

Abstract

Effects of acute organophosphorus or paraquat exposure on neuro-muscular function and efficacy of antioxidant therapy in acute paraquat poisoning

Introduction

Organophosphates (OP) are the most frequently involved pesticides in acute poisoning. Paraquat (PQ) poisoning has the highest case fatality.

As the mechanism of PQ toxicity includes free radical generation, antioxidants have been tried as a treatment. Neurotoxic effects of acute OP/PQ poisoning (OP/PQ-P) have been hitherto under-explored.

Objectives

The aims of the study were to assess the effects of acute OP/PQ-P on peripheral nerves, neuro-muscular junction (NMJ), brain-stem, cognition and psychological status. Other aims were to evaluate adherence to existing management guidelines for OP/PQ-P and to find out efficacy of antioxidant therapy in acute PQ-P.

Materials and methods

A cohort study was conducted with matched controls. Patients with acute OP/PQ-P were recruited. Nerve conduction studies, autonomic function tests, repetitive nerve stimulation (RNS), brain-stem auditory evoked potentials (BAEP), Mini Mental State Examination (MMSE) and administration of General Health Questionnaire (GHQ) were performed to assess peripheral nerves, NMJ, brain-stem, cognition and psychological status respectively. Assessments were performed at one and six weeks after the exposure.

A randomized double-blind placebo controlled clinical trial was conducted. Patients received intravenous vitamin C for 5 days. Half of them received N-acetylcysteine (NAC) and other half received 5% dextrose for 3 days.

Results

There were 70 OP (70 controls) and 28 PQ patients (56 controls).



In OP patients, motor nerve conduction velocity (MCV), amplitude and area of compound muscle action potential on distal stimulation (CMAP-D), sensory nerve conduction velocity (SCV) and F-wave occurrence were significantly reduced. At one week the significant impairment in autonomic functions were change of diastolic blood-pressure 3 min after standing, heart rate variation during deep breathing (HR-DB), amplitude of sympathetic skin response (SSR-A), post-void urine volume and size of pupil. All except HR-DB were reversed at six weeks. There was no effect on RNS.

In PQ patients, amplitude of ulnar nerve CMAP-D, CMAP-D area of median nerve and F-wave occurrence of median, ulnar and tibial nerves, blood-pressure variation after standing and SSR-A were significantly reduced at six weeks. All but F-wave occurrence remained impaired at six weeks. A significant decrement response in RNS was observed following exercise in both assessments.

There was no significant difference between BAEP and MMSE of OP/PQ-P patients and controls. GHQ showed high prevalence of psychological distress among the patients with OP/PQ-P.

There were 40 test, 24 historical-controls and 80 parallel-controls in the clinical trial. The median survival time was significantly longer in the patients treated with vitamin C when compared with the historical controls, but not with the parallel controls. NAC had no significant effect on median survival.

Atropine was commenced in 44% of patients without cholinergic features. 73% of patients developed atropine toxicity. None of the patients received the maintenance therapy of pralidoxime for the recommended duration. Of 90% PQ-P patients who received Fuller's earth, 15% did not receive it in adequate amounts.

Conclusions

The effects of OP/PQ on nervous system persist at least for six weeks. Antioxidant therapy did not show promising effects on acute PQ-P. Guidelines were not adhered to when administering antidotes in OP/PQ-P.