The use of methylene blue in abdominal aortic surgery: a case report

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ABSTRACT

The open abdominal aortic surgery includes a well-known phase in which arterial blood flow is stopped by occluding clamps, resulting in peculiar physiologic changes usually superimposed on advanced pathologic conditions. An anesthetic plan should aim at providing hemodynamic stability and preserving organ function.
Clamp removal leads to an acute fall in blood pressure following a decrease in systemic vascular resistance, caused by reactive hyperemia due to opening of the previously minimally perfused vascular beds. Several different mediators, including the nitrous oxide (NO) pathway, have been thought to be responsible for this hemodynamic effect. The massive production of NO by the inducible isoform of NO synthase could be partially responsible for the profound vasodilatation and myocardial dysfunction.
The dye methylene blue (MB) has been used as to prevent vasodilatation in other clinical situations like sepsis, cardiopulmonary bypass and liver transplantation.
We describe its use in a patient with poor hemodynamic status, who was submitted to aortic aneurism repair with infrarenal cross clamp. The intervention was also associated with a severe bleeding.
In this case MB allowed us to control hypotension with relatively low doses of vasopressors.

Keywords: *aortic aneurysm, cardiovascular anesthesia, methylene blue, ischemia-reperfusion injury, vascular surgery.*

INTRODUCTION

Vascular surgery needs the temporary interruption of arterial blood flow with occluding clamps isolating the diseased vessel tract and resulting in physiologic changes often superimposed on advanced pathologic conditions. In particular during aortic aneurism repair an increased afterload follows aortic clamp placement which can itself induce, firstly, hypertension and, afterwards, a sudden decrease in afterload with a potentially severe ischemia reperfusion injury can follow clamp removal. This phenomenon can be associated to severe hypotension, lactic acidemia, myocardial ischemia and cardiovascular collapse. Perioperative management should be aimed at providing hemodynamic stability, adequate oxygenation and preserving organ function (1).
Methylene blue (MB) has been used as a vasopressor agent in various settings (such as sepsis, liver failure and transplantation) and its role has been well described in cardiac surgery to treat vasoplegic syndrome (2, 3).
The physiological response to aortic cross clamp release is in part characterized by the production of NO, an endothelial derived vasodilator which acts on smooth cells in

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the vessel wall resulting in hypotension (4). The rationale for MB use in hypotensive syndromes is represented by the fact that MB directly inhibits nitric oxide (NO) synthases, both constitutive and inducible (3). However, at our best knowledge there are no report in literature regarding the use of MB in vascular surgery.

The recently introduced CO monitoring FloTrac™ / Vigileo™ allows CO determination from the arterial pressure waveform of any peripheral arterial line in conjunction with patients anthropometric data, with less potential complications compared to more invasive devices (5).

We describe the use of MB during an intervention of aortic aneurism repair with infrarenal cross clamp.

METHODS

The patient is 61-year old, male, with a mitral valve prolapse and dilated cardiomyopathy (Ejection Fraction 35%). He was scheduled for abdominal aortic aneurysm repair surgery. Standard monitoring was used throughout the operation, including continuous electrocardiography, pulse oximetry, capnography, bispectral index (BIS), end tidal gas analysis and urine output. A 20 gauge radial artery catheter was used to measure arterial pressure, a FloTrac™/Vigileo™ was used to measure cardiac index (CI) and stroke volume variation (SVV), an oesophageal temperature probe monitored core temperature. Fluid and drug infusion were administrated via two venous catheters and one double lumen central venous catheter. The induction of general anesthesia was obtained with i.v. propofol (1 mg/kg), sufentanyl (0.5 mcg/kg) and atracurium (0.5 mg/kg). Anesthesia was maintained with sevoflurane titrated on a BIS value of 40-50, atracurium (0.2 mg/kg/h) and sufentanyl i.v. boluses of 5 mcg as required. colloids and cristalloids were administrated to achieve a diuresis of 1 ml/kg/h, central venous pressure (CVP) of 12-15 mmHg and SVV < 12%. Ephedrine (5 mg i.v. bolus) was administered to maintain a mean arterial pressure (MAP) above 65 mmHg. Before aortic clamping, blood pressure (BP) was maintained at mean values of 90/60 mmHg with a CVP of 14 mmHg, SVV = 10 and a CI = 2.6 L/min per square meter. After infrarenal cross clamp BP increased to 110/60 mmHg, SVV = 7% and CI decreased to 1.9 L/min/m². The operation was complex: aortic clamp was maintained for 135 min. and blood losses were estimated about 4500 ml (1300 ml of blood were re-infused by a blood cell saver system, red blood cells transfusions were administered to maintain Hb value above 10 g/dl). Three minutes before clamp removal we administered i.v. MB (1,5 mg/kg) and 500 ml of colloids. Nevertheless BP decreased to 65/45 mmHg with a CVP of 6 mmHg, SVV = 14% and CI of 2.5 L/min/m².thus we administered 10 mg of ephedrine. After 10 minutes BP and CI reached the baseline values (before cross clamp).

