TOXIC EFFECTS OF TEFLUTHRIN AND ALUMINIUM ON HAEMATOLOGICAL PARAMETERS IN WISTAR RATS WITH SPECIAL REFERENCE TO AMELIORATIVE EFFECT OF ALPHA LIPOIC ACID

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Abstract: The present study was aimed to investigate the protective role of alpha lipoic acid on various altered values of hematological parameters produced by sub lethal doses of tefluthrin and aluminium alone and in combination for a period of 28 days. Forty eight wistar rats of either sex were divided into eight groups with six animals in each group. Group I served as control and were orally administered with corn oil. Groups II and III orally received tefluthrin and aluminium @ 1.1mg/Kg and 34mg/Kg respectively. Group IV animals were orally intoxicated both with tefluthrin @ 1.1mg/Kg and aluminium @ 34mg/Kg. Groups V received alpha lipoic acid @ 30mg/Kg where as groups VI, VIII and VIII respectively received tefluthrin, aluminium and combination thereof along with alpha lipoic acid. Tefluthrin and/or aluminium treatment produced a significant (P<0.05) decrease in the hematological parameters including hemoglobin (Hb), total erythrocyte count (TEC) and packed cell volume (PCV). Total leukocyte count (TEC) increased significantly (P<0.05) in all treated groups as compared to control. Groups treated with both tefluthrin and aluminium produced significant (P<0.05) changes in Hb and MCH as compared to groups treated with tefluthrin or aluminium alone. Pretreatment with alpha lipoic acid resisted the changes in hematological parameters produced by tefluthrin and/or aluminium.

Key words: Lipoic acid, Aluminium toxicity, Tefluthrin toxicity

INTRODUCTION

Pyrethroids account for 30 per cent of insecticides used globally [1]. Besides agriculture, they have a multitude of uses in veterinary, medical and household pest control [2]. Pyrethroids are also essential components of the worldwide efforts to combat malaria and other mosquito-borne diseases, despite the occurrence of resistance in some vector populations [3]. Unregulated and indiscriminate use of these chemicals have increased the risk of exposure and subsequent toxicity to humans and animals which is of considerable magnitude in India and other countries including the United States [4-7]. Tefluthrin, a fluorinated synthetic type-I pyrethroid is a colorless solid and is used to control a wide range
of insect pests both in agriculture and animal husbandry habitations and thereby have polluted the environment to great extent [8].

Aluminium is present in many natural/manufactured foods, cooking utensils, food additives, medicines (antacids, deodorants) and drinking water [9]. All this can lead to considerable exposure to this chemical which can find easy access into the bodies of humans/animals [10]. Several authors have indicated that an excessive and prolonged aluminium exposure have caused alterations in haematological and biochemical parameters after generation of free radicals along with enhanced activities of the antioxidant enzymes in plasma and tissues of animals models especially rats and rabbits [11-13].

The assessment of deleterious or toxic effects produced by concurrent exposure to commonly encountered chemicals is of great significance in order to find out toxicological consequences arising out of their interactions. Such understanding will help in comprehensive management of untoward effects produced by these chemicals. Very few studies have been attempted to assess the degree of hazard posed by simultaneous exposure pesticides and aluminium [14]. Therefore, present investigation was an attempt to study interactive toxic potential of tefluthrin and aluminium in wistar rats after their oral administration on haematological parameters for a period of 28 days and also to appraise the protective role of alpha lipoic acid in ameliorating such alterations.

MATERIAL AND METHODS

Chemicals: Aluminum chloride (AlCl₃ x 6 H₂O) as analytical grade was purchased from Hi-Media Labs Mumbai and was administered orally @ 34mg/kg after dissolution in corn oil [15]. Tefluthrin (PESTANAL®) and alpha lipoic acid as analytical standards were obtained from Sigma Aldrich and were orally administered @ 1.1mg/kg and 30mg/Kg respectively after dissolution in corn oil [16]. Alpha lipoic acid treatment in ameliorative groups was carried out 20 minutes before administration of tefluthrin and aluminium.

Animals and experimental design: Wistar rats (200-250 gm b. wt) of either sex procured from Indian Institute of Integrative Medicine (CSIR) Jammu were maintained under standard environmental conditions. The experiment was conducted strictly in accordance to the Institutional Animals Ethics committee. The animals were provided with free access to feed and water. The animal room was maintained at 21–24°C and 40–60% relative humidity with 12-h light–dark cycles, the light cycle coinciding with the day light hours.

After 2 weeks of acclimation, rats were divided randomly into 8 groups consisting of 6 rats each. The animals of group I served as control and received corn oil only. Animals in Group II were orally administered with tefluthrin @ 1.1mg/Kg where as rats in group III rats received aluminum chloride @ 34mg/Kg. Group IV received combined toxic doses of tefluthrin and aluminium @ 1.1mg/Kg and 34mg/Kg respectively. Group V animals were administered orally with alpha lipoic acid @ 30mg/kg. Animals in group VI received tefluthrin and alpha lipoic acid @ 1.1mg/Kg and 30mg/Kg respectively while as animals in group VII received aluminium chloride and alpha lipoic acid @ 34mg/Kg and 30mg/Kg respectively. Finally group VIII animals were orally administered with tefluthrin, aluminium chloride and alpha lipoic acid @ 1.1mg/Kg, 34mg/Kg and 30mg/Kg respectively. All the doses were administered in the morning continuously for 28 days and body weight was recorded at 7 days interval to adjust the dosage of application according to body weight.

