Asian Journal of Biological and Life Sciences | Original Research

Effect of Cyfluthrin on some clinical, haemato biochemical and pathological parameters in male Nubian goat kids

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Submitted : 05.05.2013 Accepted : 16.07.2013 Published : 31.08.2013

Abstract

The sequential development of the clinical signs and lesions in the organs of Nubian goat kids drenched with cyfluthrin at 500, 250 and 125 mg/kg/day b.w. was investigated. Salivation, tremors which end with choreoathetosis, upward and backward extension of the neck , respiratory rales ,bloat, greenish watery diarrhoea and recumbency were the important signs of cyfluthrin poisoning. Varying degrees of congestion and haemorrhages in different body organs, pulmonary emphysema and oedema accompanied with heart flabbiness, hepatorenal fatty change and/or necrosis and catarrhal gastroenteritis were the main pathological changes. Significant decrease ($p < 0.05$) in the PCV and in the RBC count ($p < 0.01$) accompanied with significant increase ($p < 0.01$) in the values of MCV and WBC count were the haematological changes. Significant decrease ($p < 0.05$) in the serum concentrations of total proteins, albumin and glucose and significant increase ($p < 0.05$) in the serum concentration of urea, and in the serum activity of AST were detected in cyfluthrin treated groups .

INTRODUCTION

The primary mode of pyrethroids action in both insects and mammals is disruption of voltage-sensitive sodium channels (VSSC) function [1]. In general, type II compounds delay the inactivation of VSSCs substantially longer than do type I compounds [2,3,4]. Curtis and John [10], mentioned that type I poisoning syndrome or T syndrome, is produced by esters that lack -cyano substituent and characterized mainly by hyperexcitation and whole body tremors while type II syndrome, or C.S (choreoatheteosis/salivation) syndrome is produced by esters that contain the -cyano substituentes and display coarse tremors, clonic seizures, choreoathetosis and profuse salivation without lacrimation.

Cyfluthrin is a synthetic cyano - containing pyrethroid insecticide that has both contact and stomach poison action. It is a non-systemic chemical used to control chewing and sucking insects on crops such as cotton, turf, ornamentals, hops, cereal, corn, deciduous fruit, peanuts, potatoes, and other vegetables. Cyfluthrin is also used in public health situations and for structural pest control [5].

It is well known that 90% of the Sudan population practicing agriculture and grazing animals and most of herders are nomads moving with their animals from the South of Sudan to the North following the rainy season and vice versa searching for fodder and water. Those herders are illiterate depending on their experiences in treating their animals, because the veterinary service centers are far away and mainly found in the large villages. Some of the herders used the agricultural formulations of pesticides in eradicating the external parasites infesting their animals without care to manufacturer instructions. Outbreaks due to the abuse of these pesticides lead to death of large number of animals. Casualities which were admitted to the veterinary centers were confined to animals reared in irrigated or mechanized agricultural schemes where mixed animals / farming are practiced. Widespread use of these products and the need for understanding the degree and manifestations of potential toxicities, this experiment was planned to determine the potential for acute and subchronic toxicosis in Nubian goat kids drenched with single and repeated doses of cyfluthrin.

MATERIALS AND METHODS

Animals

Fourty, apparently healthy Nubian male goat kids of 5-6 months old and weighing 10-12 kg, were purchased from Hilat Kuku Goats Market, Khartoum North. Animals were kept in standard pens at the College of Veterinary Medicine and Animal Production, Sudan University of Science and Technology. Goats were fed on forage sorghum (*Sorghum vulgarae)* and provided water *ad libitum*. The animals were kept 30 days for adaptation and acclimatization during which each animal was injected intramuscularly with Oxytetracycline (Embacycline 5% Coophavet, France) at rate of 1 ml/day/5 kg for 5 days, and drenched Albendazole (25%, AVICO, Jordan) at rate of 1 ml/5 kg for one day then, repeated after 14 days followed by Amprolium (Amprocidia 60%, ACPVD, Jordan) 0.2 gm/day/ kg for 6 consequitive days for the control of bacterial diseases, worms and coccidiosis respectively. By the end of the adaptation period, the animals were divided randomly into 4 groups each of ten. Each group was kept separately.

Cyfluthrin

Chemical name-[cyano- (4-fluoro-3-phenoxyphenyl) methyl-3- (2,2- dichloroethenyl)-2,2-dimethylcyclo-propanecarboxylate] and of molecular formula ($C_{22}H_{18}C_{12}FNO_3$) produced by (Bayer Agricultural Product, Kansas City Mo 64120). Cyfluthrin emulsifiable concentrate was used in this study at concentration of 50%.

