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Toxicologic Effect of Tri Ortho Cresyl Phosphate in Cerebellum of Chiken

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ABSTRACT
The goal of the study was to elucidate the neurotoxicity of TOCP (Tri Ortho Cresyl Phosphate) in adult hen. forty adult hens were divided equally into two groups (treated and control) for acute study for 21 days as a single dose 2.5 mg / kg a day. Moreover, chronic study was done on eighty adult hens which divided into four groups (20 hens each); control group and treated groups which in turn supplemented with TOCP at 1.25, 2.5 and 5 mg/kg a day orally for ninety days and labeled as neurotoxicity induced groups. Most of transmission electron microscopic changes (TEMc) of cerebellum occurred in the synapses associated with degeneration of myelin sheath and/or partial demyelination in the presence of myelinated nerve fiber. Additionally, neurotoxicity of TOCP revealed abnormal lamellate of mitochondria with dark stained. The other adverse effects of TOCP extended into CNS (cerebellum and spinal cord) which was characterized by the degeneration of myelin sheath of myelinated nerve fibers with lamellated bodies' formation, auto phagocytosis of degenerate myelin by oligo dendrocyte. Severe cases exhibited mitochondrial degeneration especially in the axoplasm of myelinated nerve fibers associated with calcification in the lamellated degenerated mitochondria with complete loss of neurons which lead to loss of function. These findings concluded that the histopathological results supported the clinical and biochemical findings, and the severity of nerve damage in a dose-dependent manner.

Keywords: Neurotoxicity, Cerebellum, Hen, Ultrastructure

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INTRODUCTION

The neurotoxicity of organophosphorus compounds was studied by[1],also [2] was studied the importance of the return death process in experimental and human neurological disease. The late neuropathy which can be caused by some organic phosphorus ester: the mechanism and the challenge was studied by [3]. Organic phosphorus ester causes the delayed neurotoxicity effect: action mechanism and structure/activity studies [4] .[5] the process of dyeing back. Many naturally occurring neurodegenerative disorders are commonly common and toxic. [6] Histopathological studies have done in tri dental phosphate poisoning. [7] Studied about the outbreak of polyurethane inflammation due to poisoning with tri-tradable phosphate. [8] Outbreak of krisel tri-orchphosphate poisoning (TOCP) in Durban. [9] The real cholinestraste inhibition in TOCP poisoning was studied with reinforcement by "Tween 80". [10] Some effects of experimental organic phosphorus poisoning in primates did. [11] Did not teasing from acute neurotoxicity of tri-kersili phosphate (TOCP) in the sciatic nerve of the adult hen. [12] Electron endoscopy was not the acute neurotoxicity of TOCP (tricellular chryslate phosphate) of the adult chicken's sciatic nerve. [13] Amorphous and neurotoxic analysis are evidenced by tri-krisnil phosphate poisoning in the chicken.[14] The study of the neurotoxicity of trichricephosphate (TCP) in crystalline (nycticebus coucang). [15] The effect of tri-x chrysal phosphate (TOCP) studied intoxication and termination of the sensory nerves of slow loris. [16] Delayed toxicity neurons caused by the organic phosphorus compound in wild malard duckling effect of leptophos.[17] studied about long-term neurotoxicity through a low-level local application of leptophos for hen comb.

MATERIALS AND METHODS

This study included two experiments were done on 120 adult hen , acute study included 40 chicken divided equally into two groups (treated and control) were supplemented one single dose 2.5mg/kg for 21 days, while chronic study was conducted on 80 hens divided into four groups (20 hens) each ,these groups were : untreated control , treated groups were dosed orally daily with 1.25, 2.5 and 5 mg/kg for 90 days neurotoxicity. Cerebellum was taken from scarified hens , then cerebellum was a fixed in glutaraldehyde after installing resin plastic blocks were made and cut by the super microtome 1ug section was done and stained with blue toluidine for steering and choosing the best fields for electron microscope and then made copper Graduates stained with uranyl lead acetate to examine with electron microscope.

RESULTS

An electron microscope scan showed toxic neurological changes mostly in synapses characterized by the found of dark dissolved mitochondria. fig(1,2,3,4) .Also presence of changes in myelinated nerve fiber associated with degenerate myelin fig (5,6,7) and/or partial demyelination with degenerated myelin in oligo dendrocyte as an evidence of auto phagocytoses of degenerated myelin fig (8,9,10).

