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RESEARCH ARTICLE

Hemato-Biochemical Disruptions by Lambda-Cyhalothrin in Rats

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ABSTRACT

The present study assessed *in vivo* endocrine disrupting effect of orally administered lambda-cyhalothrin (LCT) on metabolic hormones and correlated it with hematological instabilities. Adult female albino rats were divided in three equal groups; one kept as control and other two treated with 20 and 40 mg/kg BW LCT, respectively by oral gavage for 14 days. At the end of trial, blood was collected for hormonal and hematological analysis. The results showed that LCT led to reduction in serum triiodothyronine (T_3) and thyroxin (T_4) level ($P<0.001$) without modifying serum thyroid stimulating hormone (TSH) level in a dose related manner. Lambda-cyhalothrin also caused a significant ($P<0.05$) reduction in hemoglobin (Hb) concentration, red blood cell (RBC) count, total leukocyte count (TLC), platelets count, pack cell volume (PCV) and lymphocyte count. No significant variation was observed in erythrocytic indices. In sum, orally administered LCT caused reduction in feed intake and body weight along with disruption of hemato-biochemical parameters.

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INTRODUCTION

Pesticides are extensively used worldwide to combat the insects, however, their irrational use has led to growing health related problems in human and animals (Fleming *et al.,* 1999; Basir *et al*., 2011; Bakhsh, 2012; Tahir *et al*., 2012; Verger and Boobis, 2013). According to a WHO report, about 80% of the total pesticides produced are consumed in developing countries. Most of the pesticides are classified as endocrine disrupting chemicals due to their interference with signaling and functioning of various hormones (Lemaire *et al.,* 2006; Diamanti-Kandarakis *et al.,* 2009). Structural similarity of most of the pesticides with natural hormones accounts for their endocrine disrupting properties (Mnif *et al.,* 2011; Ahmad *et al.,* 2012a; 2012b). Pyrethroids are the most widely used class of pesticides and their use has increased several folds in recent years replacing the organophosphorous insecticides (Pérez *et al.,* 2010; Dahamna *et al*., 2011; Khan *et al*., 2012). The metabolites of especially synthetic pyrethroids have been found in different environmental sectors including soil, aquatic microcosms, sediments and foods (Markovic *et al.,* 2010). Some of the pyrethroids had also been detected in human samples such as breast milk and urine and exerted adverse effect on different physiological functions of the body (Sereda *et al.,* 2009).

Lambda-cyhalothrin is a new synthetic pyrethroid pesticide having activity against a wide range of chewing and sucking insects. Its residues have been identified in irrigation water and their sediments due to their extensive application in agriculture and public health (He *et al.,* 2008). The presence of LCT residues in animal meat and milk consumed by human population has been also reported recently (Muhammad *et al.,* 2012; Muhammad *et al.,* 2013). Human and animals are exposed directly to LCT through exposure in work places or indirectly through its residues in foods. Keeping in view this wide exposure, the present experimental study was designed to assess *in vivo* alterations in hemato-biochemical parameters subsequent to short-term (14-days) exposure to LCT in adult female albino rats.

MATERIALS AND METHODS

Animals and LCT treatment: Eighteen female albino rats of 10-14 weeks age and weighing 150-250 g were randomly divided in 3 equal groups and maintained at 25°C with 12h light and 12h dark cycle. Rats were provided with water and routine rat chow *ad libitum.* Keeping in view LD_{50} of LCT in female albino rats as 55 mg/kg BW per day (Mate *et al.,* 2010), two dose levels were selected. One group of rats was kept as control while other two groups were treated daily with low (20 mg/kg BW) and high dose (40 mg/kg BW) of LCT, respectively by oral gavage for 14 days. Body weight and feed intake was measured on alternate days throughout the experimental duration.

Blood/serum sampling and analysis: At the end of the experiment, blood samples were collected from jugular vein in dry glass tubes with and without EDTA. Blood with anticoagulant was used for hematological parameters including erythrocyte count (RBC), total leukocyte count (TLC), lymphocyte count, platelets count, hemoglobin concentration and hematocrit level (HCT) by standard methods (Rahman *et al.,* 2012). Erythrocytic indices including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were calculated. Serum separated from the blood samples was used for the determination of metabolic hormones (T_3 and T_4) and TSH by radioimmunoassay using the standard kit methods (Kit # IM1447-IM3286, IM1699-IM3287 and IM3712-IM3713, Beckman Coulter, Prague, Czech Republic).

