Austin Critical Care Case Reports

Open Access

Austin Publishing Group

Case Report

Multiple Organ Failure and Refractory Cardiogenic Shock due to Venlafaxine Intoxication, Successfully Treated with Veno-Arterial Extracorporeal Life Support

Le Balc'h P[1], Painvin B[1,3]*, Gicquel T[2,4] and Camus C[1,3]

[1]Service de Réanimation Médicale et des Maladies Infectieuses, Centre Hospitalier Universitaire de Rennes, Hôpital Pontchaillou, 2 rue Henri le Guilloux, 35033 Rennes Cedex 9, France

[2]Laboratoire de Toxicologie Biologique et Médico-légale, Centre Hospitalier Universitaire Pontchaillou, 2 rue Henri le Guilloux, 35033 Rennes Cedex 9, France

[3]Faculté de Médecine, Université de Rennes 1, Unité INSERM CIC 1414, IFR 140, Rennes, France

[4]Univ Rennes, INSERM, INRAE, CHU Rennes, Institut NuMeCan (Nutrition, Metabolism and Cancer) Rennes, France

***Corresponding author:** Painvin B, Service de Réanimation Médicale et des Maladies Infectieuses, Centre Hospitalier Universitaire de Rennes, Hôpital Pontchaillou, 2 rue Henri le Guilloux, 35033 Rennes Cedex 9, France

Received: December 15, 2020; **Accepted:** January 23, 2021; **Published:** January 30, 2021

Abstract

Venlafaxine has critical side effects from arrhythmias to cardiogenic shock after toxic dose ingestion. We report a case of venlafaxine intoxication with Multiple Organ Failure (MOF) treated with Veno-Arterial Extracorporeal Life Support (VA-ECLS). A 60-year old male with a history of chronic depression ingested 72 tablets of prolonged-release venlafaxine hydrochloride 75 mg (total 5400 mg). Initial EKG showed broadened QRS complexes and Transthoracic Echocardiography (TTE) revealed diffuse ventricular hypokinesia with Left Ventricular Ejection Fraction (LVEF) of 15% for which dobutamine infusion was started. Due to persistent refractory cardiogenic shock and MOF, a Medos® Deltastream® VA-ECLS was surgically implanted in our intensive care unit. On day 1, toxicology analysis found plasma concentrations of venlafaxine 3.2mg/L and its metabolite desmethylvenlafaxine at 0.92 mg/L. At day 6, we performed a weaning trial, enabling ECLS removal. Motion defect of anteroseptal and inferolateral walls was also noticed. EKGs showed a shorten R wave in the anteroseptal territory leading to the potential diagnosis of underlying ischemic cardiomyopathy. The patient was extubated at day-10 and discharged for cardiology unit at day-17. At day-20, cardiac magnetic resonance imaging showed no sign of ischemia and TTE parameters were normalized. This is the first report of refractory cardiogenic shock and MOF due to venlafaxine intoxication treated with VA-ECLS. The main objective of ECLS is to restore cardiac output especially when ventricular failure is refractory to inotropes. Our experience suggests that MOF secondary to refractory cardiogenic shock should quickly prompt the implantation of a VA-ECLS in venlafaxine critical overdose.

Keywords: Cardiogenic Shock; Ecls; Intoxication; Venlafaxine; ICU

Introduction

Venlafaxine is a bicyclic antidepressant that inhibits neuronal uptake of norepinephrine, serotonin, and to a lesser extent, dopamine. It is one of the most prescribed drugs for depression, worldwide, and ranks as the seventh out of 25 most used anti-depressants for suicidal intention in the US [1]. Critical side effects from arrhythmias to cardiogenic shock can be seen following toxic dose ingestion [2], with variation in inter-individual susceptibility [3]. We report a case of venlafaxine intoxication with Multiple Organ Failure (MOF) treated with Veno-Arterial Extracorporeal Life Support (VA-ECLS).

Case Description

A 60-year old male with a history of chronic depression was treated with oral prolonged-release venlafaxine 75 mg/day, baclofen, and oxazepam. In June 2020, he ingested 72 tablets of prolonged-release venlafaxine hydrochloride 75 mg (total of 5400 mg). Then, he was brought to a local hospital. On arrival, he developed ventricular tachycardia, which resolved spontaneously, and was intubated for respiratory failure. EKG showed broadened QRS complexes, Transthoracic Echocardiography (TTE) revealed diffuse ventricular hypokinesia with Left Ventricular Ejection Fraction (LVEF) of 15% for which dobutamine infusion was started.

