JOURNAL OF INTERNATIONAL ACADEMIC RESEARCH FOR MULTIDISCIPLINARY
Impact Factor 1.393, ISSN: 2320-5083, Volume 2, Issue 6, July 2014

TEASING OF DELAYED ACUTE NEUROTOXICITY OF TRIORTHOCRESYLPHOSPHATE(TOCP) IN SCIATIC NERVE OF ADULT HEN

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ABSTRACT

The study was done on 40 adult hen (leghorn) over six month of age, with two week acclimation, then the hens were divided in 20 control and 20 treated by oral gavage with 500 mg/kg of tri-ortho cresyl phosphate (TOCP) per hen as single dose, the birds were killed after 21 days. The results showed that sciatic of control untreated birds within normal limits with presence Ranvier node and normal myelin sheath while those hens given single dose of tri-ortho cresyl phosphate(TOCP) as 500 mg/kg orally showed varying degree of fragmented degenerate myelin with area of demyelination. The severity of fragmentation and demyelination of sciatic nerve correspond with varying degree of ataxia, in coordination and paralysis clinically appearing in the treated hens.

KEYWORDS: Tri-Ortho Cresyl Phosphate, Neurotoxicity, Hen and Sciatic Nerve.

INTRODUCTION

Concurrent signs of lesions in the peripheral and central nervous system have been already described for experimental triorthocresylphosphate (TOCP) poisoning. In previous works we reported cases showing,2-3 months following TOCP-polluted alcohol ingestion, simultaneous peripheral and central nervous system signs of lesion, predominantly in the distal portions of the longer axons, Accordingly, a "dying-back" process appears to underlie the TOCP- neuropathy, which Cavanagh has been the first to mention [1].

Most modern synthetic organophosphorus compounds are tailor-made to inhibit acetyl cholinesterase (AChE), an enzyme essential for life in humans and other animal species. Tetraethyl pyrophosphate was the 1st organophosphate synthesized as an AChE inhibitor in 1854. Later, dimethyl and diethyl phosphor fluoridates were synthesized. During World War II, organophosphorus compounds were developed primarily as agricultural insecticides, and later as chemical warfare agents. The majority of organophosphorus insecticides are organophosphorothioates; nerve agents are organophosphates or organophosphonothioates; industrial chemicals are typically organophosphates. Early studies on the mechanisms of OPIDN centered on the inhibition of the esterase's AChE and BChE by organophosphorus

esters. Subsequent studies eliminated both enzymes as targets for OPIDN. Johnson proposed an NTE—an enzymatic activity preferentially inhibited by organophosphorus compounds capable of producing OPIDN as its target. Despite numerous studies since the introduction of this concept 35 yr ago, the NTE hypothesis has not advanced our understanding of the mechanism of OPIDN because: (a) evidence for the involvement of NTE in the development of OPIDN is only correlative; (b) it has not been shown how inhibition and aging of NTE leads to axonal degeneration; (c) NTE, which is present in neuronal and non-neuronal tissues and in sensitive and insensitive species, has no known biochemical or physiological function; (d) some organophosphorus pesticides that produce OPIDN in humans do not inhibit or age NTE; and (e) phosphine's that produce Type III OPIDN do not inhibit NTE., However, the most convincing evidence against this hypothesis is the recent finding that NTE-knockout mice are sensitive to the development of OPIDN, indicating that this enzyme is not involved in the mechanisms of OPIDN [2]. Research on neurotoxicity of organo-phosphorus gose back to many years 1930 gingel jach accident of adulterated alcohol with tri-ortho cresyl phosphate(TOCP), when about 10,000 American people affected with ataxia, incoordination and paralysis and in Morocco-Agadir adulterated vegetable oil with tri ortho cresyl phosphate (TOCP), which about 600 people suffered signs of ataxia and neurotoxicity of peripheral and central nervous system effects [13].

MATERIALS AND METHODS

1.Experimental design

A total of 40 adult hen (Leghorn over six months of age, with two week acclimations) were purchased from the local market in Basrah province. The hens were divided into 20 control and 20 treated by oral gavage with 500 mg/kg of tri-ortho cresyl phosphate (TOCP) per hen as single dose, neurotoxicity of (TOCP) triorthocresylphosphate in acute delayed hypersensitivity in adult hen for 21 days, after 21 days all surviving hen were killed, sciatic nerves were taken first fixed in 10% neutral buffered formalin after fixation for over a week(post fixation in osmium tetroxide), then after that nerve fibers we separated by surgical needle under dissecting microscope, then every single nerve fiber was put on slide with drop of glycerin and cover slide and then examined under light microscope with varying magnification.