Statistical analysis: The data from each group are expressed as mean±SE. Student's t-test was applied to compare both the treated groups separately with the control group for any significant variation at P≤0.05.

RESULTS

Feed intake and body weight: There was a significant reduction (P<0.05) in feed intake in both the exposed groups as compared to the control (Fig. IA). Similarly, the group treated with low dose of LCT showed a reduction in the body weight from day 9 of the experiment and the reduction was significant (P<0.05) at day 13 and 15 of the experiment. While in the group exposed to higher dose of LCT, the reduction in body weight started from day 5 of the experiment and the reduction was significant at day 13 and 15 (Fig. IB).

Hematological parameters: Results presented that only high dose of LCT caused a significant reduction (P<0.05) in RBC count. Moreover high dose of LCT caused significant reduction in MCV as compared to control group. In contrast, none of the treated groups showed any significant effect (P>0.05) upon MCV levels. Moreover, LCT significantly reduced (P<0.001) Hb concentration at high dose but low dose exerted no significant (P>0.05) effect. Contrariwise, neither low nor high dose of LCT showed any significant variation in MCH and MCHC (Table 1).

Analysis of results revealed that high dose of LCT significantly reduced (P<0.01) TLC and platelets count but low dose of LCT had no significant effect upon these parameters. Nevertheless, both LCT treated groups showed significant reduction (P<0.05) in lymphocyte count as compared to control group. Likewise, the lymphocyte percentage in WBCs was also reduced in both LCT treated groups (Table 1).

Metabolic hormones: The serum level of T_4 and T_3 was significantly reduced (P<0.001) in both groups treated

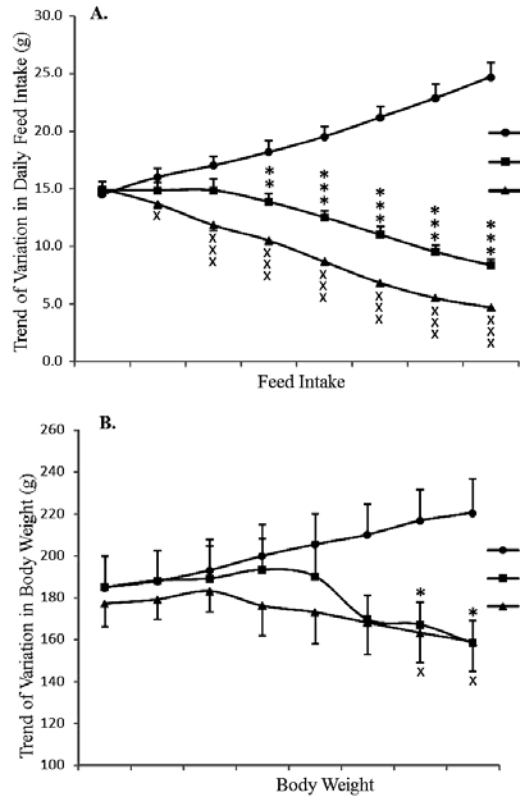

Fig. 1: Feed intake and body weight of control and LCT treated rats during the experimental duration. The level of significance is shown by * (P<0.05), ** (P<0.01) and *** (P<0.001) for control *vs* G1 or x (P<0.05) and xxx (P<0.001) for control *vs* G2. Ctl: Control group, G1: Group treated with low dose of LCT, G2: Group treated with high dose of LCT.

Table 1: Hemato-biochemical parameters (Mean±SE) in control and LCT treated groups. Significance level is shown by * (P<0.05), ** (P<0.01), *** (P<0.001) or NS (non-significant).

	Groups		
Parameters	Control	LCT (20mg)	LCT (40mg)
RBC count (10^{12}/l)	06.66±0.19	06.94±0.14^{NS}	05.37±0.32**
HCT (%)	41.60±1.16	41.23±0.79^{NS}	37.07±0.91*
MCV (fl)	59.63±0.38	59.23±0.35^{NS}	59.82±0.88^{NS}
Platelets count (10^9/l)	07.87±0.60	06.68±0.97^{NS}	04.05±0.63**
TLC (10^9/l)	05.65±0.49	04.92±0.27^{NS}	03.77±0.18**
LYM count (10^9/l)	05.48±0.46	04.18±0.24*	03.73±0.19**
LYM %age	92.23±1.04	85.13±2.69*	82.15±3.84*
Hb Conc. (g/dl)	14.90±0.26	14.47±0.26^{NS}	12.65±0.37***
MCH (pg)	20.92±0.10	20.77±0.12^{NS}	20.93±0.15^{NS}
MCHC (g/dl)	35.13±0.22	35.10±0.11^{NS}	34.95±0.67^{NS}
T_3 (nmol/l)	0.833±0.03	0.617±0.03***	0.467±0.02***
T_4 (nmol/l)	43.80±3.08	28.30±0.95***	24.70±1.54***
TSH (ng/dl)	0.1±6.2E-18	0.1±6.2E-18^{NS}	0.1±6.2E-18^{NS}

