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Hemodynamic abnormalities in sodium monofluoroacetate intoxication

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Hypotension is one of the most important predictors of mortality in sodium monofluoroacetate (SMFA) intoxication. This paper reports the hemodynamic response in one fatal and another survival case of SMFA intoxication. Despite correction of hypovolemia and with inotropic support, the patients remained in shock. Hemodynamic observations have provided evidence that shock after SMFA intoxication is due to diminished systemic vascular resistance and increased cardiac output. This is the first report in which such an invasive hemodynamic investigation has been recorded in a clinical case of SMFA intoxication.

Keywords: poisoning; sodium monofluoroacetate; Swan-Ganz catheterization

Introduction

SMFA is a potent rodenticide originally produced during World War II.[1,2] It has been removed from our market because of its high toxicity. However, some unlicensed product can be found in this country. The fluoroacetate metabolite, fluorocitric acid blocks cellular metabolism by inhibiting the Krebs cycle, producing widespread cinical effects include respiratory, neurologic, gastrointestinal, and fluid-electrolyte abnormalities. Common cardiovascular signs after ingestion include sinus tachycardia, hypotension and the rhythm may deteriorate into ventricular tachycardia or fibrillation. Previous reports identified hypotension as one of the most important predictors of short-term mortality. However, the pathophysiologic mechanism of SMFA shock is still unknown and the results of animal studies are controversial. In this report, we have reported the hemodynamic responses in two patients with SMFA intoxication.[2–6] The effects of metabolic blockade on the cardiovascular system in SMFA intoxication is discussed.

Case reports

Case 1

A 26-year-old female was transferred from local hospital 24 h after attempting suicide by swallowing 32 ml SMFA solution (1%). She was suffering nausea and vomiting and initial physical examination at our emergency department (ED) revealed low blood pressure 80/40 with dopamine support, the respiratory rate was 32 and the pulse rate was 120. Plasma creatinine was 1.8 mg/dl, blood urea nitrogen 26 mg/dl, potassium 3.3 mmol/l, total bilirubin 1.5 mg/dl, alanine aminotransferase 124 U/l, blood sugar 248 mg/dl. Arterial blood gases analysis revealed pH 7.342, PCO_2 32.1, PO_2 74.4, HCO_3- 17.4, base excess −7.2 and O_2 saturation 94.4 with 40% oxygen supply. After admission, aggressive inotropic support, fluid supply, electrolyte correction and hemodynamic monitoring were done. Hemodynamic measurement after hypovolemia was corrected. The problem here was loss of vascular tone in the arteries and elevated cardiac output: mean arterial pressure (MAP) 75 mmHg, mean pulmonary arterial pressure (MPAP) 14 mmHg, pulmonary capillary wedge pressure (PCWP) 10 mmHg, heart rate (HR) 110 beat/min, cardiac output (CO) 13 l/min, cardiac index (CI) 6.88 l/min/M2, left ventricular stroke volume (LVSW) 63 g.m, systemic vascular resistance (SVR) 745 dyne·sec·cm^{-5}, pulmonary vascular resistance (PVR) 47 dyne·sec·cm^{-5} (Table 1). After admission, progressive metabolic acidosis and profound shock were noted, followed by alternated consciousness and respiratory failure despite aggressive treatment. She expired 48 h after exposure to SMFA.

Case 2

A 62-year-old female, with past history of chronic obstructive pulmonary disease (COPD), was sent to the ED 1 h after attempting suicide by swallowing

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16 ml SMFA solution (1%). She suffered nausea and vomiting soon after intake. Initial physical examination at ED revealed blood pressure 167/78, the respiratory rate was 19 and the pulse rate was 120. The creatinine was 1.0 mg/dl, blood urea nitrogen 50 mg/dl, potassium 2.8 mmol/l, total bilirubin 1.0 mg/dl, alanine aminotransferase 65 U/l, blood sugar 478 mg/dl, and metabolic acidosis (pH 7.296, PCO_2 39.5, PO_2 123, HCO_3- 19.4, base excess −6.0 and O_2 saturation 98.3 with 28% oxygen supply). Progressive metabolic acidosis and shock developed after she was sent to the ICU. After admission, aggressive inotropic support, fluid supply, electrolyte correction and hemodynamic monitoring were done. Hemodynamic measurement after hypovolemia was corrected and with inotropic support (dopamine and norepinephrine) revealed MAP 84 mmHg, MPAP 25 mmHg, PCWP 11 mmHg, CO 9.27 l/min, CI 5.72 l/min/M2, LVSW 61 g.m, SVR 978 dyne·sec·cm^{-5}, PVR 196 dyne ·sec·cm^{-5} (Table 1). At ICU, hemodynamic compromise was corrected via inotropic agents (dopamine and norepinephrine). Upper gastrointestinal bleeding, frequent ventricular premature beats and aspiration pneumonia developed during her hospitalization and were controlled after mechanical ventilation, antibiotics, dopamine/nitroprusside therapy, bicarbonate, electrolyte and volume replacement and other medication. She was discharged without evident sequel 21 days later.

