J Anesth (2009) 23:147–150
DOI 10.1007/s00540-008-0712-5

Journal of
Anesthesia

Dexmedetomidine facilitates induction of noninvasive positive pressure ventilation for acute respiratory failure in patients with severe asthma

Yasushi Takasaki, Takanori Kido, and Kazunori Semba

Department of Anesthesia, Uwajima City Hospital, 1-1 Goten-machi, Uwajima, Ehime 798-8510, Japan

Abstract
Noninvasive positive pressure ventilation (NPPV) has been reported to be effective for acute respiratory failure in patients with severe asthma. Although NPPV requires less sedative than invasive mechanical ventilation, agitated patients with severe asthma should be given the minimum sedation necessary to facilitate the induction of NPPV. Two asthmatic patients (a 65-year-old man and a 32-year-old woman) separately presented to the intensive care unit with exacerbating respiratory failure. We initiated NPPV using bilevel positive airway pressure (PAP) ventilation. The ventilation was initially set as an inspiratory PAP of 15 cmH_2O and an expiratory PAP of 4 cmH_2O. Because they seemed too agitated to tolerate the mask ventilation, dexmedetomidine was administered intravenously, at 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 10 min, followed by a continuous infusion at 0.2–0.6 $\mu g \cdot kg^{-1} \cdot min^{-1}$. One hour after the institution of NPPV, the patients were well cooperative with the mask ventilation and the respiratory symptoms had markedly improved. While the Ramsay sedation scale was maintained at 2 or 3 during the continuous dexmedetomidine infusion, we successfully weaned the patients from NPPV by reducing the inspiratory PAP. Dexmedetomidine helped the agitated patients cooperate with mask ventilation without inducing respiratory depression. We conclude that dexmedetomidine may be a valuable sedative to facilitate the induction of NPPV.

Key words Dexmedetomidine · Noninvasive positive pressure ventilation · Respiratory failure · Asthma

Introduction

Previous clinical reports suggest that noninvasive positive pressure ventilation (NPPV) is effective for acute respiratory failure in patients with severe asthma [1–5]. Generally, NPPV requires less sedative than invasive mechanical ventilation through tracheal intubation. Agitated patients with severe asthma should be given the minimum sedation necessary to facilitate the induction of NPPV. However, sedative-induced upper airway obstruction may contribute to failure of NPPV, because the airway is not secured as it is with tracheal intubation. Dexmedetomidine has favorable respiratory and cardiovascular pharmacologic properties at therapeutic doses [6–10], and thus it may be a good candidate for the ideal sedation of patients with severe asthma who are supported by NPPV. We present two cases in which dexmedetomidine facilitated the induction of NPPV for the treatment of acute respiratory failure caused by severe asthma without inducing respiratory depression.

Address correspondence to: Y. Takasaki
This case report was presented in part at the 81st clinical and scientific congress of the International Anesthesia Research Society, Orlando, Florida, March 23–27, 2007.
Received: April 1, 2008 / Accepted: October 17, 2008

Case reports

Case 1

A 65-year-old man (weight 63 kg, height 170 cm) presented to the intensive care unit with a severe asthma attack that had developed after the ingestion of a nonsteroidal anti-inflammatory drug. He was taking several medications for chronic asthma and hypertension. Admission physical examination revealed loud wheezing on auscultation, tachypnea (>40 breaths per min), and marked use of accessory muscles for breathing. Blood pressure and heart rate were 201/114 mmHg and 150 beats per min (bpm), respectively. Arterial blood gas analysis revealed pH 7.38, Pa_{CO_2} 45 mmHg, and Pa_{O_2} 56 mmHg with supplemental oxygen delivered by face mask (7 $l \cdot min^{-1}$). Because the respiratory symptoms worsened despite initial treatment with inhaled procaterol aerosol, we initiated NPPV using bilevel-positive airway pressure (PAP) ventilation. A unique

total face mask covered the entire face, and supplemental oxygen (7 l·min^{-1}) was directly delivered from a sample port on the mask. The ventilation was initially set as an inspiratory PAP of 15 cmH_2O and an expiratory PAP of 4 cmH_2O, which worked in response to spontaneous breathing. Because of frequent complaints of dyspnea with progressive agitation, we chose dexmedetomidine for sedation (3 μg·kg^{-1}·min^{-1} via vein for 10 min for initial loading, followed by a continuous intravenous infusion at 0.2–0.6 μg·kg^{-1}·min^{-1}). Concurrently, we continued with the inhaled bronchodilator in addition to intravenous administration of methylprednisolone 500 mg and aminophylline 125 mg. Procaterol aerosol was delivered by actuating a metered-dose inhaler into a spacer placed between the mask and the ventilator circuit (two puffs every 20 min) for the first 1 h. One hour after the institution of NPPV, his respiratory symptoms were markedly improved, with respiratory and heart rates of 22 per min and 105 bpm, respectively. However, a continuous dopamine infusion (5 μg·kg^{-1}·min^{-1}) was temporarily required because of significantly reduced blood pressure. Subsequently, he was well cooperative with the mask ventilation with the continuous dexmedetomidine infusion at 0.2–0.6 μg·kg^{-1}·min^{-1} , adjusted by maintaining the Ramsay sedation scale at 2 or 3. Eighteen hours after his admission to the unit, Pa_{CO_2} had returned to 35 mmHg at an inspiratory PAP of 10 cmH_2O, and NPPV was discontinued. He was uneventfully discharged from the unit on the second post-admission day.

