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Comparison of dexmedetomidine *versus* propofol on hemodynamics in surgical critically ill patients

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ABSTRACT

Background: Sedation with dexmedetomidine and propofol may cause hypotension or bradycardia. This study aimed to compare the effects of dexmedetomidine and propofol on hemodynamics and clinical outcomes in surgical intensive care unit (ICU) patients after major abdominal surgery.

Materials and methods: Enrolled patients were randomly allocated to the dexmedetomidine or propofol group. Cardiac index was measured using a continuous noninvasive cardiac output monitor on the basis of chest bioreactance. Heart rate, blood pressure, opioid requirement, urine output, delirium incidence, ICU length of stay, and total hospital length of stay were compared between the two groups. The incidences of bradycardia, hypotension, and severe low cardiac index were compared.

Results: We enrolled 60 patients. Heart rate and mean arterial pressure were significantly lower in the dexmedetomidine group than in the propofol group. Cardiac index did not differ significantly between the two groups (dexmedetomidine group 3.1 L/min/m^2, [95% confidence interval {95% CI} 2.8-3.3] *versus* propofol group 3.2 L/min/m^2 [95% CI 2.9-3.5], $P = 0.578$). The incidences of bradycardia, hypotension, and severe low cardiac index did not differ significantly between the two groups.

Conclusions: Cardiac index did not differ significantly between the dexmedetomidine and propofol groups in surgical ICU patients after major abdominal surgery.

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Introduction

The clinical practice guidelines of the American College of Critical Care Medicine for the management of pain, agitation, and delirium have aided clinicians in efficiently managing patients in adult intensive care unit (ICU) patients.[1,2] The guidelines aim to ameliorate the harmful effects of pain, agitation, and delirium and to improve clinical outcomes. They also suggest that dexmedetomidine or propofol may be preferred over sedation with benzodiazepines to improve clinical outcomes in critically ill patients receiving mechanical ventilation.[2] Dexmedetomidine is a highly selective α_2-adrenoreceptor agonist[3,4] with sedative, anxiolytic, and analgesic effects.[5-7] Dexmedetomidine does not cause respiratory depression. Bradycardia and hypotension are the most frequent adverse events with dexmedetomidine.[8-11] Propofol acts on gamma-aminobutyric acid receptors and is commonly used in the induction of general anesthesia and sedation of critically ill patients. Bradycardia, hypotension, and respiratory depression are the most frequent adverse events with propofol, and propofol infusion syndrome is a rare but potentially lethal side effect of propofol.[11-13]

Several studies have compared the effects of dexmedetomidine and propofol on heart rate and blood pressure.[9,14,15] To the best of our knowledge, no study has compared the effects of dexmedetomidine and propofol on cardiac output in adult ICU patients. Only one study, however, reported that propofol infusion, but not dexmedetomidine infusion, can increase preload dependency and fluid responsiveness in critically ill patients with circulatory failure.[16] Low cardiac output may cause tissue hypoperfusion and multiorgan dysfunction. Thus, comparing the effect of dexmedetomidine and propofol on cardiac output is crucial. With advancements in the bioreactance technique,[17,18] cardiac output and stroke volume can be continuously measured using a noninvasive cardiac output monitor. The present study primarily compared the effects of dexmedetomidine and propofol on cardiac index in adult surgical ICU patients after major abdominal surgery. Furthermore, we compared the effects of dexmedetomidine and propofol on heart rate, blood pressure, stroke volume index (SVI), opioid requirement, urine output, delirium incidence, ICU length of stay, total hospital length of stay, and total hospital cost.

Materials and methods

Study population

This single-blinded, randomized controlled trial was approved by the Research Ethics Committee of National Taiwan University Hospital (approval number: 201407023MINA) and registered on the ClinicalTrials.gov protocol registration system (ID: NCT02393066). The study was conducted in a surgical ICU of an Academic Medical Center in Taiwan between October 2014 and June 2015. Patients aged from 20 to 99 y were evaluated by the research assistant and consented to participate in this study before undergoing major abdominal surgery. Exclusion criteria included refractory bradycardia less than 60 beats per minute (bpm), high degree atrioventricular block (second or third degree), refractory shock despite resuscitation (mean arterial pressure [MAP] <60 mm Hg), new onset of myocardial infarction, New York Heart Association Class IV heart failure, acute physiology and chronic health evaluation II score >30, severe liver cirrhosis (Child–Pugh class B or C), organ transplantation within 1 y, pregnancy, known allergic history to dexmedetomidine or propofol, enrolled in other clinical trial of dexmedetomidine or propofol within 1 mo, signed consent of do not resuscitate, other conditions determined by surgeon or primary intensivist, and non-native speaker.

Study protocol

Patients who were transferred to the surgical ICU after surgery were enrolled and randomly assigned into two groups (dexmedetomidine or propofol group) on the basis of computer-generated randomization codes in sealed envelopes. The principal investigator or research assistant assigned the sedatives to the patients, and patients were unaware of their assigned group. All patients received routine postoperative care, and the goal of postoperative pain management was to achieve an 11-point pain intensity numeric rating scale (0 = no pain and 10 = worst possible pain) of <4. When patients were arousable and had a Richmond Agitation-Sedation Scale of >0, dexmedetomidine or propofol was administered by continuous infusion according to their grouping. Patients in the dexmedetomidine group received continuous intravenous infusion of dexmedetomidine (Precedex; Hospira) with a dosage ranging from 0.1 to 0.7 mcg/kg/h. Patients in the propofol group received continuous intravenous infusion of propofol (Propofol-Lipuro 1%; B. Braun, Germany) with a dosage ranging from 0.3 to 1.6 mg/kg/h. The loading dose was omitted to prevent rapid hemodynamic changes in both groups. An infusion dosage of 0.1-0.7 mcg/kg/h of dexmedetomidine was reported to be equivalent to that of 0.3-1.6 mg/kg/h of propofol.[19] The infusion rates of dexmedetomidine or propofol were titrated to achieve a goal of Richmond Agitation-Sedation Scale of 0 to −2.[19,20] The infusion was continued for 24 h as required. After 24 h, primary intensivists selected the sedatives. We recorded the accumulated dose of analgesics, and the dose of fentanyl was converted into an equivalent dose of morphine. If the total infusion time of dexmedetomidine or propofol was <2 h or a severe bradycardia (heart rate <50 bpm for >5 min) developed, the patient was withdrawn from the study. Within the data safety monitoring plan, an interim analysis was conducted when 30 participants were enrolled to determine the safety and adequacy. If the incidence of adverse events or survival rate was significantly different between the two groups, the decision of continuance, suspension, or termination of study would be discussed and decided.

Study outcomes

The primary outcome of this study was the difference in cardiac index between the dexmedetomidine and propofol groups. Under the condition of a cardiac index of 3.0 L/min/m^2 with a standard deviation of 0.7 L/min/m^2, one side $\alpha = 0.05$,

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