Human parathion poisoning. A toxicokinetic analysis.

Abstract:

The mortality rate of suicidal parathion poisoning is particularly high, the onset of fulminant cholinergic signs, and the patients frequently present to the emergency physician with life-threatening symptoms. Despite this uniformity, subsequent clinical course differs significantly among patients, mostly not as a result of different delays in treatment or insufficiency of primary care. Probably, the differences depend on the amount of poison absorbed and/or the disposition of the active poison, paraoxon. We followed the toxicokinetics of parathion and tried to quantify the actual poison load. To this end, we monitored parathion-intoxicated patients (patients requiring artificial ventilation) for plasma levels of parathion and paraoxon along with the activity of erythrocyte acetylcholinesterase and its reactivatability. Plasma obidoxime concentrations were followed as well as the cumulative urinary para-nitrophenol conjugate excretion as a measure of total poison load. All patients received a standard obidoxime scheme of a 250 mg bolus dose intravenously, followed by continuous infusion with 750 mg per 24 hours as long as reactivation could be expected (usually 1 week). All other treatment was instituted as judged by the physician. It was recommended to use atropine at low doses to achieve dry mucous membranes, no bronchoconstriction and no bradycardia. Usually 1-2 mg/h were sufficient. Seven selected cases
are presented exemplifying toxicokinetic peculiarities. All patients were severely intoxicated, while the amount of parathion absorbed varied widely (between 0.12 and 4.4 g; lethal dose 0.02-0.1 g) and was generally much lower than anticipated from the reports of relatives. It remains open whether the discrepancies between reports and findings were due to exaggeration or to effective decontamination (including spontaneous vomiting, gastric lavage and activated charcoal). Absorption of parathion from the gastrointestinal tract was sometimes retarded, up to 5 days, resulting in fluctuating plasma profiles. The volume of distribution at steady-state (Vdss) of parathion was around 20 L/kg. Post-mortem analysis in one patient revealed a 66-fold higher parathion concentration in fat tissue compared with plasma, 16 days after ingestion. Biotransformation of parathion varied widely and was severely retarded in one patient receiving fluconazole during worsening of renal function, while phenobarbital (phenobarbitone) sedation (two cases) had apparently no effect. The proportion of plasma parathion to paraoxon varied from 0.3-30, pointing also to varying paraoxon elimination, as illustrated by one case with particularly low paraoxonase-1 activity. Obidoxime was effective at paraoxon concentrations below 0.5 microM, provided aging was not too advanced. This concentration correlated poorly with the paration concentration or the poison load. The data are discussed in light of the pertinent literature.