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 (T3) and thyroxin (T4) 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.

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 LD50 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 leucocyte 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 (T₃ and T₄) 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. 1A). 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. 1B).

**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<0.01) 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 T₄ and T₃ was significantly reduced (P<0.001) in both groups treated 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-
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 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 T3 and T4. It has also been reported that pyrethroids can decrease the activity of hepatic type I iodothyronine 5\'-monodeiodinase (5\'-D-I), a deiodinase enzyme that transform T3 and T4 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 T3 and T4. It has also been reported that pyrethroids can disrupt the metabolism and hematological values in exposed subjects. Lambda-cyhalothrin caused a reduction in the serum level of T3 and T4 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.

**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 T3 and T4 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.

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