Nicardipine Infusion for Hypotensive Anesthesia During Orthognathic Surgery Has Protective Effect on Renal Function

Ji Eun Kim, MD, [*] *Jong Seok Lee, MD,* [†] *Mi Kyeong Kim, MD, PhD,* [‡] *Seung Hyun Kim, MD,* [§] *and Ji Young Kim, MD, PhD* [‖]

Purpose: Hypotensive anesthesia may adversely affect renal function. The purpose of this study was to evaluate the renoprotective effect of nicardipine in patients undergoing orthognathic surgery under hypotensive anesthesia.

Materials and Methods: In this double-blinded randomized controlled study, healthy patients undergoing orthognathic surgery were enrolled to evaluate renal function during and after hypotensive anesthesia. The predictor variable was the agent, nicardipine vs remifentanil, used to maintain mean arterial pressure at 50 to 65 mm Hg. Primary outcome variables were renal function markers and secondary outcome variables were hemodynamic data, which were measured before hypotension, 2 hours after hypotension, 1 hour postoperatively (t3), and 24 hours postoperatively. Linear mixed model was used to analyze repeatedly measured data.

Results: Forty-six patients were randomly allocated to receive remifentanil (R group; n = 23) or nicardipine (N group; n = 23). The renal tubular function marker, urinary N-acetyl-1-β-D-glucosaminidase (NAG), was lower at t3 in the N group than in the R group ($P = .014$). In the N group, fractional excretion of sodium was significantly higher at t3 compared with baseline ($P < .0001$). The 2 groups did not show any differences in estimated creatinine clearance and serum cystatin C.

Conclusion: Subclinical and reversible renal dysfunction appears during hypotensive anesthesia in patients undergoing orthognathic surgery. Continuous infusion of nicardipine attenuated the increase in NAG, which is a marker of renal tubular injury, during hypotensive anesthesia with desflurane and remifentanil.

J Oral Maxillofac Surg 72:41-46, 2014

Hypotensive anesthesia is a state of induced hypotension during general anesthesia to decrease intraoperative blood loss[1] and improve visualization of the surgical field.[2,3] This technique is often used during hip, spine, or facial bone surgeries because bleeding from the intrabony capillary is difficult to control with conventional hemostasis. Hypotensive anesthesia is often instituted during orthognathic surgery because profound bleeding is expected owing to osteotomy and the complex vascularity of the orofacial region.

[*]Clinical Assistant Professor, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Korea.

[†]Professor, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Korea.

[‡]Assistant Professor, Department of Anesthesiology and Pain Medicine, School of Medicine, Kyung Hee University, Seoul, Korea.

[§]Resident, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Korea.

[‖]Assistant Professor, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Korea.

This study was supported by a faculty research grant of Yonsei University College of Medicine for 2010 (6-2010-0119).

Address correspondence and reprint requests to Dr J.Y. Kim: Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea; e-mail: KIMJY@yuhs.ac

Received July 12 2013

Accepted August 9 2013

0278-2391/13/01037-9$36.00/0

http://dx.doi.org/10.1016/j.joms.2013.08.011

During hypotensive anesthesia, systolic blood pressure is controlled at 80 to 90 mm Hg or mean arterial blood pressure (MAP) is decreased to 30% of baseline or 50 to 65 mm Hg to maintain adequate microcirculation of the major organs, such as the brain, heart, and kidneys.[4,5] The kidneys are particularly sensitive to decreased perfusion during hypotensive anesthesia because renal tubular cells in the medulla have a high metabolic rate.[6] In fact, some studies have reported damage to renal tubular cells during hypotensive anesthesia.[7-10]

To induce hypotensive anesthesia, an inhalation anesthetic and remifentanil can be used alone, but the need for a high concentration to achieve adequate blood pressure leads to the use of adjuvant drugs, such as vasodilators, calcium channel antagonists, or β agonists. Nicardipine is a calcium channel blocker that has been reported to decrease renal afferent arteriolar resistance and increase the glomerular filtration rate (GFR).[11-13] Previous studies have reported the protective effect of nicardipine on renal function during cardiac surgery under cardiopulmonary bypass and robotic surgery under pneumoperitoneum.

