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RECURRENT POST-HYPERVENTILATION APNEA WITH SEVERE HYPOXIA AFTER GENERAL ANESTHESIA - 2 CASE REPORTS

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ABSTRACT Post-hyperventilation hypoxemia is caused by apnea and ventilation-perfusion mismatch of the lungs, which can lead to severe hypoxemia if the duration of apnea is prolonged. Hyperventilation syndrome after general anesthesia can cause prolonged apnea due to benzodiazepine, opioid, neuromuscular blocking agent and can make severe hypoxemia due to atelectasis. We experienced two patients with recurrent apnea and sudden hypoxemia after hyperventilation syndrome after general anesthesia. We were able to treat hyperventilation, which was not treated with the drug, with a rebreathing mask and to terminate the recurrence of apnea and hypoxemia.

KEYWORDS : hypoxemia, hyperventilation, apnea, general anesthesia

INTRODUCTION

Hyperventilation syndrome ("HV") is a respiratory disorder caused by over-breathing in the absence of any underlying condition, exceeding the body's metabolic needs, resulting in a decrease in PCO_2 levels and an increase in pH levels, often causing distress, shortness of breath, chest pains, paresthesia, palpitation, and unconsciousness. HV symptoms usually disappear on their own without any particular treatment. Anxiolytics, beta blockers (Folgering H & Cox A, 1981), calcium , and potassium (Hyun Soo Moon, 2011) can be administered to treat HV, but in rare cases such treatment can result in death (Callaham M, 1989).

Hypoxia can appear as the result of the worsening of ventilation-perfusion mismatch in the lungs and apnea and may increase in severity the longer the apnea persists. It is still unclear what causes persistent apnea. Some reports have treated apnea through mechanical ventilation (Takao Munemoto et al., 2013). This study examined two patients who experienced recurring onset of persistent apnea and severe hypoxia after the onset of HV after general anesthesia while in the recovery room of the hospital where their procedures were conducted. Their HV was successfully treated with rebreathing masks. It is possible that more severe cases of hypoxia were caused by apnea in these cases, although no such reports have been made. This paper presents these patients' cases and suggestions for possible treatment methods.

First episode

The first patient was a 15-year-old male weighing 53 kg who received general anesthesia for a biopsy of the tibia osteochondroma. Anesthesia was induced using remifentanil and propofol. An injection of rocuronium bromide was administered to facilitate tracheal intubation. Sevoflurane, O_2, air, and remifentanil were used to maintain anesthesia. The procedure lasted 25 minutes and no problems with anesthesia were observed. Extubation was performed upon adequate return of neuromuscular function and the patient was moved to the recovery room once conscious.

At time of admission to the recovery room, heart rate ("HR") was 90 beats/min, respiration rate ("RR") was 14 breaths/min, and SpO_2 was 100%. SpO_2 remained at 100% 10 minutes following admission to the recovery room, but the patient exhibited an excited state and showed signs of HV and elevated HR and RR, which were 123 beats/min and 30 breaths/min, respectively. In response, 1.5 mg of midazolam was administered. The patient continued to show symptoms and began experiencing pain 15 minutes following admission to the recovery room, so 50 mcg of fentanyl and another 1.5 mg dose of midazolam were administered. The patient continued to show signs of HV, tachycardia, excitement, and lack of cooperation, so 2.0 g of propacetamol HCL, 50 mcg of fentanyl, and 20 mg of propofol were administered (first onset of HV). Respiratory examination using a stethoscope showed clear breathing sounds and chest movements were normal.

