Treatment of Severe Combined Overdose of Calcium Antagonists and Converting Enzyme Inhibitors with Angiotensin II

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Dear Sir,

Angiotensin II has been proposed as an alternative treatment for refractory septic shock unresponsive to noradrenaline [1, 2], but there are other circumstances involving severe hypotension in which it may also prove useful; we are presenting a case in point.

A 34-year-old previously healthy woman who took an overdose of 200 mg of enalapril maleate, 110 mg of ramipril, 300 mg of am-lodipine and 600 mg of nitrendipine by oral ingestion was admitted 4.5 h following ingestion. When examined, no signs of neurological deficit were evident, systolic blood pressure was 50 mm Hg, heart rate 110 beats/min and average urine output 10 ml/h. Significant serum biochemical data included: creatinine 120 µmol/l (1.35 mg/dl), glucose 5.82 mmol/l (105 mg/dl), uric acid 374 µmol/l (6.5 mg/dl), sodium 140 mmol/l, potassium 4.5 mmol/l, pH 7.39, pCO₂ 38 mmol/l and total CO₂ 22.9 mmol/l. Treatment with intravenous calcium gluconate (1,000 mg), isotonic saline solution (2.08 ml/min), dopamine (4.9 µg/kg/min) and progressive doses of noradrenaline (up to a maximum of 60 µg/min) was administered. However, 3 h later, although the central venous pressure rose to 24 cm H₂O, systolic blood pressure remained at the same level, diuresis did not improve and finally circulatory overload became apparent. Angiotensin II (Hypertensin®, Ciba) perfusion was then initiated at the rate of 5.0 µg/min and rapidly increased to 15 µg/min. Almost immediately, systolic blood pressure rose to 100 mm Hg and both improvement of the diuresis output and disappearance of the cardiac failure signs were observed. The noradrenaline dose could then be reduced to 10 µg/min but the same angiotensin II dose has to be kept up for the next 24 h to preserve hemodynamic parameters. When angiotensin was discontinued, dopamine and noradrenaline had to be increased to 24 µg/kg/min and 33 µg/min respectively and then progressively reduced until totally phased out 72 h later. On the fourth day postadmission, the patient had totally recovered and was discharged from the intensive care unit. Creatinine clearance in the convalescent phase was 96 ml/min. Serum levels of enalapril and ramipril were 1.2 and 6.5 µg/ml respectively 10 h

after drug ingestion. The reported levels 4 h after the ingestion of 10 mg of enalapril was 57.2 ± 20 ng/ml [3] and 40-50 ng/ml after 10 mg ramipril [4].

The combined effects of calcium antagonists (CA) and angiotensin-converting enzyme inhibitors (ACEI) may be greater than expected because of pharmacological interactions which interfere with intracellular calcium availability in the smooth muscle cell cytoplasm [5]. Furthermore, in some circumstances, when faced with severe hypotension and seriously impaired renal perfusion, angiotensin II plays a critical role in maintaining adequate renal vasomotor tone and glomerular filtration rate [6]. The powerful effects of high doses of long-acting CA and ACEI ingested by our patient hindered recovery when standard measures previously mentioned were employed, whereas angiotensin II administration brought about a rapid recovery.

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