

Successful Management of Severe Verapamil Overdose with VA-ECMO

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Calcium channel blocker (CCB) poisonings are the most common agents causing mortality in worldwide and new approaches and updates on antidotal and supportive treatment are still under the investigation [1, 2]. In this case report, the lifesaving effect of veno-arterial extracorporeal membrane oxygenation (VA ECMO) support on the sequel-free health of the patient when exposed to cardiovascular (CVS) system toxicity such as Verapamil+Trandolapril Isosorbide dinitrate for suicidal purposes was discussed, who developed shock not responding to pharmacotherapy and antidote treatments at the 55th hour of drug intake was discussed.

Keywords: Verapamil, Toxicology, ECMO

Short Title in English: Verapamil Toxicity

1. Introduction

Calcium channel blocker (CCB) poisonings are the most common agents causing mortality in worldwide and new approaches and updates on antidotal and supportive treatment are still under the investigation. Verapamil is a Class IV antiarrhythmic agent used most commonly for the treatment of supraventricular tachy-arrhythmia and hypertension, and the nondihydropyridine group is a Calcium Channel Blocker (CCB) (1, 2). The purpose of this case report was to discuss the clinical management of a patient who was stabilized with VA ECMO in the early period of cardiovascular failure, recovering without sequelae in late pharmacotherapy in clinical follow-up after high dose verapamil intake.

2. Case Presentation

A 36-year-old male with a history of hypertension and multiple suicide attempts presented to our emergency department (ED) approximately 45 minutes after ingesting in a suicide attempt, his own 42 tablets of Tarka forte® (Verapamil Hydrochloride/Trandolapril-Immediate Release) 240/4 mg per tablet, 9 tablets of Zestat® (Mirtazapine) 15 mg per tablet, and 14 tablets of Isordil® (Isosorbide Dinitrate) 5 mg per tablet. He was alert, oriented and cooperative. His initial vital signs were stable (heart rate: 90 beats per minute, blood pressure: 110/80 mmHg) and the electrocardiogram (ECG) showed normal sinus rhythm with no other abnormalities (Figure-1). In the ED, gastric decontamination was performed with orogastric lavage tube and activated

charcoal and a large number of tablets were aspirated via irrigation. Two hours after arrival, the blood pressure decreased to 80/50 mm Hg and the heart rate increased to 120 beats per minute. The patient's ejection fraction (EF) and wall motion was deemed normal upon bedside echocardiography performed by the emergency physician (ECHO). The patient's blood pressure improved after intravenous fluid bolus and low-dose norepinephrine infusion (0.05 mcg/kg/minute). Fifty-five hours after the ingestion, the blood pressure decreased to 70/50 mmHg and the heart rate was 62 beats per minute. He was given 3 g of calcium gluconate IV, 1 U/kg bolus of intravenous regular insulin followed by a 1 U/kg/hour insulin infusion and the patient was transferred to the general intensive care unit (ICU). The ejection fraction remained normal by bedside echocardiogram despite the low systolic blood pressure that remained low after increasing the insulin infusion rate to 10 U/kg/h and administering 4 g IV of glucagon. The patient was intubated and mechanically ventilated followed by placement on the ECMO Device in ICU with epinephrine infusion 60 hours post-ingestion. After ECMO, the patient's vital signs improved and need for vasopressors decreased, high dose insulin (HDI) therapy was weaned, urine output increased, and serum lactate decreased. Serial serum lactate levels from the admission to the 3rd day of the ECMO device are shown in Figure-2. In the bedside ultrasound imaging, the thickness of the intestinal wall was measured as 5 millimeters in this region, differential diagnosis were ischemic intestine, ileus, or pharmacobezoars however, no further imaging was obtained because the patient was attached to ECMO Device. At the 72 hours postingestion, the patient's clinical condition suddenly worsened and fifteen minutes cardiac arrest period developed, return of spontaneous circulation occurred after 15 minutes of cardiopulmonary resuscitation (CPR). Diuretic treatment was initiated due to the development of non-cardiogenic pulmonary edema. Vasopressor support was discontinued on the 7th day of post-ingestion. The ECMO catheter was discontinued on the 8th day of hospital admission and the patient was discharged on the 11th day of hospital admission. The blood drug level of the patient was analyzed with LC/MS/MS Device in the Forensic Medicine Laboratory. Mirtazapine, Trandolapril, and Isosorbide dinitrate levels were negative. Serial serum verapamil and lactate levels are shown in Figure-3.

