Deliberate Hypotensive Anesthesia With the Rapidly Acting, Vascular-Selective, L-Type Calcium Channel Antagonist—Clevidipine: A Case Report

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Deliberate hypotension is an important technique for use in select anesthetics for procedures such as orthognathic surgery, specifically LeFort I maxillary osteotomy. We present a case report of an anesthetic involving deliberate hypotension for a 17-year-old female patient who presented for a LeFort I osteotomy, bilateral sagittal split of the mandible, and a genioplasty in order to correct a skeletal class III malocclusion. After reaching a steady-state general anesthetic, deliberate hypotension was induced solely with a bolus and subsequent continuous infusion of the ultrashort acting calcium channel blocker, clevidipine. The preoperative, intraoperative, and postoperative course and anesthetic management are discussed.

Key Words: Deliberate hypotension; Bolus infusion; Dental anesthesiology; Calcium channel antagonist; Orthognathic surgery; General anesthesia; Narcotics; Hemodynamics; IV agents; Hemostasis; Pain control; Post-operative pain management; PONV; Nasotracheal intubation; Anti-emetic prophylaxis; Maxillomandibular fixation.

INTRODUCTION

Deliberate hypotension is an important tool for anesthetics provided for orthognathic surgery.¹ The maxilla is a highly vascularized area of the human body.² Since orthognathic surgery in the form of the LeFort I osteotomy involves the separation and repositioning of the maxilla, significant surgical blood loss is a risk.² One method of avoiding excessive hemorrhage is through the utilization of deliberate hypotension induced and maintained by the anesthesiologist. The target pressures for deliberate hypotension can vary, but a mean arterial pressure (MAP) of 30% below a patient's baseline MAP with a minimum MAP above 50 mm Hg in healthy patients is often considered clinically accept-

able.³ Various drugs for achieving deliberate hypotension have been investigated, including short-acting and longer-acting beta blockers, direct vasodilators, short-acting narcotics, and a combination of these techniques.⁴ No matter how the deliberate hypotension is achieved, it is important that it be performed in a controlled manner and only for as long as it is needed for the appropriate portion of the procedure. It must also leave minimal residual hypotensive effects following the procedure.⁵

CASE REPORT

A 17-year-old female patient, with a childhood diagnosis of trivial pulmonary stenosis, presented to the main operating room for a LeFort I maxillary osteotomy, mandibular bilateral sagittal split osteotomy, and a genioplasty to correct a nonpathologic, skeletal class III malocclusion. The patient underwent an echocardiogram in 2010, which showed no clinically significant findings.

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She had no past surgical history and a medical history that was otherwise not significant. She had no allergies, was taking no medications, and weighed 50 kg with an associated body mass index less than 30. Her airway was identified as a Mallampati class I and was accompanied by a full range of motion of her neck. She was currently undergoing orthodontic treatment and was judged to be an American Society of Anesthesiologists (ASA) class II physical status. The appropriate consents were obtained for educational and research purposes along with consents for her surgery and general anesthesia. The patient expressed concerns about postoperative nausea and vomiting, so she was given 40 mg of oral aprepitant prior to transfer to the operating room. Standard ASA monitors were employed, and induction was carried out with typical doses of midazolam, fentanyl, propofol, ketamine, and rocuronium. Nasotracheal intubation was accomplished with a warmed, lubricated 6.5-mm inside diameter nasal RAE tube through the left naris after preparing the nose with oxymetazoline. The endotracheal tube was advanced through the vocal cords under direct laryngoscopy with the aid of Magill forceps, and a throat pack was then placed. Bilateral breath sounds were verified, the endotracheal tube was secured, a nasogastric tube was inserted, the patient's eyes were taped closed and padded, and the head was wrapped for stability. The patient was placed on an anesthesia ventilator, and anesthesia was maintained with isoflurane and nitrous oxide in oxygen. A second 16-gauge intravenous line was established, and a right radial arterial line was placed. For additional anti-emetic prophylaxis, dexamethasone was administered intravenously, followed by a continual, low-dose infusion of propofol. Immediately after induction, a steady infusion of an analgesic dose of remifentanyl was established, taking care that the MAP was not adversely affected. Rocuronium was titrated in order to maintain neuromuscular blockade at a depth of 1 twitch of a train-of-four for the majority of the surgical procedure. After the described anesthetic was in place and stabilized, a local anesthetic was injected into the surgical field, and a low-dose baseline infusion of clevidipine (1–2 mg/h) was initiated, resulting in no significant decrease in the baseline MAP. The inhalation agents as well as intravenous infusions were kept at a constant rate for 105 minutes prior to separation of the maxilla, and the MAP remained between 68 and 72 mm Hg during this portion of the procedure.

As the surgery approached separation of the maxilla, the surgical team requested the MAP be reduced to 50–55 mm Hg. Following a bolus dose of 1 mg, the clevidipine infusion was increased to 20 mg/h that resulted in an immediate drop in the MAP from 68 mm Hg to 51 mm Hg over the course of 3 minutes. All other agents were essentially unchanged, while the clevidipine

infusion was being carefully titrated to maintain the desired MAP of 51–55 mm Hg. The clevidipine infusion dose briefly reached as high as 70 mg/h at one point during the hypotensive period until the MAP responded appropriately. The surgical procedure dictated that the deliberate hypotension remain in effect for 70 minutes while the maxilla was separated, repositioned, and affixed into place. At the conclusion of this portion of the procedure, the patient's MAP was allowed to gradually return to baseline through metered elimination of the clevidipine infusion over the course of 35 minutes. The patient's MAP returned to 70–85 mm Hg and remained near that level for the duration of the anesthetic.

