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Case Report

Successful Use of Indigo Carmine for Vasoplegic Syndrome During Coronary Artery Bypass Grafting: A Case Report

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Introduction

Vasoplegic Syndrome (VS) is characterized by profound hypotension, low systemic vascular resistance and high cardiac output. It is a known complication following cardiac surgery and is associated with significant morbidity and mortality [1,2]. The fulminant course of vasoplegia is thought to be a result of a systemic inflammatory response with pharmacologically refractory hypotension [3]. Therapy resistant vasodilation is considered to result from an imbalance in nitric oxide (NO) synthesis [3]. A number of investigations have demonstrated the efficacy of methylene blue (MB) administration in reducing NO synthesis and restoring hemodynamic stability [4]. A similar role for Indigo Carmine (IC) has been proposed [5], but less studied and documented. The purpose of this paper is to report the first successful use of IC in a case of vasoplegia following coronary artery bypass grafting (CABG).

Case Report

A 78-year male with a past medical history of hypertension and hyperlipidemia presented for coronary artery bypass grafting (CABG). Preoperative evaluation with echocardiography and cardiac catheterization demonstrated normal cardiac function, normal valvular function and severe multivessel coronary artery disease. Preoperative laboratory values were within normal limits. Preoperative medications included the following: 10 mg atorvastatin, 81 mg aspirin, 10 mg terazosin, 2.5 mg lisinopril and 25 mg metoprolol.

A left radial arterial line was placed with good waveform and blood return. General anesthesia was induced with propofol, fentanyl and vecuronium. Additional cardiac monitoring was established with a central venous catheter and a transesophageal echocardiography (TEE) probe. A quadruple CABG procedure was performed with a beating heart technique utilizing cardiopulmonary bypass (CPB) for hemodynamic support. The patient was kept normothermic and the mean blood pressure was maintained between 60 and 80 mmHg. The total CPB time was 118 minutes. All lab values throughout the case were kept within the standard range for cardiac surgery. At the conclusion of the bypass grafting, the patient was weaned off CPB. Despite good visible cardiac contractility, the patient's systolic blood pressure (SBP) remained in the 60 to 70 mmHg range. The patient was started on norepinephrine and epinephrine (both 4 mcg/min) with no improvement in BP. The CVP was 8 mmHg—intravenous crystalloid fluid administration was initiated. The TEE showed normal contractility and a relatively empty left ventricle. Additional volume was given with a single unit of packed red blood cells and two bottles of 5%



albumin (500 mls). These maneuvers raised the CVP above 10 mmHg and the hemoglobin above 10 gm/dl. Because the BP remained unchanged, the vasopressors were increased: 15 mcg/min of norepinephrine, 15 mcg/min of epinephrine, and 0.2 units/min of vasopressin. The patient's SBP remained in the 70 to 80 mmHg range. A presumptive diagnosis of vasoplegic syndrome was made and the following maneuvers were initiated: 100 mg of benadryl, 1 gm of methylprednisolone, 1 gm of calcium, and 20 mg of famotidine. The BP remained unchanged. Methylene Blue (MB) was requested but was not available due to a shortage. At this point, the decision was made to administer Indigo Carmine (IC) due to its shared mechanism of action with MB. Two doses of 40 mg of IC were administered within five minutes. The patient's SBP immediately increased to the 90-mmHg range and continued to increase to above 100 mmHg (Figure 1). Subsequently, the patient's vasopressor requirements decreased to 5 mcg/min of norepinephrine, 5 mcg/min of epinephrine, and 0.1 units/min of vasopressin. The chest was closed and the patient transferred to the Intensive Care Unit (ICU). The final TEE images showed normal cardiac function. The BP in the ICU was 102/42 mmHg. Within the first three hours postoperatively, vasopressor levels decreased and BP increased. By the first post-operative day all vasoactive drugs were discontinued. The remainder of the hospital course was unremarkable and the patient was discharged on the fifth post-operative day.

Discussion

Vasoplegic syndrome in cardiac surgery and the use of Methylene Blue (MB) to treat it has been previously described [2,4,6-8]. The use of Indigo Carmine (IC) for the treatment of vasoplegic syndrome in cardiac surgery is unreported. This paper, therefore, represents the first documentation of the therapeutic effects of IC for treatment of vasoplegic syndrome during CABG.