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RESULTS

Light microscopy of teased sciatic nerve in acute delayed neurotoxicity showed varying degrees of swollen , degenerate and fragmented myelin sheath in treated hens in comparison with untreated control, note that the severity of changes in myelin were associated with the severity of clinical signs ataxia, incoordination and paralysis and those affected teased nerve were shown in figures 1,2,3,4,5,6,7,8,9,10,11,12 and 14,with untreated control figure 13 .

Figure 1: Teasing of sciatic nerve, note fragmentation of myelin sheath.magnification. X100

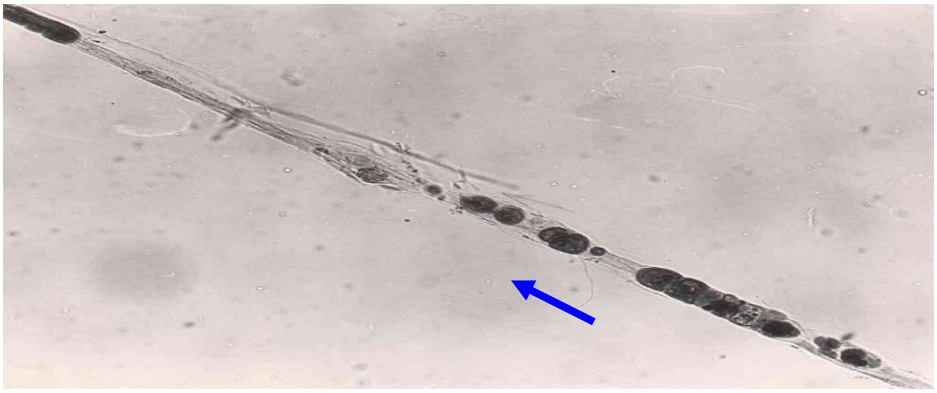

Figure 2: Teasing of sciatic nerve, note fragmentation of myelin, empty spases (arrow). High magnification .X200

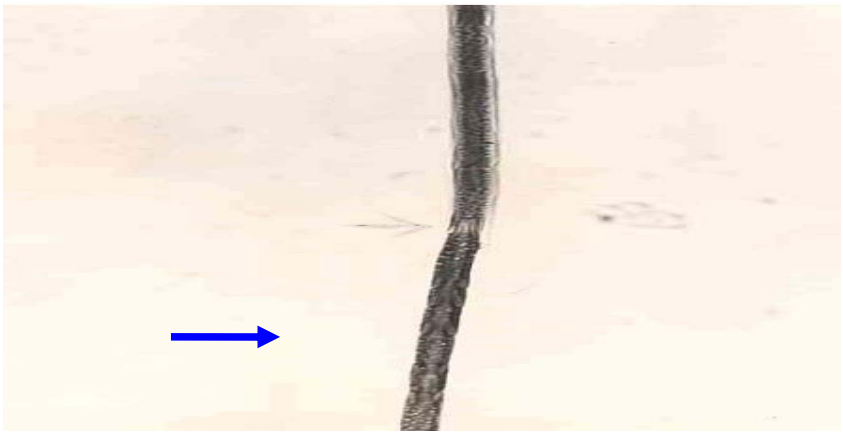

Figure 3: Teasing of nerve fiber with in normal limits, note normal myelin sheath and Ranvier node(arrow). X100.

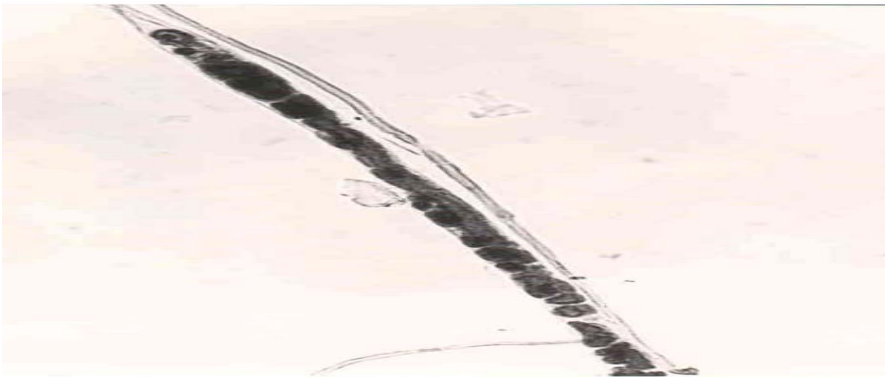

Figure 4: Teasing of sciatic nerve, note early fragmentation of nerve fiber .X 400

