Journal of Anesthesia & Clinical Research
ISSN: 2155-6148

Evora, J Anesth Clin Res 2013, 4:8
DOI: 10.4172/2155-6148.1000349

Letter Open Access

Methylene Blue Action to Treat Vasoplegic Syndrome is Time-Dependent

Paulo Roberto B Evora*

Department of Surgery and Anatomy, University of São, SP, Brazil

Abstract

We present a case report of an ultrasound-guided femoral nerve block in a seven-year-old patient with an aberrant femoral nerve. The utilization of ultrasonography enabled the identification and successful blockade of an aberrant femoral nerve within the belly of the iliopsoas muscle. A review of the literature regarding aberrant femoral nerve anatomy is included.

As stated by Blacker and Whaler, there is strong evidence that methylene blue (MB), an inhibitor of guanylate cyclase, is an excellent therapeutic option for Vasoplegic Syndrome (VS) in heart surgery. The authors reported a case of VS during an on pump coronary artery bypass grafting with no response to MB. The patient was a 63 year old male with chest pain was found to have multivessel disease and referred for elective three vessels CABG. He was 72 inches and 89 kg with a history of hypertension, hyperlipidemia, and benign prostate hypertrophy. Medications included metoprolol 50 mg once a day, enalapril, hydrochlorothiazide, Zocor, Avodart and tamsulosin. Hydrochlorothiazide had been the only held morning medication. Anesthesia procedures, including intubation and insertion of a right pulmonary artery catheter, were accomplished uneventfully. Coincidently with tranexamic acid infusion, before the beginning of CPB, a severe hypotensive episode ruled the patient hemodynamic status. Arterial hypotension persisted uncontrollable, during and after CPB, despite the use of high doses of norepinephrine. Out of CPB, CI was 2.6 L/ minute*m^2 with a Systemic Vascular Resistance (SVR) of 663 $dynes^{-s-cm-5}$, and theinitial LV function appeared normal on TEE. CPB was re-initiated. Vasopressin and norepinephrine infusions continued. In consideration of adrenal insufficiency, 125 mg hydrocortisone was given intravenously. Despite no other signs or symptoms other than hypotension, anaphylaxis were consideredand IV ranitidine and diphenhydramine were given; the latex Foley was replaced. After around 6 hours, an intra-aortic balloon pump (IABP) was placed. CPB was weanedandthe blood pressure was in the high 90/50's mmHg. Vasopressin continued as weaning would result in a MAP of 50 mmHg and tachycardia of 120 bpm. CPB was reinstituted due to persistent hypotension, a worsening lactate of 11.3 despite the IABP use. After discussion, vasoplegia was considered, and 200 mg MB was given intravenously, 6 hours after the initial episode of hypotension. There was a brief rise in the MAP to the 70's mmHg but lasted only three minutes [1].I have been "watching this movie" since the 80 s, a situation that led me to the Mayo Clinic for 2 years (1990-1992), where under the supervision of doctors Hartzell Schaff and Paul Pearson, started my expertise in endothelium/NO-dependent vasoreactivity. The conclusion was that this catastrophic situation is classified a "vasoplegic endothelial dysfunction"[2].

One problem in describing the VS is the lack of consistency in its definition. There is no clear definition, not even a single biomarker, including the determination of nitrite/nitrate (NOx), failed characterize the syndrome [3]. The VS is a constellation of signs and symptoms: hypotension, high cardiac index, low systemic vascular resistance, low filling pressures, diffuse bleeding tendency and sustained hypotension despite the use of high doses of vasoconstrictor amines.

Regarding the medications associated with the emergence of VS in cardiac surgery, heparin and angiotensin-converting enzyme are, so far,nowadaysthe only ones considered as a risk factor for VS. During 20 years daily practice, we have sought a causal relationship, and various anecdotal aspects were considered: 1) The majority of cases occurred during or after CPB; 2) In the past, there were several cases associated with the curare aloferine used during anesthesia induction; 3) More attenuated cases occurred during anesthetic induction with standardized technique (etomidate, fentanyl, diazepine and pancuronium); 4) Some cases were clearly associated with the use of protamine; 5) Frequently we had the impression that vasodilation occurred after heparin use; 6) VS was observed in non-cardiac surgeries; 7) It seems that the cases occur in outbreaks, suggesting a relationship with drug lots; 8) There is no relation with the type of heart surgery; 9) Many patients are diabetics, and; 10) Many patients, in the 80 s, had previously used the calcium antagonist diltiazem [4].

