CASE REPORTS

UDC: 615.099:615.2/.3]:616-08-039.76
https://doi.org/10.2298/VSP170926164S

Extracorporeal life support for severe cardiogenic shock induced by diltiazem intoxication

Vantelesno održavanje života kod teškog kardiogenog šoka izazvanog intoksikacijom diltiazemom

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Abstract

Introduction. Management of cardiogenic shock caused by severe drug intoxication is always challenging. In case of multidrug intoxication, a result, despite aggressive medical therapy, is often unpredictable. Utilization of extracorporeal life support devices in these cases has been suggested and reported results are promising. **Case report.** We presented a case of profound cardiogenic and distributive shock caused by suicidal intoxication with diltiazem and anionic surfactant ingestion in a 36-year-old woman. The patient ingested more than 90 tablets of diltiazem of 90 mg (ingested dose of 8.1 g), and 4 pieces of household toilet refresh agent containing anionic surfactant. During the admission, systemic blood pressure was 65/40 mmHg, heart rate 45 beats per minute, with signs of metabolic acidosis. The patient underwent several repeated gastric lavages. Emergent fluid resuscitation, calcium gluconate, insulin and vasopressive agents (dopamine and noradrenaline) infusions were administered with negligible effect. Due to progressive and refractory cardiogenic shock with signs of multiorgan failure, a decision was made to put the patient on venoarterial extracorporeal membrane oxygenator. Immediately after starting the extracorporeal membrane oxygenation, diuresis was established. During the next 36 h, an adequate end-organ perfusion was achieved with complete reversal of multiorgan failure. After the successful restoration of all major organ functions, the patient was successfully decannulated and discharged from the hospital after 10 days in a good condition. **Conclusion.** In severe cases of refractory cardiogenic and distributive shock due to diltiazem and other poison intoxication, venoarterial extracorporeal membrane oxygenation could allow additional circulatory support providing the bonus time for endogenous clearance of toxins. Venoarterial extracorporeal membrane oxygenation could be used in conjunction with the optimal medical therapy aiming to the restoration of end-organ perfusion and allowing for intrinsic drug and toxin metabolism and natural elimination.

Key words:
calcium channel blockers; extracorporeal membrane oxygenation; poisoning; pulmonary edema; shock, cardiogenic; treatment outcome.

Apstrakt

Uvod. Lečenje kardiogenog šoka izazvanog teškim trovanjem lekovima uvek predstavlja veliki izazov. U slučaju polimedikamentnog trovanja, ishod je, uprkos agresivnoj medikamentnoj terapiji, nepredvidiv. Predložena je upotreba uređaja za vantelesno održavanje života u takvim slučajevima i to sa obećavajućim rezultatima. **Prikaz bolesnika.** Prikazali smo bolesnika sa teškim kardiogenim i distributivnim šokom izazvanim suicidalnim trovanjem – ingestijom diltiazema i anjonskog surfaktanta kod 36-godišnje žene. Bolesnica je progutala više of 90 tableta diltiazema od 90 mg (ukupna doza 8,1 grama) i 4 "kuglice" sredstva za osvežavanje toaleta koje sadrži anjonski surfaktant. Tokom prijema, sistemski krvni pritisak bio je 65/40 mmHg, frekvencija srčanog rada 45/min, sa znacima metaboličke acidoze. Bolesnica je podvrgnuta ponavljanim gastričnim lavažama. Urađena je hitna nadoknada volumena, primenjen je kalcijum glukonat, kao i insulin i vazopresorni lekovi (dopamin i noradrenalin) sa zanemarljivim efektima. Usled progresivnog i refraktornog kardiogenog šoka sa znacima multiorganskog zatajenja, doneta je odluka da se započne sa venoarterijskom ekstrakorporalnom membranskom oksigenacijom. Neposredno nakon započinjanja vantelesne membranske oksigenacije, uspostavljena je diureza. Tokom narednih 36 časova postignuta je adekvatna perfuzija organa sa kompletnim povlačenjem znakova multiorganskog zatajenja. Nakon ponovnog uspostavljanja funkcije svih organa, bolesnica je podvrgnuta de-