After 28 days of daily treatment, the rats were anaesthetized with diethyl ether and blood samples were collected from retro-orbital fossa using capillary tubes in separate aliquots containing heparin and di-potassium salt of EDTA at the concentration of 10 IU/ml and 2 mg/ml of blood, respectively. Heparinized blood was used for the analysis of hemoglobin (Hb) [17] whereas, total erythrocyte counts (TEC), packed cell volume (PCV) and total leukocyte count (TLC) were analyzed in the EDTA treated blood (18). The mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular volume (MCV) were calculated mathematically [18].

Statistical analysis: The data collected during the experiment was subjected to analysis of variance which was carried in completely randomized design (CRD) and the significance was tested using Duncan Multiple Range Test [19]. The significance was assayed at 5% (P < 0.05) levels.
RESULTS

Results of the effect of tefluthrin (Tef), aluminium (Al) and alpha-lipoic acid (ALA) on haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC) and erythrocytic indices (MCV, MCH and MCHC) are presented in table 1. Compared to control, significant (P<0.05) decrease in the Hb and TEC and increase in TLC was observed in the rats exposed to either tefluthrin and/or Al with group receiving both tefluthrin and aluminium (Group IV) showed pronounced significant (P<0.05) change in haemoglobin level even in comparison to groups receiving tefluthrin (Group II) and aluminium (Group III) alone. Pre treatment with alpha lipoic acid in groups VI and VII significantly (P<0.05) increased the value of Hb, TEC and TLC values near to control value. Ameliorative group VIII showed significant (P<0.05) increase in Hb near to control but could not reverse the altered values of TEC and TLC. There was a significant (P<0.05) decrease in PCV in groups II, III and IV as compared to control group I. Ameliorative groups VI, VII and VIII significantly (P<0.05) restored the decreased value of PCV near to normal control values of group I. Also from observations depicted in table 2, no significant change in value of MCV was observed in treatment groups II, III and IV as compared to control (Group I). MCH value decreased significantly (P<0.05) only in group IV receiving both tefluthrin and aluminium from control value with non significant decrease in groups II and III receiving tefluthrin and aluminium respectively. Treatment with alpha lipoic acid has significantly (P<0.05) reversed the altered value of MCH as observed in ameliorative group VIII. No significant change was observed in MCHC in treated animals of II, III and IV as compared to control animals (Group I).

DISCUSSION

Several studies in laboratory animals have shown decreased values of hemoglobin levels, total erythrocyte count, packed cell volume and various erythrocytic indices on exposure to pyrethroids [15,20-23]. Disturbances in heme synthesis, destruction or reduction in the rate of formation of RBCs, and increased erythrocyte lipid peroxidation could be the possible reasons for such reduced hematological levels in tefluthrin intoxicated rats [25-27]. Likewise, inhibition of heme synthesis, either by inhibition of enzyme activity or interference with iron incorporation or utilization by aluminium may result in decreased hematocrit values [28]. Additionally, disturbances in the distribution pattern of trace elements viz zinc, copper, and iron together with lipid peroxidation in plasma and erythrocytes were also suggested as a mechanism of aluminum-induced anemia in rats [11]. Hemolytic activity of aluminium shown by decreased levels of haemoglobin, TEC and PCV in the present study may be due to changes in cell membrane of red blood cells. It has been reported that in the presence of aluminum ions, human erythrocytes lose their typical biconcave shape, turning into acanthocytes and stomatocytes [29]. The drastic reduction of haemoglobin and MCH in group receiving both tefluthrin and aluminium observed in present study might indicate a possible hemolytic effect of tefluthrin attenuated with aluminium which in turn can be due to increased erythrocytic lipid peroxidation in the presence of aluminium. All the treated animals in the present study showed increased leucocyte counts. Such findings are in agreement to pyrethroid intoxicated animal model studies [22,30] and aluminium exposed lab animals [23,31].

Pretreatment with alpha lipoic acid in ameliorating groups have reversed the changes in various haematological parameters. Alpha-lipoic acid (ALA) is considered as nutritional cofactor of ß-ketoacid dehydrogenase that is involved in energy metabolism of proteins, carbohydrates and fats [32]. In addition to central role in metabolism, it has also been found to alter redox status of cell by acting endogenous free radical scavenger inside and outside the cells and thereby, epitomizing itself as universal antioxidant in the body [33-35]. Tefluthrin and aluminium in present study serving as toxicants can generate free radicals due their metabolism in the body and the free radicals in turn can serve as cause for erythrocytopaenia, hypohaemoglobinemia and other altered values in haematology [36,37]. Protecting role of alpha lipoic acid in resisting the changes in various haematological parameters as observed in the present study can indirectly be justified from its capacity of quenching free radicals and maintaining the energy supply by acting as cofactor for enzymes of metabolism of tefluthrin and aluminium in the treated animals.

CONCLUSION

In conclusion, tefluthrin & aluminium chloride after repeated oral administration alone or in combination
produced marked haematological changes (Hb, PCV, TEC, and TLC). Such changes were more prominent and consistent with co-administration of these two toxicants. Haematological changes induced by tefluthrin and/or aluminium chloride were reversed significantly after pretreatment with alpha lipoic acid.

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