Arterial to end-tidal CO₂ gradient reversal during laparoscopic pheochromocytoma resection

[Le renversement du gradient du CO₂ artériel/télé-expiratoire pendant la résection laparoscopique d'un phéochromocytome]

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Purpose: We report the development of severe intraoperative hypercarbia and a pronounced arterial to end-tidal gradient reversal during laparoscopic pheochromocytoma resection. Although complex physiologic mechanisms may be responsible for this finding, anatomic alterations such as a direct communication between a capnoperitoneum and/or capnothorax and the airways resulting from prior pathology and the type of procedure should also be considered.

Clinical features: During anesthesia for laparoscopic pheochromocytoma removal we noticed an abrupt, extensive increase of the end-tidal CO₂ accompanied by a change of the capnographic CO₂ tracing and reversal of the normal arterial-to-end-tidal gradient. These changes consistently disappeared by intermittent deflation of the abdomen and at the end of surgery. A chest x-ray revealed a right-sided loculated pneumothorax with pleural thickening. Peritoneo-thoracic CO₂ tracking and pleural scaring with pulmonary adhesions resulting in a unidirectional communication between the pleural space and airways may best explain the chest x-ray and clinical findings.

Conclusion: Severe intraoperative hypercarbia and arterial to end-tidal CO₂ gradient reversal represents an intraoperative challenge. The possibility of a direct communication between the pleural space and the bronchial tree should be considered when other etiologies have been excluded. Simple maneuvers such as abdominal de- and re-inflation and analysis of the end-tidal capnographic tracing might aid in the differential diagnosis and management.

Objectif: Présenter le développement d'une hypercapnie peropératoire sévère et d'un renversement prononcé du gradient artériel/télé-expiratoire pendant la résection laparoscopique d'un phéochromocytome. Bien que des mécanismes physiologiques complexes puissent être responsables de cette situation, des modifications anatomiques comme une communication directe entre un capnopéritoine et/ou un capnothorax et les voies aériennes, résultant d'une pathologie antérieure et du type d'opération, doivent être également considérées.

Éléments cliniques: Pendant l'anesthésie pour la résection laparoscopique du phéochromocytome, nous avons noté une augmentation abrupte et importante du CO₂ télé-expiratoire accompagnée de changement du tracé du CO₂ capnographique et du renversement du gradient artériel/télé-expiratoire normal. Ces changements ont disparus avec l'affaissement intermittent de l'abdomen et à la fin de l'opération. Une radiographie thoracique a révélé un pneumothorax loculé au côté droit avec un épaississement pleural. Une fistule péritonéo-thoracique pour le CO₂ et la création d'une communication unidirectionnelle entre l'espace pleural et les voies aériennes (secondaires à des cicatrices pleurales et des adhérences) expliquent mieux cette image radiologique et les trouvailles cliniques.

Conclusion: L'hypercapnie peropératoire sévère et le renversement du gradient du CO₂ artériel/ télé-expiratoire représentent un défi peropératoire. La possibilité d'une communication directe entre l'espace pleural et l'arbre bronchique doit être considérée quand d'autres causes ont été exclues. Des manœuvres simples comme l'affaissement et le regonflement abdominal et l'analyse du tracé capnographique télé-expiratoire peuvent aider au diagnostic différentiel et au traitement.

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A modest increase in end-tidal carbon dioxide is expected during laparoscopic surgery employing carbon dioxide for peritoneal insufflation. Adjustments to the controlled ventilation during general anesthesia often suffice to maintain normocarbica and a reversal of the arterial to end-tidal carbon dioxide gradient is uncommon. However, a limited, uncomplicated reversal of this gradient has been reported during Cesarean section, gynecologic, cardiac and neurosurgical procedures.¹⁻⁴ We describe a case of extreme end-tidal carbon dioxide elevation with extensive arterial to alveolar gradient reversal during laparoscopic surgery despite controlled hyperventilation. Pertinent aspects of carbon dioxide physiology and possible explanations are discussed.

Case

Following approval of the Institutional Review Board we examined and interpreted the data presented below.

