1. Pro And Con: Methylene Blue as Rescue Therapy for Vasoplegia After Cardiac Surgery


In this Pro/Con debate on the use of Methylene Blue (MB) Therapy for vasoplegia after cardiac surgery the authors first define vasoplegia by a set of haemodynamic parameters: Mean Arterial Pressure <50mmHg, SVR<800dynes.cm⁻¹.s⁻¹, Cardiac Index>2.5L/min/m², RAP<5mmHg and LAP<10mmHg during the infusion of a vasopressor such as Norepinephrine.

They then describe the pathogenesis as multifactorial and list a number of predisposing risk factors: chronic blockade of vasoactive receptors such as occurs in patients taking B-Blockers, Calcium Channel Blockers or Angiotensin Antagonists, long CPB, preoperative Heparin therapy, acute Amiodarone therapy and haemodynamic instability pre-CPB. The major physiologic disturbance in this syndrome is vasopressin deficiency and excess Nitric Oxide production.

Low dose vasopressin infusion started pre CPB has been shown to significantly decrease perioperative vasopressor support requirements.

Methylene Blue (MB) is an antagonist of Nitric Oxide. It binds to the heme moiety of soluble guanylate cyclase inhibiting its action,
scavenges nitric oxide and inhibits synthetase to decrease nitric oxide production.

MB is available as solution (10mg/ml) and is administered orally or intravenously. Single Bolus Dose is 1-2mg/kg over 20-30mins. Haemodynamic effects occur fairly rapidly.

The pro authors, Riha and Augoustides, explain that the use of MB has generally been reserved as a last resort in vasoplegic patients unresponsive to other therapy but that 2 randomised trials have reported MB to be effective and safe as prophylactic therapy for decreased vascular tone after cardiac surgery. They state further trials are required to elucidate its role as preemptive therapy.

The con author, Michael Andritsos, lists several points of contention in the routine use of MB for vasoplegia: Non-standardised timing and dosing of MB administration, data supporting the use of MB existing mostly in the form of case reports and only few small randomised trials exist and it is not a benign drug.

Side effects include cardiac arrhythmias, coronary vasoconstriction, it may counteract the benefit of inhaled NO or prostaglandin, transiently turns skin, urine and faeces greenish-blue, interferes with pulse oximetry readings and cerebral oximetry readings giving a spuriously low oxygen saturation reading, neurologic complications have been reported in rats, MB is a potent monoamine oxidase inhibitor and potentially life threatening serotonin toxicity may occur as a result of interaction between serotonergic agents and MB. They also list renal
impairment as an absolute contraindication to the use of MB as it is predominantly renally excreted.

He concludes that questions remain and data is scarce and until we have further data, the use of MB should only be considered with extreme caution.

The Pro Authors on the other hand conclude with the statement that MB has generally been shown to be safe, that further case reports have highlighted its usefulness in non-cardiac surgery (liver transplant surgery and phaeochromocytoma resection) and that given its safety, low cost and general availability, its indications are likely to expand.

**Comment:** A potentially very useful drug, especially as vasopressin is not freely available in South Africa. There isn’t enough evidence available to administer routinely but important to keep in mind.

2. **Protective Effects of Steroids in Cardiac Surgery: A Meta-Analysis of Randomized Double-Blind Trials**

   *Journal of Cardiothoracic and Vascular Anesthesia, Vol25, No1, 2011:pp156-165*

   In this systematic review of randomized double-blind trials, Cappabianca et al set out to evaluate the effects of steroid treatment on mortality and morbidity after cardiac surgery.

   They reviewed 31 trials (1974 patients) of adult patients undergoing cardiac surgery. 80% were undergoing isolated CABG surgery. Most were small trials, only 4 trials enrolled
>100 patients. They found steroid prophylaxis provided a protective effect in preventing postoperative atrial fibrillation, reducing postoperative blood loss, reducing ICU stay and in reducing hospital stay. It had no effect on postoperative mortality.

The authors argue that the first finding of this review of steroids in cardiac surgery was that the use of steroids during cardiac surgery is safe and this analysis represents the best evidence on this topic (safety of steroids) at the moment.

The use of steroids was not associated with a higher incidence of postoperative infection.

They also highlight the effect of steroids on the (30% reduced) onset of atrial fibrillation. They comment that recent literature has emphasized the role of inflammation in the pathogenesis of postoperative atrial fibrillation.

The limitations of the meta-analysis are identified as follows: variety of types and dosages of steroids used in these studies, the trials included are from a 30 year span, the patients in these trials were generally very low risk and therefore the data cannot be automatically extended to high-risk patients.

They conclude that a forthcoming large RCT will probably be able to evaluate the unanswered questions:

(Steroids In caRdiac Surgery Trial (SIRS Trial)) (SIRS trial is a large simple study in which high-risk patients undergoing cardiac surgery requiring the use of cardiopulmonary bypass (CPB) are randomly allocated to receive a pulse dose of Methylprednisolone or a matching placebo. Cardiopulmonary bypass initiates a systemic inflammatory response that facilitates development of post-operative
complications. SIRS will confirm or deny the potential clinical benefits of suppressing this response through the use of systemic steroids. Specifically, does 250 mg of intravenous Methylprednisolone given twice, once on anesthetic induction and again on CPB initiation, result in improved early survival and less myocardial infarction in high-risk cardiac surgery patients requiring CPB?)

**Comment:**

Will be very interesting to follow the outcome of the SIRS Trial. In the meantime I believe there is a role for steroids in adult cardiac surgery. It is already relatively well established in paediatric cardiac surgery.