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kanulaciji nakon čega je, desetog dana, otpuštena iz bolnice u dobrom stanju. **Zaključak.** U slučajevima refraktornog kardiogenog i distributivnog šoka usled trovanja diltiazemom i ostalim agensima, venoarterijska ekstrakorporalna membranska oksigenacija može pružiti dodatnu cirkulatornu podršku i omogućiti dodatno vreme za endogeno uklanjanje toksina. Venoarterijska ekstrakorporalna membranska oksigenacija bi trebalo da se koristi zajedno sa optimalnom medikamentnom terapijom u cilju uspostavljanja perfuzije krajnjih organa čime se podstiče metabolizam lekova i toksina i njihova prirodna eliminacija.

Ključne reči:
kalcijum, blokatori; oksigenacija; ekstrakorporalna, membranska; trovanje; pluća, edem; šok, kardiogeni; lečenje, ishod.

Introduction

Cardiovascular drugs are one of the most frequent substance category involved in human exposures/intoxications, according to the American Poison Control Centers' National Poison Data System [1]. Among cardiovascular drugs, single most frequent intoxicating agents are calcium channel blockers (CCB) and beta blockers (BB). Multidrug intoxication may potentially lead to more deleterious effects resulting in higher mortality rate [2], but is less common than single agent intoxication [1]. Trend of household detergents and germicides intoxication is on increase as well. Impact of mixing several intoxicating agents, namely cardiovascular drugs and household detergents containing anionic surfactants, remains largely unknown [3].

Diltiazem and verapamil are among the most commonly used drugs for accidental, or suicidal overdose [3, 4]. Diltiazem is associated with negative inotropic and chronotropic effect, often coupled with extensive peripheral vasodilatation effects contributing to shock development. Knowing that diltiazem is designed and produced as sustained release medication, might explain delayed onset and prolonged duration of toxicity [5]. Additional surfactant intoxication can contribute to deterioration of clinical course. Surfactant composition varies among products. Surfactants are frequently encountered in human environment in the form of household cleaning products.

The application of the concept of extracorporeal life support (ECLS) in drug induced cardiogenic shock is possible, but clinical experience is still limited with inadequate evidence to support a high-grade recommendation.

Case report

A 36-year-old female was admitted to the Intensive Coronary Care Unit (ICCU) due to ingestion of large amount of tablets in a suicidal attempt. The patient's relatives reported ingestion of near 90 tablets of diltiazem (90 mg) – total ingested dose of 8.1 g, 50 tablets of metoprolol (100 mg) and 4 pieces of toilet refreshment agent (Bref® - Henkel).

During the admission, the patient was unconscious – Glasgow Coma Scale 9 (Eye-2, Verbal-3, Motor-4), cyanotic, tachypnoic (respiratory rate 30/min), hypotensive (blood pressure 65/40 mmHg), with a heart rate of 45 beats per min. Initial electrocardiogram (ECG) revealed atrioventricular (AV) conduction abnormalities with second (Figure 1) and third degree AV block. The standardized scale for grading severity of poisoning – Poisoning Severity Score (PSS) [6] – yielded grade 3, designating poisoning affecting more organ systems: cardiovascular, respiratory and central nervous system. Laboratory findings revealed complex abnormalities. The arterial blood gas analyses showed severe lactate acidosis [pH 7.14, normal range (nr) 7.35–7.45, lactate 9.2 (nr less than 1.0), base excess (BE) -18.6 mmol/L (nr: -3 mmol/L to +3 mmol/L)], sodium of 118 mmol/L (nr 135–145 mmol/L), potassium of 2.6 mmol/L (nr 3.6–5.2 mmol/L), and ionized calcium of 0.8 mmol/L (nr 1.0–1.2 mmol/L)]. A glucose level at admission was 16 mmol/L (nr 3.9–5.5 mmol/L).

