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Original article

Severe and acute hypercapnia, subsequent to the mistaken connection of a carbon dioxide cylinder on the nitrous oxide manifold: a report of three simultaneous cases

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Abstract

Ensuring the delivery of correct gas mixtures during anesthesia is of paramount importance for perioperative patient safety. Accidents resulting from a problem with the supply of medical gases to the operating theater are rare; however, the consequences can be serious. Given the continuous advances in safety measures for the administration of medical gases, it is reasonable to assume that current patients consistently receive the intended gas, as requested by the anesthesiologist. Nevertheless, it is necessary to acknowledge that human error may still occur, despite the automation and safety protocols in place.
Simultaneously in three operating rooms, we observed abrupt and sever cases of hypercapnia that occurred during general anesthesia when nitrous oxide was requested. These incidents were due to a carbon dioxide cylinder connected in the place of a nitrous oxide cylinder on the manifold.
Patient management, operating theater supervision and factors responsible for this serious adverse event will be discussed in this report. This problem appears to be fairly specific to Belgium where the standard cylinder fittings for the two gasses involved are either the same or close enough to be misconnected on the manifold. Local measures, as well as general recommendations, are proposed to prevent a similar incident in the future.

Keywords: **Hypercapnia, Nitrous Oxide, Cylinder fittings.**

Introduction

Patient safety necessitates the prevention of any avoidable harm that may occur during the administration of medical care[1]. Ensuring the delivery of correct gas mixtures during anesthesia is of paramount importance for perioperative patient safety. Any deviation from the intended gas mixture administered can have significant consequences, including inadequate oxygen supply, compromised ventilation, or adverse reactions to anesthetic agents. It continues to be challenging for the anesthesiologist to control the gas content before administering it to the patient. The anesthesiologist observes the gas received by the patient through the monitoring of the anesthesia machine during his administration. This contrasts sharply with the visual confirmations possible when medication is administered by syringe, such as with epidural or IV treatments. In the latter cases the anesthesiologists have direct control over the drug they draw and inject, a process facilitated by the labelling and the packaging of the product.

According to current recommendations for perioperative oxygenation and ventilation, monitoring of blood oxygenation by pulse oximetry is a universal standard among all professional organizations[1]. It is also recommended by all surveyed organizations to detect the presence of end-expired carbon dioxide ($EtCO_2$), but only after intubation or placement of a supraglottic airway[1]. Surprisingly, despite their importance to patient safety recommendations, monitoring of inhaled and exhaled agents are not uniform[1]. Considering the evolution of safety in the administration of medical gases[2,3], it would be assumed nowadays that the patient does indeed receive the correct gas requested

by the anesthesiologist on the anesthesia machine. Many anesthesiologists take this for granted, but this might not always be the case[4,5,6]. The anesthesia machine verification procedure, as part of the checklist, does not allow adequate control for all gas delivery.

We describe here abrupt and sever cases of hypercapnia related to an improper administration of CO_2 in three operation rooms when N_2O was requested, consequently to an accidental mistaken connection of a CO_2 cylinder on the N_2O manifold. The description of this event aims to alert any anesthesiologist about the possibility that such an incident can reoccur since there is no international safety regulation that addresses the issue of continuous gas supply control at the level of the central distribution.

Case series

First case

A 40-year-old female patient, classified as ASA 2 according to the American Society of Anesthesiology, presented to the day clinic for the placement of an intragastric balloon under general anesthesia. Her medical history included sever obesity with a body mass index of 38 kg/m^2, as well as cervical and lumbar arthropathy.

Her past surgical history included wisdom tooth removal, abdominoplasty, and laparoscopic appendectomy. She had allergies to latex and penicillin. The patient was able to perform efforts requiring more than four metabolic equivalents. Her clinical examination was unremarkable.

Preoperative blood test results were within the normal range. She was the first patient to be operated at 8 a.m. on that day in the endoscopy room. Before the patient was admitted, the operating room equipment, including the anesthesia machine was checked in accordance with the standard procedure for the equipment.