The patient was referred to our unit for VA-ECLS evaluation. He presented with signs of hypoperfusion, anuria and liver failure with MAP of 62 mmHg while receiving dobutamine 15µg/kg/min. An EKG showed a non-significant ST elevation from V1 to V3 without mirroring. TTE revealed no Takotsubo cardiomyopathy but biventricular hypokinesia, LVEF of 10%, and low subaortic Velocity Time Integral (VTI) at 8cm. Due to persistent refractory cardiogenic shock and MOF, a Medos® Deltastream® VA-ECLS was surgically implanted in the right femoral triangle. Initial settings were Pump Motor Speed (PMS) 4010 revolutions per minute (rpm), resulting in a Blood Flow Rate (BFR) of 5.3 L/minute, sweep gas flow rate 4.5 L/minutes with oxygenator at 80%. Heat exchanger was set at 36°C. Initial characteristics and evolution are summarized in Table 1.

On day 1, toxicology analysis found plasma concentrations of: venlafaxine 3.2mg/L and its metabolite desmethylvenlafaxine 0.92 mg/L, baclofen 0.37mg/L, acetaminophen 6 mg/L, and oxazepam 0.3 mg/L.

Over the next days, ECLS setting remained: PMS at 3635 rpm (BRF 5.3L/min), oxygenator at 50% with a sweep gas flow rate of 3L/

Citation: Le Balc'h P, Painvin B, Gicquel T and Camus C. Multiple Organ Failure and Refractory Cardiogenic Shock due to Venlafaxine Intoxication, Successfully Treated with Veno-Arterial Extracorporeal Life Support. Austin Crit Care Case Rep. 2021; 5(1): 1021.

Table 1: Patient's characteristics and Extra Corporeal Life Support settings.

Variables	Admission time, referral medical ICU	Admission day	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 20 Cardiology unit
						Continuous veno-venous haemodiafiltration				
pH	7.12	7.48	7.54	7.49	7.45	7.45	7.42	7.42	7.35	NA
PaO2 - mmHg	82	372	43	65	100	75	69	82	71	NA
HCO3 - mmol/L	17	19	33	32	32	41	26	25	23	NA
Lactates - mmol/L	19	19	5.4	3.2	2.6	1.5	0.9	NA	1.2	NA
Total /conjugated bilirubin - µmol/L	34/30	20/25	34/27	41/39	36/34	36/34	NA	NA	31/29	13
AST / ALT - IU/L	7290 / 2802	1208 / 2716	15570 / 2900	3609 / 2177	1332 / 1560	511 / 1067	NA	NA	117 / 359	45 / 69
Creatinine - µmol/L	190	235	357	495	656	790	470	230	333	165
Daily diuresis (mL/24h)	NA	225	170	170	200	210	200	100	97	NA
factor V-%	12	NA	41	71	115	132	146	NA	NA	NA
INR	2.91	NA	2.42	1.92	1.32	1.15	1.16	NA	1.03	1.2
SOFA score	15	16	18	20	20	19	12	9	13	1
Norepinephrine (µg/kg/min)	2	0.75	0.2	0.04	None	None	None	None	None	None
Dobutamine (µg/kg/min)	15	12,5	2,5	None	None	None	None	None	None	None
lowest MAP (mmHg)	61	77	68	66	70	78	80	80	81	NA
Subaortic VTI (cm)	10	6	NA	12	NA	13	NA	18	18	18
LVEF (%)	10	10	NA	15	NA	20	NA	30	30	65
Extra Corporeal Life Support settings	Extra Corporeal Life Support									
PMS (RPM)	NA	4010	3680	3630	3630	3630	3630	3100	NA	NA
BFR (L/min)	NA	5.3	5.2	5.2	5.2	5.2	5.2	4.2	NA	NA
Oxygenator $Fi0_2$ (%)	NA	80	60	60	50	50	50	40	NA	NA
Sweep gas flow rate (L/min)	NA	4.5	3	3	3	3	3	3	NA	NA

Abbreviations: AST: Aspartate Transaminase; ALT: Alanine Transaminase; BFR: Blood Flow Rate; ICU: Intensive Care Unit; INR: International Normalized Ratio; MAP: Mean Arterial Pressure; NA: Non-Applicable; SOFA: Sequential Organ Failure Assessment; VTI: Velocity Time Integral; LVEF: Left Ventricular Ejection Fraction; PMS: Pump Motor Speed; RPM: Revolution Per Minute; BFR: Blood Flow Rate

min (Table 1). At day 6, we performed a weaning trial: BRF was set at 1 L/min for 1 hour. TTE then showed LVEF of 25%, with subaortic VTI at 16cm (Table 1) enabling ECLS removal. Motion defect of anteroseptal and inferolateral walls was also noticed. EKGs showed a shorten R wave in the anteroseptal territory leading to the potential diagnosis of underlying ischemic cardiomyopathy.

The patient was extubated at day-10 and discharged for cardiology unit at day-17. At day-20, cardiac magnetic resonance imaging showed no sign of ischemia and TTE parameters were normalized (Table 1).