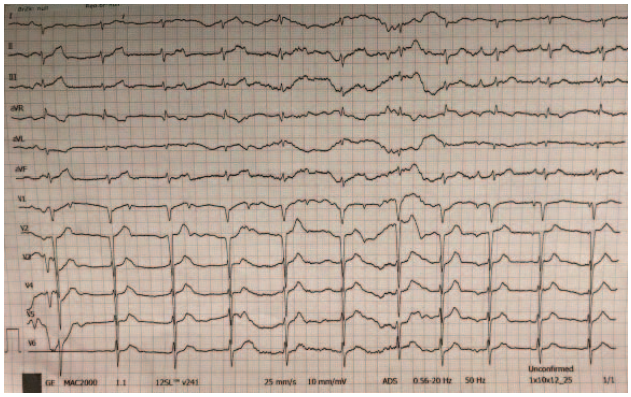

Fig. 1 – Second-degree atrioventricular block – Mobitz 2.

Immediately after the admission, the patient was endotrachealy intubated and mechanical ventilatory support was instituted. Following the nasogastric tube insertion and initial elimination of 500 mL of gastric content, additional repeated gastric lavage was performed, eliminating some particles of undigested tablets. Knowing that the patient ingested anionic surfactant, a decision was reached not to use additional charcoal through the nasogastric tube.

Volume resuscitation (total amount of 1.5 L) with saline infusions was started during the first 2 h. Due to a lack of prompt response, and persistent hypotension and bradycardia, dopamine (10–20 μg/kg/min) and noradrenaline (0.2–2.0 μg/kg/min) were administered. Sodium bicarbonate in total amount of 25 mmol during the first 10 h was also administered along with 20 mmol of calcium gluconate.

Chest X-ray was performed indicating the presence of pulmonary edema (Figure 2). A computed tomography (CT) scan confirmed a massive amount of undigested tablets in the patient's stomach (Figure 3), confirming the diagnosis of pulmonary edema with bilateral pleural effusion. Echocardiography revealed slightly depressed left ventricular systolic function. Summarizing all the data gained through various diagnostic modalities and clinical presentation, a diagnosis of cardiogenic and distributive shock with acute multiorgan failure was established.

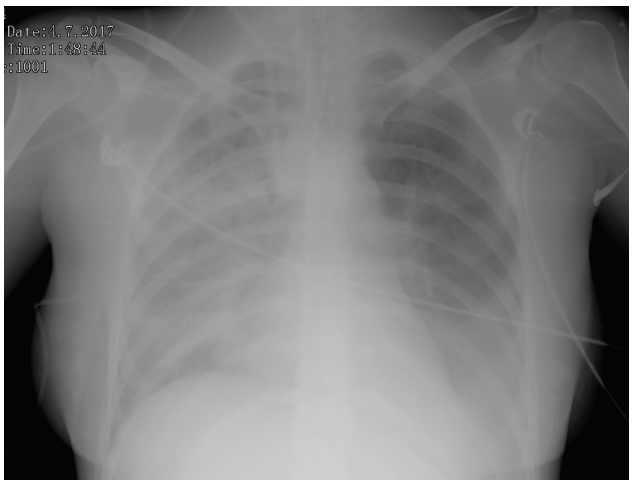

Fig. 2 – Chest X-ray demonstrating pulmonary edema.

The blood samples taken immediately after the admission of patient to the ICCU (approximately 7 h after ingestion) were sent to a reference toxicology laboratory for a detailed quantitative analysis. The diltiazem blood level was 6,200 ng/mL (therapeutic range 50–200 ng/mL). No traces of BB or its metabolite were found. Thus, BB intoxication was excluded. There were no possibilities to confirm anionic surfactants poisoning due to lack of reagents in laboratory.

The initial treatment strategy with inotropic and vasopressor agents was unsuccessful. The signs of progressive and refractory cardiogenic and distributive shock were apparent. The National Poison Control Center (Military Medical Academy in Belgrade) was contacted for further assistance. Additional treatment with lipid emulsion therapy (LET) was proposed. Unfortunately, LET was not available at the time, and it could not have been ordered and delivered in acceptable period.

Eight hours after continuous conservative treatment with slight, or no improvement in hemodynamic and general state of the patient, decision was made to put the patient on venoarteriral extracorporeal membrane oxigenator (VA-ECMO). A percutaneous cannulation of the left superficial femoral artery was achieved with 17 French arterial cannula with a distal perfusion protection using 7 French arterial sheet. Simultaneously, the percutaneous right femoral vein cannulation using 19 French cannula was performed (Figure 4). ECMO flow was set to around 3 L/min with a pump speed set to 3,000 rounds per minute. Within minutes, hemodynamic stability was achieved and spontaneous diuresis appeared. Initial lactate level of 9.2 mmol/L was reduced to 0.97 mmol/L in matter of 15 h following the ECMO commencement.