with low and high dose of LCT (Table 1). The group exposed to higher concentration of LCT was more severely affected as compared to the group treated with lower concentration indicating a dose related response. There was no significant change (P>0.05) in the level of TSH in both treated groups (Table 1).

DISCUSSION

Pyrethroids are group of pesticides that may act as endocrine disruptors (Brander *et al.,* 2012) and lead to physiological oddities in the exposed animals and humans (Manikkam *et al.,* 2012; Li *et al.,* 2013). Lambda-cyhalothrin, a pyrethroids insecticide, is being used widely all over the world and it might pose threat to human health and environment due to which there is a growing concern about its safety (Bradberry *et al.,* 2005; Amarasekare and Shearer, 2013). Previous studies showed that pyrethroids resulted in metabolic disruption; however the underlying *in vivo* mechanisms were not well-defined.

In current study, 10-14 week adult female albino rats were kept to evaluate endocrine disrupting potential of LCT. The reduction in body weight due to pyrethroids exposure is previously reported (Akhtar *et al.,* 1996); however the primary mechanism is not well understood. The reduction in body weight in rats exposed to lambda-cyhalothrin could be either due to reduced daily feed intake or disturbances in level of metabolic hormones. The reduction in level of thyroid hormones due to other pyrethroids has been reported in different studies (Saravanan *et al.,* 2009; Goldner *et al.,* 2010). It could be assumed that decreased level of thyroid hormones might had led to reduction in basal metabolic rate that subsequently resulted into decreased feed intake ultimately leading to significant reduction in body weight. The thyroid hormones might have decreased either due to direct impact on thyroid follicles or due to lack of sensitivity of thyroid glands to TSH (Van-Sande *et al.,* 1995). As there was no effect on TSH level, our results suggested that LCT directly affected pituitary gland and decreased its sensitivity to respond to decreased metabolic hormone. Along with it LCT might also directly affect the thyroid follicles resulting in decreased production of T_3 and T_4. It has also been reported that pyrethroids can decrease the activity of hepatic type I iodothyronin 5´-monodeiodinase (5´ D-I), a deiodinase enzyme that transform T_3 and T_4 and boost up the serum TSH levels (Wang *et al.,* 2002). Many pesticides including organochlorine, organophosphorous and pyrethroid pesticides lead to a reduction in serum level of T_3 and T_4 and lead to a significant increase in TSH (Akhtar *et al.,* 1996). The reason behind these alterations might be the deficiency of pituitary response to LCT.

Thyroid hormones are involved in expression of erythropoietin gene and hence increase the production of erythropoietin (Ng *et al.,* 2013). In another *in vitro* study thyroid hormones were proved to stimulate the growth of erythroid colony that indicated its role in erythropoiesis (Schindhelm *et al.,* 2013). This research was further extended and it was found that thyroid hormones activated the progenitor cells that were erythroid committed. Therefore, a reduction in serum level of thyroid hormones due to any reason might lead to decreased erythropoiesis. In present study LCT resulted in a reduction in serum level of thyroid hormones and the disturbances observed in erythrocyte count and other hematological parameters might be due to anti-metabolic hormonal effects of LCT.

Recently it has been shown that LCT and cypermethrin exerted genotoxic and cytotoxic effects on human blood lymphocyte culture (Muranli, 2013). Some of other pyrethroids (cypermethrin, deltamethrin, fenvalerate) also disrupt the hematological parameters resulting in an increased number of leukocytes in blood (Haratym-Maj, 2002). In contrast, LCT in our trial resulted in a diminution in TLC and also reduction in lymphocyte percentage in leukocytes. At the same time LCT also reduced platelets count and lymphocyte count. Lambda-cyhalothrin exerted no effect on MCH and MCHC, however, Hb concentration decreased as a result of reduction in RBC count. Cypermethrin, a pyrethroid pesticide, has been reported to show similar effects when administered to rabbits (Dahamna *et al.,* 2009) and resulted in decreased RBC count, TLC and Hb by an unknown mechanism. Endogenous estradiol has a suppressive effect on erythropoietin (Horiguchi *et al.,* 2005). As the estrogenic effect of LCT has also been reported, hence its effect on hematological parameters might be due to its estrogenic action.

