EVALUATING THE EFFECTS OF HYPERCAPNIA ON RECOVERY TIME AND NAUSEA IN THE POST ANESTHESIA CARE UNIT

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Abstract—Hypercapnia is often used to accelerate emergence from general anesthesia in the operating room, but little is known about the postoperative effects that may carry over to recovery in the post anesthesia care unit. We have designed two studies to address this topic, one of which has been completed. The first study monitored 22 patients undergoing eye surgery who received general anesthesia using desflurane. During emergence, half of the patients were hypercapnic and ventilated at twice their minute volume. After the desflurane was turned off the hypercapnic group open their eyes on command 4.1±1.4 min later, while the control group took 6.5±2.3 min. The hypercapnic group was also able to state their first and last name, birthdate, and current year in 10.9±5.1 min; the control group took 18.2±9.7 min. In the PACU, several subjective measures including alertness, orientation, conversant, and an Aldrete score > 8 were used to access recovery. Hypercapnic patients fared better in all categories. They also experienced less nausea and received fewer doses of antiemetic. A second study has been designed to quantify more fully the results of the first study. Pending approval of the Institutional Review Board, 44 more patients will be monitored in a similar fashion except that expired gas levels and ventilation parameters will be recorded during recovery in the PACU.

INTRODUCTION

The cardiovascular and respiratory systems work in tandem to provide the necessary gas exchange for cellular metabolic activity throughout the body. The respiratory system exchanges O₂ and CO₂ between the atmosphere and blood; the circulatory system delivers the O₂ to cells throughout the body and transports CO₂, a byproduct of cellular respiration, from the cells back to the lungs. When the concentration of CO₂ in the blood fluctuates, the cardiovascular and respiration systems are adjusted to compensate. For example, if the arterial partial pressure of CO₂ (PₐCO₂) rises, the respiratory rate will increase and vaso-dilation will occur, increasing blood flow and gas exchange in the lungs in order to flush the body of excess CO₂. When PₐCO₂ is reduced, the opposite occurs. In the operating room (OR), this principle is frequently taken advantage of to aid patients during recovery from general anesthesia.

Induced hypercapnia, or elevated PₐCO₂, can be used to accelerate a patient’s recovery from anesthesia by washing anesthetic vapors from the body in the same way that excess CO₂ is removed[1], [2]. A device developed by our lab, called the QED-100 (Anecare, Salt Lake City, UT), accomplishes this task during the emergence phase of anesthesia in the OR[3]. The QED-100 incorporates a rebreathing reservoir to induce hypercapnia and a charcoal filter to soak up expelled anesthetic gases. Studies have shown that the QED-100 is capable of reducing emergence times by approximately 55%[3], [4], [5]. This result translates not only into a cost savings from time spent in the OR, but perhaps more importantly, it produces a patient that can enter the PACU with less anesthetic in their system and a stronger respiratory drive, which in turn could lead to a faster, safer, and more satisfactory recovery.

Studies have shown that of 42,000 patients monitored, 23–24% experienced complications in the PACU, while only 3.8–5.1% encountered difficulties in the operating room[6], [7], [8]. One of the reasons for this is that as a patient becomes more alert in the PACU, a greater awareness of pain is attained, often resulting in the administration of additional analgesics, which can react synergistically with trace amounts of anesthetic still in the patient’s system and induce any number of adverse clinical events, including difficulties breathing and even loss of consciousness. If a patient enters the PACU with less anesthetic in their system, the probability of encountering complications may decrease.

Although the effects of using hypercapnia during emergence from anesthesia have been well established, little is known about the effects that may carry over into the PACU. We have designed two studies to address this topic, one of which has been completed. In the first study we hypothesized that a hypercapnic patient, entering the PACU with less anesthetic in their system and a stronger respiration drive, would progress through the phases of recovery faster, experience less nausea, and require fewer rescue antiemetics.

Owing to the success of the first study we wish to perform a second study that further quantifies the results.
of the first. The principle difference will be that the patient’s CO₂, O₂, and anesthetic gas levels as well as tidal volume and respiratory rate will be recorded during recovery in the PACU. We hope this data can be used to create a numerical model that can give further insight into how hypercapnia benefits a patient during recovery.

