Laboratory Investigations

Venous gas embolism – a comparison of carbon dioxide and helium in pigs

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Purpose: The use of helium for insufflation during laparoscopic surgery avoids hypercarbia and acidosis associated with absorbed CO₂, but the effects of helium gas embolism are unknown. We compared the effects of CO₂ with He gas embolism on survival, haemodynamic variables, oxygenation, and ventilation in pigs.

Methods: Anaesthetized juvenile pigs were given progressively larger boluses of either CO₂ (n=5) or He (n=4) into the right atrium. Measurements of haemodynamic variables, oxygenation, and P_{ET}CO₂ were made before and after each gas injection.

Results: All animals survived injections of 300 ml CO₂ while no animal survived more than 120 ml He (P < 0.01). Mean arterial pressure decreased more after 60 ml He (99 ± 14 to 44 ± 20 mmHg) than after 60 ml CO₂ (110 ± 12 to 88 ± 14 mmHg, P < 0.001). Cardiac output did not change at any injection volume. The P_{ET}CO₂ decreased more after 60 ml He (30 ± 2 to 3 ± 6 mmHg) than after 60 ml CO₂ (35 ± 3 to 30 ± 3 mmHg, P < 0.001). Only the He group showed a decrease in PaO₂ (190 ± 51 to 68 ± 22 mmHg at 60 ml, P < 0.05).

Conclusion: Helium gas embolism has a greater deleterious effect than CO₂ gas embolism on survival, MAP, P_{ET}CO₂, and PaO₂. These different effects of gas embolism should be recognized when considering the use of helium or other insoluble gases for abdominal laparoscopic insufflation.

Objectif : Pendant la chirurgie laparoscopique, l'insufflation d'hélium permet d'éviter l'hypercarbie et l'acidose consécutives à l'absorption du CO₂. Nous ignorons toutefois les effets de l'embolie gazeuse à l'hélium. Nous avons comparé chez des cochons les effets de l'embolie au CO₂ à ceux de l'embolie à l'hélium sur la survie, les variables hémodynamiques, l'oxygénation et la ventilation.

Méthodes : Des cochons juvéniles anesthésiés ont reçu des bolus progressifs de CO₂ (n=5) ou d'hélium (n=4) dans l'oreillette droite. Les variables hémodynamiques, l'oxygénation et la P_{ET}CO₂ ont été mesurées avant et après chaque injection de gaz.

Résultats : Tous les animaux ont survécu à l'injection de 300 ml de CO₂ alors qu'aucun n'a survécu à des injections de 120 ml d'He et plus (P < 0,01). La pression artérielle moyenne s'abaissait plus après 60 ml d'He (99 ± 14 à 44 ± 20 mmHg) qu'après 60 ml de CO₂ (110 ± 12 à 88 ± 14 mmHg, P < 0,001). Le débit cardiaque ne changeait pas quel que soit le volume injecté. La P_{ET}CO₂ diminuait plus après 60 ml d'He (30 ± 2 à 3 ± 6 mmHg) qu'après 60 ml de CO₂ (35 ± 3 à 30 ± 3 mmHg, P < 0,001). Seul le groupe He a subi une chute de la PaO₂ (190 ± 52 à 68 ± 22 mmHg à 60 ml, P < 0,05).

Conclusion : L'embolie gazeuse à l'He a des effets plus nocifs que l'embolie au CO₂ sur la survie, la PAM, la P_{ET}CO₂ et la PaO₂. Il faut tenir compte de cette différence si on considère utiliser l'hélium ou tout autre gaz insoluble pour l'insufflation abdominale pendant la laparoscopie.

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VISUALIZATION during laparoscopic surgery depends on separation of the anterior abdominal wall from intra-abdominal viscera. Although mechanical retractors have been advocated for this purpose, intra-peritoneal gas insufflation is the most common method used to aid visualisation. Of the potential gases available for insufflation, CO₂, N₂O and He have been advocated. Carbon dioxide is most commonly used because of its low cost, non-flammability, and high blood solubility which allows for rapid blood absorption and lung excretion. However, absorption of CO₂ can result in hypercarbia with respiratory acidosis particularly in patients who have pre-existing pulmonary disease or increased dead space (obese, elderly, chronic obstructive pulmonary disease).¹ Nitrous oxide insufflation can be used for diagnosis only and not for surgery due to its flammability. Mechanical retractors are also useful but have not yet become widespread due to cost and poor visualisation for many procedures. Recently, the use of inert gases such as helium and argon has been suggested to eliminate the effect of CO₂ absorption from insufflation.^{2,3} However, the use of He, or other gases with low solubility, may alter the physiological effects of gas embolization.

