LETTER TO THE EDITOR

Could extracorporeal albumin dialysis be considered as an adjunct therapy in calcium channel blocker overdose?

D. Vodovar[1,2], B. Mégarbane[1,2]*

[1]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, Paris, France, [2]INSERM UMRS 1144, Paris-Diderot University, Paris, France, *corresponding author: tel.: +33-149958961, fax: +33-149956578, email: bruno-megarbane@wanadoo.fr

To the Editor,

Recently, Rietjens et al. presented an up-to-date stepwise strategy to manage calcium channel blocker (CCB) overdose including supportive care (mechanical ventilation, vasopressors and inotropic drugs), gastrointestinal decontamination and evidenced antidotes (calcium salts and high-dose insulin). In life-threatening CCB poisoning, refractory to standard therapies, they advised to consider lipid emulsion and extracorporeal life support.[1] We agree with this strategy and would like to clarify the role of extracorporeal albumin dialysis mentioned by the authors.

All CCBs have some similar pharmacokinetic properties including high protein binding rates (up to 80%), octanol-water partition coefficients (logP > 2.8) and distribution volumes (up to 5 l/kg), making them non-removable by dialysis. The rationale for extracorporeal albumin dialysis is based on the ability of albumin contained in the circuit to enhance the elimination of the toxicant released from the proteins by physicochemical interactions with the membrane and cleared from the blood by diffusion.[2] Four refractory CCB poisonings (diltiazem [n = 2], verapamil [n = 1] and amlodipine [n = 1]) were treated with the Molecular Adsorbent Recirculating System (MARS).[3,4] Significant tapering of the catecholamine infusion rate was reported and attributed to the faster drop in blood CCB concentrations during MARS.[3] However, in the case of amlodipine poisoning, the fraction of amlodipine removed by MARS (< 1%) was negligible,[4] questioning the exact mechanisms involved in MARS-attributed improvement of CCB-poisoned patients. Interestingly, extraction of diltiazem, verapamil and their respective active metabolites by MARS has not been investigated.[3]

Several hypotheses can explain how MARS contributes to improvement in CCB poisoning. CCBs induce vasodilatation by stimulating endothelial nitric oxide (NO) synthase and increasing the production of cyclic guanosine monophosphate, a potent vasodilator. In acute and decompensated chronic liver failure patients, MARS was shown to remove NO from plasma by binding NO to the albumin contained in the circuit as S-nitrosothiol-albumin.[5] MARS may thus act in CCB-poisoned patients by scavenging the overproduced NO. Additionally, as in liver failure patients, removal of pro-inflammatory cytokines by MARS may explain the observed improvement in haemodynamics.[2] Finally, although elevation of liver enzymes and decrease in prothrombin time were not reported in the CCB-poisoned patients treated by MARS,[3,4] significant alteration in liver function due to cardiovascular failure cannot be ruled out. Since all involved CCBs are strongly metabolised by the liver, liver function support using MARS may explain the reported clinical benefit by maintaining CCB metabolic clearance. However, since its usefulness is still low-evidenced, the routine use of extracorporeal albumin dialysis cannot be recommended to manage CCB poisoning.

DISCLOSURES

The authors report no conflicts of interest. No funding or financial support was received.

REFERENCES

1. Rietjens SJ, de Lange DW, Donker DW, Meulenbelt J. Practical recommendations for calcium channel antagonist poisoning. Neth J Med. 2016;74:60-7.

2. Wittebole X, Hantson P. Use of the molecular adsorbent recirculating system (MARS™) for the management of acute poisoning with or without liver failure. Clin Toxicol (Phila). 2011;49:782-93.

3. Pichon N, Dugard A, Clavel M, et al. Extracorporeal albumin dialysis in three cases of acute calcium channel blocker poisoning with life-threatening refractory cardiogenic shock. Ann Emerg Med. 2012;59:540-4.

4. Gérard L, Galloy AC, Capron A, Hantson P. Mixed amlodipine/valsartan overdose treated by the molecular adsorbent recirculating system (MARS™). Clin Toxicol (Phila). 2015;53:573-7.

5. Guo LM, Liu JY, Xu DZ, et al. Application of Molecular Adsorbents Recirculating System to remove NO and cytokines in severe liver failure patients with multiple organ dysfunction syndrome. Liver Int. 2003;23:16-20.