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Is Vasoplegia, a common phenomenon in liver transplantation: A Case Report

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Abstract

A 23 year old male patient with primary sclerosing cholangitis and biliary cirrhosis was treated with liver transplantation. Intra operatively he developed resistant hypotension which was not responding to conventional doses of vasopressure agents. This vasoplegic episode was managed aggressively with high doses of epinephrine intra operatively as well as early post operatively without compromising liver graft function.

Key words: vasoplegic syndrome, liver transplantation, epinephrine, norepinephrine, methylene blue, vasopressin and hydroxycobalamine

Introduction:

Vasoplegic syndrome [1] is a phenomenon of refractory hypotension commonly seen in cardiac surgeries[2,3]. In the setting of liver transplantation vasoplegic syndrome shares similar features of low systemic vascular resistant, high cardiac output and refractory hypotension[4]. The mechanism behind this refractory hypotension is still unclear but thought to be due to profound vasodilation seen in cirrhosis[5]. Management of vasoplegia perioperatively is very much challenging to anaesthesiologist[10]. Early diagnosis and treatment of vasoplegia can prevent liver graft failure and renal dysfuction in liver transplant surgery[6].

Case report

A 23 year old male patient with BMI of 22kg/m^2 , diagnosed with primary sclerosing cholangitis and biliary cirrhosis was treated with liver transplantation. His MELD score was 16 at the time of induction. His preoperative all investigations were within normal limits except serum bilirubin which was 13 mg%. Preoperative cardiac evaluation which included 2 D echo with RVSP and DSE were within normal limits. Routine monitoring was established and anaesthesia was induced. Anaesthesia was maintained with fentanyl and atracurium infusion and midazolam intermittent bolus doses.

Approximately 20 min after initiation of surgery, Patient's arterial blood pressure rapidly dropped (lowest was 37/12mmHg). Fluids were administered via rapid infusion system to maintain a central venous pressure in the range of 8–10 mm Hg. Vasopressors, norepinephrine and vasopressin was started in maximum doses. But blood pressure responded poorly to the treatment. At that time his cardiac output was high (11.4 L/min), and the systemic vascular resistance

was very low (386 dyn s/cm^5). Therefore, epinephrine was administered (10 µg bolus). In response to that blood pressure was increased. So epinephrine infusion was started and dose adjusted (0.5µg/kg/min) to maintain mean ABP more than 55mmHg. Norepinephrine and vasopressin infusion gradually tapered and stopped. Anhepatic phase lasted for 58 minutes. Total cold ischemia time was 7 hours 38 minutes. Total surgical time was 11 hours and 30 minutes

In the reperfusion phase of the surgery epinephrine requirement remained same. Post operatively patient was shifted to Liver ICU with epinephrine infusion (0.5µg/kg/min) and endotracheal tube in situ. Epinephrine infusion gradually tapered and stopped 24 hours after the surgery. Patient was discharged from the intensive care unit on day 3 and from the hospital on day 21 without any further complications and with optimal liver graft function.

Discussion

Perioperative hypotension is a well-recognized and relatively common problem during surgery. Vasoplegic syndrome is one such condition which is characterized by severe persistent hypotension with normal to high cardiac output and low systemic resistance[1]. It is commonly seen in patients undergoing cardiac surgery on cardiopulmonary bypass[2,3] with incidence ranging from 5 -15%[7].

The mechanism of vasoplegic syndrome is still unclear and multifactorial[7]. The pathogenesis of cardiac vasoplegia involves the activation of contact, coagulation and complement systems and the activation of leukocytes, platelets and endothelial cells resulting in an imbalance in the regulation of the vascular tone leading to postcardiac surgery vasoplegia[1].Majority of mechanisms associated with vascular hyporesponsiveness to vasopressors are inflammation, nitric oxide (NO), potassium and calcium channels, adrenomedullin, and free radicals[8]. They are common to all types of shock including septic, haemorrhagic, cardiogenic (including in post-cardiopulmonary bypass patients), anaphylactic and during ischemia-reperfusion, such as cardiac arrest or multiple trauma[9,11,12]. All this condition leads to activation of pro-inflammatory and inflammatory triggers which induces nitric oxide synthase (*iNOS*) expression and overproduction of NO. This molecule activates cyclic guanosine monophosphate as a mediator of profound vasodilation and vasoplegia[13,14,15]. Norepinephrine-refractory vasoplegia is associated with a higher post-operative morbidity and mortality. So its prompt, accurate diagnosis and aggressive management are paramount to reduce its peri-operative morbidity and mortality[16].

Vasopressors are the main stem of management therapy as only fluid resuscitation can't help to overcome this refractory hypotension. Bruno Levy et al in his latest study has demonstrated that conventionally catecholamines, norepinephrine is the first line treatment in vasoplegia[8]. The latest Surviving Sepsis Campaign guidelines also consider that combination of multiple vasopressors, including norepinephrine and early prescription of vasopressin is best therapeutic management of vasoplegia[12]. However, Hajjar LA et al demonstrated superiority of vasopressin over norepinephrine in the treatment of vasoplegic shock after cardiac surgery. He suggested regarding lower incidence of renal insufficiency, atrial fibrillation and shorter hospitalization time after using vasopressin in postoperative cardiac patients[17]. Outcome of norepinephrine resistant vasoplegia is poor in perioperative period[17]. Hosseinian et al demonstrated

efficacy of methylene blue in the treatment of vasoplegia in critically ill cardiac and liver transplant patients[19]. There is an evidence that methylene blue is very effective in improving systemic hemodynamics in the setting of vasoplegia, with reportedly few side effects by inhibiting nitric oxide synthase[20]. Whether methylene blue should be the first line of therapy in patients with vasoplegia is a matter of debate, and there is inadequate evidence to support its use as a first line drug[21]. More scientific evidence is needed to define the role of MB in the treatment of catecholamine refractory vasoplegia. For patients who do not respond to epinephrine, methylene blue can be used[19,20,21].

Intravenous hydroxycobalamine is now recently being used by Brent T et al for the treatment of vasoplegia during liver transplantation[22]. Intravenous hydroxycobalamin can be used as a rescue in - methylene blue resistant vasoplegic syndrome in cardiac surgery [23, 24].

Our patient's arterial blood pressure decreased rapidly almost 20 min after the starting of the operation (lowest value was 37/12 mm Hg). The patient responded poorly to volume infusions and increasing doses of norepinephrine and vasopressin. In response to bolus dose of epinephrine 10 µg, blood pressure showed improvement. Therefore, intravenous infusion of epinephrine was started and continued in dose of 0.5µg/kg/min to maintain the mean arterial blood pressure of 55mmHg during intraoperative and early postoperative period. Maintaining blood pressure during liver transplantation appears to have a positive effect on perioperative liver and renal function. So early identification and effective management with high doses of epinephrine was the key factor in salvaging of the patient in our case without compromising liver graft and renal function.

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