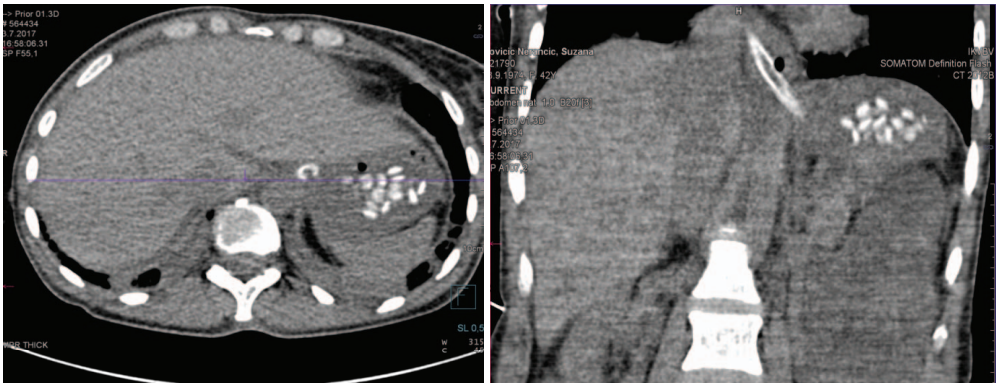

Fig. 3 – Computed tomography (CT) scan of the abdomen showing massive amount of undigested tablets in the stomach.

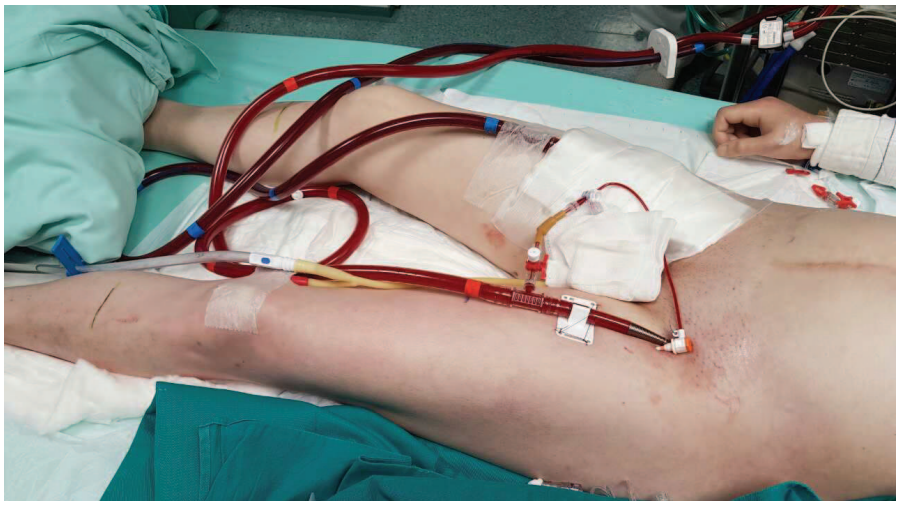

Fig. 4 – Venoarterial extracorporeal membrane oxygenator (VA-ECMO) – the left superficial femoral artery with distal perfusion protection and the right femoral vein

During the following 36 h, a gradual hemodynamic stabilization was established allowing successful weaning (gradual reduction of ECMO flow to 0.5 L/min with sustained hemodynamic stability) and decannulation from VA-ECMO 72 h after the ECMO commencement. A full recovery of all affected organs was established. The patient was discharged from our hospital 10 days after.