A 72 kg, 5' 4", 65-yr-old woman presented for laparoscopic resection of a right adrenal pheochromocytoma. She had a history of hyperparathyroidism, and never smoked. The preoperative medical preparation consisted of daily prazosin 24 mg and metyrosine 1.5 g *po* for three weeks.

Following left radial artery catheterization on the day of surgery, a blood gas analysis (ABG) on room air revealed: pH 7.49, $P_a\text{CO}_2$ 42 mmHg, $P_a\text{O}_2$ 94 mmHg, bicarbonate 32 mmol·L⁻¹. In the operating room invasive and non-invasive blood pressure, oxygen saturation (SpO_2), and electrocardiographic monitors were attached to the patient. An uneventful induction of general anesthesia was achieved with the administration of lidocaine 40 mg *iv*, propofol 130 mg, sufentanyl 25 µg and rocuronium 80 mg. Following endotracheal intubation, the lungs were ventilated volume controlled with a tidal volume of 625 mL, a respiratory rate of 8 breaths·min⁻¹ and an FiO_2 of 0.4. The peak inspiratory pressure (PIP) was 18 cm H₂O and the end-tidal carbon dioxide ($P_{\text{ET}}\text{CO}_2$) was 34 mmHg. A right internal jugular central venous line was inserted prior to surgical incision. Anesthesia was maintained with isoflurane in oxygen and air with an FiO_2 of 0.45, and a continuous sufentanyl infusion of 0.1 µg·kg⁻¹·hr⁻¹. Neuromuscular block was maintained with intermittent *iv* boluses of rocuronium guided by train-of-four monitoring. Vasoactive short acting *iv* medications were prepared and readily available should hemodynamic instability ensue.

Prior to peritoneal CO₂ insufflation to a target pressure of 15 mmHg, the $P_{\text{ET}}\text{CO}_2$ was 33 mmHg and an ABG showed a $P_a\text{CO}_2$ of 35 mmHg. The PIP and the

$P_{\text{ET}}\text{CO}_2$ increased to 28 and 38 mmHg respectively. Dense adhesions in the right upper quadrant required extensive surgical adhesiolysis to separate the liver from the diaphragm. No diaphragmatic injury was apparent. Thirty-five minutes into the case, a sudden increase of the $P_{\text{ET}}\text{CO}_2$ was noted on the capnograph (model M1026A, Philips, Boeblingen, Germany) to values greater than 70 mmHg accompanied by a change in the shape of the capnograph tracing. The previous end-expiratory (alveolar) plateau was replaced by a very steep and irregular CO₂ pattern, and each expiration differed from the previous one. The PIP increased from 28 to 30 mmHg. The surgeon was notified, and manual hyperventilation was begun with an FiO_2 of 1.0. During this episode, the patient was hemodynamically stable, and no desaturation occurred. Chest wall *sc* emphysema as an indication of extensive CO₂ tracking was absent at this time, bilateral ventilation was confirmed by auscultation to exclude the possibility of a pneumothorax, and there was no new heart murmur suggestive of a CO₂ embolism. The CO₂ absorber was exchanged to exclude absorber exhaustion as a cause of the observation. Rebreathing was excluded by an unrevealing examination of the anesthesia circuit, the in- and expiratory ventilator valves and the expiratory gas sample tubing. The ABG values at this time were not suggestive of a possible malignant hyperthermia episode: pH 7.45, $P_a\text{CO}_2$ 39.3 mmHg, $P_a\text{O}_2$ 219 mmHg and bicarbonate 27.8 mmol·L.

