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CASE REPORT

Methemoglobinemia should be suspected when oxygen saturation apparently decreases after prilocaine infiltration during intravenous sedation

Ryo Wakita & Haruhisa Fukayama

Section of Anesthesiology and Clinical Physiology, Division of Oral Health Sciences, Department of Oral Restitution, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan

Correspondence
Ryo Wakita, Section of Anesthesiology and Clinical Physiology, Division of Oral Health Sciences, Department of Oral Restitution, Graduate School, Tokyo Medical and Dental University, 1-5-45, Yushima, Bunkyo-ku, Tokyo 113-8549, Japan.
Tel: +81 3 5803 5549; Fax: +81 3 5803 0206;
E-mail: ryoanph@tmd.ac.jp

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Key Clinical Message

During intravenous sedation, a decrease in SpO2 is usually the result of respiratory failure. However, we experienced a case with SpO2 decrease that was caused by methemoglobinemia in prilocaine infiltration anesthesia during sedation. This indicates that methemoglobinemia should be considered if low SpO2 is sustained unrelated to sedation level.

Keywords

Methemoglobinemia, monitored anesthesia care, prilocaine, pulse oximetry, sedation.

Introduction

Infiltration anesthesia using 3% prilocaine containing 0.03 IU felypressin (3%Prilo+F; Citanest-Octapressin, Dentsply-Sankin, Tokyo, Japan) is used as an alternative for patients with cardiovascular disease or arrhythmia, instead of 2% lidocaine containing 12.5 μg/mL adrenaline (2%Lid+E; ORA Inj, Showa Yakuhin Kako, Tokyo, Japan), because catecholamines should be avoided for such patients. However, methemoglobinemia (MetHbemia) may occur as a result of prilocaine administration, and the maximum dosage is 300–600 mg [1, 2]. A decrease in the pulse oximetry (SpO2) reading is sometimes observed in patients with MetHbemia because of the difference in absorbance spectrum between O_2Hb and MetHb [3].

Intravenous sedation is a common method in oral surgery, but may decrease SpO2 because of respiratory depression. It is difficult to distinguish respiratory depression from MetHbemia as the cause of a SpO2 decrease in a patient who receives peripheral nerve block using prilocaine under intravenous sedation because both prilocaine and sedation are risk factors for a SpO2 decrease. Here, we describe the case of a patient with MetHbemia due to prilocaine infiltration anesthesia under intravenous sedation. Written consent for publication was obtained from the patient.

Case History

A 43-year-old woman was scheduled to undergo bone grafting from the right mandibular bone for implant preparation in the area of the right anterior teeth. Her height was 158 cm and body weight was 49 kg. The patient had already undergone several dental implant operations under intravenous sedation. She had no other relevant medical history. Because of the longer operation (estimated time of 90 min), intravenous sedation was

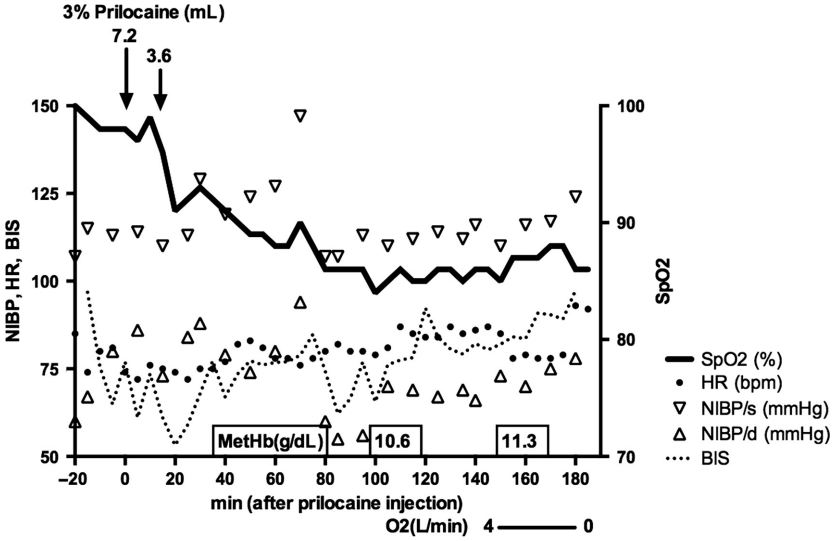

Figure 1. The changes of vital signs during sedation. After prilocaine injection, SpO2 was decreased and was become stable around 85%.

