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Vasoplegic syndrome after pediatric cardiac surgery

Abstract

Vasoplegic syndrome (VS) is a form of vasodilatory shock that occurs in the early period in patients who undergo cardiac surgery requiring cardiopulmonary bypass (CBP). Vasoplegic syndrome, reported between 9 and 44%, is characterized by severe hypotension,severe decrease in systemic vascular resistance, decreased arteriolar reactivity, need for increased volume, and decreased response to norepinephrine, despite normal ardiac outflow. Vasoplegia is associated with high mortality and morbidity, especially in pediatric patients. The pathophysiology of vasoplegic syndrome includes disruption of the arteriolar tone, which is regulated by endothelial function and neurohumoral system.Methylene blue is safely used when administered at a dose below 2mg/kg while more prospective randomized controlled trials are needed to determine the effective dose range.

Keywords: vasoplegic syndrome, pediatric, cardiac surgery, methylene blue, cardiyopulmoner bypass, prostaglandin infusion, pleth variability index, cross clamp

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Pınar Yıldırım Özkan,[1] Ahmet Akyol,[1] İpek Erus,[2] AhuBaysal Çitil,[1] Ayşe Duygu Kavas,[1] Ahmet Eroğlu[3]

[1]The University of Health Sciences, Ümraniye Training and Research Hospital, Clinic of Anesthesiology and Intensive Care, Turkey

[2]Koc University, Medical Faculty, Clinic of Anesthesiology and Intensive Care, Turkey

[3]KTU, Medical Faculty, Clinic of Anesthesiology and Intensive Care, Turkey

Correspondence: Assoc. Prof.Dr.Ahmet AKYOL, The University of Health Sciences, Ümraniye Training and Research Hospital, Clinic of Anesthesiology and Intensive Care, ElmalikentMah. AdemYavuz Cad. No: 1. (34764) Ümraniye, İstanbul, Turkey, Tel +90 533 6331369, Email ahmetakyol9598@gmail.com

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Introduction

Vasoplegic syndrome (VS) is a form of vasodilatory shock that occurs in the early period in patients who undergo cardiac surgery requiring cardiopulmonary bypass (CBP). Vasoplegic syndrome, reported between 9 and 44%, is characterized by severe hypotension,severe decrease in systemic vascular resistance, decreased arteriolar reactivity, need for increased volume, and decreased response to norepinephrine, despite normal cardiac outflow.[1,2] Vasoplegia is associated with high mortality and morbidity, especially in pediatric patients. Prolonged use of ACE inhibitor, calcium channel blockers, use of amiodarone and heparin, low cardiac reserve (EF <35%), symptomatic congestive heart failure and diabetes mellitus are among perioperative risk factors in adults.[3] On the other hand, pre- and post-CPB hematocrit, pre-bypass mean arterial pressure (MAP), surgery type, duration of bypass, use of antifibrinolytic and/or vasopressor before bypass, hypothermia and needed dose of vasopressin for terminating bypass have been found intraoperative risk factors in pediatric cases.[4]

Increased IL-1 and ANP levels following CPB resulting in vasodilation due to increased intracellular cGMP or irregularity in the synthesis of mediators such as NO and prostacyclin have been accused to be the underlying pathophysiology.[5] NO release and increased levels of cGMP induce relaxation in vascular smooth muscle cells.

Clinical case

The patient, delivered by cesarean section at week 37, was examined at a different institution with the symptom of cyanosis. At 3-day old, the patient was admitted to our hospital and detected with muscular middle inlet VSD, PFO, BAT with 68% of EF on the echocardiogram. During the ICU evaluation for preoperative anesthesia, the skin color was icteric, turgor and tonus was normal. Lung sounds were bilaterally equal and rough. Spontaneous breathing revealed a 3/6 systolic murmur. With the infusion of prostaglandin (0.02mcg/kg/min), SpO2 was 85%, BP 69/37 mmHg, and pulse 168/min at room temperature. Abdominal examination revealed hepatosplenomegaly. When 11-day-old, the patient was taken to the operation room after the necessary preparations were made. Anesthesia induction was started after the basal values were recorded by performing a five-ECG test, pulse oximeter from two different extremities, noninvasive dynamic measurement of changes in perfusion and pleth variability index, NIRS and noninvasive blood pressure monitoring. Induction was performed with 0.15 mg/kg of dormicum, 2mcg/kg/min of fentanyl and 0.6mg/kg of esmeron given to the baby weighing 2950 gr. on the operation day. During the operation, intravenous anesthetics were administered. 10 mg/kg of prednisolone, 25 mg/kg of ceftazidime, and 0.5 mg/kg of pantaprosol were administered intravenously. Right jugular venous catheterization (4f 8cm) and left femoral artery catheterization (2f 3cm) were applied. Milrinonee infusion (0.5 mcg/kg/min) was initiated following catheterization. Rectal temperature probe, nasogastric catheter and urine catheter (6f silicone) were inserted. Milrinone infusion was continued in the peroperative period. After the cross-clamp was removed, adrenaline (0.05 mcg/kg/min), dopamine (3 mcg/kg/min) and perlinganite (0.25 mcg/kg/min) infusion was started. The total cross-clamp time of the patient undergoing arterial switch operation was 147 min and the duration of cardiac pulmonary bypass (CPB) surgery was 203 min. The patient was cooled to 30 degrees during CPB. After the cross-clamp was removed and the patient was warmed up, administration of inotropic agents, 0.05 mcg/kg/min of adrenaline, 3mg/kg/min of dopamine and 0.25 mcg/kg/min of nitroglycerin for peripheral perfusion, was initiated. 0.1 mcg/kg/min of noradrenaline was started for the patient with hypotensive course. Cryoprecipitate, erythrocyte suspension, platelet and fresh frozen plasma replacement were performed. The curarized and intubated patient receiving inotropic support was transferred to the pediatric intensive care for monitorization. On postoperative day 1, the echocardiogram showed pericardial hematoma and the patient was operated again. The hematoma was cleared, and the sternum

