

Large Dose Dexmedetomidine in a Patient during Sedation for Invasive Oral Procedure

In Yeob Baek, JiUk Yoon, Nam Won Kim, Hyun Su Ri, Cheul Hong Kim*, Ji Young Yoon*

Department of Anesthesia and Pain Medicine School of Medicine, Pusan National University,

*Department of Dental Anesthesia and Pain Medicine School of Dentistry, Busan, Korea

Certain oral procedures require a sedated patient who is responsive to allow for the mouth opening and position change. Dexmedetomidine is a relatively selective alpha₂-adrenoceptor agonist with sedative, analgesic, amnestic, and anesthetic-sparing effects. Large dose dexmedetomidine is suitable as a single agent for sedation and anxiolysis for plate removal in a patient with bilateral sagittal split osteotomy and Lefort 1 osteotomy with genioplasty.

Key Words: Dexmedetomidine, Sedation, Oral procedure

In oral surgery, sharing the airway with a surgeon can present challenges to the anesthesiologist. In addition, in certain oral procedures, keeping the patient responsive can be important. Selection of optimal sedative should be based on the ability to achieve adequate sedation and minimal respiratory depression and maintenance of cardiovascular homeostasis. Dexmedetomidine is a relatively selective alpha₂-adrenoceptor agonist with sedative, analgesic, amnestic, and anesthetic-sparing effects. It reduces anesthetic requirements, makes early recovery, and blunts the sympathetic nervous system [1]. Minimal respiratory depression and easy reversibility from sedation to responsiveness make dexmedetomidine a commonly used drug for "asleep-awake-asleep" anesthesia. Large dose dexmedetomidine as a single agent for sedation and anxiolysis in a patient undergoing oral procedure for plate removal is presented. Patient's permission was obtained to publish this case report.

CASE REPORT

A 25-year-old, 50 kg, 160 cm woman with surgical history of bilateral sagittal split osteotomy (BSSO) and Lefort 1 osteotomy with genioplasty, was scheduled for plate and screw removal. In the operating room, standard ASA monitors were applied with a MAC-safe nasal cannula to monitor end-tidal CO₂ concentration (Fig. 1). Dexmedetomidine was initiated with an intravenous (IV) loading dose of 1 mcg/kg delivered over 10 minutes, followed by an infusion rate of 1 mcg/kg/hr. Subsequently, the dexmedetomidine infusion was titrated to effect and stopped when the main part of the procedure was completed.

The patient was then prepped and draped in a standard fashion for an orthognathic surgical procedure. The patient's oropharynx was thoroughly irrigated and suctioned free of debris. 10 ml of 2%

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Corresponding Author: Ji Young Yoon, Department of Dental Anesthesia and Pain Medicine, School of Dentistry, Pusan National University, Beomeo-ri, Mulgeu-eup, Yangsan-si, Gyung-sangnam-do 626-787, Korea

Tel: +82.55.360.5379 Fax: +82.51.242.7466 email: dryoonji@pusan.ac.kr

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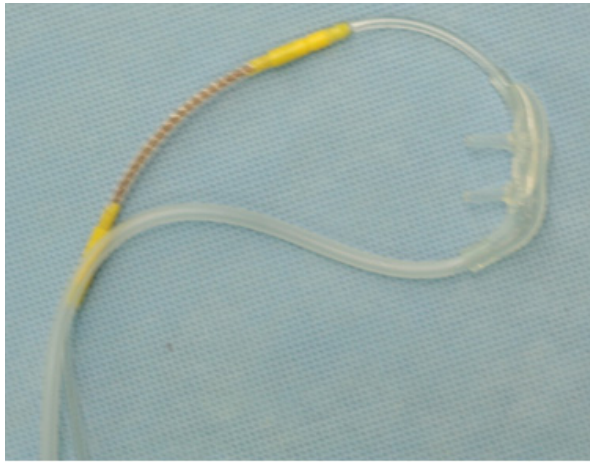


Fig. 1. MAC-safe nasal cannula to monitor end-tidal CO₂

lidocaine with 1 : 100,000 epinephrine was infiltrated into the maxillary vestibule in the areas of the Lefort 1 osteotomy and then, 8 ml of 2% lidocaine with 1 : 100,000 epinephrine was next infiltrated into the mandibular vestibules bilaterally in the areas of the BSSO and genioplasty. Lidocaine infiltration and removal of Lefort 1 osteotomy plate induced severe pain. So during this period, dexmedetomidine infused at 2-3 mcg/kg/hr and followed by an infusion 0.4-1 mcg/kg/hr.

The patient maintained spontaneous respiration while breathing O₂ at 2 L/min. Arterial oxygen saturation, as measured by pulse oximetry, was maintained between 98% and 100%, and her end-tidal CO₂ was stable except in one instance when the airway obstructed and a chinlift was necessary. In the beginning, her blood pressure gradually declined from 150/80 mmHg to 90/55 mmHg. Blood pressure then stabilized around 110/70 mmHg after the dexmedetomidine infusion was discontinued. Her heart rate (HR) remained at approximately 70 beats per minute (bpm). Total surgery time was 2 hours. The patient was then admitted to the recovery room in stable condition and observed in the hospital over the next 24 hours.

DISCUSSION

Certain dental procedure requires continuous intraoperative visualization of intraoral structure with position change, in order to assess the extent of the disease and the results of the procedure. Consequently, the patient needs to remain responsive and to cooperate when asked to open mouth. Traditional sedatives such as fentanyl, midazolam and propofol do not always easily achieve such cooperation. In addition, these agents have well-known respiratory depression. Dexmedetomidine is an alpha-2 adrenoreceptor agonist with α_1 : α_2 receptor selectivity of 1 : 1620. Dexmedetomidine provides adequate sedation [2].