Mechanical ventilation was adjusted by increasing the respiratory rate to 12 breaths·min⁻¹. The capnograph subsequently displayed a question mark in lieu of a numerical $P_{\text{ET}}\text{CO}_2$ value and was replaced by a Datex-Ohmeda gas analyzer (model 525, Ultima, Helsinki, Finland) suspecting monitor malfunction. The new monitor briefly revealed $P_{\text{ET}}\text{CO}_2$ values between 100 to 115 mmHg. No significant inspiratory CO₂ was detected. The minute ventilation was re-adjusted, and a positive end-expiratory pressure of 5 cm H₂O was added, resulting in an increase of the PIP to 34 cm H₂O. Curiously, with each removal of a laparoscopic instrument and subsequent desufflation of the peritoneum, a sharp decline of the $P_{\text{ET}}\text{CO}_2$ and normalization of the capnographic $P_{\text{ET}}\text{CO}_2$ tracing was observed. The Table summarizes intraoperative $P_{\text{ET}}\text{CO}_2$ and $P_a\text{CO}_2$ values. We attributed abrupt intraoperative bidirectional hemodynamic fluctuations to tumour manipulation rather than hypercarbia, because of the poor correlation in the timing of their respective occurrence. Sixty minutes following the initial event, hypercarbia resulted in acute respiratory acidosis (pH to 7.27) which improved by adjusting the ventilation (pH 7.31). A chest *x-ray* at the completion of

surgery, following extubation in the operating room, showed a loculated pneumothorax at the right lateral costophrenic angle with pleural thickening. At this time, right shoulder *sc* emphysema was also detected. A follow-up chest *x-ray* four hours later demonstrated resolution of both findings, and the patient recovered uneventfully.

Discussion

In an ideal lung, end-capillary and alveolar P_aCO_2 are in equilibrium. However, even in normal individuals ventilation-perfusion (V/Q) mismatch contributes to a positive gradient of 2 to 5 mmHg between P_aCO_2 and $P_{ET}CO_2$. Smoking, age and pulmonary disease alter the V/Q ratio,⁵⁻⁸ which is the principal pulmonary determinant of the gradient. Increasing dead space ventilation with increasing age or in patients with emphysema, hypotension, hypovolemia and/or low cardiac output will increase the ratio, and hence the gradient. During positive pressure ventilation the alveolar dead space and the arterial to end-tidal CO_2 gradient decrease with increasing tidal volume and a low respiratory rate, because of a more even gas distribution and improved ventilation of slow units.⁷ Although the gradient is also affected by cardiac output and index,⁸ a gradient reversal due to cardiac output or index abnormalities has not been described.

We report an unexpected and sudden increase in $P_{ET}CO_2$, an associated change of the capnographic $P_{ET}CO_2$ waveform, and the reversal of the P_aCO_2 to $P_{ET}CO_2$ gradient during laparoscopic adrenalectomy for pheochromocytoma. During laparoscopy in healthy subjects, the CO_2 gradient either remains unchanged or may increase,^{9,10} with an exaggerated response in the presence of cardiopulmonary disease.¹¹ The differential diagnosis of sudden intraoperative hypercarbia including *sc* emphysema absorption, pneumothorax, CO_2 embolus, malfunction of the ventilator, circuit or capnograph, as well as CO_2 absorber exhaustion were systematically ruled out. In retrospect, additional information from an intraoperative chest *x-ray* may have been helpful. However, this would have been difficult to obtain and interpret in a patient in the semi-lateral position with "bean bag" support. The initial expected positive gradient in our patient was found to be reversed following detection of an abrupt increase of $P_{ET}CO_2$, and remained highly negative even after adjustments of the ventilation.

Subcutaneous emphysema and pneumothorax are well-recognized complications of pneumoperitoneum^{12,13} and extraperitoneal laparoscopic surgery. Both are more common when the procedure is close to the diaphragm,¹³ as during an adrenalectomy or fundoplication,

FIGURE End-tidal CO_2 trace following lung puncture during transthoracic endoscopic sympathectomy as described by Olsfanger *et al.*¹⁵ (used with permission). During CO_2 insufflation, the end-tidal CO_2 increases beyond normal limits in an irregular pattern (1) and does not return to zero during ventilation (2,3). This pattern most closely resembles our intraoperative observation.

and *sc* emphysema may be exacerbated by retroperitoneal CO_2 insufflation.¹⁰ Carbon dioxide may enter the pleural cavity or *sc* tissue via congenital or acquired defects in the diaphragm^{12,13} or via free spread within the retroperitoneal space. Injury to the falciform ligament may also be implicated.¹³ Extensive adhesiolysis to mobilize the liver in our patient could have caused diaphragmatic as well as falciform ligament injury. Intraoperatively we did not detect any signs of pneumothorax or *sc* emphysema, but severe hypercarbia instead. The PIP changed minimally, air entry was bilateral and equal, and the oxygen saturation was maintained.