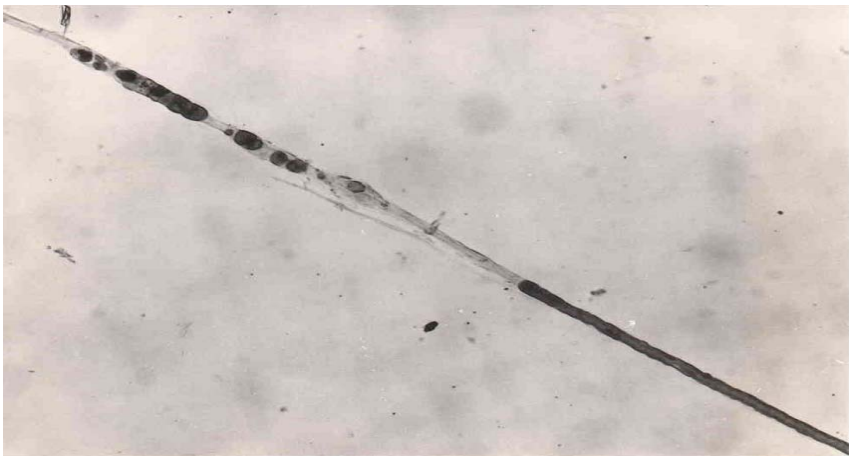

Figure 5: Teasing of sciatic nerve, note fragmentation myelin,varying size of demyelination and part of no change. X 200.

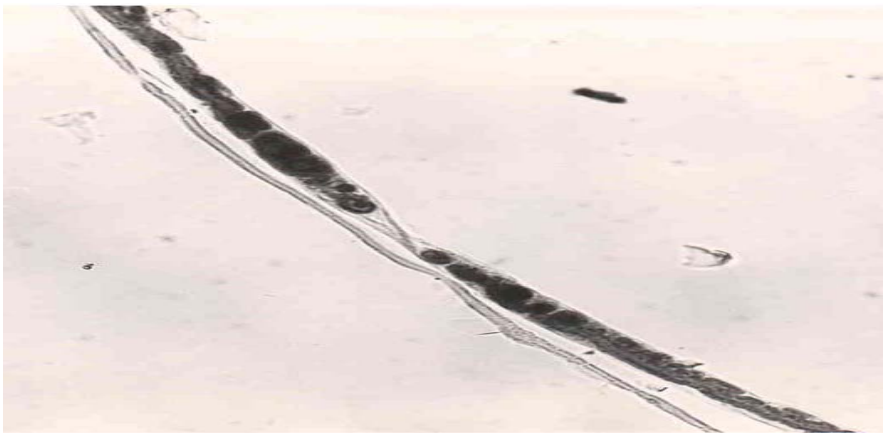

Figure 6: Teasing of sciatic nerve, note fragmentation of myelin sheath, in the early stage of fragmentation, just one small space of demyelination. X400 .

Figure 7: Teasing of sciatic nerve, note swollen , degenerate myelin, with varying degree of Fragmentation. X200.

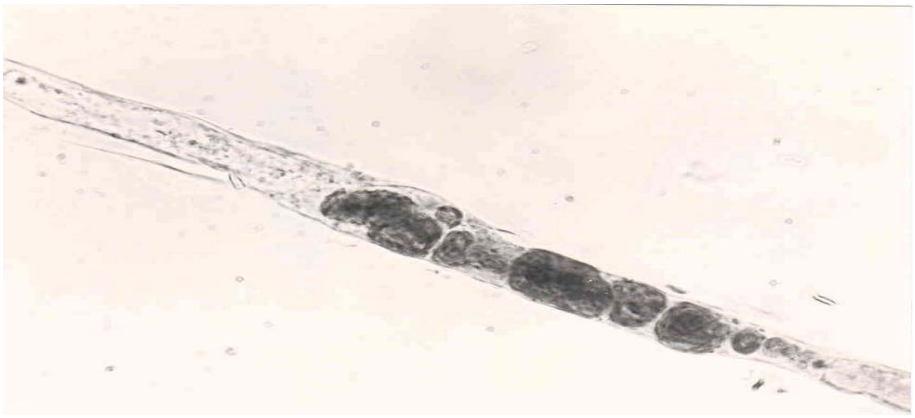

Figure 8: Teasing of sciatic nerve, high magnification , note fragmentation of myelin as varying masses of myelin as clumps and area of demyelination X400.