3. Discussion

Previous reports of verapamil poisoning where serial serum verapamil levels were measured, have shown that the peak serum level was achieved and then gradually dropped at earlier hours of presentation (3-6). In this case report, serum verapamil levels peaked at 55 hours after the ingestion despite being an immediate-release formulation. This can be due to hypotension-induced hypoperfusion of the intestinal tract and secondary slowing of peristalsis. Again, the

decrease in peristalsis due to the antimuscarinic effect of mirtazapine, which was another medication ingested by the patient, may have contributed to slowing peristalsis although the ingestion of this drug was not confirmed by LCMS. Also, it was reported in the literature that pharmaco bezoars occur in intestinal structures in multidrug overdoses, and that causes delayed serum peaks and deterioration in the patient's clinical manifestation with the dissolution of these bezoars in decreased intestinal motility (7). It is recommended to start HDI early in cases of CCB poisoning in cases of hemodynamic insufficiency with impaired cardiac contractility (8). Although cardiac EF was checked twice, EF did not decrease, and HDI treatment was given due to the patient's non-responsive status to IV fluid, IV vasopressor and IV calcium, but no clinical response was obtained. ECMO should be considered early in cases where the history and initial clinical findings point towards a critical overdose with high risk of death. VA-ECMO in high dose metoprolol and amlodipine intoxication, and VV-ECMO in high dose verapamil intoxication were successful when applied before cardiac arrest (9,10). In this case, the early recommendation of VA-ECMO in addition to the advance therapies administered, had a likely role in the favorable outcome of this critical poisoning.

4. Conclusion

Considering the potential risk of cardiac collapse in severe calcium-channel and betablocker poisonings, it is important to plan for potential need of advanced therapies like ECMO.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Consent Form

'Additional informed consent was obtained from all patients for which identifying information is included in this article.'

5. References

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Figure-1: A) ECG during the patient's admission, B) The patient's ECG just before being placed on ECMO after 55 hours

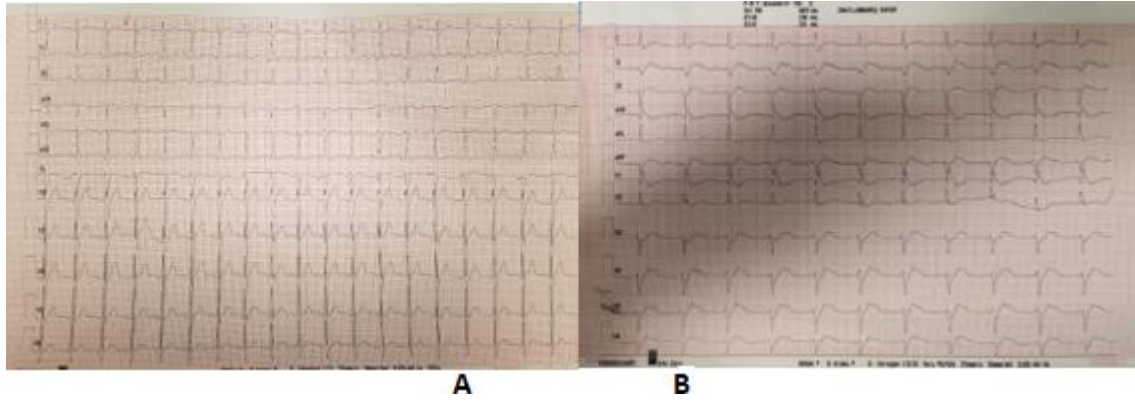


Figure-2: Serum Verapamil (ng/mL) and Lactate (mg/dL) levels