Carbon dioxide embolization is a possible but rare complication of laparoscopy. The classic presentation includes an abrupt reduction of $P_{ET}CO_2$, hypotension, cyanosis, arrhythmia or asystole and possibly a mill wheel murmur.^{12,13} However, there are reports of CO_2 embolization with a modest increase, rather than decrease of the $P_{ET}CO_2$.^{12,13} We did not detect any new cardiac murmur or sudden hemodynamic instability during the procedure.

A direct communication between the peritoneal cavity and the broncho-alveolar tree via thoracic tracking of CO_2 as a cause for our observation is supported by the abnormal capnographic waveform, and the sudden reversal of the P_aCO_2 to $P_{ET}CO_2$ gradient. Termination of peritoneal CO_2 insufflation should result in a linear decline of $P_{ET}CO_2$ over time.¹⁴ In our patient however, intermittent abdominal port release and finally removal at the end of surgery resulted in an abrupt decrease of the capnographic $P_{ET}CO_2$ values, normalization of the waveform and a positive arterial to end-tidal CO_2 gradient. This suggests an unusual ball-valve mechanism for direct CO_2 entry into the airways. Pleural thickening and a loculated pneumothorax at the right lateral costophrenic on the postoperative chest *x-ray* suggest prior pleuro-pulmonary

TABLE Measured arterial partial pressure of carbon dioxide ($P_a\text{CO}_2$) and end-tidal partial pressure of carbon-dioxide ($P_{ET}\text{CO}_2$) values and their gradient during laparoscopic pheochromocytoma removal with corresponding arterial pH values

Time	$P_a\text{CO}_2$ (mmHg)	$P_{ET}\text{CO}_2$ (mmHg)	$P_a\text{CO}_2 - P_{ET}\text{CO}_2$ (mmHg)	pH _a
9:55 (5 min prior to incision)	35	33	+ 2	7.52
10:41 (time of initial observation)	39.3	> 70	> - 30	7.46
10:55	56	78	- 22	7.36
11:15	67.6	88	- 20.4	7.30
11:50	66.3	86	- 13.7	7.27
13:05 (port removal & end of surgery)	59.3	49	+ 10.3	7.31

disease with subsequent scarring, which may explain such a mechanism in our patient. We believe that peritoneo-thoracic CO_2 tracking resulted in sudden unidirectional opening of this valve-like pleural pathology, each time a certain laparoscopic threshold pressure was surpassed. Two reports describe direct CO_2 entry from the pleural cavity into the bronchial tree during transthoracic endoscopic surgery using CO_2 insufflation.^{15,16} Olsfanger *et al.*¹⁵ reported a capnographic waveform resulting from an intraoperative lung puncture that was very similar to our observation: no distinct expiratory upstroke and plateau phase, and each expiration differed from the previous one (Figure). Although not present during the initial intraoperative exam, a *sc* emphysema was revealed postoperatively. It may take time for such a finding to develop, and repeated examination may be necessary to detect it. Its presence suggests extensive CO_2 tracking and absorption, contributing to the large, unphysiologic positive CO_2 gradient from CO_2 reabsorption and mobilization at the end of surgery (Table).

This case also illustrates the technical limitation of a capnograph monitor when $P_{ET}\text{CO}_2$ values exceed 76 mmHg. The display of a question mark instead of a numerical value may indicate excessive $P_{ET}\text{CO}_2$.

In conclusion, this case describes the possibility of a significant intraoperative CO_2 gradient reversal in the setting of hypercarbia during laparoscopic surgery when certain anatomical alterations are present. Such an event poses an intraoperative challenge, and is difficult to interpret. Close collaboration with the surgical team facilitates patient management and establishment of a differential diagnosis.

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