Figure 9: Teasing of sciatic nerve, note degenerate, fragmentated myelin and an area of demyelination X400.

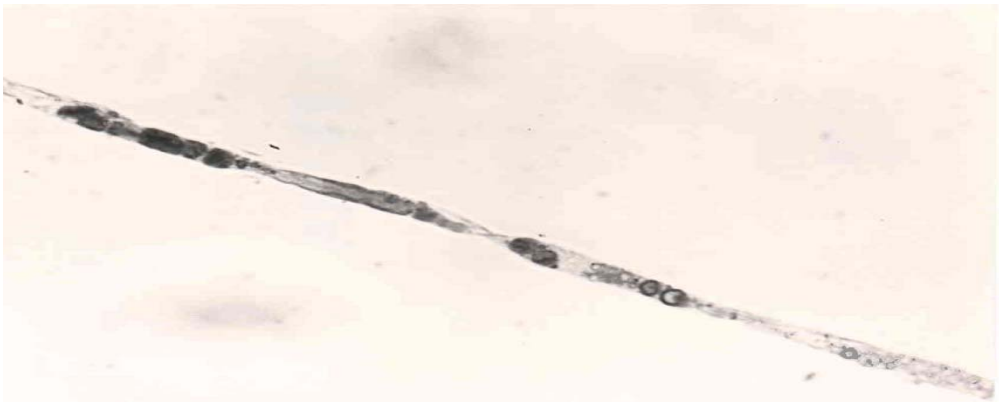

Figure 10: Teasing of sciatic nerve, note areas of demyelination and fragmentated myelin sheath, with an area of no change. X200.

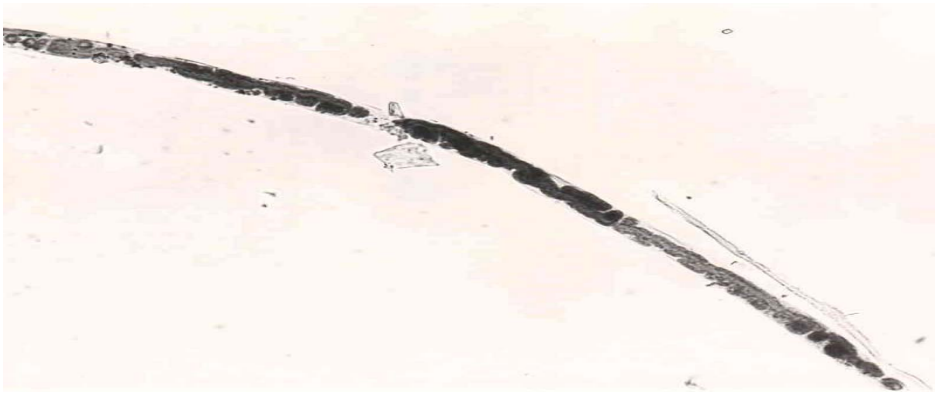

Figure 11: Teasing of sciatic nerve, note varying degrees of degenerate, fragmented myelin.. X200.