scheduled. Her latest sedation record showed sneezing caused by oxygen flow from the nasal catheter and sinus tachycardia after infiltration anesthesia with use of 2% Lid+E. Therefore, we decided to administer 3%Prilo+F to prevent tachycardia and to skip oxygen administration using a nasal catheter.

Blood pressure (BP), atrial oxygen saturation (SpO2), and ECG (lead II) were monitored using a vital sign monitor (BSM 9101; Nihon Kohden, Tokyo, Japan), and bispectral index (BIS) was also monitored (A-2000; Covidien, Boulder, CO) from the start of the procedure. End-tidal carbon dioxide was not measured (Fig. 1). On arrival in the operating room, her heart rate (HR) was 86 bpm, BP was 108/61 mmHg, SpO2 was 98%, and BIS was 97. After securing the IV route and administering 2 mg of midazolam, propofol was continuously given using a target-controlled infusion method to achieve a plasma propofol concentration (PPF[Ci]) of 1.0 μg/mL, using an infusion pump (TE-371; Terumo, Tokyo, Japan). Several minutes after starting sedation, her observer's assessment of alertness/sedation (OAA/S) score was 3 and BIS was about 70. Local infiltration anesthesia of 7.2 mL of 3%Prilo+F was then administered. HR increased temporarily and recovered to baseline within 5 min, and thereafter SpO2 was 96–98% and BP was stable. The operation was started and PPF[Ci] was raised to 1.3 μg/mL. Fifteen minutes after the start of the operation, SpO2 had gradually decreased to 94%, and the respiratory rate was around 15–20 breaths/min. As there were no symptoms of respiratory depression, the same PPF[Ci] was maintained. After an additional 3.6 mL of 3%Prilo+F was added (10.8 ml in total), SpO2 gradually decreased to around 90%.

The patient complained of surgical pain, and an additional 3.6 mL of 2%Lid+E was administered. At that time, SpO2 was around 86–88%. Her position was changed to the Fowler position and deep breathing was promoted. Although PPF[Ci] decreased to 1.0 μg/mL, SpO2 did not recover. Thirty minutes later, additional 2%Lid+E was administered because she complained of local surgical pain. As SpO2 gradually decreased to 85%, propofol infusion was suspended. PPF[Ci] reached 0.7 μg/mL within several minutes. BIS recovered to about 90 and the OAA/S score rose to 5, but SpO2 was still about 85%. A venous blood sample was found to be a dark chocolate color. Blood gas analysis and CO-oximetry (ABL800FLEX; Radiometer, Tokyo, Japan) revealed pH 7.314, partial pressure of oxygen in venous blood (PvO2) 26.6 mmHg, partial pressure of carbon dioxide in venous blood (PvCO2) 53.5 mmHg, total hemoglobin (tHb) 11.2 g/dL, and MetHb 10.6%. There was no cyanosis in her extremities, and the patient appeared to be in no discomfort, including no problems with respiration, but she was completely awake.

2%Lid+E was used to relieve surgical pain and allow continuation of the operation. Propofol infusion was resumed and PPF[Ci] was kept at 0.7 μg/mL to maintain BIS at 80–90 until the end of the operation. Throughout the operation, BP and HR were stable and SpO2 (85%) was unchanged. After successful completion of the operation, SpO2 remained at about 85–86% despite starting oxygen therapy through a face mask (4 L/min). A second venous blood sample showed tHb 11.2 g/dL and MetHb 11.4%. The patient was transferred to the ward and continued to receive monitored care with oxygen therapy (Fig. 2). SpO2 recovered to 92% with the use of 4 L/min