Case 2

A 32-year-old woman (weight 105 kg, height 150 cm) with exacerbated asthma presented to the intensive care unit. She had a 7-year history of chronic asthma and was taking several medications for the condition. She was also taking antihypertensive drugs. Admission physical examination showed loud wheezing on auscultation, tachypnea (>30 breaths per min), marked use of accessory muscles for breathing, profuse sweating, and mild fever. Blood pressure and heart rate were 264/141 mmHg and 136 bpm, respectively. Arterial blood gas analysis revealed pH 7.25, Pa_{CO_2} 48 mmHg, and Pa_{O_2} 66 mmHg with supplemental oxygen delivered by face mask (5 l·min^{-1}). As soon as paradoxical respiratory movement with agitation developed, we initiated NPPV, using bilevel-PAP ventilation with dexmedetomidine administered intravenously at 3 μg·kg^{-1}·min^{-1} for 10 min for initial loading, followed by a continuous infusion at 0.2–0.6 μg·kg^{-1}·min^{-1}. The ventilation was initially set as an inspiratory PAP of 15 cmH_2O and an expiratory PAP of 4 cmH_2O with supplemental oxygen (5 l·min^{-1}) delivered from the total face mask's sample port. In addition, procaterol aerosol was inhaled by actuating a metered-dose inhaler into a spacer (three puffs every 20 min) for the first 1 h and dexamethasone 4 mg and aminophylline 250 mg were administered intravenously. Because laboratory data suggested respiratory tract infection (white blood cell count, 16.300 μl^{-1} and C-reactive protein, 10.4 mg·dl^{-1}), intravenous antibiotic was also administered. One hour after the institution of NPPV, the paradoxical respiratory movement had almost disappeared, and the gas exchange had improved (Pa_{CO_2} 36 mmHg). Heart rate and blood pressure were 108 bpm and 160/105 mmHg, respectively. With the continuous dexmedetomidine infusion at 0.2–0.6 μg·kg^{-1}·min^{-1}, the Ramsay sedation scale was maintained at 2 or 3 and she was able to cough sufficiently to excrete infectious sputum. We gradually weaned her from NPPV by reducing the inspiratory PAP. Sixty-seven hours after her admission to the unit, NPPV was discontinued with her recovery from the respiratory infection and she was uneventfully discharged from the unit on the fourth post-admission day.

Discussion

Dexmedetomidine was extremely effective and safe for sedation when we instituted respiratory support with NPPV for two patients with severe asthma and acute respiratory failure. After the initial loading of dexmedetomidine, subsequent maintenance at 0.2–0.6 μg·kg^{-1}·min^{-1} kept both of them at Ramsay sedation scale of 2 or 3, and they seemed to be comfortable with the mask ventilation. Both patients were also able to develop spontaneously, or by means of verbal prompting by the intensive care personnel, sufficient cough to clear tracheobronchial secretions despite the continuous sedation with dexmedetomidine. Because both patients responded well to pharmacologic therapies for their asthma, including inhaled bronchodilator and systemic glucocorticosteroids, we could successfully wean them from the mechanically ventilated support without major adverse events. However, the second patient needed longer respiratory support with NPPV for impaired pulmonary oxygenation until she had fully recovered from the concomitant lower airway infection. In spite of the extended requirement for dexmedetomidine infusion, the patient did not experience brain dysfunction (such as coma and delirium), which is occasionally induced by other sedative drugs. Of note, a clinical randomized controlled trial demonstrated that dexmedetomidine compromised brain function less than lorazepam in attaining optimal sedation for mechanically ventilated patients [11].

Because the airway is not secured by the insertion of a tracheal tube when noninvasive mechanical ventilation is employed, one should avoid the use, wherever