In 2009, targeting MB for VS treatment in heart surgery, we published a personal statement including fifteen years (now eighteen years) of questions, answers, doubts and certainties. Some observations, again anecdotal, would be applied to the VS: 1) In the recommended doses it is safe (the lethal dose is 40 mg/kg); 2) The use of MB did not cause endothelial dysfunction; 3) The MB effect appears in cases of NO up-regulation, and; 4) MB is not a vasoconstrictor, by blocking of the cGMP pathway it releases the cAMP pathway, facilitating the epinephrine vasoconstrictor effect; 5) It is possible that the MB acts through this "cross talk" mechanism and is not right use of MB as a drug of first choice, or their use solely in the treatment of anaphylactic shock, is beyond any rational therapeutic option; 6) The most used dosage is 2 mg/kg as IV bolus followed by the same continuous infusion because plasma concentrations strongly decays in the first 40 minutes; 7) Although there are no definitive multicentric studies, the MB used to treat heart surgery VS, at the present time, is the best, safest and cheapest option, but; 8) There is a possible 'window of opportunity' for the MB's effectiveness [4].

The VS concepts are a valuable Brazilian contribution to cardiac surgery. Gomes described the syndrome and the MB treatment

***Corresponding author:** Paulo Roberto B. Evora, Department of Surgery and Anatomy, RibeirãoPreto School of Medicine, University of São, Paulo, SP, Brazil, E-mail: prbevora@gmail.com

Received August 05, 2013; **Accepted** August 27, 2013; **Published** August 29, 2013

Citation: Evora PRB (2013) Methylene Blue Action to Treat Vasoplegic Syndrome is Time-Dependent. J Anesth Clin Res 4: 349. doi:10.4172/2155-6148.1000349

was proposed by Evora et al. However, the clinical practice shows that the MB sometimes works and sometimes not [5-7]. A possible explanation, emphasized by Blacker & Whaler, was given by Fernandes in his academic thesis. Using a mouse sepsis model, three eight-hour windows of guanylate cyclase activity were evidenced [8]. Sepsis like VS is a state of profound refractory vasodilation. In the first eight hours, there is increased nitric oxide synthase activity and upregulation of guanylate cyclase. The second eight hours there is an absence of guanylatecyclase expression and a down regulation of nitric oxide synthase. The third eight hour window occursand there is an upregulation of guanylatecyclase and nitric oxide synthase.

Retrospectively, discussing the presented case: 1) SV diagnostic by observing amine resistant hypotension after tranexamic acid infusion; 2) MB 2 mg/kg infusion before starting the CPB; 3) MB continuous infusion during CPB based on the need of overflow and high dose NOR; 3) The IABP would be contraindicated because it is a situation of vasoplegia and 4) As additional measures, consider the use anti-inflammatory doses of corticosteroids andlow doses of metoprolol to counteract the phenomenon of beta receptors "downregulation".

The motivation of this long letter to the editor was the authors contribution, practical and education, singularly fundamental aspects: 1) The disclosure of the team to use the MB window opportunity syndrome vasoplegic in heart surgery, and; 2) The need for the establishment of this window in humans, perhaps choosing cGMP as biomarker since our attempt to use nitrite/nitrate, measured by chemiluminescence was frustrating [3]. Congratulations to the authors by the attitude of seeking, in retrospect, why the MB had a transient effect not just dismissing its action as often happens. In addition, I guess that it has introducedan easier concept to understand than the "Window of Opportunity" definition…"MB ACTION TO TREAT VASOPLEGIC SYNDROME IS TIME-DEPENDENT".

References

1. Blacker SN, Whalen FX (2013) Vasoplegic Syndrome: Does the Timing of Methylene Blue Matter?J Anesthe Clinic Res 4.
2. Evora PR (2013) Endothelium dysfunction classification: keeping the discussion opened. Nitric Oxide 1: 54-55.
3. Viaro F, Baldo CF, Capellini VK, Celotto AC, Bassetto S, et al. (2008) Plasma nitrate/nitrite (NOx) is not a useful biomarker to predict inherent cardiopulmonary bypass inflammatory response. J Card Surg 23: 336-338.
4. Evora PR, Ribeiro PJ, Vicente WV, Reis CL, Rodrigues AJ, et al. (2009) Methylene blue for vasoplegic syndrome treatment in heart surgery: fifteen years of questions, answers, doubts and certainties. Rev Bras Cir Cardiovasc 24: 279-288.
5. Gomes WJ, Carvalho AC, Palma JH, Gonçalves I Jr, Buffolo E (1994) Vasoplegic syndrome: a new dilemma. J Thorac Cardiovasc Surg 107: 942-943.
6. Evora PR, Ribeiro PJ, de Andrade JC (1997) Methylene blue administration in SIRS after cardiac operations. Ann Thorac Surg 63: 1212-1213.
7. Evora PR (2000) Should methylene blue be the drug of choice to treat vasoplegias caused by cardiopulmonary bypass and anaphylactic shock? J Thorac Cardiovasc Surg 119: 632-634.
8. Fernandes D, da Silva-Santos JE, Duma D, Villela CG, Barja-Fidalgo C, et al. (2006) Nitric oxide-dependent reduction in soluble guanylatecyclase functionality accounts for early lipopolysaccharide-induced changes in vascular reactivity. Mol Pharmacol 69: 983-990.