Symptoms of HV, tachycardia, and excitement had subsided, but hypoventilation, apnea, a sharp decrease in peripheral oxygen saturation, and a loss of consciousness were observed 45 minutes following admission to the recovery room. Bag-mask assisted ventilation was conducted intermittently for approximately 25 minutes (apnea following first onset of HV), which resulted in a decrease in SpO_2 to 83%. The patient regained consciousness and again began experiencing HV and excitement 75 minutes following admission to the recovery room with an HR of 149 beats/min, an RR of 60 breaths/min, and SpO2 at 100% (second onset of HV). HV was relieved temporarily before symptoms returned by administering 20 mg of propofol and 10 minutes thereafter the patient experienced the second onset of HV and loss of consciousness. Bag-mask assisted ventilation was conducted intermittently (apnea following second onset of HV), and causing the patient to regain consciousness before another onset of HV and tachycardia with difficulty breathing occurred (third onset of HV) (Fig. 1). Nasal prong $EtCO_2$ monitoring was conducted through capnography (Microstream , Drager, Germany). A mask with a reservoir bag (high concentration oxygen mask adult, Hsiner, Taiwan) (Fig. 3) with the middle check valve removed to allow for rebreathing was used to administer 500ml/min of oxygen until rebreathing was observed. After four minutes, the patient regained consciousness and HR, RR, $EtCO_2$ and oxygen saturation all returned to normal levels, prompting the removal of the rebreathing mask. There were no further onsets of HV or apnea, so the patient was transferred to a bed in the patient ward. The total time spent in the recovery room was 170 minutes.

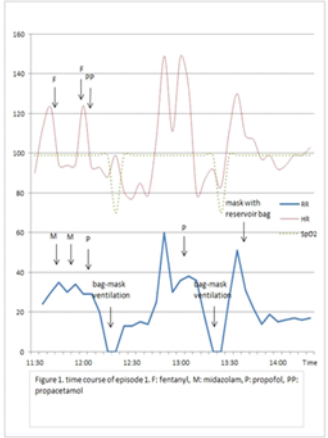
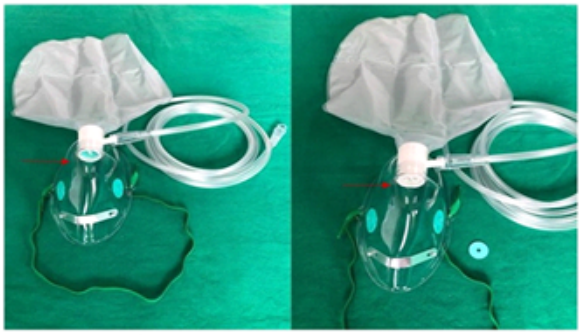


Figure 1. time course of episode 1. F: fentanyl, M: midazolam, P: propofol, PP: propacetamol



(A) (B)

[figure.3] (A) mask with reservoir bag (B) mask with reservoir bag without inspiratory check valve

Second episode

The second patient was a 6-year-old female weighing 21 kg who received general anesthesia for a tonsillectomy with adenoidectomy. Prior to the procedure, the patient exhibited minor anxiety, but otherwise had no underlying or pre-existing conditions. Anesthesia was induced using intravenous fentanyl and ketamine. Rocuronium bromide was injected to facilitate tracheal intubation. Anesthesia was maintained using oxygen, air, and sevoflurane. The procedure lasted 55 minutes and no problems with anesthesia were observed. Extubation was performed upon adequate return of neuromuscular function.

The patient was moved to the recovery room once conscious. At time of admission to the recovery room, HR was 147 beats/min, RR was 20 breaths/min, and SpO2 was 100%. The patient displayed agitation due to pain, prompting the administration of 10 mcg fentanyl and 600 mg propacetamol HCl. The patient then showed a stable HR and RR until 24 minutes after admission to the recovery room when HR increased to 124 beats/min and RR increased to 33 breaths/min accompanied by the onset of HV, excitement, shortness of breath, and lack of cooperation (first onset of HV). Respiratory examination using a stethoscope showed clear breathing sounds and normal chest movements. In response, 10 mcg fentanyl was administered and HV continued for approximately 20 minutes followed by the rapid onset of hypoventilation, loss of consciousness, and hypoxia with SpO2 at 60%. Bag mask ventilation was conducted immediately (apnea following first onset of HV) (Fig. 2). Apnea following HV persisted for approximately 15 minutes. The second onset of HV occurred as the patient regained consciousness and persisted for approximately 15 minutes. This onset was followed by five minutes of apnea accompanied by hypoxia, prompting immediate bag mask ventilation (apnea following second onset of HV). The patient experienced a third onset of HV that persisted for 15 minutes with five minutes of apnea for which 100 mcg of naloxone was administered. The patient then experienced a fourth onset of HV for 15 minutes with five minutes of apnea.Approximately 120 minutes after being admitted to the recovery room, the patient experienced a fifth onset of HV and a mask with reservoir bag (high concentration oxygen mask adult, Hsiner, Taiwan) (Fig. 3) with the middle check valve removed to allow for rebreathing was used to administer oxygen at 500ml/min until rebreathing was observed. Venous blood gas analysis and capnography were conducted at the same time. The fifth onset of HV persisted for approximately 10 minutes. The patient showed no signs of hypoxia, apnea, HV, excitement, or lack of cooperation following this and was capable of voluntary breathing.