As soon as the patient arrived, the anesthesiologist proceeded to implement a standard monitoring (3-lead electrocardiogram (ECG), non-invasive blood pressure, pulsed oxygen saturation). Preoxygenation was started with an inspired fraction of oxygen (FiO_2) set at 100 %. The induction of anesthesia was initiated with sufentanil (0.1 µg/kg), propofol (2 mg/kg) and celocurine (1mg/kg) after obtaining an expired oxygen fraction (EtO_2) of 90%. The oro-tracheal intubation was uneventful and the patient was connected to the anesthesia machine set to a volume-controlled ventilation mode. The available features on the anesthesia machine (Perseus A500, Dräger, Wemmel, Belgium) used included O_2, CO_2, N_2O, and sevoflurane monitoring. Maintenance of the anesthesia was performed with sevoflurane and a mixture of oxygen (O_2) and N_2O (50%/50%). The gastroenterologist then started his procedure. The CO_2 insufflation pressure given by the gastroscope was normal (9 mmHg). Within a few seconds, the anesthesiologist heard the CO_2 alarm, with the capnometer showing an end-tidal CO_2 partial pressure ($EtCO_2$) at 330 mmHg and inspired carbon dioxide fraction ($FiCO_2$) at 298 mmHg. There was no differentiation between expiratory and inspiratory phases on the capnograph; a plateau persisted on the monitor. Gas monitoring demonstrated an absence of inspired and exhaled N_2O. The soda lime granules quickly became saturated and turned purple. The other vital parameters were within the normal range.

In the hypothesis of possible malignant hyperthermia, the administration of sevoflurane was stopped. In addition, N_2O was stopped and FiO_2 at 100 % was administered. In parallel, the gastroenterologist was made aware of the situation, stopping the CO_2 insufflation and swiftly completing his operation.

The physical examination and cardiopulmonary auscultation of the patient remained normal. There was no hyperthermia objectified by rectal temperature monitoring. There was no trismus of the masseter muscle. A quick analysis of the gas circuit showed no apparent defects.

A change of soda lime was performed. The anesthesiologist ventilated the patient with an open circuit and a fresh gas flow at 12 liters/minute. The expiratory and inspiratory phases of CO_2 reappeared with a progressive decrease of the expired CO_2 to normal values after 25 minutes of ventilation under 100 % of FiO_2. The patient was kept under sedation with intravenous propofol during that period. She was extubated as soon as she had spontaneous ventilation and exhibited typical signs of awakening.

Then, the patient was transferred to the recovery room. The physical examination was without particularity, as were the arterial blood and the 12-lead ECG. A blood test (creatine kinase, renal-hepatic function, and troponin kinetics) was performed and showed results within the normal range. There was no myoglobinuria.

Note that the two anesthesiologists who worked in the two other opened operating rooms had been called for help during the incident. However, they could not come to aid because they were experiencing a similar situation in their own operating theaters simultaneously.

Second and third cases

In the second operating room, a 35-year-old male ASA 1 underwent general anesthesia for urinary tract stone removal. In the third operating room, a 32-year-old ASA 1 patient underwent general

anesthesia for circumcision surgery. They were also the first patients to be operated in these operating rooms for the day. Operating room equipment had been checked as per the standard procedure.

During their anesthesia, the patients were monitored using standard methods. The inductions were performed with sufentanil (0.1 µg /kg) and propofol (2mg/kg) without using any myorelaxant drug. Patients' laryngeal masks were connected to the anesthesia machine (Perseus A50, Dräger, Wemmel, Belgium) in pressure-controlled ventilation mode. The maintenance phases were also performed with sevoflurane and a mixture of O_2 and N_2O (50%/50%).

Then, the sequence of events was the same for these two patients as for the patient in the first operating room. Two minutes after turning on the N_2O, the capnometers showed severe $EtCO_2$ and $FiCO_2$ with a persisting plateau on the monitors. There was also no differentiation between inspired and exhaled N_2O displayed on the capnographs. Gas monitorings demonstrated also an absence of inspired and exhaled N_2O. The other vital parameters were within normal range. The soda lime granules quickly became saturated.

