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# Selected Topics: Toxicology

# EXTRACORPOREAL LIFE SUPPORT AND PLASMAPHERESIS IN A CASE OF SEVERE POLYINTOXICATION

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☐ **Abstract—Background: Resuscitation without return to spontaneous circulation in patients with suicidal ingestion of cardiotoxic drugs necessitates alternative bridging therapies for drug removal. Objectives: To show the effectiveness of emergency extracorporeal membrane oxygenation (ECMO) and plasmaspheresis in severe polyintoxication. Case Report: A 21-year-old woman developed asystole after suicidal polyintoxication with 1.75 g carvedilol, 300 mg amlodipine, 6 g amitriptyline, 500 mg torsemide, 1.5 g ketoprofen, 28 g nicotinic acid, and 16 g gabapentin. After 3 h of cardiopulmonary resuscitation without return to spontaneous circulation, ECMO was used as a bridging therapy and a temporary pacemaker was inserted. Plasma peak levels were measured for amlodipine (29.3 μg/L), amitriptyline (1456 μg/L), carvedilol (585 μg/L), and gabapentin (126.8 mg/L). To facilitate drug removal, therapeutic plasma exchange was performed. The patient could be weaned from ECMO at day 4 and extubated on day 8 after admission without neurologic sequelae. Conclusion: ECMO and plasma exchange should be considered as a therapeutic option in selected patients under resuscitation without return to spontaneous circulation after severe intoxication.** © 2014 Elsevier Inc.

☐ **Keywords—resuscitation; ECMO; plasmapheresis; intoxication; β-blocker; tricyclic antidepressant; calcium channel blocker**

## INTRODUCTION

Polyintoxication with more than four substances is rare, with cardiovascular drugs and cyclic antidepressants belonging to the drugs most frequently ingested for suicide (1).

Toxicity of β-blockers is significantly increased after co-ingestion of further cardioactive drugs, especially calcium channel antagonists or tricyclic antidepressants (2). The cardiotoxic action of the ingested drugs represents a potentially reversible cause that prevents return to spontaneous circulation (ROSC) even under sufficient resuscitation measures. Thus, enhanced drug removal, for example, by plasmapheresis, is an effective but time-consuming treatment of cardiac failure under these circumstances. Extracorporeal membrane oxygenation (ECMO) could serve as a bridging tool to maintain a sufficient circulation until the complete drug removal enables ROSC.

## CASE REPORT

A 21-year-old woman was found unconscious with bradycardia (30 beats/min) by her relatives after suicidal ingestion of 70 tablets of 25-mg carvedilol (1750 mg), 40

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**Table 1. Summary of Ingested Drugs**

| Drug | Ingested Dose | Maximal Therapeutic Single Dose | Substance Class | Mode of Action | Symptoms in Overdose | Ref. |
|---|---|---|---|---|---|---|
| Carvedilol | 1750 mg | 100 mg | β-blocker (β1, β2, β1) | Reduction of intracellular cAMP, negative inotropic/ chronotropic/ dromotropic | Bradycardia, cardiogenic shock, asystole, asthma | (4) |
| Amlodipine | 300 mg | 10 mg | Peripheral calcium channel antagonist | Inhibition of calcium influx via voltage-dependent calcium channels | Hypotension, cardiogenic shock | (5) |
| Amitriptyline | 6000 mg | 300 mg | Tricyclic antidepressant | Blockade of neuronal norepinephrine re-uptake/cardiac inward sodium channels/ postsynaptic peripheral α-adrenergic receptors | Dysrhythmia, cardiac arrest, coma, hypotension, respiratory arrest, seizures, anticholinergic syndrome | (3) |
| Torsemide | 500 mg | 200 mg | Loop diuretic | Inhibition of renal $Na^+K^+2Cl^-$ symporter | Alkalosis, hypokalemia | (6) |
| Ketoprofen | 1500 mg | 200 mg | Antipyretic | Inhibitor of cyclooxygenase-2 | Delirium, gastrointestinal, bleeding, cardiac insufficiency, hemolysis | (7) |
| Gabapentin | 16 g | 3.6 g/day | Antiepileptic | Still debated | Seizures, myoclonic jerks, somnolence | (8) |
| Nicotinic acid | 28,000 mg | 200 mg (max. 3 g/day) | Lipid-lowering drug | Part of NAD, NADP | Flush, tachycardia, hypotension, DIC | (9) |

cAMP = cyclic adenosine monophosphate; DIC = disseminated intravascular coagulation; NAD = nicotinamide adenine dinucleotide; NADP = nicotinamide adenine dinucleotide phosphate.

tablets of 400-mg gabapentin (16,000 mg), 60 tablets of 5-mg amlodipine (300 mg), 60 tablets of 100-mg amitriptyline (6000 mg), 50 tablets of 10-mg torsemide (500 mg), 56 tablets of 500-mg nicotinic acid (28,000 mg), and 30 tablets of 50-mg ketoprofen (1500 mg). Details of the ingested drugs are listed in Table 1. She became pulseless shortly after the arrival of the emergency physician, and cardiopulmonary resuscitation (CPR) was started immediately. Due to catecholamine-refractory cardiac failure, the patient was transferred after 60 min to our intensive care unit still undergoing CPR.

After admission, CPR was continued for another 120 min. Because no ROSC could be achieved, extracorporeal membrane oxygenation (ECMO; Medtronic BioMedicus; Medtronic, San Francisco, CA) was performed as a bridging therapy via right femoral arteriovenous access (flow rate 5 L/min), which stabilized the mean arterial pressure at 65 mm Hg under augmented vasopressor therapy (norepinephrine/adrenaline). The time course of intensive care unit treatment is depicted in Figure 1. Laboratory results upon arrival are shown in Table 2 (3–9). Therapeutic hypothermia (33.5°C) was initiated. First, spontaneous electrical cardiac activity was detected 3 h after admission, showing a sinoatrial blockade with narrow complex escape rhythm (33 beats/min) with complete myocardial akinesia. On day 2 after admission, when echocardiography showed minimal cardiac contractions (Video 1), a temporary right ventricular pacemaker was inserted (80–100/min) to avoid intraventricular thrombus formation. Spontaneous heart rate began to increase from day 3, with an improved ejection fraction of 45% on day 6 and a normal left and right ventricular function on day 7 (Figure 1A, Video 2). The patient could be successfully weaned from ECMO on day 5. After demonstration of normal sinus rhythm, the temporary pacemaker was removed on day 5. Catecholamines were tapered until day 6, and extubation was possible on day 8 after admission (Figure 1A).

Specific treatment for intoxication is summarized in Figure 1B. For the β-blocker and calcium channel antagonist intoxication, high-dose insulin/euglycemia therapy (25 units/h for 5 days), calcium gluconate (free calcium serum concentration 1.0 mmol/L, for 3 days), glucagon (10 mg/h for 24 h), and 10 mg milrinone (3 h) were administered. Sodium bicarbonate was applied for 5 days to inhibit the activity of amitriptyline on the sodium channel. Due to the enormous doses of carvedilol, amlodipine, and amitriptyline with a high plasma protein binding and half-life, plasma exchange was performed on days 1, 2, 3, and 4 for accelerated drug elimination. Initial drug plasma concentration of carvedilol, amlodipine, and amitriptyline and their time course under plasmapheresis are shown in Figure 2.

The course was complicated by a cannula-induced dissection of the deep femoral artery. Although perfusion