The mask was left on to maintain 28–33 mmHg of $EtCO_2$ for approximately 10 minutes and was removed once the patient regained consciousness. During the fifth onset of HV, venous blood gas analysis results showed a pH of 7.564, 24.5 mmHg of PCO_2, 33.8 mmHg of PO_2, HCO_3 of 21.7 mmol/L, SvO_2 of 75.7%, Na of 138, K of 3.68, and Ca of 1.18. The total time spent in the recovery room was 210 minutes.

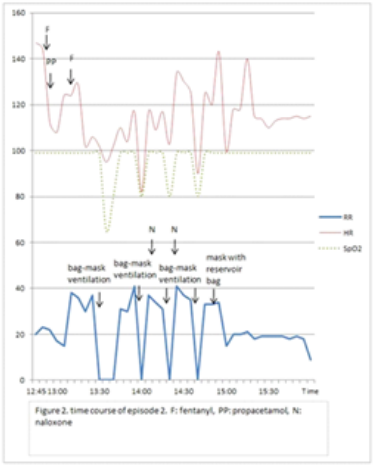


Figure 2. time course of episode 2. F: fentanyl, PP: propacetamol, N: naloxone

DISCUSSION

Alkalosis resulting from decreased $PaCO_2$ levels following HV syndrome can lead to negative feedback of central chemoreceptors, resulting in apnea.In most cases, when $PaCO_2$ levels return to normal, hydrogen ions bind to chemoreceptors to facilitate normal breathing. However, hypoxia can occur during this process and the persistence of apnea for any reason, it can lead to severe hypoxia. Although the source of persistent apnea is unclear, there are several possible explanations.

First, although alveolar and arterial CO_2 levels may have returned to normal, the brain may take longer to recover from normocapnea, inhibiting central chemoreceptors and causing persistent apnea (Cummin AR, Telford RJ & Saunders KB, 1991) .Also, according to Leevers et al., once breathing occurs following HV, $PetCO_2$ levels are higher than apneic threshold $PetCO_2$ levels . Second, the central nervous system may affect persistent apnea due to its role in maintaining alertness (Mangin P, Krieger J, Kurtz D, 1982; Ohi M, et al., 1994) According to Mangin, a high rate of healthy patients who experience HV also experienced apnea while sleeping. Mangin suggested that the central neural mechanism is closely related to alertness and active breathing can provide neural facilitation to stop apnea caused by chemical deficiencies (Mangin P, Krieger J, Kurtz D, 1982).

Furthermore, according to Chin et al., HVS patients show normal hypoxic and hypercapnic ventilatory responses. In this study, apnea and severe hypoxia were observed in sleeping or unconscious, post-HV patients, not in alert, HV-induced patients(Chin K et al., 1997)

Post-HV hypoxia occurred as the result of apnea and ventilation-perfusion mismatch in the lungs following HV. Much less oxygen is stored in the body than CO_2 so extended periods of ventilation to return exhausted CO_2 supplies back to their normal levels following HV can lead to hypoxia. Hypoxia can become more severe following HV as a result of ventilation-perfusion mismatch in the lungs caused by changes in blood gas and pH levels (Nolan SR et al., 2004).

According to Nolan et al., as HV becomes more severe, hypoxia does as well, not as much due to ventilation itself but due to V/Q mismatch caused by changes in pulmonary blood flow caused by an increase in pH and a decrease in CO_2 levels.

In the cases of the two patients featured in this study, recurring onset of persistent HV caused near-exhaustion of internal CO_2 levels, which led to apnea and, consequently, severe hypoxia. Both patients were unconscious following HV, which most likely also affected the onset of apnea. Both patients also experienced recurring decreases in peripheral oxygen saturation levels following apnea, most likely due to ventilation-perfusion mismatch in the lungs cause by alkalosis and hypoxia.