was left open. Despite the inotropic support on the 6th postoperative day, the patient was still hypotensive. Following, 1mg/kg bolus of methylene blue was administered intravenously, and infusion was continued at 1mg/kg/h. While BP was 46/30 mmHg, it was measured as 71/38 mmHg 1 hour after the intravenous administration of bolus. The doses of inotropes were reduced after the patient's blood pressure was found within normal limits. The patient, who was hypotensive at the 24th hour of the methylene blue infusion, was again administered increased doses of inotropes, but no response was obtained. The patient who did not respond to CPR was accepted exitus.

Discussion

Vasoplegic syndrome is a common complication of cardiac surgery requiring CPB. CPB is also described as a type of SIRS induced by surgical trauma, nonspecific activity, blood transfusion and hypothermia.[6] The pathophysiology of vasoplegic syndrome includes disruption of the arteriolar tone, which is regulated by endothelial function and neurohumoral system. Increased IL-1 and ANP levels following CPB resulting in vasodilation due to increased intracellular cGMP or irregularity in the synthesis of mediators such as NO and prostacyclin have been accused to be the underlying pathophysiology. NO release and increased cGMP lead to vascular smooth muscle cell relaxation. NO and cGMP is related to profound vasodilatation, myocardial depression, and decreased response to catecholamines.[5]

Methylene blue, which has come into use in the treatment of vasoplegic syndrome, inhibits NO synthesis and cGMP synthesis, which form the basis of pathophysiology, prevents vasodilation in vascular smooth muscles and increases the effect of norepinephrine. The interaction between methylene Blue (MB) and the cholinergic system also contributes to the hemodynamic response. It binds to muscarinic receptors acting as a cholinesterase inhibitor. It reduces endothelial NO release by binding to endothelial M3 receptors. Although the recommended MB dose is 1-3 mg/kg, 2 mg/kg of iv bolus is the most commonly used dose. Since the duration of action is 40 minutes, it should be switched to infusion at the same dose following iv bolus administration. In their study, Hassan et al. applied a single dose of 1.5 mg/kg infusion over 20 minutes and received a response.[7] Although there are promising findings regarding the use of methylene blue in vasoplegic syndrome, there are no prophylactic and therapeutic guidelines or therapeutic window. The lethal dose is reported as 40mg/kg.

Del Ducaet al.[8] described the use of methylene blue in vasoplegic syndrome. It inhibits vascular smooth muscle relaxation by preventing the increase of NO and cGMP that is accused in pathophysiology. MB acts as a cholinesterase inhibitor by binding to endothelial muscarinic (M3) receptors and contributes to the correction of hemodynamic response by reducing basal NO release.

MB solution is available as an ampoule containing 10 mg/ml. A single bolus dose can be applied, or it can be switched to infusion where it is not ineffective. Although no clear dose is defined for pediatric population, it has been shown to be safe when administered below 2mg/kg.

Leyhet al.[9] applied 2mg/kg of MB infusion over 20 min in their study. MAP increased from 68 mmHg to 72mmHg in the first hour of MB infusion and the norepinephrine dose decreased from 0.5 mcg/kg/min to 0.35 mcg/kg/min. In 6 hours, MAP was 71 mmHg and needed norepinephrine was 0.2mcg/kg /min while a significant decrease was observed in cardiac output and serum lactate level in 24 hours compared to the control group.[9] In our case, infusion was maintained at a dose of 1mg/kg/hr following the administration of 1mg/kg bolus. BP increased from 46/30 mmHg to 71/38 mmHg while the dose of inotropes was reduced.

Levin et al.[10] also applied 1.5 mg/kg infusion over 1 hour in 28 adult patients who developed VS following CPB. In two hours, VS was completely corrected, and they reported a significant decrease in the rate of mortality, renal failure, respiratory failure, neuropathy, arrhythmia, sepsis and multiple organ failure compared to the control group.[10].

Driscolet al.[11] administered 1mg/kg/h iv to 5 neonatal patients with refractory hypotension following a high-dose of inotropic, corticosteroid and colloid loading, and obtained a significant hemodynamic response. Inotropic support was completely ceased in three patients within 72 hours.[11] In a case report published by Bhalla et al.,[12] a 5-year-old with hypoplastic left heart syndrome underwent a heart transplant after a failed Fontan attempt. 1 mg/kg of methylene blue was applied over 5 minutes in a patient developing inotrope-resistant hypotension in the postoperative period after sufficient cardiac function was verified on the echocardiogram. In 1 hour, an additional 1mg/kg bolus was applied, and MAP increased from 30mmHg to 60 mmHg in 10 minutes. Inotrop support was completely ceased within the next 12 hours.[12]

Conclusion

There are no defined risk factors for VS seen following pediatric cardiac surgery. Methylene blue is safely used when administered at a dose below 2mg/kg while more prospective randomized controlled trials are needed to determine the effective dose range.

Authors' contributions

AA and AE designed the study and drafted the manuscript. PYÖ, İE, ABÇ, ADK, and AA collected the clinical and laboratory data. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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