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Plasmapheresis in fatal overdose with verapamil

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Sir: Verapamil intoxication is a life-threatening condition with a far too often fatal outcome. The established therapeutic approach consists of gastric lavage, administration of activated charcoal and symptomatic therapy in an intensive care setting whereas extracorporeal verapamil elimination is still under debate [1, 2].

In two patients, severe suicidal intoxication by 2.4 g and 9.6 g of verapamil orally resulted in life-threatening hypotension and bradycardia with the need of heart-pacing and resuscitation. The blood levels (5180 and 1856 ng/ml) on admission to the hospital exceeded at least twofold the 687 ng/ml, which was reported to be fatal [2]. On account of clouded consciousness, no gastric irrigation was carried out in the first patient at the patient's home. This case, with the higher verapamil blood level despite lower verapamil ingestion in comparison to the second patient, underlines the importance of early drug decontamination.

Plasmapheresis (PP) (plasmafilter: Haemoselect, B.Braun Melsungen, filtration 1000 ml/h, total volume 3000 ml, which was completely balanced by human albumin 5 %) was started within 4 h after intoxication. In the first patient the verapamil concentrations in blood decreased considerably below 8 h half-life concentrations (1272 vs 4356 ng/ml 4^{th} h, 1150 vs 2824 ng/ml 9^{th} h, 500 vs 1412 ng/ml 17^{th} h). In the second patient the verapamil blood level declined before PP approximately as calculated by an 8 h half-life (1349 vs 1561 ng/ml 4^{th} h). As in patient 1, the verapamil blood level decreased markedly below the calculated level (485 vs 1204 ng/ml 7^{th} h) during the time of PP. Due to the gastrointestinal resorption, the verapamil levels increased again after 17 h (438 vs 506 ng/ml) and remained above the calculated level after 31 h (262 vs 150 ng/ml). A dramatic improvement of cardiovascular stability was already observed during plasmapheresis. However, the first patient died 38 h after admission at the time of a verapamil plasma level below 500 ng/ml due to multiorgan failure. The outcome was attributed to the long period of cardiogenic shock, which was reflected by a high serum lactate (17.8 mmol/l) on admission. The second patient survived without infirmity in spite of the higher verapamil ingestion.

In vitro PP with the blood of pigs was performed to verify the effectiveness of the extracorporeal detoxification. PP removed verapamil out of the blood by a clearance to the amount of the filtration rate (29.2–30 ml/min) at a blood flow rate of 200 ml/min.

In conclusion, the primary therapy should include a vigorous gastrointestinal lavage with repeated administration of active charcoal to reduce gastrointestinal absorption of the drug, which is blamed for the second rise in verapamil levels in the second patient. The mainstay of treatment is support in an intensive care setting. All symptoms of verapamil intoxication are self-limiting within 48 h under the condition of cardiovascular stability and normal hepatic clearance [3, 4]. However, in circulatory breakdown and/or impaired hepatic verapamil clearance, PP is an effective treatment to stabilize the clinical situation and to allow time for the hepatic detoxification.

References

1. Watling SM, Crain JL, Edwards TD, Stiller RA (1992) Verapamil overdose: case report and review of the literature. Ann Pharmacother 26: 1373–1378
2. Rosansky S (1991) Verapamil toxicity – treatment with hemoperfusion. Ann Intern Med 114: 340–341
3. Sauder P, Kopferschmitt J, Dahlet M, Tritsch L, Flesch F, Siard P, Mantz JM, Jaeger A (1990) Les intoxications aigues par le verapamil. A propos de 6 cas. Revue de la litterature. J Toxicol Clin Exp 10: 261–270
4. Watson NA, FitzGerald CP (1991) Management of massive verapamil overdose. Med J Aust 155: 124–125

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