure to low doses of chlorpyrifos in lactating rats. *Toxicology and Industrial Health*, 27, 213–224.

Mc Collister, S.B., Kociba, R.J., Humiston, C.G., Mc Collister, D.D., & Gehring, P.J. (1974). Studies of the acute and long-term oral toxicity of chlorpyrifos. *Food and Cosmetict Toxicology*, 12, 45–61.

Nelson, S.K., Bose, S.K., Grunwald, G.K., Myhill, P., & Mc Cord, J.M. (2006). The induction of human superoxide dismutase and catalase in vivo: a fundamentally new approach to antioxidant therapy. *Free Radical Biology & Medicine*, 40, 341–347.

Nisar, N.A., Sultana, M., Raina, R., Waiz, H.A., Baba, N.A., Ahmed, I., & Zargar, F.A.(2013). Experimental Studies on the effect of Chlorpyrifos and Lead Acetate on Biochemical Parameters in Wistar Rats with Special Reference to Ameliorative Effect of Vitamin C. *The Proceedings of the National Academy of Sciences, India, Section B: Biological Sciences* , 84(4).

Orabi, S.H., Elbialy, B.E., & Shawky, S.M. (2013). Ameliorating and Hypoglycemic effects of Zinc against Acute Hepatotoxic Effect of chlorpyrifos. *Global Veterinaria*, 10, 439–446.

Ranibar, A., Solhi, H., Mashayeki, F.A., Susanabdi, A., Razaei, A., & Abdollahi, M. (2005). Oxidative stress in acute human poisoning with organophosphorus insecticides; a case control study. *Environmental Toxicology and Pharmacology*, 20, 80–91.

Reygner, J., Lichtenberger, L., Elmhiri, G., Dou, S., Bahi-Jaber, N., Rhazi, L., Depeint, F., Bach, V., Khorsi-Caue, H., & Najar, L. (2016). Inulin supplementation lowered the metabolic defects of prolonged exposure to chlorpyrifos from gestation to young adult stage in offspring rats. *PLoS One* 11(10), e0164614.

Rezg, R., Mornagui, B., Kamoun, A., El-Fazaa, S., & Gharbi, N. (2007). Effect of subchronic exposure to malathion on metabolic parameters in the rat. *CR Biologies*, 330,

Sidhu, I., Bhatti, J.S., & Bhatti, G.K. (2014). Modulatory action of melatonin against chlorpyrifos induced hepatotoxicity in Wistar rats. *Asian Journal of Multidisciplinary Studies*, 2, 123–131.

Syed, F., John, P.J., & Soni, I. (2016). Neurodevelopmental Consequences of gestational and lactational exposure to pyrethroids in rats. *Environmental Toxicology*, 31, 1761–1770.

Tanvir, E.M., Afroz, R., Alamgir Zaman Chowdhury, M., Ibrahim Khalil, Md, Sabir Hossain, Md, Abdurrahman, Md, Harunur Rashin, Md, & Siew Hua Gan. (2015). Honey has a protective effect against chlorpyrifos-induced toxicity on lipid peroxidation, diagnostic markers and hepatic histoarchitecture. *European Journal and Integrative Medicine*, 7, 525–533.

Uchendu, C., Ambalia, S.F., Ayo, J.O., Lasisi, I.O.., & Umosen, AY. (2013). Subacute chlorpyrifos induced alterations in serum lipids and some oxidative stress biomarkers in male Wistar rats: beneficial effect of acetyl-L-carnitine. *Toxicology and Environmental Chemistry*, 95, 483–494.

WHO. (1997). The WHO Recommended classification of pesticides by Hazard 1996-1997. *International programme on chemical safety*. WHO/IPCS, 96, 3.

Zama, D., Meraihi, Z., Boubekri, N., Amrani, A., Tebibel, S., & Baali, N. (2005). Assessment of the changes in some diagnostics enzymes and other parameters in wistar albino rats treated with pesticides during gestation. *Sciences &Technologie*, *C* 23, 51–56.

Zhang, Y., Han, S., Liang, D., Shi, X., Wang, F., Liu, W., Zhang, L., Chen, L., Gu, Y., & Tian, Y. (2014). Prenatal Exposure to Organophosphate Pesticides and Neurobehavioral Development of Neonates: A Birth cohort study in Shenyang, China. *PLOS ONE*, 9(2), e88491.