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STUDYOFACUTEDELAYEDNEUROTOXICITYOFTRI ORTHO CRESYLPHOSPHATE(TOCP) OF SPINAL CORDBY LIGHT MICROSCOPE IN ADULT HEN

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ABSTRACT

Acute delayed neurotoxicity of spinal cord of adult hens treated with TOCP(triorthocresylphosphate) as positive control for organophosphorus, histopathology of light microscopy of Toluidine blue stains showed occasional nerve fibers with partial demyelination also nerve fibers with clumps or masses of degenerate myelin.

KEYWORDS: Tri-Orthocresyl Phosphate, Light Microscope, Spinal Cord, Acute and Hen.

INTRODUCTION

The present review describes a group of organophosphorus compounds with delayed neurotoxic properties [1]. Delayed neurotoxicity is a delayed onset of prolonged loco motor ataxia resulting from a single or repeated exposure to an organophosphorus compound [2, 3]. For many years, the effect was wrongly termed "demyelization" or "demyelinating disease" because of the early misinterpretation of pathological lesions as reflecting demyelination instead of being primary axonal degeneration followed by demyelination [4]. Since 1978, this effect has been termed organophosphorus ester-induced delayed neurotoxicity or OPIDN [5]. OPIDN was first recognized at the end of the nineteenth century in humans poisoned with TOCP[6, 7]. Snce then an estimated 40,000 cases of delayed neurotoxicity in humans have been documented. In the 1920s about 20,000 persons in the United States developed "Ginger-Jake" paralysis after the consumption of an extract of ginger called "Jamaica Ginger" that had been adulterated with TOCP [8-16]. Later this syndrome was recognized in Europe, South Africa, and India as a result of the deliberate or accidental use of TOCP-containing preparations [17-29]. In 1951 three persons were poisoned with a then newly developed insecticide, mipafox, and developed symptoms of delayed neurotoxicity [30]. Between 1974 and 1975 the experimental insecticide leptophos was implicated in the poisoning and paralysis of some workers in the Texas factory where it was manufactured and packaged [31, 32]. Symptoms associated with TOCP [33-37] and mipafox [30, 38] poisoning in human

subjects are well documented. The clinical conditions of persons in the leptophos incident were diagnosed as multiple sclerosis, encephalitis, or psychiatric disorder [30,32,39].

MATERIALS AND METHODS

Experimental design

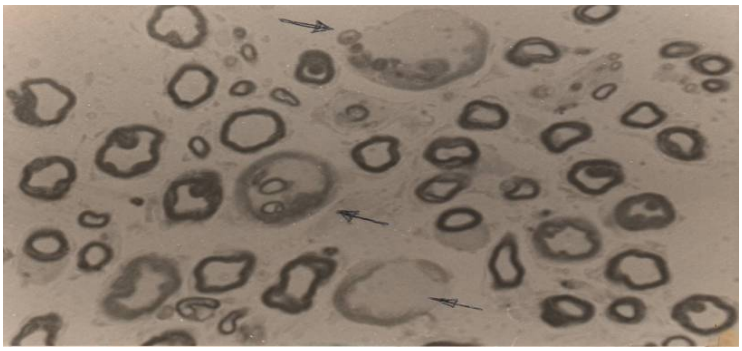
Twenty adult hen were divided in two groups, 10 untreated control and 10 dosed orally with single TOCP (triorthocresylphosphate) as positive control for organophosphorus of 500 mg/kg delayed acute neurotoxicity for 21 days, clinical signs appeared after 10 days of treatment and progressed till the end of 21 days, symptoms various from in coordination, ataxia and paralysis, there were grades of those changes from 1 to 6, samples of spinal cord were taken, sections of spinal cord were made on different levels such as cervical, thoracic, lumber and sacral region, those were stained with Toluidine blue, those were photographed at different level and at different powers.

