Clinical, Biochemical and Electrophysiological Correlates of Intermediate Syndrome following Acute Organophosphate Poisoning

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Clinical biochemical and electrophysiological correlates of intermediate syndrome following acute organophosphate poisoning

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Introduction: Intermediate syndrome (IMS) remains a major contributor to the high morbidity and mortality in acute organophosphate (OP) poisoning. The pathophysiology of IMS is not clearly understood. Acetylcholinesterase inhibition is generally believed to cause IMS. Neuromuscular transmission has been studied in IMS using repetitive nerve stimulation (RNS) and single fiber electromyography. However there are no previous studies which have evaluated patients with serial RNS from the onset of poisoning to describe sequential electrophysiological changes that correlate with clinical severity in IMS. Further there are no clinical, biochemical or electrophysiological predictors for the development of IMS.

Objectives: The objectives were to describe the clinical and electrophysiological features that correlate with the development of IMS, develop an RNS predictor for IMS, investigate the relationship between admission red blood cell acetylcholinesterase (RBC-AChE) level,

butyrylcholinesterase (BuChE) level, serum organophosphate level and the development of IMS and evaluate their predictive value, and investigate the relationship between RBC-AChE inhibition, BuChE inhibition, serum OP level and the development of IMS.

Methods: Seventy eight consenting symptomatic patients with OP poisoning were assessed prospectively with daily physical examination and RNS. RNS was done on the right and left median and ulnar nerves at 1, 3, 10, 15, 20 and 30Hz. In a sub set of patients blood was collected on admission and 1, 4, 12, 24 hours after admission and daily thereafter to assess RBC-AChE, BuChE and serum OP.

Results: Seventy eight patients were recruited for the clinical and electrophysiological study and of those 59 chlorpyrifos patients were recruited for the biochemical study. IMS was diagnosed in 10/78 patients using apriori clinical diagnostic criteria and 5 of them developed respiratory failure. All 10 patients showed progressive RNS changes correlating with the severity of IMS. A decrement-increment was observed at intermediate and high frequencies preceding the onset of clinical signs of IMS. As the patient developed clinical signs of IMS, decrement-increment was progressively noted at low and intermediate frequencies and a combination of decrement-increment and repetitive fade or severe decrement was noted at high frequencies. Severe decrement preceded respiratory failure in 4 patients.

Thirty patients developed *forme fruste* IMS with less severe weakness not progressing to respiratory failure whose RNS was characterized by decrement-increment or a combination of decrement-increment and repetitive fade but never severe decrements.

Admission RBC-AChE, BuChE and serum chlorpyrifos level had a poor predictive value in predicting the development of IMS and *forme fruste* IMS. RBC-AChE inhibition and the serum chlorpyrifos level was significantly associated with the development of IMS spectrum disorder.

Conclusions: Characteristic changes in RNS, preceding the development of IMS, help to identify a subgroup of patients at high risk of developing respiratory failure. The *forme fruste* IMS with the characteristic early changes on RNS indicates that IMS is a spectrum disorder. RNS changes are objective and precede the diagnosis and complications of IMS. Thus they may be useful in clinical management and research. RBC-AChE inhibition is strongly but not uniquely associated with the development of IMS spectrum disorder. The contribution of other factors in the development of IMS needs to be further investigated.