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Effect of perinatal beta cypermethrin exposure on the biochemical profile of rat off spring

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Abstract
Cypermethrin, a broad spectrum pesticide, extensively used for pest management and animal husbandry practices has resulted in severe environmental pollution and health hazards. Previous studies have shown that cypermethrin has teratogenic effect on rat foeti born to exposed dam or buck with no information on its effect on their biochemical profile. The present study was aimed to measure the serum and tissue biomarkers (AST, ALT, MDA, CA, SOD and GSH) of rat offspring exposed to beta cypermethrin (β-cyp) during the perinatal period. Fifteen pregnant animals (Day 0 = day of mating, average body-weight = 190g) were randomly divided into 3 groups. Group A (Control) received 0.5ml olive oil, Group B (15 mg/kg β-cyp) and Group C (30 mg/kg β-cyp) by oral gavage from gestational day (GD) 1 – post natal day (PND) 20. On PND 21, blood, liver and kidney samples were collected from 5 pups from each group for biochemical assay. β-cyp caused a significant ($p< 0.05$) increase in the AST activities and slight but not significant ($p>0.05$) increase in activities of ALT of the β-cyp exposed rat offspring relative to the control. β-cyp also caused a significant ($p<0.05$) reduction in the Hepatic MDA and CA levels and a non significant ($p>0.05$) change on the hepatic GSH & SOD, and the renal MDA, CA, GSH and SOD of exposed rat offspring relative to the control. It is therefore concluded that β-cyp can alter the biochemical profile of albino rat offspring exposed during the perinatal period.

Keywords: beta cypermethrin, perinatal, biochemical, biomarkers

1. Introduction
Pesticides are used in agriculture and public health to control insects, animals and vectors of disease. These pesticides cause hazardous effects at different levels to non target species, producing significant histopathological changes. Pyrethroids are among the most widely used synthetic pesticides. Their use has increased in the past decades with the declining use of organophoshate pesticides, which are more acutely toxic to birds and mammals than the pyrethroids. However, this change to less acutely toxic pesticides, while generally beneficial, has introduced certain health related issues [1]. The toxicity of pyrethroid insecticides has received much attention in recent times. Cypermethrin, a Type II pyrethroid is reported to have toxic effects on birds, fishes and mammals [2, 4].

Pesticides trigger the release of tissue damaging Reactive Oxygen Species (ROS) which in turn results in oxidative stress [5, 6]. Oxidative stress is an outcome of an increased generation of free radicals and/or reduced activity of the antioxidant defence mechanism of the body. Although the production of ROS is a normal physiological event resulting from normal metabolic processes and interaction with the environmental stimuli, the over production can induce oxidative stress, leading to cell damage which can culminate in cell death. ROS comprise both free radical and non free radical oxygen containing molecules such as hydrogen peroxide, superoxide, singlet oxygen and the hydroxyl radical which could attribute to increased oxidative stress and impair the redox balance [7].

Several studies have demonstrated that maternal pesticides exposure can cause damage to the foeti such as increased mortality of offspring, organ and skeletal abnormalities and other forms of teratogenesis [8, 9]. The studies on teratogenic effect of pyrethroids in rodents limited the maternal exposure to the period of gestation; but the present work, using beta cypermethrin as an example, extended the maternal exposure to the period of lactation. The aim of the present study therefore is to assess the biochemical profile of rat offspring exposed to beta cypermethrin during the perinatal period.

2. Materials and Methods
2.1 Chemicals and Reagents
Beta cypermethrin (a mixture of the alpha and theta forms of the insecticide) at 95.8% purity was purchased from Haihang Industry Company, Limited, China as white to light yellow crystalline powder with CAS No: 52315-07-8 and Batch No: 20140517. The desired doses were prepared in olive oil which was purchased from the supermarket. All other chemicals were of the finest analytical grade.

2.2 Animals and Treatment
Fifteen mature female albino rats weighing an average of 190g, procured from the Animal House of Department of Pharmacology, College of Health Sciences, University of Port Harcourt, Nigeria were used for the study. The rats were acclimatized for two (2) weeks before commencing the study. They were fed *ad libitum* with commercially sourced feed (Top Feeds Nigeria Limited) and supplied with clean drinking water all through the study.

Following acclimatization, one female was paired with a male in a cage overnight. Mating was confirmed the following day by the presence of sperm cells in vaginal smear or presence of vaginal plug and designated gestational day (GD) 0. They were then grouped into 3, each group housed in a cage. Group A (Control) received 0.5 ml olive oil, Group B (15 mg/kg β-cyp) and Group C (30 mg/kg β-cyp,) by oral gavage from gestational day (GD) 1 – post natal day (PND) 20. Animal's weight was taken daily and the dose adjusted accordingly.

2.3 Sample collection

a) Serum Analysis

On PND 21, five (5) pups were randomly selected from each of the three (3) groups and anaesthetized under chloroform. Blood samples were collected from the retro orbital plexuses using the micro haematocrit capillary tube. The activities of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) were measured in serum according to Reitman and Frankel [10] using the diagnostic kits from Randox Laboratories, Northern Ireland.

b) Tissue Homogenate Preparation

Liver and kidney samples were also dissected out through laparatomy and homogenized immediately in a cold medium. The homogenate of each tissue was centrifuged at 4000 rpm for 15 mins at 4℃. The supernatant was collected and used for the estimation of the oxidative stress markers in the tissues. Malondialdehyde (MDA) was determined measuring the formation of thiobarbituric acid reactive substances (TBARS) according to the method of Ohkawa *et al*. [11]. The method of Sedlak and Lindsay [12] was followed in estimating the level of reduced glutathione (GSH) level. Catalase (CA) activity was determined according to Clairborne [13]. The activity of superoxide dismutase (SOD) was determined by the method of Misra and Fridovich [14].