Examination

Samples for histopathological examination were taken from spinal cord, those were cut in pieces of 2 to 3 cubic centimeters, samples were fixed in 10% phosphate buffered formalin and left in fixative for several days, the materials were embedded in paraffin, then paraffin blocks were made and cut by microtome as 5-7 microtones passing through different concentration of alcohol for dehydration and then rehydration to remove the paraffin then sections were stained by Toluidine blue. Stained sections were examined with light microscope on different powers for histopathological changes (40)

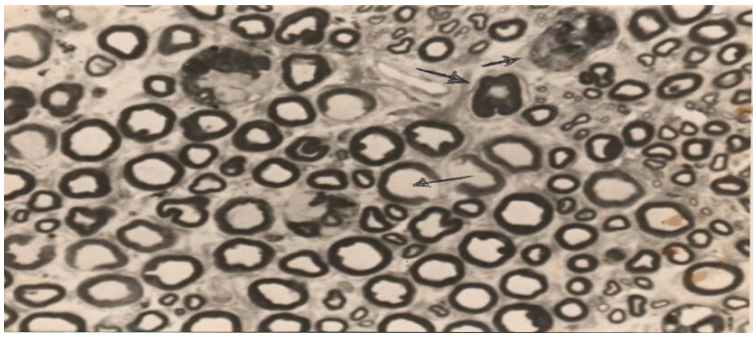
RESULTS

Light microscopy of spinal cord from treated adult hens of acute delayedneurotoxicity showed partial demyelination of some nerve fibers as in (fig1), while in another figures there were degenerate myelin(fig2). Furthermore some birds showed degenerate nerve fibers with clumps of degenerate myelin and partial demyelination in others (fig3), same changes were present at low magnification in (fig4). In addition in (fig5) a number of demyelinated nerve fibers, in another section, fields of nerve fibers with degeneration associated with clumps of degenerate myelin(fig6).on some condition some sections of spinal cord where majority of nerve fibers appeared without changed (fig7).

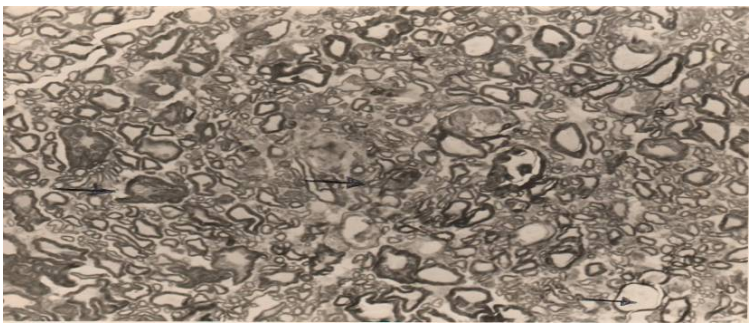


Fig(1): neurotoxicity of TOCP, spinal cord note partial demyelination of nerve fibers.(arrows) (20X, Toluidine blue stain, light microscope).

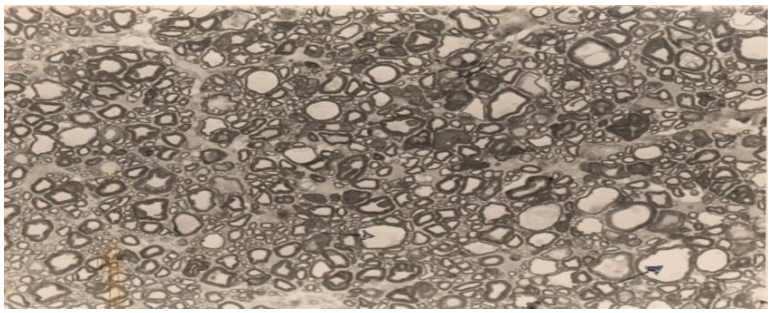
Fig(2): neurotoxicity of TOCP, spinal cord note masses of degenerate myelin in degenerate nerve fibers.(arrows) (40X, Toluidine blue stain, light microscope).