The anesthesiologists immediately notified the events to the surgeons who stopped the procedures. The N_2O and the sevoflurane were stopped. Clinical examinations were also unremarkable. Soda limes were also changed.

The anesthesiologists ventilated the patients at 100% FiO_2 for 20 minutes to lower their $EtCO_2$ to 40 mmHg, under propofol sedation. Laryngeal masks were removed when the patients had spontaneous ventilation and exhibited appropriate signs of awakening.

They were then transferred to the recovery room. Physical and complementary examinations were without particularity.

Post Operation

A discussion was held among the three anesthesiologists after their patients had been secured in the recovery room. Not knowing the origin of the problem, the operating program for the day was interrupted. The hypothesis of malignant hyperthermia was considered unlikely given the similarity of the problem and the absence of other pathognomonic signs of this metabolic disorder for the three patients. The fact that the soda lime granules quickly became saturated, proved that there had been a high concentration of CO_2 in the gas delivery system.

The similarity of the sequence of events after the introduction of N_2O in the respiratory system led to the hypothesis that the problem was due to a general gas supply problem. Having checked the proper connections of the wall outlets for medical gases, they concluded that the problem was external to the operating rooms. The biomedical department was quickly made aware of the incident.

A technician was sent to check the gas delivery system in the basement who was able to identify a CO_2 cylinder mistakenly connected on the N_2O manifold (Figure 1). The CO_2 cylinder appeared to have the same fitting as the N_2O cylinder.

Fig. 1 — CO_2 cylinder (grey shoulder) mistakenly connected to the N_2O manifold (N_2O cylinders with blue shoulders). Photo taken by the technician during his checkup of the gas delivery system. 1: CO_2 cylinder, 2: N_2O cylinders, 3: connection of the fitting on the thread, 4: connecting lines.

This explained the high $FiCO_2$ and the absence of inhaled N_2O when the gas was requested by the anesthesiologists. The alert was immediately given to the medical management team, who ordered the closure of the operating theatre. Contact was made with the hospital's medical gas supplier to understand how this incident could have occurred. The CO_2 cylinder was removed and a complete purge of the network and anesthetic equipment was carried out on the same day. An analysis was performed that evening to ensure the conformity and quality of the gas distributed so that the operating theaters could reopen the following day. The analysis showed full compliance.

The three patients were informed of the events that took place. The three anesthesiologists allowed the patients to go home at the end of the day, after close and prolonged monitoring in the recovery room, following this acute CO_2 poisoning.

Patients were advised to go to the emergency room if their state of health deteriorated. They were referred to their general practitioners within 24 to 48 hours for an overall reassessment.

Discussion

In this case study, we describe three simultaneous cases of acute and severe hypercapnia caused by the iatrogenic administration of CO_2, which was driven by improper gas supply. A technician accidentally connected a CO_2 cylinder on the N_2O manifold. Correct use of the recommended monitoring enabled hypercapnia to be identified and anesthesiologists to be quickly alerted to the problem. To our knowledge, this is the first case of the mistaken connection of a CO_2 cylinder on the N_2O manifold.

A multitude of gas supply errors can occur throughout the entire process of gas supply, spanning from the cylinders to the anesthesia machine[4,5,6]. Cylinder-related errors encompass mislabeling, inadequate gas supply and the inadvertent introduction of incorrect gases. Progressing along the gas supply chain, challenges may arise during the transfer of gases from the cylinders to the anesthesia machine, encompassing crossed pipelines, leaks, or suboptimal pressure. Subsequently, within the anesthesia machine itself, potential errors can stem from faulty flow meters or dysfunctional pressure regulators.

In our case, all these possibilities have been ruled out. The mistaken connection of the CO_2 cylinder on the N_2O manifold could occur because these cylinders had the same fittings.