Dosing

Goats in groups 1, 2 and 3 were drenched daily doses of

Cyfluthrin at the rate of 500,250 and 125 mg/kg/ b.w. respectively. Goats in group 4 were not drenched and used as controls. The duration of the experiment is 45 days.

Blood Sampling

Each experimental animal was subjected to blood sampling on days 1,3, 7, 14, 21, 28, 35 and 45- post dosing. Additional samples were taken from animals in moribund condition. A volume of 10 ml blood was collected from the jugular vein puncture using a disposable 10 ml syringe with 18.5 gauge needle. Immediately, 1 ml of the collected blood sample was poured into a small clean 5 ml vacutainer containing anticoagulant EDTA (ethylene diamine-tetra-acetic acid) for the measurement of haemoglobin concentration (Hb), packed cell volume (PCV), red blood cells count (RBC), white blood cells count, (WBC), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) according to the methods described by Dacie and Lewis [6].

Another 1 ml was poured into a small clean 5 ml vacutainer containing fluoride oxalate as an anticoagulant and used immediately for glucose determination using enzymatic colorimetric kit (GOD-PAP method. Fouz Diagnostics Laboratory) (FDL) and the concentration was read in spectrophotometer (Perkin -Elmer 2380, Germany).The remaining blood was kept to clot, centrifuged at 3000 r.p.m. for 5 minutes and sera were collected and kept at -20 °C for the measurement of the activities of aspartate aminotransferase (GOT,AST,E.C.2.6.1.1.), alanine aminotransferase(ALT,GPT, E.C.2.6.1.2,), alkaline phosphatase (ALP, E.C. 3.1.3.1.) and for the concentrations of total proteins, albumin , total bilirubins, and urea using commercial kits, (Plasmatec Laboratory Products Ltd., England), and absorbance was measured in a spectrophotometer (Unicam 8625 uv / vis Spectrometer PU , England). The concentration of serum globulins was obtained by subtracting values of serum albumin from the total proteins. Serum concentration of sodium (Na), potassium (K), calcium (Ca), inorganic phosphate (PO_4), magnesium (Mg), copper (Cu) and iron (Fe) was determined using the method described by Allen [7]. Calibration curve was prepared for each element. The sample solution was aspirated along with the standard according to the specific cathode lamp used and they were read out in the atomic absorption spectrophotometer (Perkin Elmer 2380, Germany) against the deionized water as blank.

Clinical Signs

Experimental animals were closely observed for clinical signs and behavioral changes.

Postmortem lesions

Dead or sacrificed animals were immediately underwent postmortem examinations and lesions were recorded. Specimens of the brain, spinal cord, lungs, heart, liver, spleen, pancreas, kidneys, abomasum, omasum and small intestines were collected and fixed in 10 % neutral buffered formalin, embedded in paraffin wax, sectioned at 5µm and stained with haematoxylin and eosin (H&E) for histopathological investigations.

Statistical analysis

The data were analyzed using Students t- test [8].

RESULTS

Clinical signs

Goats in group (1) showed 5 minutes postdosing, profuse frothy salivation , chewing movements of the jaws, licking or chewing inanimate objects and pressing forward with the head then coarse tremors which end with choreoathetosis , upward and backward extension of the neck (Fig.1), abduction of the elbows and respiratory rales . One hours later the animals suffered off food, bloat, greenish watery diarrhoea, downward arching of the back and straddling of the legs, depression, staggering, then fall down, recumbent and the head carried around towards the flank with difficult respiration. These animals died on day 1. Goats in group (2) showed the same clinical signs as in group (1) but were moderate in severity.These signs started two hours postdosing and continued for 5 hours then disappeared gradually specially those of the neuromuscular nature. These animals died on days 9-11.

Fig. 1. Goat in group (2) drenched with cyfluthrin 250 mg/kg /day which died on day 16 and showing upward and backward extension of the head and neck.

Goats in group (3) showed mild clinical signs, which started three hours postdosing and lasted for one hour and consisted mainly as dullness and the animals separated from each other, then these animals retained their normality. These animals were sacrificed on day 45.

Goats of group (4) were not drenched with cyfluthrin, remained healthy and were sacrificed on day 45.

Postmortem lesions

Generally, congestion and haemorrhages were the dominating features in the different organs of the drenched groups. The lesions were dose - dependent. Pulmonary emphysema and oedema, heart flabbiness accompanied with hydropericardium, scattered foci of fatty change and/or necrosis in the liver and kidneys and haemorrhagic foci on the internal surface of the small intestines were the most prominent lesions in cyfluthrin - drenched goats. No apparent lesions were observed in the rumen, reticulum, omasum, spleen, cutaneous blood vessels and lymph nodes. No lesions were observed in the control goats of group 4.

Histopathological findings

Brain: The cerebrum and cerebellum showed widening of the perivascular spaces , congestion, small foci of haemorrhages, and slight gliosis.