Conclusion: Analyzing all the results of the present experimental study, it could be concluded that LCT disrupted the metabolism and hematological values in exposed subjects. Lambda-cyhalothrin caused a reduction in the serum level of T_3 and T_4 without affecting TSH level. It also led to drop in feed intake and body weight in the exposed rats. Furthermore, LCT disrupted the hematological values and caused a significant reduction in Hb concentration, RBC count, TLC, platelets count, and HCT.

REFERENCES

Ahmad L, A Khan and MZ Khan, 2012a. Pyrethroid-induced reproductive toxico-pathology in non-target species. Pak Vet J, 32: 1-9.

Ahmad L, A Khan, MZ Khan, I Hussain, F Mahmood, MK Sleemi, LA Lodhi and I Abdullah, 2012b. Toxico-pathological effects of cypermethrin upon male reproductive system in rabbits. Pest Biochem Physiol, 103: 194-201.

Akhtar N, SA Kayani, MM Ahmad and M Shahab, 1996. Insecticide-induced changes in secretory activity of the thyroid gland in rats. J Appl Toxicol, 16: 397-400.

Amarasekare KG and PW Shearer, 2013. Laboratory bioassays to estimate the lethal and sublethal effects of various insecticides and fungicides on *Deraeocoris brevis* (Hemiptera: Miridae). J Econ Entomol, 106: 776-785.

Bakhsh K, 2012. Environmental and technical efficiency analysis in bitter gourd production. Pak J Agric Sci, 49: 583-588.

Basir A, A Khan, R Mustafa, MZ Khan, F Rizvi, F Mahmood and A Yousaf, 2011. Toxicopathological effects of lambda-cyhalothrin in female rabbits (Oryctolagus cuniculus). Human Exp Toxicol, 30: 591-602.

Bradberry SM, SA Cage, AT Proudfoot and JA Vale, 2005. Poisoning due to pyrethroids. Toxicol Rev, 24: 93-106.

Brander SM, G He, KL Smalling, MS Denison and GN Cherr, 2013. The *in vivo* estrogenic and *in vitro* anti-estrogenic activity of permethrin and bifenthrin. Environ Toxicol Chem, 31: 2848-55.

Dahamna S, D Harzallah, A Guemache and N Sekfali, 2009. Biochemical investigation of cypermethrin toxicity in rabbits. Commun Agric Appl Biol Sci, 74: 149-153.

Dahamna S, A Belguet, D Bouamra, A Guendouz, M Mergham and D Harzallah, 2011. Evaluation of the toxicity of cypermethrin pesticide on organs weight loss and some biochemical and histological parameters. Commun Agric Appl Biol Sci, 76: 915-921.

Diamanti-Kandarakis E, JP Bourguignon, LC Giudice, R Hauser, GS Prins, AM Soto, RT Zoeller and AC Gore, 2009. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr Rev, 30: 293-342.

Fleming LE, JA Bean, M Rudolph and K Hamilton, 1999. Mortality in a cohort of licensed pesticide applicators in Florida. Occup Environ Med, 56: 14-21.

Goldner WS, DP Sandler, F Yu, JA Hoppin, F Kamel and TD Levan, 2010. Pesticide use and thyroid disease among women in the Agricultural Health Study. Am J Epidemiol, 15: 455-464.

Haratym-Maj A, 2002. Hematological alternations after pyrethroids poisoning in mice. Ann Agric Environ Med, 9: 199-206.

He LM, J Troiano, A Wang and K Goh, 2008. Environmental Chemistry, Ecotoxicity and Fate of Lambda-Cyhalothrin. Springer, New York, USA, pp: 71-91.

Horiguchi H, E Oguma and F Kayama, 2005. The effects of iron deficiency on estradiol-induced suppression of erythropoietin induction in rats: implications of pregnancy-related anemia. Blood, 106: 67-74.

Khan A, L Ahmad and MZ Khan, 2012. Hemato-biochemical changes induced by pyrethroid insecticides in avian, fish and mammalian species. Int J Agric Biol, 14: 834-842.

Lemaire G, W Mnif, JM Pascussi, A Pillon, F Rabenoelina, H Fenet, E Gomez, C Casellas, JC Nicolas, V Cavaillès, MJ Duchesne and P Balaguer, 2006. Identification of new human pregnane X receptor ligands among pesticides using a stable reporter cell system. Toxicol Sci, 91: 501-509.