Discussion

This is the first report of refractory cardiogenic shock and MOF due to venlafaxine intoxication treated with VA-ECLS. Unlike beta-blockers or calcium channel inhibitors, the effectiveness of ECLS for cardiogenic failure due to other cardio tropic drugs is not established. Management of venlafaxine intoxication is not consensual, because of its complex cardiovascular toxicity [4], and the lack of any specific antidote. At therapeutic dose, this drug is not associated with a higher risk of cardiotoxicity compared to other commonly used antidepressants [5], yet the opposite seems to occur in case of overdose [6]. Large dose ingestion increases serotonin and noradrenaline plasma concentration, leading to stunning of cardiac cells, and most cardiovascular effects. These effects extend from increased heart rate or blood pressure, to malignant arrhythmias or cardiac conduction effects [7-11]. Left ventricular failure and cardiogenic shocks are described with great doses ingestion, between 2000 and 18000 mg [2;12]. The main objective of VA-ECLS is to restore cardiac output especially when ventricular failure is refractory to inotropes [13-14].

Conclusion

Our experience suggests that MOF secondary to refractory cardiogenic shock should quickly prompt the implantation of a VA-ECLS in venlafaxine critical overdose.

Author Contributions

BP conceptualized the study and participated in its design, data acquisition and analysis, literature research, and manuscript drafting. LBP participated in data acquisition and analysis, literature research and manuscript drafting. GT participated in data acquisition and analysis and manuscript drafting. ME participated in analysis and manuscript drafting. CC participated in data acquisition and analysis, revising of the article for important intellectual content and manuscript drafting. All authors read and approved the final manuscript.

Conflicts of Interest Statement

The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper. The manuscript has been read and approved by the authors. The authors certify that the submission is not under review at any other publication. The authors declare no financial disclosures.

References

1. White N, Litovitz T, Clancy C. Suicidal antidepressant overdoses: a comparative analysis by antidepressant type. J Med Toxicol. 2008; 4: 238-250.
2. Batista M, Dugernier T, Simon M, Haufroid V, Capron A, Fonseca S, et al. The spectrum of acute heart failure after venlafaxine overdose. Clinical Toxicology. 2013; 51: 292-295.
3. Karlsson L, Green H, Zackrisson AL, Bengtsson F, Jakobsen Falk I, Carlsson B, et al. ABCB1 gene polymorphisms are associated with fatal intoxications involving venlafaxine but not citalopram. Int J Legal Med. 2013; 127: 579-586.
4. Ellahi R. Serotonin syndrome: a spectrum of toxicity. BJ Psych Advances. 2015; 21: 324-332.
5. Martinez C, Assimes TL, Mines D, Delloaniello S, Suissa S. Use of venlafaxine compared with other antidepressants and the risk of sudden cardiac death or near death: a nested case-control study. BMJ. 2010; 340: c249.
6. Whyte IM, Dawson AH, Buckley NA. Relative toxicity of venlafaxine and selective serotonin reuptake inhibitors in overdose compared to tricyclic antidepressants. Q J Med. 2003; 96: 369-374.
7. Isbister G. Electrocardiogram changes and arrhythmias in venlafaxine overdose. Br J Clin Pharmacol. 2009; 67: 572-576.
8. Howell C, Wilson AD, Waring WS. Cardiovascular toxicity due to venlafaxine poisoning in adults: a review of 235 consecutive cases. Br J Clin Pharmacol. 2007; 64: 192-197.
9. Höjer J, Hulting J, Salmonson H. Fatal cardiotoxicity induced by venlafaxine overdosage. Clin Toxicol. 2008; 46: 336-337.
10. Khalifa M, Daleau P, Turgeon J. Mechanism of sodium channel block by venlafaxine in guinea pig ventricular myocytes. J Pharmacol Exp Ther. 1999; 291: 280-284.
11. Fossa AA, Gorczyca W, Wisialowski T, Yasgar A, Wang E, Crimin K, et al. Electrical alternans and hemodynamics in the anesthetized guinea pig can discriminate the cardiac safety of antidepressants. J Pharmacol Toxicol Methods. 2001; 55: 78-85.
12. Schroeder I, Zoller M, Angstwurm M, et al. Venlafaxine intoxication with development of takotsubo cardiomyopathy: successful use of extracorporeal life support, intravenous lipid emulsion and CytoSorb®. Int J Artif Organs. 2017; 40: 358-360.
13. Masson R, Colas V, Parienti JJ, et al. A comparison of survival with and without extracorporeal life support treatment for severe poisoning due to drug intoxication. Resuscitation. 2012; 83: 1413-1417.
14. De Lange DW, Sikma MA, Meulenbelt J. Extracorporeal membrane oxygenation in the treatment of poisoned patients. Clin Toxicol (Phila). 2013; 51: 385-393.