
42. Intoxication with Alpha-Lipoic Acid: Case Reports and Toxicokinetic Analysis

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Objective: Alpha-lipoic acid (ALA) is an OTC preparation used in the treatment of diabetic polyneuropathy or as antioxidative dietary supplement. Although ALA causes severe and even fatal intoxications, few pharmacokinetic data so far been published and almost nothing is known about its toxicokinetic properties. In this presentation clinical representation of six patients intoxicated with ALA are analyzed and toxicokinetic parameters are derived from two suicidal poisonings. Methods: (a) The clinical courses of six patients, who ingested >200 mg ALA per kg body weight and who were reported to poison information centres were monitored by follow-up reports. (b) For toxicokinetic analysis plasma concentrations of ALA from a 69 year old male, who ingested ALA twice within four months in a dose of 340 mg/kg and 510 mg/kg respectively, were measured by RP-HPLC before, during and after haemodialysis until 72 hours after ingestion. Oral bioavailability, elimination half-life, volume of distribution and efficacy of haemodialysis were computed based on linear kinetics and compared to pharmacokinetic data published elsewhere. Results: In all patients symptoms of intoxication encompassed disturbances of the CNS ranging from agitation to convulsions, increasing lactate acidosis, hyperglycaemia and disseminated intravascular coagulation occurring within 1 to 6 hours after ingestion. In at least three cases lactate acidosis was treated with haemodialysis or haemofiltration, respectively. Quantification of ALA in plasma samples obtained from a single patient with an ingested 510 mg ALA per kg allowed estimation of a prolonged elimination half-life ranging from 80 to 160 min, which was not significantly reduced by high-flow haemodialysis. Additionally, ongoing absorption was observed until approx. 40 hours after ingestion. Estimated oral bioavailability in intoxication (26.7% at dose 340 mg/kg) did not significantly differ from that found under therapeutic dose (29.1% at dose 2.7 mg/kg), indicating non-saturable absorption of ALA with a substantial hepatic first-pass effect. Conclusion: (a) Occurrence and severity of symptoms are more related to peak plasma concentration of ALA than to ingested dose. (b) Early gastric emptying and repeated application of charcoal/cathartic appears to be of major importance in reducing peak plasma concentration of ALA and the occurrence of delayed absorption, thus reducing severity and duration of symptoms. (c) Haemodialysis or haemofiltration are ineffective in enforced elimination of ALA, but may be lifesaving in ALA poisonings with severe lactic acidosis. References: Teichert J, Kern J, Tritschler HJ, Ulrich H, Preiss R, Teichert J. *Int J Clin Pharmacol Ther* 1998; 36(12):625–628. Hermann R, Ruus P, Preiss R. *J Clin Pharm* 2003; 43:1257–1267.

43. Pharmacokinetics of Digoxin-Like Substances in the Plasma of Patients with Yellow Oleander (*Thevetia peruviana*) Self Poisoning

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Objective: Self-poisoning with seeds from the yellow oleander tree (*Thevetia peruviana*) occur worldwide, but is particularly common in Sri Lanka. The pharmacokinetics of the cardenolides in yellow oleander poisoning, and the effect of administration