Fig 1: Cerebellum, synapses, some with swollen mitochondria others with dark stained degenerated mitochondria (EM 30000X)

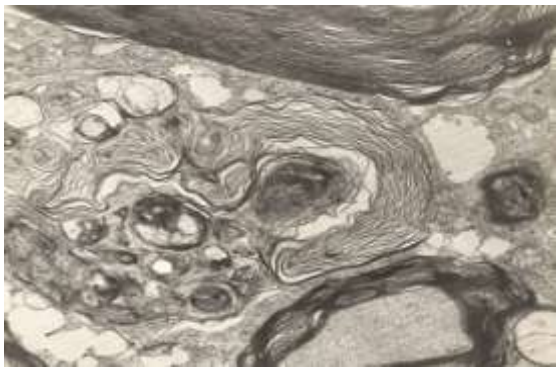

Fig 2: Cerebellum, degenerated myelin also present of dark stained degenerate lamellated mitochondria. (EM 20000X)

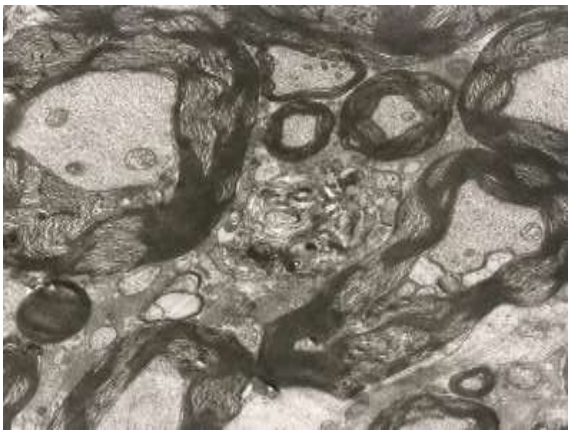

Fig 3: Cerebellum, synapses with dark stained degenerate mitochondria (EM 20000X)

Fig 4: Cerebellum, synapses with degenerated dark stained lamellated mitochondria (EM 30000X)

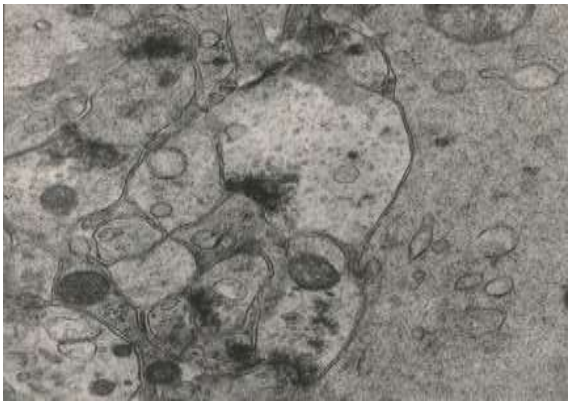

Fig 5: Cerebellum, nerve ending synapses, note pre and post synapses (EM 15000X)

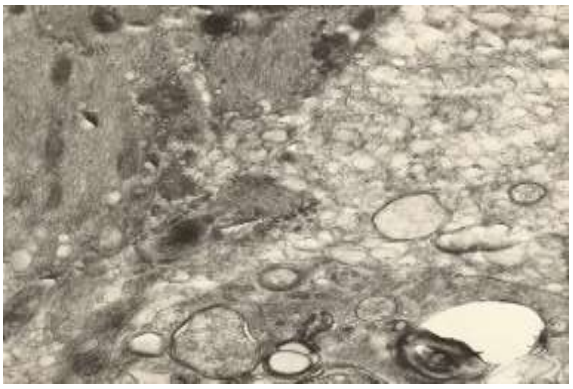

Fig 6: Cerebellum, degenerated demyelinated nerve fibers (EM 20000X)

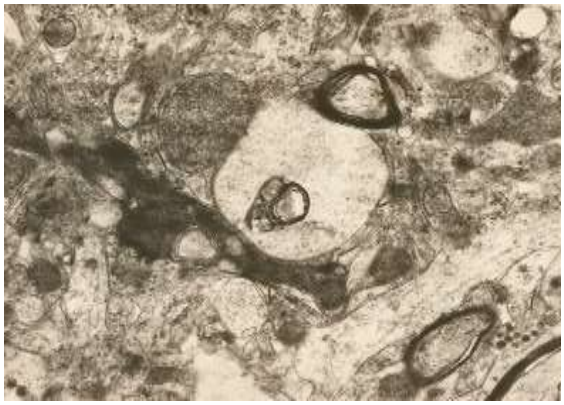

Fig 7: Cerebellum, note synapses with degenerated lamellated mitochondria (EM 20000X)

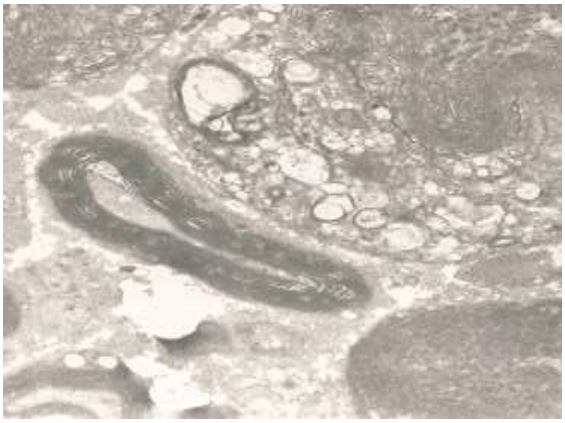

Fig 8: Cerebellum, nerve fiber with degenerated myelin associate with lamellation and ovoid body formation (EM 20000X)