Gas embolization is a potentially lethal complication of intra-abdominal insufflation. Carbon dioxide gas embolism during laparoscopic surgery has been reported to cause haemodynamic compromise.^{4,5} The incidence of gas embolism during laparoscopic surgical procedures is not well documented. In one report of 113,253 laparoscopies there were 15 patients who had clinically relevant CO₂ embolism, yielding a rate of 0.01%.⁶ In contrast, CO₂ embolism has been detected in 69%⁷ to 100%⁸ of patients during laparoscopic cholecystectomy by transoesophageal echocardiography. While this degree of CO₂ embolization was asymptomatic,^{7,8} the physiological effects of helium embolism have not been described. If the effects of helium are more severe than those of CO₂ embolism then the incidence of clinically relevant embolism could increase when He is used for intra-abdominal insufflation.

In a porcine model of gas embolism, we asked: 1) Is there a difference in survival between pigs suffering gas embolism with CO₂ vs He? 2) Are there differences in haemodynamic variables, oxygenation, and ventilation between animals embolized with CO₂ or He?

Methods

The protocol was approved for study by the Animal Care Committee of the University of British Columbia and conforms to NIH standards for animal experiments.

Instrumentation and preparation

Nine juvenile pigs (25–35 kg) were fasted overnight and premedicated with 0.5 mg lorazepam *im* on the morning of the experiment. Anaesthesia was induced with 500 mg ketamine *im* and 250 mg sodium thiopentone *iv*. Tracheostomy was performed and the lungs were ventilated at a minute ventilation adjusted to maintain PaCO₂ at 35–45 mmHg (Harvard ventilator). Anaesthesia was maintained with isoflurane (0.75%), air/oxygen (FiO₂=0.50), 125 mg·hr⁻¹ ketamine *iv*, 2.5 mg·hr⁻¹ pancuronium bromide *iv* and an infusion of 0.9% NaCl (15 ml·kg⁻¹·hr⁻¹). Arterial, central venous, and pulmonary artery catheters were placed by cut-down in the neck. A 7.5F venous catheter was placed via the right internal jugular vein with the catheter tip just above the right atrium. Correct position was confirmed by fluoroscopy. Carbon dioxide or He gas was delivered via this catheter with a number of syringes arranged in series of increasing volume, and connected to a gas cylinder of either CO₂ or He. A precordial phonocardiograph microphone confirmed the presence of intracardiac gas (Versatone, Meda Sonics, 340 Pioneer Way, Mountain View CA, 94042). A foley catheter was placed in the bladder.

Measurements

Mean arterial pressure (MAP), central venous pressure (CVP), and pulmonary artery pressure (PAP) were recorded continuously (DIREC Physiologic Recording System, Fine Science Tools Inc., Vancouver, B.C.). Pressure transducers were calibrated at the start of each experiment. Cardiac output (CO) was measured by thermodilution (Model 9520, American Edwards Laboratories) and P_{ET}CO₂ via capnography (Ohmeda 4700 Oxicap, BOC Group, Louisville CO, 80027). Arterial blood gases were measured using a blood gas analyzer (ABL30 Blood Gas Analyzer, Radiometer, Copenhagen).

Experimental protocol

After 30 min of haemodynamic and ventilatory stability following instrumentation, CO₂ was injected in five (n=5) animals and He in four (n=4) animals. Baseline measurements were made before each injection of intravenous gas. Intravenous gas was injected manually using sequentially larger volumes (15, 30, 45, 60, 75, 90, 120, 150, 180, 240, and 300 ml) or until the animal had irreversible cardiac failure. The duration of the injection for all volumes was less than two seconds. After each venous gas injection, haemodynamic variables and blood gases were measured and recorded when MAP reached its nadir. The next venous gas injection was performed once MAP had

returned to the baseline value. Mechanical ventilation was adjusted to keep the PaCO_2 between 35–45 mmHg. Otherwise, no other resuscitation intervention was performed.