The Total amount of fluids required was 5500 ml of crystalloids, 1350 ml of colloids and 1250 ml of red blood cells.

The operation was concluded and the patient was moved to the intensive care unit (ICU). After 2 days he was discharged uneventfully

DISCUSSION

The classic investigation of Gelman (6) represents a cornerstone of our knowledge of the pathophysiology of hemodynamic changes during aortic cross clamping and unclamping. Aortic clamping increases mean arterial pressure (MAP) and systemic vascular resistances (SVR) up to 50%, due to mechanical afterload increase as well as

a physiologic increase because of the activation of renin and release of cathecolamines, prostaglandins, and other active vasoconstrictors. Because of the increased SVR, CO initially decreases (6, 7).

Unclamping of the aorta can result in severe reduction in MAP, SVR and even CO unless aggressive therapy is undertaken prior to unclamping. Most anesthesiologists use fluid administration together with vasoconstrictors (i.e norepinephrine) or other drugs as calcium chloride to offset the negative inotropic and dromotropic effects caused by the reperfusion-induced release of factors such as e potassium, acids and other mediators.

Although the main factor contributing to hypotension is volume redistribution to the lower body after clamp release, many humoral mediators are released from the underperfused areas and exacerbate the hemodynamic changes. Such factors are as follows: renin, angiotensin, epinephrine, norepinephrine, PGI 2, endothelin, tromboxane, lactate, potassium, oxygen free radicals, platelet activator, cytokines, activated complement and neutrophil sequestration (8, 9). Another mechanisms contributing to the reduction in SVR occurring after reperfusion is represented by abnormalities in NO synthesis and vascular smooth muscle cell guanylate cyclase activation. NO is produced by two types of nitric oxide synthase, a constitutive type and an inducible one. NO activates soluble guanylate cyclase to produce Cyclic guanosine monophosphate (cGMP) which causes vasodilation and may also decrease myocardial contractility (5).

MB directly inhibits both types of NO synthases band it is also believed to act in competition with NO in binding guanylate cyclase, thus reduction cGMP production, and indirectly counterbalancing reperfusion-induced (3).

MB has been studied in different clinical situations such as sepsis, cardiopulmonary bypass, liver failure an transplantation (11-15). These studies used different doses and modalities of drug administration, but most of them reported an improvement of hemodynamics in the patients treated with MB.

However there is not a general agreement on this topic. In fact some investigations found an increase in SVR with no changes in CI, while others supposed that this drug mainly exerted its effects on a action on myocardial function (2, 10-13).

Similarly, some experimental and in vitro studies support this hypothesis reporting a direct effect of MB in increasing myocardial contractility (3, 16).

Adverse effects of MB include cardiac arrhythmias, coronary vasoconstriction, angina, decreased CO, renal blood flow and increased pulmonary vascular pressure. Other side effects are headache, fever, hemolytic anemia, nausea, vomiting and abdominal pain. These side effects are unlikely with MB doses < 2 mg/kg. A dangerous interaction with MAO inhibitors is described and it can result into a postoperative serotonin syndrome.

Nevertheless the most common side effect noted with MB is the self limiting discoloration of skin and urine (13, 17).

In regard to our patient, the possibility that MB administration could have favorably affected hemodynamics can be considered.

Our findings might be explained through a first effect of MB on myocardial function which sustained hemodynamic immediately after reperfusion, this effect is mostly mediated by guanylate cyclase inhibition; the effects on NO induced vasodilatation are likely to be gradual and slower, but unfortunately we did not measure NO products in our investigation.

As far as MB dose is concerned, we arbitrarily chose the dose and modalities previously described in liver transplantation (12) with a single bolus of MB. We cannot

exclude that could be better a bolus followed by a continuous infusion, in order to obtain the immediate improvement of myocardial function and the effect on endothelial NO.
Limitations: a potential limitations of this case report is the use of FloTrac™/Vigileo™ during aortic cross clamp, since a randomized controlled trial on this concern has never been performed. However FloTrac™/Vigileo™ is validated in many surgical settings (5), and there are no reasonable motivations against its reliability in this setting.
The whole intraoperative management including fluid and vasopressors administration have contributed to the hemodynamic finding and the good outcome and they cannot be ascribed only to MB use, thus we cannot draw any definitive conclusion regarding MB use is this setting with a case report.
Randomized controlled trials are needed to assess the clinical effects of MB in vascular surgery as well the most efficacious doses and administration modalities.

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