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Clinical Study

The effect of milrinone on induced hypotension in elderly patients during spinal surgery: a randomized controlled trial

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Abstract

BACKGROUND CONTEXT: Induced hypotension is widely used intraoperatively to reduce blood loss and to improve the surgical field during spinal surgery.

PURPOSE: To determine the effect of milrinone on induced hypotension during spinal surgery in elderly patients.

STUDY DESIGN/SETTING: Prospective randomized clinical trial.

PATIENT SAMPLE: Forty patients, 60 to 70 years old, ASA I–II, who underwent elective lumbar fusion surgery.

OUTCOME MEASURES: Intraoperative hemodynamics, blood loss, hourly urine output, and grade of surgical field.

METHODS: All patients were randomized to group M or N. The study drug was infused after perivertebral muscle retraction until complete interbody fusion. In group M, 50 μg/kg/min of milrinone was infused over 10 minutes as a loading dose followed by 0.6 μg/kg/min of milrinone as a continuous dose. In group N, an identical volume of normal saline was infused in the same fashion. This study was not funded by commercial or other sponsorship and the authors confirm no conflicts of interest, financial or otherwise.

RESULTS: During infusion of the study drug, the systolic and mean blood pressures were maintained within adequate limits of induced hypotension in group M. Intraoperative blood loss was 445.0±226.5 mL in group M and 765.0±339.2 mL in group N ($p=.001$). Hourly urine output was 1.4±0.6 mL in group M and 0.8±0.2 mL in group N ($p<.001$). The grade of the surgical field was better in group M than in group N ($p=.004$).

CONCLUSIONS: We conclude that milrinone is useful for induced hypotension in elderly patients during spinal surgery.

Keywords: Milrinone; Induced hypotension; Lumbar spinal surgery

Introduction

Induced hypotension is a commonly used anesthetic technique to obtain a bloodless operative field in many types of surgeries [1]. Induced hypotension has been advocated to control local bleeding during spinal surgery since the 1970s [2,3]; however, many patients undergoing spinal surgeries are elderly, limiting the use of induced hypotension due to the risk of hypoperfusion.

Milrinone is a selective phosphodiesterase (PDE) type III inhibitor with both inotropic and vasodilatory effects [4]. It is usually used in patients with congestive heart failure or during cardiac surgery.

We conducted this study to determine whether continuous infusion of milrinone during spinal surgery under general anesthesia would achieve induced hypotension, reduce intraoperative blood loss and the number of transfusions required, improve the surgical field, and maintain perfusion of vital organs, especially in elderly patients.

Materials and methods

This study was a prospective, double-blind, balanced (1:1), randomized controlled, parallel-group trial and came

FDA device/drug status: Not applicable.

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from the department of anesthesiology, part of the university hospital in Korea. There were no changes to the design or protocol during the course of the study. The institutional review board of our hospital approved this study, and all participants provided written consent. Eligible patients were 40 patients with American Society of Anesthesiology (ASA) class I or II, aged between 60 and 70 years, who were scheduled for elective posterior lumbar interbody fusion. Exclusion criteria included cardiovascular disease (uncontrolled hypertension, ischemic heart disease, arrhythmia, congestive heart failure), pulmonary disease, liver disease, renal disease, cerebrovascular disease, hematologic disease, prior treatment with anticoagulants, diabetic neuropathy, body mass index (BMI) less than 16 kg/m^2 or more than 30 kg/m^2, and refusal to participate.

Patients were randomized into the following two groups using computer software: the milrinone group (group M, n=20) and the normal saline group (group N, n=20). The group allocation was concealed in opaque envelopes that were opened by an anesthesiologist just before the induction of anesthesia. The anesthesiologist aware of the randomization code prepared a covered-syringe pump with milrinone or the placebo solution. A second anesthesiologist, who was blinded to group allocation, conducted the entire course of anesthesia and recorded all of the parameters. A single surgeon performed all of the surgeries using the same technique. The patients and the surgeon in charge were blinded to group allocation for the duration of the study.

All patients fasted for at least 8 hours before surgery and premedication was omitted. After arrival in the operating room, anesthesia was induced with 1.5 mg/kg propofol and 0.5 mg/kg atracurium under standard monitoring. Anesthesia was maintained with 1.0 vol% sevoflurane and 50% oxygen in medical air until surgical incision, and muscle relaxation was achieved by a 5-μg/kg/min atracurium infusion during the entire surgery. Ventilation was mechanically controlled and adjusted to maintain peak inspiratory pressure below 20 cmH_2O and an end-tidal carbon dioxide of 30 to 35 mm Hg. An arterial line was inserted into the radial artery and connected to a FloTrac/Vigileo system (Edwards Lifesciences, Irvine, CA, USA) to measure arterial blood pressure and cardiac output. During surgery, lactated Ringer solution at 10 mL/kg/h was infused continuously. When bleeding occurred, 6% hydroxyethyl starch was infused at the same volume of the blood lost. The hemoglobin was maintained at a level of more than 10 g/dL with transfusion of packed red blood cells (RBCs).

Patients were placed in a prone position on a Wilson frame, paying particular attention not to interfere with venous return. After skin incision, the end-tidal concentration of sevoflurane was controlled to 1.5 vol%. This concentration was obtained from a preliminary study to maintain the Bispectral index value at 40 to 55 during the same kind of surgery in this age group. If the systolic blood pressure was more than 10% of the baseline value, 0.5 to 2.0 mg of nicardipine was injected. After retraction of the perivertebral muscles, the study drug was infused. In group M, 50 μg/kg milrinone was administered over 10 minutes as a loading dose, followed by 0.6 μg/kg/min of continuous infusion until interbody fusion was completed. In group N, an identical volume of normal saline was infused in the same fashion as group M. When the systolic blood pressure (SBP) dropped below 70% of the baseline value or the mean blood pressure (MBP) was less than 60 mm Hg during infusion of the study drug, 5 to 10 mg of ephedrine was injected.

In all patients, 4 mg ondansetron was injected 30 minutes before the end of surgery for prophylaxis of postoperative nausea and vomiting. The infusion of muscle relaxant was discontinued at the beginning of wound irrigation. Neuromuscular block was reversed with 0.4 mg glycopyrrolate and 10 mg pyridostigmine. After surgery, the train-of-four ratio was measured and the patients were extubated.

The primary outcome measure was intraoperative blood loss estimated by measuring collected blood in the suction bottle and weighing the wet gauzes at the end of surgery. The secondary outcome measure was the visibility of the surgical field graded using the quality scale proposed by Fromm and Boezaart (Table 1) [5]. The surgeon assessed the surgical field after the interbody fusion was completed. Hemodynamic values, including SBP, diastolic blood pressure (DBP), MBP, heart rate (HR), cardiac output (CO) and cardiac index (CI), were recorded at seven points, as follows: before induction (T0); before (T1) and after (T2) the loading dose; at 30 (T3), 60 (T4), 90 (T5) minutes after the loading dose; and at 30 minutes after termination of

EVIDENCE & METHODS

Context
Induced intraoperative hypotension is sometimes used to decrease bleeding during spine surgery. The authors present their experience with milrinone to achieve this effect.

Contribution
In this RCT comparing milrinone to saline, the study drug induced controlled hypotension and appeared to reduce blood loss and improve visualization in the field without observed complication.

Implications
Assuming other surgical factors were similar, the findings are helpful as blood loss not only makes the surgery more difficult, in older patients it can be associated with greater likelihood of complications. Of note, the study may be underpowered to provide insight into less common and potentially serious complications of the drug.
—*The Editors*