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Effect of intraoperative dobutamine on splanchnic tissue perfusion and outcome after Whipple surgery☆

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Abstract

Purpose: Splanchnic hypoperfusion during abdominal surgery contributes to postoperative gut sepsis and mortality. Dobutamine is an inotrope with vasodilator properties that improve hepatosplanchnic perfusion. The aim of this study was to examine the effect of intraoperative dobutamine infusion during Whipple surgery on splanchnic perfusion, hemodynamic, and overall postoperative outcome.

Methods: Sixty patients were randomly allocated to receive intraoperatively (3 μg/kg per minute or 5 μg/kg per minute) doses of dobutamine or saline. Baseline measurements included hemodynamic parameters, gastric tonometric parameters, and arterial and mixed venous gases. These patients had a follow-up for development for in-hospital morbidity and mortality.

Results: Intraoperative use of dobutamine increased oxygen-derived parameters as evidenced by increased mixed venous oxygen saturation. Tonometered gastric mucosal pH, a surrogate for splanchnic perfusion, increased in patients who received intraoperative dobutamine. Patients in the dobutamine groups demonstrated significant higher heart rates, premature ventricular contraction arrhythmias, and electrocardiographic signs of ischemia. Mean arterial blood pressure demonstrated no significant difference among groups. The overall incidence of postoperative complications was higher in control group 70 % vs 20% to 40% in dobutamine groups.

Conclusion: Intraoperative use of dobutamine improved global oxygen delivery, splanchnic perfusion, and postoperative outcome after Whipple surgery. These findings may be of clinical importance when the therapeutic goal is to improve gut perfusion.

1. Introduction

Splanchnic hypoperfusion has been demonstrated in the perioperative period of major abdominal surgery secondary to hypotension, blood loss, myocardial depressant effect of volatile anesthetics, and gut manipulations [1-3]. An impaired splanchnic perfusion leads to gastrointestinal

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mucosal ischemia with increased permeability and gut barrier failure [4,5] and subsequent bacterial and endotoxins translocation from gut lumen to systemic circulation [5,6]. Reperfusion of ischemic gut initiates an inflammatory cascade, which contributes to multiorgan dysfunction syndrome (MODS) and acute respiratory distress syndrome [3,7]. Prevention of mucosal hypoperfusion avoids this cascade and improves postoperative outcome.

Gut mucosal acidosis is a better predictor of the development of MODS than global indices of oxygen delivery (DO2) [8] because gut mucosa is one of the earliest organs that experience ischemia/hypoxia. Gut tonometry is a reliable indicator of gut mucosal perfusion [9]; it allows early prevention of gastric mucosal acidosis better than treatment of an already developed acidosis [10]. Furthermore, it provides an effective monitoring tool for of disease worsening and treatment success [11,12].

The main goal of anesthetic management is to maintain adequate systemic oxygenation and tissue perfusion and to decrease the risk of perioperative hypoperfusion and postoperative complications and, hence, improve survival after major surgery [13]. Among agents used for this purpose is dobutamine, which is a catecholamine with the beneficial effect of combining positive inotropic support with peripheral vasodilatation and after load reduction [14,15]. The splanchnic and renal vasodilatory effects of low-dose dopamine (0.5-3 μg/kg per minute) enhance sodium and water excretion, making this agent attractive for use in patients following open heart procedures [16].

Dobutamine has been found to most consistently decrease mucosal-arterial P_{CO_2} difference and increase gastric mucosal blood flow. Dobutamine has been shown to improve both splanchnic oxygenation and gastric mucosal pH (pHi) in septic patients [17] and after coronary artery bypass graft [18].

In this study, we hypothesized that dobutamine can improve splanchnic perfusion during major abdominal surgery and, consequently, decrease the incidence of postoperative complications. The aim of this prospective randomized, double-blind, controlled study was to evaluate the effect of intraoperative dobutamine infusion on splanchnic perfusion assessed by gastric tonometry and to examine the impact of this intervention on the postoperative outcome.

2. Patients and methods

2.1. Patients

The present study was single-center, prospective randomized, double-blind, placebo-controlled trial started in August 2009 and ended in August 2010. The study took place in the operating room and intensive care unit (ICU) of Mansoura Gastroenterology Surgical Center. The study was approved by the Hospital Clinical Ethic and Scientific Committee, and written informed consent was obtained from each patient. Sixty patients, with American Society of Anesthesiologists (ASA) physical status I to III, who underwent Whipple surgery (pancreatoduodenectomy) for the treatment of pancreatic carcinoma were included in this study.

Exclusion criteria for this study included severe preexisting pulmonary, renal, hepatic, and cardiac disease. Prior decision was made to exclude postrandomization any patient who had intraoperative blood loss greater than 10 mL/kg and required perioperative inotropic support or postoperative mechanical ventilation support during first 72 hours of postoperative period. Furthermore, any patients who had advanced malignancy and required shorter procedure with minimal dissection were also excluded. All patients were operated on by the same surgical team of 3 senior staff surgeons and 3 surgical fellows according to standardized surgical techniques.

2.2. Anesthesia management

Patients were premedicated with 50 mg ranitidine, morphine 0.07 mg/kg, and 0.05 mg/kg midazolam intravenously (IV). Before anesthesia induction, all patients received preoperative single-shot lumbar epidural analgesia at L2 to 3 vertebral interspaces with 14 mL of 0.25% bupivacaine and 2 mg morphine. The standardized anesthetic protocol for anesthesia induction included the following: 1.5 μg/kg fentanyl and 4 mg/kg of 2.5% thiopental sodium. Endotracheal intubation was facilitated with 0.1 mg/kg vecuronium. Mechanical ventilation parameters were regulated to maintain the end-tidal CO_2 around 35 mm Hg. Stable depth of anesthesia was maintained throughout the surgery using hemodynamic parameters instead of end-tidal isoflurane level monitoring. Inspired isoflurane concentration was titrated to maintain hemodynamic variables, heart rate (HR), and mean arterial pressure (MAP), within 20% of its basal value. The average concentration of isoflurane required to maintain hemodynamic stability was approximately 0.5 minimum alveolar concentration. Hemodynamic instability during anesthesia was defined, and treatment plan was placed in the study protocol. Persistent hypertension (defined as an average MAP value $>$120% of the preincisional baseline MAP lasting longer than 6 minutes after increasing the anesthetic concentration) was treated with 10 mg IV labetalol. Persistent tachycardia (defined as an HR $>$100 beats per minute lasting longer than 6 minutes after deepening anesthesia and increase of the fluid infusion rate) was treated with 15 mg IV esmolol as needed. Hypotension (ie, an average MAP value $<$80% of the baseline MAP lasting longer than 6 minutes) was treated by decreasing the isoflurane administration and increasing fluids infusion rate. In the absence of hypotension, persistent bradycardia (ie, HR $<$45 beats per minute lasting $>$6 minutes) was treated with 0.2 mg IV glycopyrrolate or 5 mg IV ephedrine. At the end of surgery, isoflurane was withheld, and the residual neuromuscular blockade was antagonized by 0.04 mg/kg IV neostigmine and 0.02 mg/kg IV atropine. On completion of the surgical procedure, all patients were extubated in the operating room, monitored in ICU, and