It binds the α_2 adrenoceptor subtypes α_2A , α_2B , and α_2C . The former two subtypes are present in the pre-synaptic membranes of neuron regulating neurotransmitter release [3]. The three α_2 adrenoceptor subtypes may produce adenylatecyclase inhibition or activation, and subsequent decrease or increase of cyclic AMP [4]. Activation of the α_2A receptors located in the locus ceruleus induce the sedative, analgesic, and sympatholytic effects of dexmedetomidine [4,5]. This specific mechanism of dexmedetomidine by α_2 receptors may allow cortical neurons to continue functioning upon stimulation in comparison to propofol or barbiturates, which would induce a generalized neuronal hyperpolarization from the opening of chloride channels. This sedation is unique in that patients are sedated and sleepy, but are easily aroused when stimulated and are able to follow commands [6]. Dexmedetomidine also produces analgesia [2] and amnesic effects [7], and it has antisialagogue properties [8].

Dexmedetomidine shows a rapid distribution phase with a distribution half-life of 6 minutes and a terminal

elimination half-life of two hours [3]. Its protein binding is around 94%, but there is no significant protein binding displacement of other drugs [9]. Gender or ages do not affect the metabolism of dexmedetomidine in patients older than 18 years. There are no pharmacokinetic data in pediatric patients. However, in previous pediatric studies, there is no marked prolongation of its effects were reported. Pharmacodynamic effects of dexmedetomidine show a dose-dependent sedation that resolves approximately two hours after stop of the infusion [10]. Caution should be used when administering the loading dose because hypotension, hypertension, bradycardia, and asystole have been described following by rapid administration. The manufacturer recommends that dexmedetomidine be loaded over 10 minutes to avoid these side effects [11]. The effect of dexmedetomidine on blood pressure can be biphasic. First, there is a short hypertensive phase mediated by α_2B , α_2C , and α_1 receptors, followed by hypotension due to the activation of α_2A receptors.

The optimal dosage strategy of dexmedetomidine for conscious sedation is still under development, and even adult doses listed in the package insert often exceed the upper limit of 0.7 mcg/kg/hr [12]. Dexmedetomidine has a wide safety margin that includes the production of stable respiratory parameters even though the sedation state of dexmedetomidine is dose dependent and, therefore, at large doses, deep sedation or even general anesthesia is possible [7]. Jordan et al. [13] reported three adult dexmedetomidine overdoses in patients concomitantly receiving opioids. Two patients received a 10-fold increase in dosage because of a decimal error, and one patient received a 60-fold increase secondary to dosing the drug per minute rather than per hour. Their patients had a deep level of sedation that corrected

after discontinuation of the drug infusion. Dexmedetomidine do not depress respiratory function even when administered in higher than recommended doses for sedation [14]. These properties renders dexmedetomidine ideal for use in intraoral procedure.

We suggest that sedation with short term large dose dexmedetomidine is a promising technique in patients who are scheduled for invasive intraoral procedure which meets the goals of minimum anesthetic intervention with maximum safety.

REFERENCES

1. Aantaa R, Kanto J, Scheinin M, Kallio A, Scheinin H: Dexmedetomidine, an alpha 2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor gynecologic surgery. *Anesthesiology* 1990; 73: 230-5.
2. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ: Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. *AnesthAnalg* 2000; 90: 699-705.
3. Dyck JB, Maze M, Haack C, Vuorilehto L, Shafer SL: The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. *Anesthesiology* 1993; 78: 813-20.
4. Eason MG, Kurose H, Holt BD, Raymond JR, Liggett SB: Simultaneous coupling of alpha 2-adrenergic receptors to two G-proteins with opposing effects. subtype-selective coupling of alpha 2C10, alpha 2C4, and alpha 2C2 adrenergic receptors to gi and gs. *J BiolChem* 1992; 267: 15795-801.
5. Philipp M, Brede M, Hein L: Physiological significance of alpha(2)-adrenergic receptor subtype diversity: One receptor is not enough. *Am J PhysiolRegulIntegr Comp Physiol* 2002; 283: R287-95.
6. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M:

- The alpha₂-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiology* 2003; 98: 428-36.
7. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colino MD: The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiology* 2000; 93: 382-94.
 8. Scher CS, Gitlin MC: Dexmedetomidine and low-dose ketamine provide adequate sedation for awake fiberoptic intubation. *Can J Anaesth* 2003; 50: 607-10.
 9. Venn RM, Bryant A, Hall GM, Grounds RM: Effects of dexmedetomidine on adrenocortical function, and the cardiovascular, endocrine and inflammatory responses in post-operative patients needing sedation in the intensive care unit. *Br J Anaesth* 2001; 86: 650-6.
 10. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M: The alpha₂-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiology* 2003; 98: 428-36.
 11. Arain SR, Ebert TJ: The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. *Anesth Analg* 2002; 95: 461, 6, table of contents.
 12. Finkel JC, Johnson YJ, Quezado ZM: The use of dexmedetomidine to facilitate acute discontinuation of opioids after cardiac transplantation in children. *Crit Care Med* 2005; 33: 2110-2.
 13. Jordan VS, Pousman RM, Sanford MM, Thorborg PA, Hutchens MP: Dexmedetomidine overdose in the perioperative setting. *Ann Pharmacother* 2004; 38: 803-7.
 14. Ramsay MA, Luterma DL: Dexmedetomidine as a total intravenous anesthetic agent. *Anesthesiology* 2004; 101: 787-90.