The N_2O and CO_2 cylinders were connected at a distance from the operating room in the hospital's basement where anesthesiologists could not visually verify them. In the gas storage and distribution room, the cylinders are connected on the manifold via a connecting line ending in a fitting. The fitting is connected to the thread of the cylinder. The manifold is then connected to the hospital network (Figure 1). These cylinders have the same volume (50 liters) and pressure (50 bars). The colors of the gas cylinder shoulder (grey for CO_2 and blue for N_2O) comply with the European standard EN 1089-3[7]. However, with regard to cylinder fittings, each country in Europe has its own national standard for cylinder fittings and there is no standardized European standard for cylinder fittings. It should be noted that in Belgium, standard NBN 226 applies[8]. This standard dates from 1950 and has never been revised.

The fittings defined in the NBN 226 standard and used for CO_2 and NO_2 cylinders, regardless of the gas producer in Belgium, are the following:

- type B4 fitting = 21.700, pitch 1.814, R, EXT
- type B5 fitting = 21.800, pitch 1.814, R, EXT

Measurements taken at fittings B4 and B5 indicated that there is a difference of 0.2 millimeters in the internal diameter between these two fittings; 19.3 mm versus 19.5 mm respectively. Measurements taken at the thread of N_2O and CO_2 cylinders for a B4 fitting show that they have the same diameter and length.

It is therefore possible to connect a N_2O cylinder or a CO_2 cylinder via a B4 or a B5 connection on the manifold without forcing. This erroneous maneuver was tested in our center and showed high reproducibility. Thus, even if the two possible fittings are used for the different gasses within a facility, they are so similar that a mistaken connection is still possible.

The main gas companies that supply medical gases in Belgium, are Air Liquide, Messer, BTG and Strombeek. When contacted, they all responded that the type of connection used for these cylinders varied across gas companies (Table I).

When we examined the data, we noticed that all the gas suppliers in Belgium were consistent in their use of connections, either B4 or B5, for both their CO_2 and N_2O cylinders (Table I). In contrast, most European countries use the B4 or B5 fittings for CO_2 cylinders but not for N_2O cylinders, for which different fittings act as an added safety measure to ensure specific use.

Medical gas cylinders currently undergo rigorous testing and inspection to guarantee their safety and reliability[2]. Despite this human error is still possible and must be compensated for in procedure and built-in safety measures such as incompatible fittings. We recommend that the

Table I. — Fittings used for N_2O and CO_2 cylinders by the Belgian gas companies.

Gas suppliers in Belgium	Fittings for Nitrous oxide	Fittings for Carbon dioxide
Air Liquide	B4	B4
Messer	B5	B5
Strombeek	B5	B5
BTG	B4	B4

Belgian Society of Anesthesiology, Resuscitation, Perioperative Medicine and Pain-management (BeSARPP) requests a specific connection for N_2O to all medical gas suppliers in Belgium as is already the practice in most countries in Europe.

In the meantime, new procedures have been put in place within our hospital to avoid a similar incident:

- A specific training for the hospital technicians has been designed, informing on the dangers and specificities of each cylinder.
- A more visible identification, including a label on the wall and a matching color-coded marking on the ground (Figure 2).
- The process of changing cylinders now requires a double-check with the supervision of the hospital pharmacist.

Conclusions

Anesthesiologists are trained to work in an operating room and to manage incidents that occur during surgery with the implementation of automatic control systems, strict protocols, and decision trees. However, when faced with a situation outside the operating room, they step out of their routines, relying on their own experience, clinical judgment, and monitoring to manage such situations.

The event that we have described reminds us that anesthesiologists do not have total control over the flow of medical gases in operating theaters. Anesthesiologists using N_2O and CO_2 cylinders must be careful when requesting N_2O from the anesthesia machine. A concomitant rise in $FiCO_2$ and $EtCO_2$ should alert the practitioner of any technical issue.

Fig. 2 — A visible identification of the cylinders via clear labeling on the wall and via a color-coded marking on the ground.

Anesthesiologists should find out what measures are in place in their institutions and consider whether other measures can be introduced to minimize the risk of cylinder misconnection. The BeSARPP must support new standards to ensure the production of a specific connection for N_2O in Belgium.

Finally, this incident reminds us of the importance and the necessity of using a complete monitoring system for all procedures under general anesthesia.

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