The purpose of this study was to elucidate the effect of nicardipine on renal function during hypotensive anesthesia. The investigators hypothesized that nicardipine infusion would prevent the decrease in renal function during hypotensive anesthesia in patients undergoing orthognathic surgery. The specific aim of this study was to compare renal parameters, the primary outcome of this study, such as estimated creatinine clearance (CrCl), fractional excretion of sodium (FE_{Na}), urinary N-acetyl-1-β-D-glucosaminidase (NAG), and serum cystatin C, in 2 groups of patients with and without nicardipine infusion for hypotensive anesthesia.

Materials and Methods

STUDY DESIGN

To evaluate the renoprotective effect of nicardipine during hypotensive anesthesia, a double-blinded randomized controlled study was designed. This study was approved by the institutional ethics committee of the Yonsei University Health System (3-2009-0196) and registered at www.ClinicalTrials.gov (NCT01175746). Informed consent was obtained from all patients. The study population was composed of all patients presenting for preanesthetic evaluation for orthognathic surgery from April 2011 through December 2011. To be included in the study sample, patients' American Society of Anesthesiologists Physical Status had to be 1 or 2 and the orthognathic surgery must have included mandibular osteotomy and Le Fort I osteotomy. Patients with known diabetes mellitus, subalimentation, anemia, cerebrovascular accidents, coronary artery diseases, heart failure, peripheral vascular diseases, respiratory insufficiency, anemia, abnormal liver or renal function, hormonal or hypertensive diseases, and previous treatment with diuretics or antihypertensive drugs were excluded.

VARIABLES

The primary predictor variable was the hypotensive agent used to maintain the MAP at 50 to 65 mm Hg, which was nicardipine (N group) or remifentanil (R group). The primary outcome variables were renal function parameters, such as the estimated CrCl, FE_{Na}, NAG, and serum cystatin C. The secondary variables were hemodynamic data, such as MAP, heart rate (HR), and cardiac index (CI), which can affect renal perfusion during and after hypotensive anesthesia.

DATA COLLECTION

MAP, HR, CI, and arterial blood gas data were recorded before hypotension (t1), 2 hours after hypotension (t2), 1 hour postoperatively (t3), and 24 hours postoperatively (t4). Serum creatinine (Cr), sodium, potassium, and cystatin C, spot urine Cr, sodium, and potassium, and NAG were measured at t1, t2, t3, and t4. Estimated CrCl and FE_{Na} were calculated at t1, t2, t3, and t4. The amount of fluid administered and urine output were recorded hourly during surgery.

To calculate estimated CrCl, a modified Cockcroft-Gault equation was used: CrCl for men = ([140 − age] × weight)/P_{Cr}; CrCl for women = ([140 − age] × weight × 0.85)/P_{Cr}, where P_{Cr} is plasma Cr concentration (milligrams per deciliter). Then, the value was corrected for body surface area: estimated CrCl = CrCl × 1.73 m^2 per body surface area. FE_{Na} was calculated according to the following formula: $FE_{Na} = (U_{Na} \times P_{Cr})/(P_{Na} \times U_{Cr}) \times 100$, where U_{Na} is urinary sodium concentration (millimoles per liter), P_{Na} is plasma sodium concentration (millimoles per liter), and U_{Cr} is urinary Cr concentration (milligrams per deciliter).

METHODS

Patients received midazolam 0.02 mg/kg and glycopyrrolate 0.004 mg/kg for premedication. On arrival in the operating room, pulse oximetry, electrocardiography, and noninvasive blood pressure monitors were used. Anesthesia was induced with propofol 1.5 mg/kg and remifentanil 0.3 μg/kg, and nasotracheal intubation was facilitated with rocuronium bromide 0.6 mg/kg. Patients were mechanically ventilated to maintain end-tidal carbon dioxide at 35 to 40 mm Hg at 50% inspired oxygen with air. Anesthesia was maintained with remifentanil 0.05 μg/kg/min and 6.0 vol% expired desflurane. A 20-gauge catheter was inserted into the radial artery for continuous arterial blood pressure monitoring and blood sampling. The arterial catheter was connected to a FloTrac/VigilioTM system (Edwards Lifesciences, Irvine, CA) to monitor the CI.