**STUDY 1**

**Methods**

Following Institutional Review Board (IRB) approval, written informed consent was obtained from 22 ASA class I-III patients of both genders scheduled to undergo eye surgery at the John A. Moran Eye Center. Exclusion criteria included a history of renal or hepatic disease, chronic alcohol or drug abuse, disabling neuropsychiatric disorder, hypersensitivity or unusual response to other halogenated anesthetics, pulmonary hypertension, increased intracranial pressure, seizure disorder or personal/familial history of malignant hyperthermia.

Patients were premedicated with fentanyl and then induced with a remifentanil infusion and a lidocaine, propofol, and rocuronium or succinylcholine bolus at the anesthesiologists discretion followed by tracheal intubation. Anesthesia was maintained at 6% desflurane along with a remifentanil infusion, although clinician’s could deviate and titrate remifentanil and fentanyl as needed during periods of increased stimulus. O₂ flow was maintained at 2 L/min, blood pressure within ±20% of baseline, and EtCO₂ at 35 mmHg (by adjusting ventilation). Ondansetron 4mg was given prophylactically before the end of surgery.

Near the end of surgery, a sealed envelope was opened that randomly assigned the patient to either the control or treatment group—opening the envelope at this point prevented any bias during induction and maintenance of anesthesia on behalf of the attending clinician. At the end of surgery, the remifentanil infusion and desflurane were turned off and both groups were given O₂ at 10 L/min. For the treatment group, a QED-100 was placed between the endotracheal tube and breathing circuit and switched on to induce mild hypercapnia. At the same time, minute volume was doubled by doubling the respiratory rate and adjusting tidal volume as needed. No changes were made to the control group.

Every 30 seconds during emergence the study investigator asked the patient to open their eyes by verbal command and gentle prodding. The time from when anesthesia was turned off until the patient was able to complete the task was noted.

In the PACU, a second study nurse, who was blinded to which study group the patient was assigned, monitored and noted the patient’s progress during the first 60 minutes of recovery. Every five minutes the study nurse assessed whether the patient was alert, conversant, and in pain. The patient was considered alert if they responded to their name being called and conversant if they volunteered information. Pain was assessed on a scale from 0-10. If the patient’s actual pain score exceeded their tolerable pain score, fentanyl was administered at the discretion of the PACU nurse in increments ranging from 25-150 mcg. Every ten minutes the study nurse assessed orientation, Aldrete score[9], and nausea. The patient was considered oriented if they could state their first and last name, birthdate, and current year. Questioning was stopped after two consecutive correct answers. Nausea was ranked as either none, mild, or moderate. The patient was given antiemetics if the nausea persisted or increased through two assessments and at the discretion of the PACU nurse.

**Results**

Twenty-two patients were enrolled in this study who underwent either eye muscle surgery, intraocular lens implantation, or resection of eye lesions. Patient demographics are shown in Table I. All patients were premedicated with 1.1±0.4 mcg/kg of fentanyl and induced with 2.5±0.6 mg/kg of propofol. Drug dosing during maintenance of anesthesia is listed in Table II.

At the end of surgery, the PₐCO₂ for the hypercapnic group was 34.4±2.3 mmHg, for the control group it was 35.1±1.5 mmHg; at extubation their PₐCO₂ was 36.1±6.5 and 48.1±3.8 mmHg (Table I) respectively (note that n=6 for the hypercapnic group at extubation because the CO₂ sampling tube was misplaced).

Figure 1 shows the times to awake and oriented. The time to awake (when the patient opened their eyes on command) for the hypercapnic group was 4.1±1.4 min, the control group took 6.5±2.3 min. Time to oriented (when the patient could state their first and last name, birth date, and current year) was 10.9±5.1 min for the hypercapnic group and 18.2±9.7 min for the control group. A Student t-test revealed p-values of 0.009 and 0.039 for awake and oriented respectively. A Bonferroni correction showed that the differences for both are statistically significant.

Figure 2 shows the times to reach the various phases of recovery. The top two plots, awake and oriented, were already discussed in Figure 1. Alert, conversant, and Aldrete > 8 were inherently subjective measurements made by the blinded PACU study nurse, and as such, were not included in the statistical analysis. The extubation measurement was also excluded because the attending
Fig. 1. The survival curve on the left shows the time from when anesthesia was discontinued until patients opened their eyes on verbal command. The survival curve on the right shows how long the patients took to state their first and last name, birth date, and current year after anesthesia was turned off. In both curves, the dark line represents the hypercapnic group, the gray represents the control group.

