

Poster Abstracts

PO-15

REDUCING CELL MACROMOLECULE DAMAGE PROTECTS RATS AGAINST MONOCROTOPHOS INDUCED TYPE 1 PARALYSIS

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Acute severe organophosphate pesticide induced Type I paralysis is a common medical condition in most of Asia particularly India that can lead to Type II paralysis which is associated with significant morbidity and mortality. Type I paralysis is a consequence of cholinergic hyper stimulation and prevention would improve outcome of poisoned patients. This paper will present an animal model of stress induced protection against monocrotophos induced Type I paralysis.

Objectives: To study the mechanism of noise stress induced protection against Type I paralysis in monocrotophos poisoned rats

Methods:

1. Rats were exposed to noise stress (75-90dBA, 3-4hrs / day, six days a week, 8 months).
2. Non-stressed control and noise-stressed rats were subject to severe monocrotophos poisoning (0.8LD50)
3. The development and temporal profile of cholinergic symptoms and muscle weakness were observed in all rats.
4. Rats were sacrificed on recovery from muscle weakness and blood and muscle acetylcholinesterase levels, muscle oxidative damage, anti-oxidant levels and mitochondrial function and activity determined.
5. The results were analyzed for significant differences between stressed and non-stressed rats by Student's t test for parametric data and by the Mann-Whitney test for non-parametric data. Significance at $p < 0.05$.

Results: Noise stress significantly

- Reduced lipid peroxidation 3 fold and elevated glutathione peroxidase 3.5 fold in rat muscle.
- Lowered oxygen uptake through mitochondrial Complex 1 40%, reduced Complex 1 activity 60% and increased Complex IV activity 2.7 fold in rat muscle. On monocrotophos poisoning:

Poster Abstracts

- Onset of cholinergic symptoms of chewing, body tremors, salivation and lacrimation were delayed significantly by 2.5, 5.5, 5 and 7 minutes respectively and muscle weakness by 10 minutes in stressed compared to non-stressed rats.
- Stressed rats did not develop paralysis while non-stressed rats developed paralysis.
- Inhibitions of blood (>80%) and muscle (>50%) cholinesterases were similar in stressed and non-stressed rats.
- Oxidative damage was not induced in muscle of stressed or non-stressed rats.
- Muscle mitochondrial function and complex activities were not affected in stressed or nonstressed rats.

Conclusion: This study indicated that noise stress improved the structure of cell macromolecules through reduced oxidative damage and protected muscle from the effects of monocrotophos induced cholinergic hyper stimulation despite significant inhibition of acetylcholinesterase. The role of macromolecule structural integrity in reducing organophosphate pesticide induced muscle weakness and the potential of drugs that raise and maintain a high redox potential of muscle to prevent muscle weakness will be discussed.