Li YF, C Pan, JX Hu, J Li and LC Xu, 2013. Effects of cypermethrin on male reproductive system in adult rats. Biomed Environ Sci, 26: 201-208.

Manikkam M, R Tracey, C Guerrero-Bosagna and MK Skinner, 2012. Pesticide and insect repellent mixture (permethrin and DEET) induces epigenetic transgenerational inheritance of disease and sperm epimutations. Reprod Toxicol, 34: 708-719.

Markovic M, S Cupac, R Durovic, J Milinovic and P Kljajic, 2010. Assessment of heavy metal and pesticide levels in soil and plant products from agricultural area of Belgrade, Serbia. Arch Environ Contam Toxicol, 58: 341-351.

Mate MS, RC Ghosh, S Mondal and DB Karmakar, 2010. Effect of lambda cyhalothrin on rats: an acute toxicity study. J Indian Soc Toxicol, 6: 25-28.

Mnif W, AH Hassine, A Bouaziz, A Bartegi, O Thomas and B Roig, 2011. Effect of endocrine disruptor pesticides: A review. Int J Environ Res Public Health, 8: 2265-2303.

Muhammad F, I Javed, ZU Rahman, MM Awais, MK Saleemi and MI Anwar, 2012. Quantitative structure activity relationship and risk analysis of some pesticides in the milk of cattle in Faisalabad, Pakistan. Pak Vet J, 32: 589-592.

Muhammad F, MM Awais, M Akhtar and MI Anwar, 2013. Quantitative structure activity relationship and risk analysis of some pesticides in the goat milk. Iranian J Environ Health Sci Eng, 10: 4.

Muranli FD, 2013. Genotoxic and cytotoxic evaluation of pyrethroid insecticides λ-cyhalothrin and α-cypermethrin on human blood lymphocyte culture. Bull Environ Contam Toxicol, 90: 357-363.

Ng YY, HD Lin, SC Wu, CY Yang, WC Yang, HH Liou, FH Hu, CC Hou, SS Tseng, NY Ku, NY Hsiao, WC Wu, HM Tu, TJ Lien, CC Lee, KK Tsang, CS Cheng, J Hu and RP Lin, 2013. Impact of thyroid dysfunction on erythropoietin dosage in hemodialysis patients. Thyroid, 23: 552-561.

Pérez JJ, MK Williams, G Weerasekera, K Smith, RM Whyatt, LL Needham and DB Barr, 2010. Measurement of pyrethroid, organophosphorus and carbamate insecticides in human plasma using isotope dilution gas chromatography-high resolution mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci, 878: 2554-2562.

Rahman ZU, JA Khan, T Khaliq and A Ali, 2012. Manual of Physiology-I. 5th Ed, University of Agriculture, Faisalabad, Pakistan, pp: 12-55.

Saravanan R, K Revathi and PB Murthy, 2009. Lambda cyhalothrin induced alterations in Clariasbatrachus. J Environ Biol, 30: 265-270.

Schindhelm RK, E Ten-Boekel, NE Heima, NM van Schoor and S Simsek, 2013. Thyroid hormones and erythropoiesis: A complex relation? Eur J Intern Med, 13: 102-107.

Sereda B, H Bouwman and H Kylin, 2009.Comparing water, bovine milk, and indoor residual spraying as possible sources of DDT and pyrethroid residues in breast milk. J Toxicol Environ Health Part A, 72: 842-851.

Tahir T, S Mushtaq, SA Rana and MA Shiekh, 2012. Farmers' awareness about spider as natural predator of cotton pests and hazardous effects of pesticides on their health from three districts of Punjab cotton belt: past findings and future priorities. Pak J Agric Sci, 49: 381-386.

Van-Sande J, J Parma, M Tonacchera, S Swillens, J Dumont and G Vassart, 1995. Somatic and germline mutations of the TSH receptor gene in thyroid diseases. J Clin Endocrinol Metab, 80: 2577-2585.

Verger PJ and AR Boobis, 2013. Global food supply. Reevaluate pesticides for food security and safety. Science, 16: 717-718.

Wang S, N Shi, Z Ji and G Pinna, 2002. Effects of pyrethroids on the concentrations of thyroid hormones in the rat serum and brain. Zhonghua Lao Dong Wei Shen Zhi Ye Bing Za Zhi, 20: 173-176.