Fig. 2. Times to reach the various phases of recovery after desflurane anesthesia. The hypercapnic group is represented by the dark filled boxes, the control group by the open boxes. P-values were less than 0.05 for all phases except for Aldrete > 8.
TABLE I
PATIENT DEMOGRAPHICS: MEAN±STANDARD DEVIATION (MEDIAN)

<table>
<thead>
<tr>
<th>Group</th>
<th>Gender (F/M)</th>
<th>Weight (kg)</th>
<th>Age (yrs)</th>
<th>Duration of Surgery (min)</th>
<th>( P_{\text{ET}} CO_2 ) at End of Surgery (mmHg)</th>
<th>( P_{\text{ET}} CO_2 ) at Extubation (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=11)</td>
<td>7/4</td>
<td>73.3±20.0 (64.6)</td>
<td>40.4±15.0 (40)</td>
<td>52±30 (43)</td>
<td>35.1±1.5 (35.4)</td>
<td>36.1±6.5 (36.7)</td>
</tr>
<tr>
<td>Treatment (n=11)</td>
<td>6/5</td>
<td>75.8±13.0 (77.0)</td>
<td>43.7±15.1 (42)</td>
<td>90±63 (73)</td>
<td>34.4±2.3 (34.1)</td>
<td>48.1±3.8 (48.1)</td>
</tr>
</tbody>
</table>

†Surgery for one patient in the treatment group lasted 4 hours.
‡n=6 because the sampling tube was misplaced in 5 of the cases.

TABLE II
PERIOPERATIVE AND POSTOPERATIVE DRUG DOSING FOR THE TREATMENT AND CONTROL GROUPS.

<table>
<thead>
<tr>
<th>Group</th>
<th>Desflurane MAC-hrs ± (mg)</th>
<th>Average MAC at End of Surgery (mg)</th>
<th>Propofol Infusion Rates (mcg/kg/min)</th>
<th>Remifentanil Infusion Rates (mcg/kg/min)</th>
<th>Fentanyl Infusion Rates (mcg/kg/min)</th>
<th>Fentanyl in PACU (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=11)</td>
<td>0.82±0.46 (0.76)</td>
<td>0.80±0.07 (0.81)</td>
<td>0.77±0.16 (0.81)</td>
<td>2.36±0.92 (2.0)</td>
<td>0.095±0.035 (0.10)</td>
<td>50.0±76.6 ( )</td>
</tr>
<tr>
<td>Treatment (n=11)</td>
<td>1.46±1.02 (1.22)</td>
<td>0.81±0.08 (0.85)</td>
<td>0.78±0.11 (0.82)</td>
<td>2.82±1.25 (2.0)</td>
<td>0.11±0.016 (0.10)</td>
<td>25.0±33.0 ( )</td>
</tr>
</tbody>
</table>

The nausea experienced by the patients in the PACU is shown in Figure 3. The top charts show the duration of the nausea and the severity as reported by the patients. The patients have been ranked according to severity and duration of nausea. Six control patients reported nausea, only one of them vomited; three hypercapnic patients reported mild nausea. The dark gray bars represent moderate nausea while the light gray represent mild nausea. The bottom charts show the corresponding doses of antiemetic given to the patients in the top charts. Six of the control patients received antiemetics in the OR, only one in the hypercapnic group received a single dose. It should be noted that patient 3 in the control group and patient 1 in the hypercapnic group experienced severe pain and the PACU nurse chose to treat the pain and nausea with fentanyl rather than antiemetics. Also patient 8 in the control group received ondansetron 4 mg upon standing just before discharge from the PACU.

Discussion

When patients were hyperventilated and hypercapnic during the emergence phase of anesthesia they woke up 2.4 min sooner than the control group—a 37% decrease in wake up time. This result follows what was seen in a previous study where hyperventilation and hypercapnia shortened emergence time by 64%[2]. The differing result between these studies may be attributed to the fact that hypercapnic patients in the other study reached a \( P_{\text{ET}} CO_2 \) of 58 mmHg whereas the patients in this study only reached 48 mmHg. Ito et al. has shown that hypercapnia can increase cerebral blood flow by as much as 6% per mmHg increase in \( P_{\text{ET}} CO_2 \)[10]. This means that the cleansing effect that cerebral blood flow provides was not available to the same degree for these patients as those in the other study. Also, the remifentanil infusion was turned off 10 min before the desflurane was discontinued in the other study; in our study they were both turned off at the end of surgery. The remifentanil still present in the the patient’s system and the possibility that it reacted with desflurane may have increased the emergence time in this study.