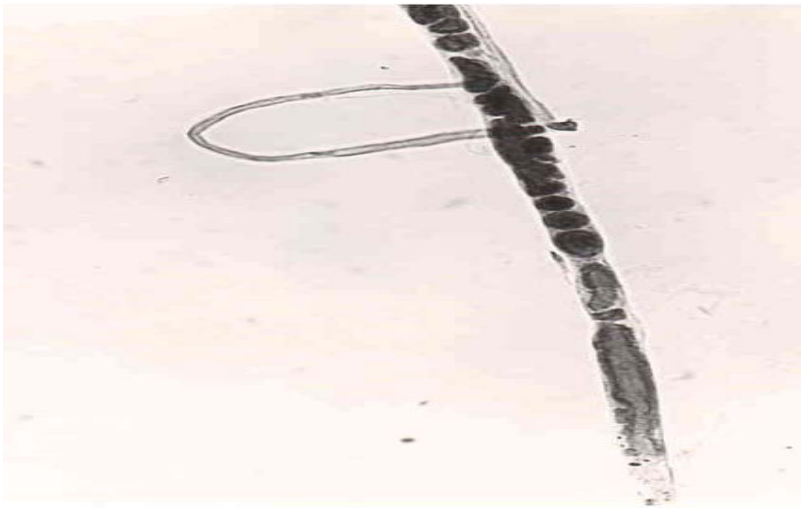

Figure 12: Teasing of sciatic nerve, note fragmented myelin sheath, while other part still normal. X200.

Figure 13: Teasing of sciatic nerve, note very early fragmented myelin (arrow) . X200.

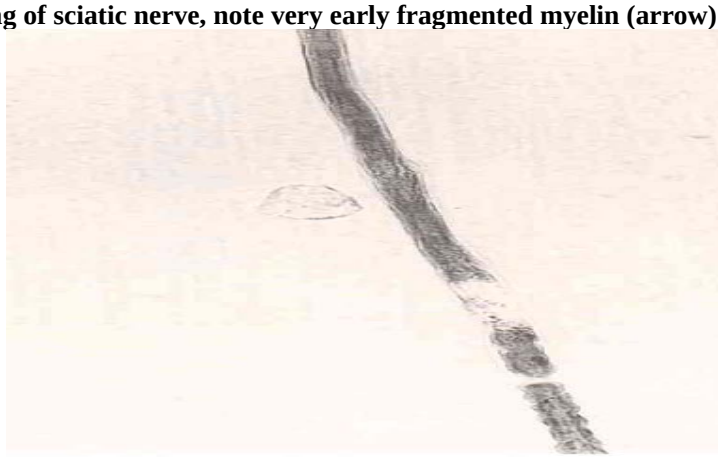

Figure 14: Teasing of sciatic nerve, note varying early demyelination and fragmented myelin . X200

DISCUSSION

The present research was done on neurotoxicity of TOCP (triorthocresylphosphate) as positive control for organophosphorus, using adult hen as a model for neurotoxicity as it give nearly similar clinical light and electron microscopic changes in peripheral and central nervous system with acute delayed neurotoxicity as it was reported by[1&2] and other incited by[3,4,5,6,7,8,9&10].

Furthermore, teasing of nerve fibers was also used to identify age related in peripheral nerve fibers in rats and mice as was reported by [11&12], the changes in the peripheral nerve fibers of aged rats and mice were similar to the changes of TOCP in adult hen as it was characterized by segmentation and fragmentation of peripheral nerve fibers with clumps of degenerate myelin and areas of demyelination the changes in teased peripheral nerve fibers were the main nerve toxic changes in acute delayed neurotoxicity as was reported by [1&2], as it was single oral dose of TOCP of 500 mg/kg in corn oil, changes only started to appear after 10 days and progressed to the end of the acute delayed neurotoxicity which was 21 days, the cause of calling this mechanism as delayed neurotoxicity because clinical symptoms as ataxia, incoordination and paralysis only appear after 10 days of the beginning of the oral dose and that was agreed by[1&2].

Finally, [13] found that teasing of peripheral nerve fibers is very good and important approach for diagnosis of neurotoxicity of TOCP(triorthocresylphosphate) as positive control for neurotoxicity of organophosphorus and for using this to identify neurotoxicity of any newly formed products of insecticides.

Research highlights

We believe the present article is quite interesting because it brings interesting and important findings in neurotoxicity of organophpsphorus using TOCP (triorthocresylphosphate) as positive control.

Finding and policy aspects

As it shows that adult hen can be used as very good model for neurotoxicity of organophosphorus in comparison to human.

Justification of research

The present article showed the importance of research on neurotoxicity of organophosphorus

using adult hen as model and doing teasing of nerve fibers to demonstrate the treatment related neurotoxic effects.

Conclusion

The present research work showed the importance of using teasing of nerve fibers of very interesting method to identify the neurotoxicity of organophosphorus.

Recommendation

Further research on neurotoxicity of any chemical or insecticide can use teasing of nerve fibers as a way to study the neurotoxic effects.

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