2.4 Statistical Analysis

Statistical analysis was done using SPSS 21. All values were expressed as mean ± SEM and data were assessed by one-way ANOVA followed by the Tukey post-test. The significance level was set at $p<0.05$.

3. Results

Exposure of rat offspring to beta cypermethrin during the perinatal period caused a significant *($p<0.05$)* increase in the serum Aspartate Aminotransferase (AST) activity and a slight increase in the serum Alanine Aminotransferase (ALT) activity though not significant *($p>0.05$)* when compared with the control (Table 1).

Table 1: Serum biomakers of rat offspring exposed to β-cyp during the perinatal period

Parameters	Group A	Group B	Group C
AST (U/L)	71.00±2.55	105.75±7.15*	108.40±5.98*
ALT (U/L)	22.20±2.27	28.50±3.28	29.20±2.33

Values are given as mean ± SEM for each group.***** indicate significant difference ($p<0.05$) compared to group A (control group).

The hepatic malondialdehyde (MDA) and catalase (CA) levels of rat offspring exposed to beta cypermethrin during the perinatal period decreased significantly ($p<0.05$) in a dose dependent manner relative to those in the control group (Table 2). There is no significant ($p>0.05$) change in the level of hepatic Glutathione (GSH) and Superoxide dismutase (SOD) in rat offspring exposed to beta cypermethrin during the perinatal period when compared with the control (Table 2).

Table 2: Hepatic biomakers of rat offspring exposed to β-cyp during the perinatal period

Parameters	Groups		
	A	B	C
MDA (µmol MDA/mg protein)	2.80±0.64	0.90±0.34*	0.89±0.38*
GSH (µg GSH/min/mg protein)	1.47±0.08	1.61±0.11	1.43±0.04
CAT(µmol/min)	11.98±0.28	6.41±0.73*	4.84±1.20*
SOD (µmol/mg)	1.54±0.06	1.98±0.53	1.09±0.13

Values are given as mean ± SEM for each group.* indicate significant difference ($p<0.05$) compared to group A (control group).

Exposure of rat offspring to beta cypermethrin during the perinatal period did not cause significant *($p>0.05$)* change in Renal biomarkers level (Table 3). However, there is a dose dependent decrease in the catalase level of exposed rat offspring relative to the control. (Table 3)

Table 3: Renal biomarkers of rat offspring exposed to β-cyp during the perinatal period

Parameters	Groups		
	A	B	C
MDA (µmol MDA/mg protein)	0.47±0.16	0.39±0.15	0.69±0.22
GSH (µg GSH/min/mg protein)	1.49±0.03	1.49±0.12	1.52±0.07
CAT (µmol/min)	8.22±0.58	5.70±1.44	4.81±1.20
SOD(µmol/mg)	0.90±0.04	0.80±0.06	1.05±0.10

Values are given as mean ± SEM for each group.* indicate significant difference ($p<0.05$) compared to group 1 (control group).

4. Discussion

Oxidative stress is a harmful process that can mediate damage to cell structures, including lipids, proteins, RNA and DNA

which lead to a number of diseases [15]. During pyrethroid metabolism, Reactive Oxygen Species (ROS) are generated and result in oxidative stress in intoxicated animals [16]. The level of oxidative stress in these animals is commonly assessed by measuring some biological markers in the serum and some targeted organs such as the liver and kidney.

Our study demonstrated that perinatal β-cyp exposure of rat offspring elevates the serum biochemical enzymes – ALT and AST. This result is in agreement with the findings of Omonona and Jarikre [17] and Amir *et al*., [18] in studies carried out in male wistar rats and guinea pigs respectively using cypermethrin. ALT and AST are normally found inside liver cells. However, when the liver is damaged or inflamed, these enzymes can be released into the bloodstream resulting in increased serum level. ALT and AST tests are markers for liver damage but ALT is more specific to the liver, as AST is also found in other organs such as heart, kidneys, brain and muscles. As revealed in the study, the significant increase in the level of AST in β-cyp exposed rat offspring relative to the control and slight but not significant increase in ALT Levels in exposed rat offspring relative to the control suggests that the damage may be from a different part of the body other than the liver.

This study also demonstrated a significant decrease in the hepatic MDA levels of β-cyp exposed rat offspring relative to the control. This result is in contrast with other studies that measures MDA levels in rodents exposed to [19-21]. The reason for this disparity with other studies could be as result of unreliability of malondialdehyde as a biomarker of oxidative stress. According to Khoubnasabjafari *et al*. [22]. MDA assay may not able to provide valid analytical data for biological samples due to its high reactivity and possibility of various cross-reactions with co-existing biochemicals. Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxidation in the cells. An increase in free radicals causes overproduction of MDA hence MDA level is commonly known as a marker of oxidative stress [23].

The dose dependent significant decrease in the hepatic catalase (CAT) activity of β-cyp exposed rat offspring relative to the control indicates depletion in the enzyme level as a result of increased oxidative stress in the cells. Catalase is an antioxidant enzyme found in almost all the body cells. The non-significant change in the renal biomarkers - MDA, CA, SOD, GSH, shows that β-cyp did not cause any significant damage to the kidneys of exposed rat offspring.

5. Conclusion

The study suggests that perinatal exposure of rat offspring to beta cypermethrin has the potency to induce oxidative stress as well as cause damage to the body evidenced by the alteration in some of the biochemical profile.

6. References

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