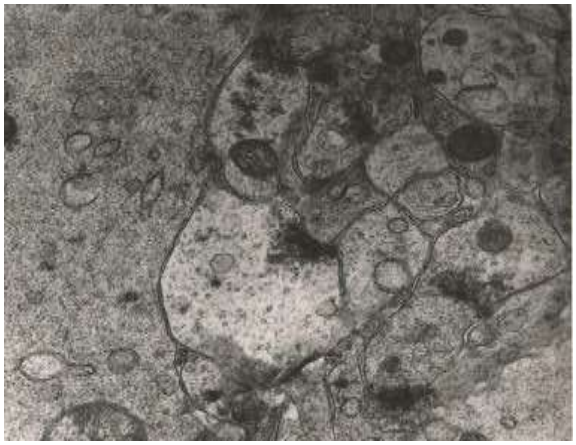

Fig 9: Cerebellum, synapses, note cleft formation with pre and post synaptic process and also dark stained degenerate mitochondria in other synapses (EM 30000X)

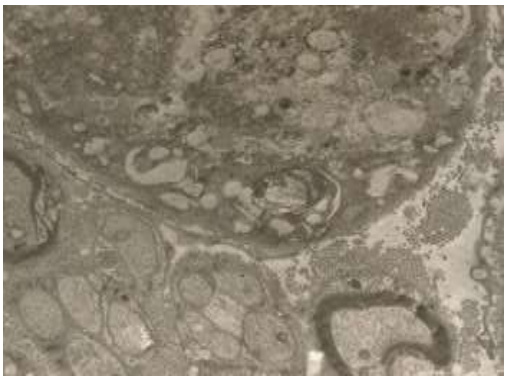

Fig 10: Cerebellum, synapses and nerve fiber with demyelination associated with degenerated myelin with ovoid body formation (EM 20000X)

DISCUSSION

Neurotoxicity of organophosphorus compounds with anticholine esterase activity was studied by [1]. In the present study, lesion where it is found in cerebellum which is induced by neurotoxicity by organophosphorus due to the inhibition of cholinesterase which was already reported by [1]. Dying back neurotoxicity effect of organophosphorus was explained by [2] , the present study stated by [2] due to the neurotoxic effect of organophosphorus on central nervous system especially cerebellum. The delayed neuropathy caused by some organic phosphorus ester: mechanism, challenge was studied by [3]which supporting the result of the current study. The delayed neurotoxic effect of organophosphorus stressing on mechanism and action was studied by [4] ,The present study supported [4] .There were clear electron microscopic changes related to the treatment with organophosphorus. The toxic neuropathies associated with dying back process was examined by [5] and the present study support [5]. There were electron microscopic changes due to neurotoxicity of organophosphorus. The histopathology of organophosphorus poisoning, was shown by [6] and the present study supported [6] .Clear evidence of electron microscopic changes due to neurotoxic effect of organophosphorus was stated by [7] that reported a polyneuritis due to poisoning by organophosphorus, the current study showed electron microscopic changes induced by organophosphorus and supported [7]. The current study found electron microscopy changes due to neurotoxicity of organophosphorus and it was supported by [8] who studied outbreak of poisoning induced by tri-ortho-cresyl phosphate (TOCP). The inhibition of true cholinesterase in TOCP poisoning was studied by [9] , in the present study, electron microscopic study was done and found neurotoxicity changes, therefore; it supported by [9]. The experimental organophosphorus intoxication in primates was examined by [10] who reported treatment related changes, and this study showed electron micro changes caused by neurotoxicity by TOCP in agreement with [10]. It was shown by [11] that the control of sciatica of untreated birds within normal limits with the presence of a reaper node and normal myelin sheath while those chickens are given a single dose of tri ortho cresyl phosphate (TOCP) as 500 mg/kg orally showed varying degree of dissolved myelin, fragmented with the myelin removal area. The severity of fragmentation and the removal of melanomas from the sciatic nerve corresponds to a varying degree of ataxia, coordination and paralysis that appear clinically in hens. The subject of current research has not studied electron microscopic on the mitochondria in the central nervous system of adult chicken cause dislocated by TOCP. [12] The result of the electron microscope of the sciatic nerve showed myelin degeneration in spinal nerve fibers characterized by myelin deformation, myelin clumping, spherical body formation of myelin, and the brilliant body of degenerated myelin, exoplasm showed increased neurofilament also present of degenerative mitochondria stained darkness. The current study focused on electronic microscopy changes in mitochondria in the central nervous system caused by the neurotoxicity of TOCP in adult hens.

CONCLUSIONS

In the present study, it was proven that the regular oral administration of Tri Ortho Cresyl Phosphate (TOCP) in adult hen for (21 and 90) days as neurotoxicity inducer has the ability to degenerate the peripheral and central nervous system and loss of function in a dose, time-dependent manner. Furthermore, it was concluded from this study of

the microscopic electron showed changes in cerebellum cannot be seen by a light microscope.

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