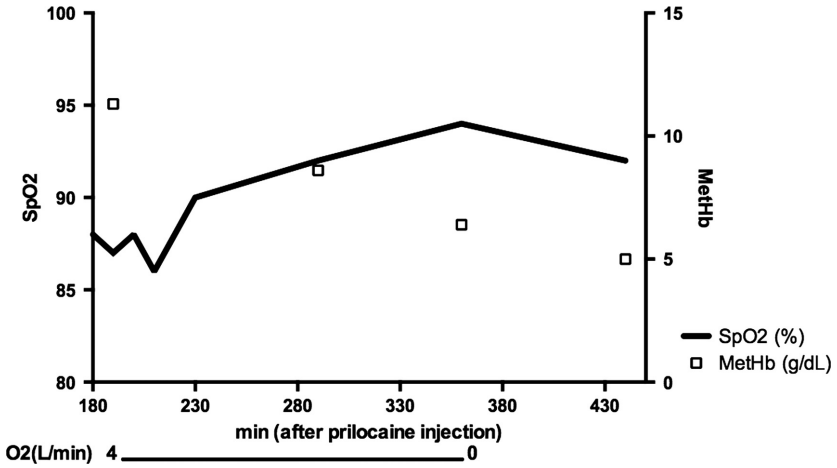

Figure 2. SpO2 and MetHb changes after sedation. MetHbemia was gradually recovered over 400 min.

of oxygen and MetHb decreased to 8.6% 4.5 h after the first prilocaine injection. After 7 h, MetHb was reduced to 5.0% and SpO2 was 95% without oxygen therapy. The patient was discharged 8 h after the first injection of prilocaine. One week later, when she visited our clinic, the wound was healing properly, SpO2 was 99% in room air, and venous blood analysis showed pH 7.380, PvO2 32.5 mmHg, PvCO2 43.9 mmHg, tHb 12.1 g/dL, and MetHb 0.3%.

Discussion

We encountered a rare case of MetHbemia that occurred during intravenous sedation and was almost misdiagnosed as respiratory depression. To diagnose MetHbemia, blood gas analysis with CO-oximetry for arterial blood is required to measure various types of hemoglobin, including MetHb, and to assess arterial blood oxygenation. In this case, we suspect that MetHb was increased due to the use of a large amount of prilocaine, but the patient did not complain of respiratory discomfort, even after recovery of consciousness. In addition, arterial blood gas (ABG) sampling is invasive for conscious patients and is too difficult and challenging to perform in office-based dentistry, such as in our case. Therefore, ABG was not examined and venous blood was sampled only to diagnose MetHbemia. However, ABG should be used to evaluate respiratory and oxygenation status, or for a patient with respiratory difficulty, especially if the cause is unclear. Thus, ABG analysis should have been performed to detect hypoxemia. Furthermore, for a case with severe hypoxemia, oxygen therapy or mechanical ventilation with airway control should be considered, as in general anesthesia. However, blood analysis has a disadvantage of not measuring MetHb continuously [4]. We note that a multiwavelength pulse oximeter (pulse CO-oximeter) for noninvasive and continuous measurement has recently become available, and this allows for easier detection of MetHbemia [5].

When MetHb increases, SpO2 in conventional pulse oximetry approaches about 85% because of the difference in absorbance spectrum between oxyhemoglobin and MetHb [3]. Thus, a pulse oximeter reading is considered to be unreliable and not useful in cases of MetHbemia. However, we found that pulse oximetry was still useful in the absence of a CO-oximeter, especially as MetHbemia manifested and progressed. Although accurate MetHb levels cannot be determined from SpO2, an abnormal SpO2 decrease after local anesthesia does suggest onset of low to moderate MetHbemia. Moreover, SpO2 readings hovering around 85% often suggest severe MetHbemia [3, 4]. A decrease of SpO2 was found 15 min after local anesthesia and SpO2 remained at 85–87% for 45 min while MetHb was 10–11% in our case. We concluded that MetHb developed 15 min after prilocaine infiltration from the anesthetic record and previous reports, in which MetHbemia has been found to occur within 20 min after exposure to prilocaine [6, 7]. However, it was difficult to show that MetHb was responsible for the SpO2 decrease because the patient was also sedated at that time.