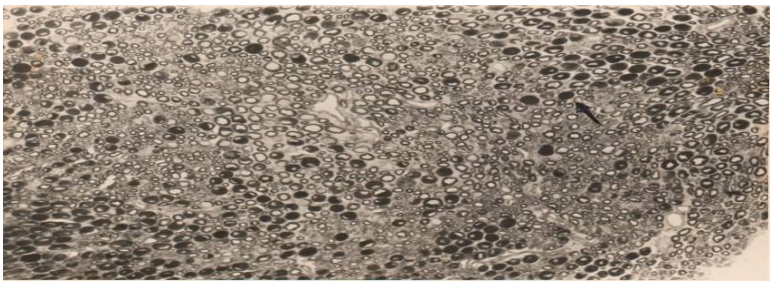
Fig(3): neurotoxicity of TOCP, spinal cord note clump of degenerate myelin in nerve fibers and partial demyelination.(arrows) (40X, Toluidine blue stain, light microscope).



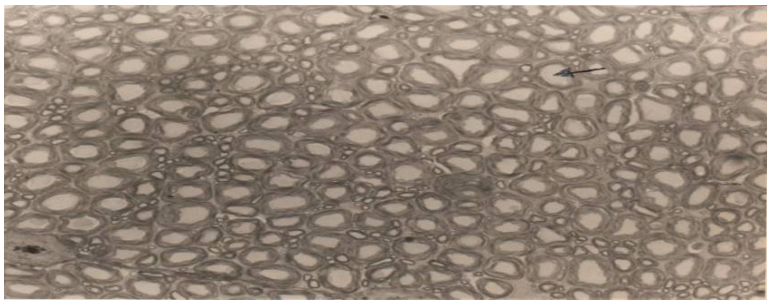
Fig(4): neurotoxicity of TOCP, spinal cord note clump of degenerate myelin in nerve fibers and partial demyelination. (arrows) (20X, Toluidine blue stain, light microscope).



Fig(5): neurotoxicity of TOCP, spinal cord note high number of demyelinated nerve fibers. (arrow) (20X, Toluidine blue stain, light microscope).



Fig(6): neurotoxicity of TOCP, spinal cord note high number degenerate nerve fibers with clumps of myelin. (arrow) (10X, Toluidine blue stain, light microscope).



Fig(7): neurotoxicity of TOCP, spinal cord note majority of nerve fibers appear normal. (arrow) (20X, Toluidine blue stain, light microscope).

DISCUSSION

The neurotoxicity of TOCP(tri-ortho-cresyl-phosphate) phosphorus, with acute delayed neurotoxicity, single oral dose of 500 mg/kg with corn oil in adult hen, the age related and species related effects of TOCP neurotoxicity was discussed by[1] and this applied on the present study as it was found that adult hen the best model for delayed organophosphorus delayed neurotoxicity, even with development of the lesions affecting long tract of myelinated nerve fibers. In addition[41] discussed mechanisms of organophosphorus stressing the fact that TOCP and some other organophosphorus induced delayed neurotoxicity with clinical signs and light microscopic lesions in spinal cord. Delayed

neurotoxicity by TOCP and some other organophosphorus compounds were in references [1-5]. The lesions reported were in agreement with the light microscopic findings in spinal cord also agreed with clinical findings too, [1]review the neurotoxicity of organophosphorus and reported OPIDN due to TOCP and that agreed with our findings in spinal cord of adult hen, including the clinical signs, but one thing that the lesions in sciatic nerve in acute delayed neurotoxicity more severe than those of spinal cord, some which only recede in subchronic neurotoxicity of peripheral nerve which will be less and that of spinal cord will progress and that will be in OPIDN. [6-39],the history of organophosphorus with clinical signs and pathological neural lesions were in agreement with what we found clinically and on base of light microscopy of spinal cord. In spinal cord in acute neurotoxicity the changes of spinal cord were less than sciatic nerve.

Research highlights

The present investigation brings important knowledge about neurotoxicity of organophosphorus, using TOCP as positive control, on spinal cord.

Finding and policy aspects

The neurotoxic findings of organophosphorus in spinal cord brings the attention on neurotoxicity of spinal cord and push the need to examine the spinal for future research on neurotoxicity.

Justification of research

The findings of neurotoxicity of organophosphorus in spinal cord preserved the need to examine the spinal for any treatmentrelated neurotoxic effects.

Conclusion

The results demonstrate that spinal cord can show treatment -related neurotoxic effects.

Recommendation

Future neurotoxicity research needs to include spinal cord, as it can give interesting treatment - related neurotoxic changes.

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