The treatment of vasoplegia is challenging and occasionally unsuccessful. The unbalanced inflammatory reaction produces massive vasodilatation resulting in hypotension and poor organ perfusion leading to increased morbidity and mortality [3]. The pathophysiology of vasoplegia involves the activation of complement and coagulation systems resulting in over-activity of leukocytes, platelets and endothelial cells, creating a proinflammatory state causing abnormal regulation of vascular tone [9]. Although a complex process, it is basically a lack of vascular smooth muscle contraction. It has been suggested that the vasoplegia is dependent on cytokine and nitric oxide-mediated smooth muscle relaxation, catecholamine receptor down regulation and endothelial injury [6]. Nitric oxide is synthesized by nitric oxide synthase (NOS) which has two isoforms: 1) a calcium dependent constitutive isoform, which is responsible for constant, low level NO synthesis and 2) a calcium-independent Inducible isoform, which produces NO as needed. The inducible isoform of NOS is considered the mediator of distributive shock and is responsible for mitochondrial dysfunction, apoptosis and multi-organ failure [10]. In one study of vasoplegic syndrome in cardiac surgery, the mortality rate approached 25% in patients who had persistent hypotension into the postoperative period [8].

Vasoplegia is a fairly common complication of cardiopulmonary bypass procedures under general anesthesia with an incidence ranging between 8-10% in general cardiac surgical patients and up to 50% in those taking renin-angiotensin system (RAS)

antagonists [1]. With regard to the maintenance of BP under normal conditions, the RAS is one of three important pathways—the other two include the sympathetic nervous system and the vasopressinergic system [11]. Anesthesia affects all the systems and contribute to BP fluctuations depending on the interplay between the patient, anesthetics, and other medications either administered preoperatively or intraoperatively. The anesthetic drugs work by reducing the sympathetic drive on vascular tone. Therefore, under general anesthesia, the maintenance of vascular tone is mainly dependent on the RAS and the vasopressinergic system [12]. RAS antagonists, such as angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), block the action of renin-angiotensin in maintaining vascular tone and contribute to hypotension. ACEIs block the conversion of angiotensin I (ATI) to angiotensin II (ATII) causing a reduction in arterial resistance leading to increased vascular capacitance and increased cardiac output. ARBs block the action of angiotensin II on ATII receptors, resulting in a similar effect. Therefore, patients undergoing general anesthesia who take an ACEI or ARB are deprived of the beneficial effects of renin-angiotensin in maintaining blood pressure, and consequently are more prone to develop profound refractory hypotension. Data from the literature advise discontinuation of ACEIs/ARBs prior to anesthesia to reduce the incidence of hypotension [13].

The treatment of hypotension following cardiac surgery is complex, challenging, and at times multi-factorial. In the setting of normal or supra-normal cardiac contractility with associated hypotension, vasoplegic syndrome must be considered. Initial treatment often begins with high doses of vasopressors for hypotension in the hope that vascular tone can be restored [8]. For true vasoplegic syndrome, fluid administration is added to maintain adequate circulatory volume in the setting of profound vasodilatation. Systemic steroid and histamine blockers are added as well and the use of MB has proven to be useful as described earlier in cardiac surgery and in other forms of vasodilatory shock [7,14]. The use of IC, on the other hand, has seen efficacy in non-cardiac conditions including cystoscopy. Indigo Carmine, a dye known commonly for its diagnostic importance in procedures such as cystoscopy, has actions similar to MB in blocking the accumulation of cGMP [5]. Until this report, the use of IC for vasoplegic syndrome treatment in cardiac surgery was unknown. The clinical features of the case support the features of vasoplegic syndrome during CABG surgery and the BP response to IC was dramatic (Figure 1).

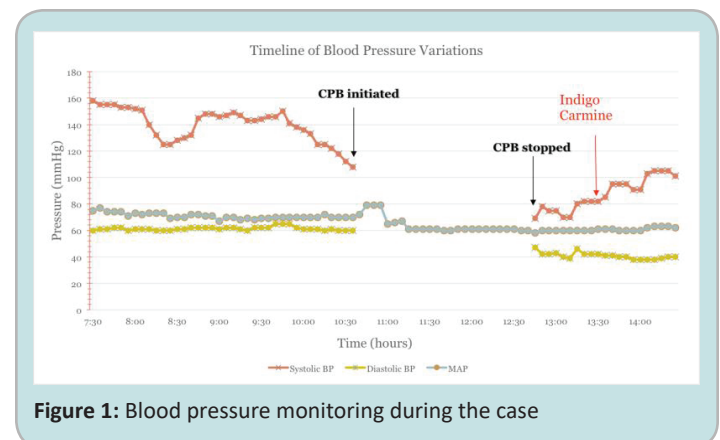


Figure 1: Blood pressure monitoring during the case

In conclusion, this is the first reported case of Indigo Carmine use for the treatment of vasoplegic syndrome in cardiac surgery.

This compound, like methylene blue, should be studied further and considered for use in future cases.

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