The possible role of anesthesia in causing severe hypoxia and persistent apnea must also be taken into consideration.

Approximately 85–90% of patients who receive local anesthesia experience atelectasis, which can cause shunts (Karcz M & Papadakos PJ, 2013). The effects of shunts caused by local anesthesia can also lead to severe hypoxia.

Further, fentanyl raises the apneic threshold of PCO_2 and reduces the hypoxic ventilatory drive. Midazolam also reduces ventilatory response to CO_2 and has a synergistic effect when administered together with opioids, which may also have contributed to the persistent apnea observed in the two patients.

However, it can be determined that naloxone and midazolam were not the definitive causes of apnea given that naloxone has no effect on apnea and that midazolam was only administered for a short period of time.

Hypocalcemia can occur as a result of HV, intensifying the residual effects of neuromuscular blocking. It is possible that inhibited carotid body chemosensitivity as the result of neuromuscular blocking could have interfered with the hypoxic ventilatory response while in a hypoxic state, resulting in persistent apnea and prolonging the time that it took for breathing to return to normal (Eriksson LI, Sato M, Severinghaus, JW,1993; Eriksson LI, 1996)). However, this possibility does not seem to have occurred in these two patients' cases, as neuromuscular blocking had adequately subsided prior to the onset of symptoms. The second patient did not exhibit hypocalcemia, which indicated that there was no inhibition of the hypoxic ventilatory response due to residual effects of neuromuscular blocking.

Bag and mask ventilation (Takao Munemoto et al., 2013) is the standard treatments for post-HV apnea. Treatment for HV includes treatment of symptoms using anxiolytics, beta blockers, calcium, potassium, or haloperidol along with the plastic bag method. However, such methods are related to side effects, including severe hypoxia, myocardial infarction, and even death. As such, there are limited examples of these methods used during treatment and thus are not recommended (Callaham M, 1989).

The medications which were administered to the two patients included midazolam, propofol, fentanyl, naloxon, and propacetamol HCl. Midazolam and propofol only temporarily relieved HV and were not effective in preventing recurring onsets. Also, there is no evidence showing that propofol is effective in treating HV whereas there is evidence showing that it is not effective (Tomioka S et al., 2001). Both patients exhibited recurring HV, suggesting that they had very low CO_2 levels. In order to prevent hypoxia while increasing CO_2 to its normal level, 500 ml/min of oxygen was administered at the onset of HV and a mask with the inspiratory check valve removed bag was used with a reservoir.

The masks available in these cases were equipped with bags which could adjust the rate of oxygen flow and which featured one-way inspiratory check valves. These valves were removed and airflow bags were modified to allow for the flow of CO_2. Patients who weigh 20 kg with a tidal volume of 200ml and a RR of 20 breaths/min, the alveolar gas mixture per breath is 13.2% O_2, 74.4% N_2, 5.3% CO_2, 0.9% inert gas, and 6.2% H_2O. If 500 ml/min of oxygen are given using a mask, the mixture becomes 22.8% O_2, 66.1% N_2, 4.7% CO_2, 0.8% inert gas, and 5.5% H_2O along with 188ml/min of CO_2. Most of the approximately 45–55 ml/dl of CO_2 in the body is stored in the blood. A 20 kg patient contains approximately 700 ml of CO_2. Therefore, CO_2 can be raised to normal levels through the moisture created by rebreathing.

The first and second patients underwent four and 10 minutes of rebreathing, respectively, to increase the $ETCO_2$ to normal levels. As a result, there was no subsequent onset of HV, distress, shortness of breath, loss of consciousness, or apnea, so the most likely cause of these symptoms were low CO_2 levels and alkalosis, which is why the masks were an effective treatment method.

CONCLUSION

HV following general anesthesia can result in apnea and hypoxia. Administering benzodiazepines, opioids, and neuromuscular blockers in patients receiving general anesthesia should be carefully considered as general anesthesia often leads to atelectasis, thus increasing the chances of persistent apnea and severe hypoxia occurring after HV. Furthermore, using a ventilation mask while administering oxygen, it is the most effective treatment method for treating HV following general anesthesia in patients who have no underlying respiratory system problems.

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