Prior to completion of the procedure, the patient regained spontaneous ventilation with the gradual elimination of the remifentanyl, while increments of fentanyl were titrated according to the desired 8–14 respirations/min. Just prior to emergence, the surgical team determined that the patient's dental occlusion was not acceptable, so they reopened the surgical field to make the adjustments. Thus, the inhalational anesthetic was increased accordingly, and the patient was placed back on the ventilator until the corrective procedure was completed. When satisfied with the surgical result, the surgery team readministered the local anesthetic for postoperative pain control and began placing maxillomandibular wire fixation after removal of the throat pack. The anesthetic was again titrated downward. Four full twitches were present in the train-of-four test, spontaneous ventilation was resumed, and neostigmine with glycopyrrolate were administered to ensure full reversal of neuromuscular paralysis. Droperidol, metoclopramide, and ondansetron were administered for antiemetic prophylaxis. After an uneventful emergence and extubation, the patient was responsive to verbal commands, denied pain and nausea, and was delivered with the nasogastric tube in place to the postanesthesia care unit. She underwent an uneventful postoperative course, and following an overnight hospital admission, was discharged the following morning.

DISCUSSION

Maxillary LeFort I osteotomy is a surgical procedure that carries a risk of significant hemorrhage that can be a danger to the patient. Hemorrhage can also flood the surgical field, increasing surgical time and altering the outcome. Deliberate hypotension is a useful method to help bypass these complications. The goal is to induce a hypotension that lasts for the indicated portion of the procedure and can be discontinued or reversed when it is no longer needed.

Deliberate hypotension can be achieved with a number of medications, each having their advantages and

disadvantages. Labetalol is commonly used to induce depression of blood pressure, but has a prolonged duration of action, a slow onset of peak effect, and an unpredictable dose requirement. The use of beta blockers can be further complicated by bradycardia, cardiac conduction delays, left ventricular dysfunction, and bronchospasm. Deliberate hypotensive effects of sodium nitroprusside or nitroglycerin result from the dilation of capacitance vessels, and are often used for inducing deliberate hypotension, but can carry potential complications such as increased intracranial pressure. Remifentanyl has also been used, but it tends to have a ceiling effect and carries risks such as chest-wall rigidity and bradycardia.

Clevidipine has properties that are very well suited for a limited course of deliberate hypotension. Approved by the US Food and Drug Administration in 2008, it is a rapidly acting, vascular-selective, L-type calcium channel antagonist that lowers blood pressure by reducing systemic vascular resistance. It has a high clearance (0.05 L/min/kg) and is rapidly hydrolyzed by plasma and tissue esterases. Clevidipine elimination is unlikely to be influenced by hepatic or renal dysfunction. Owing to its fast onset and offset of blood pressure-lowering activity (clinical half-life is less than 1 minute), clevidipine can be easily titrated to effect, allowing for effective, rapidly adjustable blood pressure management.⁶ The recommended administration technique for clevidipine is to start the intravenous infusion at 1–2 mg/h for initiation and then titrate by doubling the dose every 90 seconds. As the blood pressure approaches the goal, the infusion rate should be increased in smaller increments and titrated less frequently. The maximum sustained infusion rate for Cleviprex is 32 mg/h. Most patients in clinical trials were treated with doses of 16 mg/h or less.

In this case report, clevidipine was administered both off-label as an initial bolus as well as via an infusion, delivering the desired results with no lasting residual effects and no significant influence on other aspects of the anesthetic. After giving the initial bolus of 1 mg clevidipine and increasing the infusion rate as dictated by the patient's vital signs, the MAP dropped predictably from 68 mm Hg to 51 mm Hg, and was maintained between 51 and 54 mm Hg throughout the necessary portion of the surgical procedure. Close monitoring of the MAP via the arterial line permitted the rapid MAP reduction to be accomplished safely. Furthermore, as the infusion was titrated downward, the patient's MAP responded very closely and predictably, and readily returned to baseline MAP.

It is noteworthy that upon administration of the infusion, the patient's heart rate increased from 70–80/min to 90/min and remained in sinus rhythm. This modest increase was likely due to either the reflex tachycardia in response to the lowered MAP by the clevidipine or to the surgical

stimulation, but it was deemed acceptable and no corrective intervention was performed.

The only analgesic given after induction was a 0.1 µg/kg/min remifentanyl infusion, negating the need for narcotic bolus throughout the procedure. Many agents used for their hypotensive effects, such as beta blockers and nitroglycerin, also mask variations in vital signs that are due to surgical stimulation. Predictably, this may lead to excessive or insufficient narcotic administration which can hinder a metered return to a baseline MAP and a timely, gradual emergence. In our case, the remifentanyl infusion permitted all other elements of the anesthetic to be maintained at a steady-state throughout the case and was easily titrated downward near the end so that longer-acting narcotics for postoperative analgesia could be titrated. It also provided an environment where hypotension through modification of the clevidipine dosage alone could be effectively employed.

CONCLUSION

The ultra-short-acting calcium channel blocker clevidipine was very effective in inducing deliberate hypotension and avoiding residual effects upon cessation of the medication. The combination of bolus-dosing and a titrated infusion proved very effective in obtaining and maintaining the desired lowered MAP only for the desired hypotensive period. The anesthetic was otherwise unaffected by the administration of clevidipine and enabled the anesthesiologist to maintain tight control over the patient's MAP. Clevidipine's characteristics of having both a rapid onset and a short clinical half-life make this medication an intriguing option for surgical procedures where deliberate hypotension is indicated.

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