Oxygen therapy is commonly recommended in guidelines for intravenous sedation and usually maintains SpO2 over 97% during sedation [8]. MetHbemia should be suspected if a decrease in SpO2 occurs independently of sedation level or respiratory status [9, 10]. In our case, we did not use oxygen because of a concern that airflow from the nasal catheter could cause sneezing, as in the previous sedation of the patient. It is well known that SpO2 can be lowered following respiratory depression caused by sedative drugs, especially in the absence of

oxygen therapy. Thus, a low SpO2 level under oxygen omission initially misled us to suspect respiratory depression in our case, while SpO2 was unchanged after facilitating deep and frequent breaths and after suspending propofol infusion. In addition, the patient did not complain of respiratory discomfort, and her thoracic movement and breath sounds were normal. For these reasons, we finally concluded that desaturation was not due to respiratory failure. There is no doubt that ABG measurement is important for confirming a diagnosis of hypopnea. From our experience, we strongly recommend supply of oxygen during sedation, which is important for safety and earlier identification of a MetHb-related decrease in SpO2.

Patients with MetHbemia have many symptoms that depend on their MetHb levels. Guay et al. described cyanosis (≥5%), tachycardia (≥10%) and hyperventilation (≥11.5%) [9], and cyanosis, which occurs at >1.5 g/dL of MetHb, may be the first symptomatic sign [11]. In our case, none of these symptoms were found at a MetHb level of about 11% (estimated MetHb of 1.4 g/dL). However, the blood color was chocolate brown, as in previous reports; and this color is one of the important symptoms for diagnosis of MetHbemia [9, 12]. Methylene blue is the first choice for treating MetHbemia, but medication is not necessarily required and oxygen therapy alone can promote oxygen transport by residual hemoglobin in a case with no symptoms and MetHb <20% [6, 12]. In our case, neither methylene blue nor ascorbic acid was administered because of the absence of symptoms.

In previous operations on our patient, SpO2 reduction was not observed. Prilocaine was the only drug used for the first time in the latest procedure and was certainly the cause of MetHbemia. We administered a total of 324 mg (approximately 6.6 mg/kg) of prilocaine into the oral cavity, where drugs are rapidly absorbed. The maximum recommended prilocaine dosage is 600 mg, but this varies among countries from 300 to 600 mg with felypressin [1, 2, 13]. The relationship of the prilocaine dose with the concentration of MetHb and incidence of MetHbemia are unclear. Vasters et al. [14] found a large interindividual variation in MetHb from 0.9 to 15.4% after administration of 300–400 mg of prilocaine for peripheral nerve block. A review suggested that the maximum dose should be 2.5 mg/kg [9] and we agree with this as the maximum clinical dose.

There is a variable time for reconversion from MetHb to deoxy-Hb, with the time to recovery to a MetHb level of 2.0% varying from 15 to 36 h [9]. The adult effective half-life of MetHb is approximately 160 min [15]. In our case, 7 h after prilocaine administration, the estimated MetHb was below 3.0% and the actual MetHb was 5.0%. This indicated that the pathway for reduction of MetHb was effective and we were able to discharge the patient. One week later, we confirmed that her MetHb level had returned to the normal range.

In conclusion, we have reported a case with MetHbemia during intravenous sedation. An abnormal SpO2 decrease after local anesthesia should lead to suspicion of MetHbemia, and CO-oximetry is helpful for accurate diagnosis. Moreover, it is important to administer supplemental oxygen and maintain a constant sedation level for safety and earlier detection of a MetHb-related SpO2 decrease. Administration of prilocaine at a dose <2.5 mg/kg may prevent MetHbemia.

Authorship

RW: managed the case, collected and interpreted data, and write the manuscript. HF: made critical review of the manuscript. Both authors: approved the final version of the manuscript.

Conflict of Interest

None declared.

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