In the PACU, however, the effects of hypercapnia and hyperventilation seem to have carried over from the OR since treated patients, in general, reached each stage of recovery sooner than the control group. Hypercapnic patients also experienced less nausea and required fewer rescue antiemetics.

Two mechanisms are responsible for the decrease in emergence and recovery time: increased cerebral blood flow, caused by increased \( P_{\text{ET}} CO_2 \) hypercapnia; and increased ventilation, which removes anesthetic quickly from the lungs, decreasing the alveolar concentration and increasing the concentration gradient between arterial blood and brain tissue[10], [11], [12]. A patient with lower anesthetic levels and increased ventilation drive due to hypercapnia may have faired better in the PACU because they were more awake, oriented, and able to
interact with PACU nurses in addressing their needs.

It has been hypothesized that “high inspired-oxygen concentrations may counter the tissue hypoxia resulting from surgical manipulation, thereby preventing serotonin release,” which is believed to be one of the factors affecting the nausea and vomiting centers in the nervous system—especially during abdominal surgery[13]. Greif et al. found that patients undergoing colon resection who received 80% inspired oxygen during surgery and 2 hours postoperatively and no prophylactic antiemetics experienced twice the reduction in postoperative nausea and vomiting compared to those that received only 30% inspired oxygen[14]. Fleischmann et al. and Ratnaraj et al. both have shown that hypercapnia with high concentrations of inspired oxygen aid in subcutaneous, colonic, and intestinal oxygenation[15], [16]. The reduction of nausea and vomiting seen in this study may be the result of a similar phenomenon where hypercapnia and high concentrations of inspired oxygen provide adequate oxygenation to the tissues being manipulated during surgery so as to suppress the release of serotonin that occurs when tissue becomes hypoxic. Future studies could verify the link between oxygenation and nausea in patients undergoing eye surgery since this type of surgery is known to produce a high frequency of nausea and vomiting.

STUDY 2

Methods

Pending IRB approval, written informed consent will be obtained from 44 ASA class I-III patients scheduled to undergo eye muscle surgery at the John A. Moran Eye Center. A similar protocol to the previous study will be followed with just a couple of exceptions: a more stringent protocol as to the administration of antiemetics will be used and ondansetron 4mg will be the preferred rescue antiemetic. Additionally, CO₂, O₂, and anesthetic levels as well as tidal volume and respiratory
rate will be recorded in the PACU during the first 30 min of recovery. Two monitors will be used: the Capnomac Ultima (Datex, Helsinki, Finland) and Respitrace Calibrator (Ambulatory Monitoring, Inc., Ardsley, NY). The Capnomac Ultima is capable of measuring five parameters. However, to obtain accurate volume measurements, the patient must wear a tight fitting mask, and unfortunately many patients are irritated by even the loose fitting oxygen mask presently used in the PACU. Also, supplemental oxygen will most likely be given to the patient during this process, which will interfere with the tidal volume measurements. The Respitrace monitor provides an alternative approach to measuring tidal volumes.

The Respitrace monitor provides a method of measuring tidal volume and respiratory rate without using a mask. It measures the expansion of the chest and abdomen due to breathing using impedance readings from special elastic bands placed around the patient. The impedance reading can then be calibrated to produce volumetric information. With this configuration the tidal volume and minute volume will be measured using the Respitrace monitor, and CO₂, O₂, and anesthetic levels will be measured using the Capnomac Ultima through a nasal cannula.

Custom software has been developed to integrate the two monitors into one system that will sample and record relevant information from both monitors simultaneously. Both monitors have analog outputs that can be sampled using the USB-1208LS analog-to-digital converter (Measurement Computing, Middleboro, MA). To calibrate the Respitrace, the patient must breath into a mouth piece for 15 seconds so that flow data can be recorded using the Capnomac Ultima.

Once the initial calibration is made, data will be gathered for the first 30 min the patient spends in the PACU. Recalibration will occur every 5 minutes since the calibration can altered if the patient moves too much. This will also provide at least 5 direct measurements of gas volumes and concentrations in case the nasal cannula or elastic bands fail to record accurately.

CONCLUSIONS

Hypercapnia after anesthesia with desflurane does reduce emergence time, and the effects of hypercapnia carry over to the PACU where a patient seems to pass through the phases of recovery sooner with less nausea.

Our upcoming study will further quantify the prolonged effects of a hypercapnic emergence. The data collected in the PACU regarding a patient’s respiratory parameters will be of great interest since little has been published concerning this aspect of recovery.

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REFERENCES