possible, of sedatives, which depress respiration and can cause upper airway obstruction. On the other hand, agitation is known to be one of the mental manifestations in patients with severe asthma and dyspnea. Initially, they may be too agitated to cooperate with mask ventilation and may thus require some degree of sedation for the induction of NPPV. Also, it has been reported that one of the crucial causes leading to failed NPPV in patients with respiratory failure is intolerance of mask ventilation [5]. Dexmedetomidine is, therefore, a valuable sedative for NPPV because it provides a proper sedation level at therapeutic doses without inducing respiratory depression [6–8], as was shown in our patients. Additionally, Groeben et al. [12] suggested, from the results in an animal study with histamine-induced bronchoconstriction, that dexmedetomidine infusion may have a therapeutic effect to decrease airway reactivity in patients with asthma. Besides showing the above beneficial properties for the respiratory system, dexmedetomidine affords favorable cardiovascular stabilizing effects through a reduction of sympathetic activity [9,10] in patients with severe asthma, in whom extensive hemodynamic stress responses such as tachycardia and hypertension are often evident. The trend toward decreased heart rate and blood pressure observed in our patients may be attributed not only to the relief of the respiratory symptoms but also to direct cardiovascular drug effects. Although the first patient required dopamine infusion because of notable hypotension following the administration of dexmedetomidine, his blood pressure increased rapidly in response to the low-dose dopamine infusion, and it was discontinued within 6 h.

In the respiratory management of patients with severe asthma and acute respiratory failure, NPPV may be useful because it ameliorates various factors associated with deterioration (such as augmented intrinsic positive end-expiratory pressure, fatigued respiratory muscles, and abnormal alveolar gas exchange) as effectively as the standard mechanical ventilation [1–5]. Although the efficacy of NPPV has been reported in patients with various types of acute respiratory failure [5], practical evidence-based guidelines have not yet been established for the use of NPPV in patients with severe asthma [13]. Therefore, we must deliberately make decisions in choosing to employ NPPV or invasive mechanical ventilation, based on the severity of individual cases. Both of our patients showed remarkable improvement in respiratory symptoms and physical condition within 1 h after being supported by NPPV, and thus we were able to avoid conversion to invasive mechanical ventilation. In fact, analysis of our patients suggests that the early institution of NPPV prior to the development of excessive respiratory acidosis or hypercapnea may be of importance in leading to successful treatment. This suggestion is partially supported by the results of previous clinical studies, which showed significantly less severe respiratory symptoms, in terms of both pH and Pa_{CO_2} values, at presentation in patients who received NPPV than in those who received invasive mechanical ventilation [1,2]. Moreover, the combination of the simultaneous use of sedation with dexmedetomidine with the early induction of NPPV may increase the possibility of effective NPPV, especially in agitated patients who initially do not seem to tolerate mask ventilation. However, it should be kept in mind that NPPV cannot always replace invasive mechanical ventilation with tracheal intubation. If improvement is not observed within 1 h following the initiation of NPPV, we consider that invasive mechanical ventilation should be introduced without delay.

Finally, we conclude that consideration of previous reports, combined with our experience, shows that large clinical trials are warranted to define the indications for NPPV and to clarify conditions under which sedation with dexmedetomidine should be used for patients with severe asthma and acute respiratory failure.

References

1. Meduri GU, Cook TR, Turner RE, Cohen M, Leeper KV. Noninvasive positive pressure ventilation in status asthmaticus. Chest. 1996;110:767–74.
2. Fernandez MM, Villagra A, Blanch L, Fernandez R. Noninvasive mechanical ventilation in status asthmaticus. Intensive Care Med. 2001;27:486–92.
3. Soroksky A, Stav D, Shpirer I. A pilot prospective, randomized, placebo-controlled trial of bilevel positive airway pressure in acute asthmatic attack. Chest. 2003;123:1018–25.
4. Soma T, Hino M, Kida K, Kudoh S. A prospective and randomized study for improvement of acute asthma by non-invasive positive pressure ventilation (NPPV). Intern Med. 2008;47:493–501.
5. Mehta S, Hill NS. Noninvasive ventilation. Am J Respir Crit Care Med. 2001;163:540–77.
6. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care. 2000;4:302–8.
7. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000;90:699–705.
8. Martin E, Ramsay G, Mantz J, Sum-Ping ST. The role of the α2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. J Intensive Care Med. 2003;18:29–41.
9. Talke P, Li J, Jain U, Leung J, Drasner K, Hollenberg M, Mangano DT, The Study of Perioperative Ischemia Research Group. Effects of perioperative dexmedetomidine infusion in patients undergoing vascular surgery. Anesthesiology. 1995;82:620–33.
10. Talke P, Chen R, Thomas B, Aggarwall A, Gottlieb A, Thorborg P, Heard S, Cheung A, Son SL, Kallio A. The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. Anesth Analg. 2000;90:834–9.
11. Pandharipande PP, Pun BT, Herr DL, Maze M, Girard TD, Miller RR, Shintani AK, Thompson JL, Jackson JC, Deppen SA, Stiles RA, Dittus RS, Bernard GR, Wesley Ely E. Effect of seda-

tion with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. JAMA. 2007;298:2644–53.
12. Groeben H, Mitzner W, Brown RH. Effects of the α2-adrenoceptor agonist dexmedetomidine on bronchoconstriction in dogs. Anesthesiology. 2004;100:399–63.
13. Ram FS, Wellington S, Rowe BH, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma. Cochrane Database Syst Rev. 2005;1:CD004360.