Discussion

Standard treatment of CCB and BB intoxication consists of several general measures and specific activities for sustaining normal cardiovascular function allowing the endogenous detoxification [7]. The initial treatment of symptomatic BB and CCB poisoning is supportive. This includes early airway and respiratory support. After the ingestion of CCB, it is important to determine formulation of drugs – whether it is a slow- release, or intermediate-release drug formulation [4]. Gastrointestinal decontamination is considered one of the first procedures needed to be performed. Administration of activated charcoal within 4 hours of CCB ingestion is suggested, especially in the case of immediate release CCB formulation ingestion. Whole bowel irrigation (WBI) with a polyethylene glycol electrolyte mixtures recommended in the case of slow-release CCB ingestion and should be considered in all patients. Activated charcoal administration is contraindicated after the ingestion of corrosive substances (e.g., inorganic acids), surfactants, or liquid hydrocarbons, and whenever the respiratory tract has not been protected by intubation [5].

Specific measures suggested for a treatment of CCB poisoning include administration of high dose of insulin, calcium, dopamine, noradrenaline or LET [7–10]. As demonstrated in our case, most of the recommended therapeutic options were performed with no satisfactory result, prompting another approach – extracorporeal life support. Although VA-ECMO was used in this clinical scenario with a clear survival benefit, no large scale studies have been performed examining the efficacy of ECMO in the setting of drug induced cardiogenic and distributive shock [11–13]. In the observational study published by Masson et al. [8] ECMO support was associated with a lower mortality when initiated in a group of 14 patients compared to conventional therapies provided to a group of 48 patients (48% vs. 86%) after adjustment for the Simplified Acute Physiology Score (SAPS) II and BB intoxication. Most human case series reported the positive functional outcomes in the majority of survivors with acceptable rate of procedure- related complications.

Lange et al. [14] performed a search of several scientific databases using the keywords: “extracorporeal membrane oxygenation”, “extracorporeal life support”, “ECMO”, “ECLS”, “assist-device”, and “intox*” or “poison*”. A total of 46 publications were selected (case reports and case series) and thoroughly examined. The authors concluded that ECLS could be safely used as a bridge-to-recovery for severely intoxicated patients with cardiogenic shock. They also defined main contraindications: absolute – uncontrolled coagulopathy and severe intracranial bleeding; relative – advanced age, severe irreversible brain injury, untreatable metastatic cancer, severe organ dysfunction and high positive pressure ventilation for more than 7 days. Most commonly observed complications of ECMO are the cannulation site bleeding and intracranial bleeding.

Recently published paper from Lyon group [15] looked at the high-rate arterial complications supported by ECLS for drug induced cardiogenic shock. In the period 2010–2015 they performed 12 ECLS. Drug intoxication was mainly due to BB and/or CCB (83.3%) and 5 (41.7%) patients had multiple drugs overdose. A success rate – hospital discharge and no major neurological sequel – was 75% (9 patients) with the mean support time of 2.4 ± 1.1 days. It is interesting that 6 (50%) patients developed lower limb ischemia that had to be dealt with decannulation and other vascular procedures. For this reason, we advocate routine use of distal perfusion protection with 7 French arterial sheet.

An interesting observation came from Lee et al. [16] about the adverse effects associated with the combined use of intravenous LET and ECMO. They were able to identify 7 papers in which simultaneous use of LET and VA-ECMO was described. There is an evidence that such a combined therapy is linked with the higher rate of fat depositions in the VA-ECMO circuits and increased blood clot formation warranting increased awareness of the managing personnel. In our patient, we also engaged combined LET and VA-ECMO approach with no adverse effect that we contribute to short ECLS time, only 72 hours. Kolcz et al. [17] proposed a way to reduce emergency ECLS time through initiating therapeutic plasma exchange. This approach allowed them to circulatory support the patient while performing exogenous clearance of plasma.

Conclusion

In severe cases of refractory cardiogenic and distributive shock due to diltiazem and other poison intoxication, VA-ECMO could give additional support and provide the bonus time for endogenous clearance of toxins. ECLS could be used in conjunction with the optimal medical therapy aiming to restoration of end-organ perfusion and allowing for intrinsic drug and toxin metabolism and natural elimination. An increasing body of evidence is accumulating for the use of ECLS in drug-induced cardiogenic shock, but further rigorous clinical trials and strong evidence are warranted.

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Received on September 26, 2017.
Revised on October 22, 2017.
Accepted on October 24, 2017.
Online First November, 2017.