Analysis

Survival was plotted and compared between CO_2 and He using a Fisher Exact Analysis for $2 \times n$ tables.⁹ Changes in measured variables (MAP, CO, $\text{P}_{\text{ET}}\text{CO}_2$, PaO_2) as a function of increasing venous gas injection volume were analyzed using a 2 way repeated measures ANOVA. When this analysis indicated differences between groups ($P < 0.05$) we tested for specific differences in variables at the 60 ml injection volume (the greatest volume at which all animals were still alive) using an unpaired Student's *t* test. Statistical analysis was performed using Systat for Macintosh version 5.1 (Evanston, IL). Data are reported as mean $\pm$ 1 SD.

Results

Figure 1 shows survival curves for the two experimental groups. There were no deaths in the group injected with CO_2 up to 300 ml injection volume. Thus, a lethal volume for CO_2 embolization was not reached in this model. No animal in the helium group survived an injection volume > 120 ml. There was a difference in survival between the two groups ($P = 0.0079$).

The MAP decreased after each venous gas injection and the magnitude of decrease in MAP increased as the volume of gas injection increased ($P < 0.03$) (Figure 2). The decrease in MAP was greater in the He than in the CO_2 group at the 60 ml injection volume ($P < 0.001$). At a venous gas injection volume of 60 ml, the MAP in the CO_2 group decreased from 110 ± 12 mmHg to 88 ± 14 mmHg and MAP in the He group decreased from 99 ± 14 mmHg to 44 ± 20 mmHg.

FIGURE 1 Survival curves for CO_2 and He groups. No animal survived beyond the 120 ml injection in the He group ($P = 0.0079$).

The decrease in cardiac output as a function of increasing intravenous gas injection volume in both groups was not statistically significant ($P = 0.08$) (Figure 3).

In both groups $\text{P}_{\text{ET}}\text{CO}_2$ decreased as a function of increasing intravenous injection volume ($P < 0.001$), indicating increased dead space ventilation from gas embolism (Figure 4). The $\text{P}_{\text{ET}}\text{CO}_2$ at the 60 ml venous gas injection volume decreased from 35 ± 3 mmHg to 30 ± 3 mmHg in the CO_2 group and from 30 ± 2 mmHg to 3 ± 6 mmHg in the He group. The decreases in $\text{P}_{\text{ET}}\text{CO}_2$ was more pronounced in the He group than in the CO_2 group ($P < 0.001$).

There was a decrease in PaO_2 from baseline with injection of both gases (Figure 5). However, the decrease in PaO_2 was much larger using He than CO_2 gas injection. At the 60 ml venous gas injection volume, the PaO_2 changed from 244 ± 22 mmHg to 203 ± 23 mmHg in the CO_2 group ($P = \text{NS}$) and from 190 ± 51 mmHg to 68 ± 22 mmHg in the He group ($P < 0.05$).

FIGURE 2 MAP for CO_2 (upper panel) and He (lower panel) injected groups. There was a decrease in MAP with both CO_2 and He embolization ($*P < 0.05$). However, the effect was more pronounced in the He group ($†P < 0.001$). Note that in the He group, the first death occurred after the 60 ml injection and no animal survived beyond the 120 ml injection.

FIGURE 3 Cardiac output for CO₂ (upper panel) and He (lower panel) injected groups. *P*: NS.

FIGURE 4 $P_{ET}CO_2$ for the CO₂ (upper panel) and He (lower panel) groups. $P_{ET}CO_2$ decreased in the He embolism groups (* $P < 0.001$). The decrease was more profound in the He group († $P < 0.001$).

FIGURE 5 PaO_2 for CO₂ (upper panel) and He (lower panel) groups. A decrease in PaO_2 with increasing embolus volume was found only in the He embolism group (* $P < 0.05$) which was different from the CO₂ embolism group († $P < 0.05$).

Discussion

We found that He gas embolism in this porcine model was fatal at considerably lower volumes than CO₂ gas embolism. Both CO₂ and He had profound effects on haemodynamic variables and upon gas exchange but deleterious effects of He embolism were more severe than CO₂ embolism at each volume injected.

The ideal insufflation agent for laparoscopy should be physiologically inert, pure, non-flammable, and inexpensive. It should also have low tissue solubility to conserve the amount used. Carbon dioxide has been traditionally used because it is inexpensive and not flammable. Its high blood solubility ensures rapid absorption and, in turn, is readily eliminated via the lungs. However absorption of CO₂ can result in hypercarbia and acidosis. On the other hand, He is chemically inert, non-reactive, and has low aqueous solubility which minimizes tissue absorption and its use would not be associated with hypercarbia. These properties have led several groups to investigate He as an insufflation gas for laparoscopy.^{2,3}