Discussion

The clinical presentation of SMFA intoxication has an extraordinarily wide variation in both sensitivity to effects and in clinical signs in various species of animals. In human beings, nausea, vomiting, and abdominal pain occurs initially, followed by respiratory distress, anxiety, agitation, muscle spasm, stupor, seizure, and coma.[1–5] Reversible acute renal failure, either oliguric or nonoliguric was reported in SMFA intoxication.[7] Sinus tachycardia and hypotension are the common cardiovascular signs and the cardiac rhythm may deteriorate into ventricular tachycardia/fibrillation or sudden cardiac arrest.[5] Hypocalcemia and hypokalemia are the most common electrolyte abnormalities. After a lethal dose of SMFA was ingested, severe cases resulted in death within 72 h. A previous study shows that early presentations with metabolic acidosis, shock and/or increased serum creatinine value are associated with poor short-term survival.[6] These prognostic variables can be useful to all clinicians that choose the optimal care for patients with suspected SMFA intoxication.

Table 1 The hemodynamic profiles in two cases of sodium monofluoroacetate intoxication

	Case 1	*Case 2*
Heart rate (beat/min)	110	107
Mean arterial blood pressure (mmHg)	75	84
Mean pulmonary arterial pressure (mmHg)	14	25
Central venous pressure (mmHg)	11	14
Pulmonary artery wedge pressure (mmHg)	10	11
Cardiac output (l/min)	13	9.27
Cardiac index (l/min/m2)	6.88	5.72
Systemic vasculat resistance (dyne·sec·cm^{-5})	745	978
Pulmonary vascular resistance (dyne·sec·cm^{-5}	47	196

Hypotension is a common finding in severe SMFA intoxication. However, the pathophysiologic mechanism of shock in SMFA is still unknown and the result of animal studies was controversial. Animal study of citrate metabolism in the tricarboxylic acid (TCA) cycle with monofluoroacetate has been shown to cause an increase in myocardial blood flow without any change in cardiac output, blood pressure, or O_2 consumption. Pulmonary arterial blood pressure and vascular resistance increased after administration of fluoroacetate, but neither systemic hemodynamics or myocardial contractility changed significantly. Administration of normal saline had no effect on any of the parameters. Neither myocardial oxygen consumption nor left ventricular work changed.[8] Other studies of citrate metabolism in the TCA cycle with monofluoroacetate also showed that blood flow did not increase to any organs examined other than the heart, including resting limb skeletal muscle. This unique response of myocardium to TCA cycle inhibition suggested a unique metabolic control of cardiac vasodilation. An alternative explanation is that after monofluoroacetate, blood flow to active muscles of breathing as well as to the heart became abnormally elevated with respect to mechanical work, and loading evoked no further increase in blood flow.[9]

How does SMFA cause the vasodilatation and subsequent shock in humans? We presumed two possible mechanisms: (1) direct effect on vessel wall by inhibiting the cellular Krebs cycles and (2) metabolic acidosis caused by the block of whole body cellular aerobic metabolism. In the initial course of our two patients, the factor of hypovolemic shock was unable to be ruled out due to initial severe vomiting, diarrhea and prerenal azotemia. However, persistent profound shock was still noted despite administration of large amount of intravenous fluids. The following hemodynamic measurement by Swan-Ganz catheterization revealed low systemic arterial and right heart pressure, low systemic vascular resistance, and elevated values for cardiac output. The results in decreased vascular tone were similar to the initial warm phase of septic shock. Otherwise, the fatal one (Case 1) showed a low pulmonary vascular resistance,

which differed from the survival one (Case 2). However, the meanings of low pulmonary vascular resistance are unknown on SMFA shock and wait for further investigation.

Our report seems to be the first one about the invasive hemodynamic study of SMFA shock in the worldwide literature. We presumed direct effect on vessel wall by inhibiting the cellular Krebs cycles and metabolic acidosis caused by the block of whole body cellular aerobic metabolism are responsible for SMFA induced vasodilatation and shock. Hemodynamic observations have provided evidence that shock after SMFA intoxication is diminished systemic vascular resistance and increased cardiac output. The authors hope that the findings in these cases may be helpful in providing information about the pathophysiology of SMFA intoxication and in dealing with such patients.

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