Spinal cord: slight perivascular lymphocytic infiltration (cuffing).

Lungs: In groups 1and 2 many alveoli were coalesced due to rupture of alveolar walls and filled with pinkish fibrinous exudates while in group 3 the interlobular septa were thickened and infiltrated with lymphocytes and some of the bronchioles showed peribronchiolar lymphocytic infiltration.

Heart : Some of the cardiac muscle bundles had hyaline degeneration. Cardiac bundles were separated by pinkish homogenous material which infiltrated with inflammatory cells and RBC.

Liver: Moderate centrilobular hepatocytic cytoplasmic vacuolations were seen in group 1. While in groups 2 and 3 these lesions were extended to the portal areas with slight bile ductules hyperplasia .The sinusoids were congested severely in group1 and moderate to mild in groups 2 and 3 respectively.

Pancreas: Slight congestion, some of the acini were degenerated.

Kidneys: The cortical renal tubular epithelial cells showed severe to moderate hydrophilic cytoplasmic vacuolations, and others were coalesced or degenerated. Some of the cortical renal tubles were dilated . Some of the glomeruli were shrunk and resulted in widening of Bowman's space, others were lobulated or hypercellular.

Abomasum: The mucosal epithelial cells were eroded. Congestion and scattered foci of haemorrhages were seen in the submucosa and *lamina propria*.

Small intestines: The lumen contained shreds of epithelial cells , inflammatory cells and RBC. Foci of haemorrhages were seen in the submuosa and *lamina propria.*

No lesions were observed in the spleen and the omasum. No histopathological changes were seen in control group (4).

Haematological and serobiochemical findings

No samples were taken from goats in group 1 because they were died within 24 hours. No significant changes were observed in the Hb concentration, MCH and MCHC of goats in groups 2 and 3. Significant decreases in the levels of PCV ($P<0.05$) and in the RBC count ($P<0.01$) were recorded in goats in groups 2 and 3.Significant increase in the WBC count and in the values of MCV ($P<0.01$) were recorded in these goats.

Animals in groups 2 and 3 showed no significant changes in serum concentrations of sodium, potassium, calcium, inorganic phosphorus, magnesium, iron , copper and globulins ,total bilirubin and in the ALT activity. It was noticed that serum concentrations of total proteins and albumin and glucose had decreased significantly ($P<0.05$) in groups 2 and 3 while the serum concentration of urea and AST activity had increased significantly ($P<0.05$) in the same groups. The increase in serum ALP activity is still within the reference interval.No significant changes were observed in the serum values of group (4).

DISCUSSION

The objective of this study was to investigate the toxic effects of cyfluthrin in Nubian goat kids as many casualities suspecting exposure to this insecticide had been admitted to veterinary centers in irrigated agricultural schemes of the Sudan. The present study displays toxicity with fatal events in goat kids receiving 250 mg/kg /day and above by drench. Repeated daily dosing of 125 mg/kg caused mild clinicopathological effects and tolerated by the animals. The oral L D_{50} of cyfluthrin in sheep > 1000 mg/kg [9] which indicates that goat kids are more sensitive than sheep. The nervous signs which appeared among the treated animals were attributed to cyflurthin neurotoxicity [11,12].

The cardiopulmonary functions were adversely affected and were a part of the neurotoxic effect of cyflthurin.The hepatorenal lesions as well as the increase in serum urea concentration and the decrease of total proteins and albumin concentration indicate that cyfluthrin had hepatonepheric enrolement. The profuse salivation and diarrhoea which accompanied by gastroenteritis may be attributed to the irritating effect of cyfluthrin or achieved as part of stimulation of the parasympathetic system. On the other hand, colic manifested by arching of the back might be due to hepatorenal or gastroenteritis . The clinical signs and pathological lesions which observed in this study were more or less similar to that observed by Mohamed and Adam (1990)[13] when studied the toxicity of sumicidin (Fenvalerate) to Nubian goats.

The present study demonstrated the presence of macrocytic normochromic anaemia as a result of decreases in the PCV and RBC and an increase of the MCV and leukocytes count values. In cases of chronic haemorrhage the loss of blood is not always easy to appreciate, and at early stage the cells will be macrocytic [14] . These haematological changes point to that, cyfluthrin might had an endotheliotoxic effect.

CONCLUSION

The present study conclude that cyfluthrin is fatal when given once at 500 mg/kg and at 250 mg/kg repeated for 11 days. Doses such as 125 mg/kg/day can be tolerated by the animals in this study. The cause of death can be due to the consequences of the neurotoxic effects of cyfluthrin on the vital organs.

Further studies are needed to illustrate functional and physiological effect of cyfluthrin in vital body organs in the different species of animals.

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