Haemodynamic effects of gas embolism are minimized by both dissolution of gas in the blood stream

and permeation of the gas into surrounding tissues. Solubility of CO₂ in blood is 50 times greater than that of He in the pressure range used during laparoscopy¹⁰ (solubility coefficient at body temperature: 670 ml CO₂·l⁻¹ water compared with 10 ml He·l⁻¹ water).¹¹ Gas permeation through the surrounding cardiac ventricular tissue is the product of both diffusion and partition coefficients for a particular gas. Although He has a three fold higher diffusion coefficient than CO₂, the net effect is that He permeation into cardiac ventricular tissue is slower than CO₂ by a factor of about 17.¹⁰ Therefore, because of its relative insolubility and slower tissue permeation, He gas embolism would be predicted to cause more mechanical obstruction from gas locking in the pulmonary outflow tract than that of an equivalent volume of CO₂. Our results support this theoretical argument by showing that a large animal model tolerated He gas embolism poorly compared with CO₂ gas embolism.

The incidence of gas embolism during laparoscopy is not well documented but two large series reported 1 in 5,000–10,000 laparoscopies^{6,12} suggesting that clinically important CO₂ embolism was unlikely.¹³ However, criteria for diagnosis are not uniform and undetected emboli may be more common. Couture and colleagues found that transoesophageal echocardiography was the most sensitive method for detecting CO₂ emboli.¹⁴ Using transoesophageal echocardiography during laparoscopic cholecystectomy gas emboli were detected in 11 of 16 patients by Derouin *et al.*⁷ Thio and Reichert detected gas embolism in all patients during laparoscopic cholecystectomy.⁸ The small amount of CO₂ embolism observed by these investigators had no important physiological effects. However, on the basis of our findings, a similar degree of He embolization may have greater physiological effects. Therefore, our results raise the possibility that more widespread use of He as an insufflation gas may increase the rate of clinical gas embolism.

One limitation of our study is that we cannot directly extrapolate from the observed differences between CO₂ and He *iv* injection and the clinical observation of gas emboli during laparoscopy^{7,8} to determine the likely clinical importance. We observed that 15 ml He embolism resulted in a reduction in P_{ET}CO₂ that was only matched by 20 times the volume of CO₂ embolism. Couture *et al.* observed that clinically important P_{ET}CO₂ and haemodynamic changes occurred at *iv* CO₂ infusion rates > 0.1 ml·kg⁻¹·min⁻¹.¹⁴ If 1/20th the He infusion rate results in a comparable clinical effect then, given these data, it is reasonable to consider the possibility that clinically observed gas embolism during laparoscopy^{7,8} may be important if the gas were He.

Further limitations of our study include necessity of caution with respect to extrapolating results of a study in anaesthetised, paralysed animals to the clinical situ-

ation in humans. However, we believe that the porcine model has haemodynamic and respiratory responses that approximate the human response. We acknowledge that our study did not address the issue of whether an embolism was more or less likely with CO₂ or He, which would be an important consideration given the relatively rare occurrence of massive gas embolisation during laparoscopic surgery. Nor did we investigate the effects of slower rates of gas embolism that may be important in extrapolating our study of bolus intravenous gas injection to peritoneal gas emboli during laparoscopic surgery. While we have shown that CO₂ gas embolism had a lesser detrimental effect than He gas embolism, it is possible that adverse effects of CO₂ such as hypercapnia may outweigh this potential benefit.

In summary, gas embolism using He is fatal at lower volumes than with CO₂. Both CO₂ and He embolisation have deleterious effects on haemodynamic variables, oxygenation and dead space ventilation but the deleterious effects are more profound with He embolism than with CO₂. These different effects of gas embolism should be recognised when considering the use of helium or other insoluble gases as abdominal laparoscopic insufflation gases.

References

- 1 Fitzgerald SD, Andrus CH, Baudendistel LJ, Dahms TE, Kaminski DL. Hypercarbia during carbon dioxide pneumoperitoneum. *Am J Surg* 1992; 163: 186–90.
- 2 Bongard FS, Piani NA, Leighton TA, *et al.* Helium insufflation for laparoscopic operation. *Surg Gynecol Obstet* 1993; 177: 140–6.
- 3 Leighton TA, Liu S-Y, Bongard FS. Comparative cardiopulmonary effects of carbon dioxide *versus* helium pneumoperitoneum. *Surgery* 1993; 113: 527–31.
- 4 Diakun TA. Carbon dioxide embolism: successful resuscitation with cardiopulmonary bypass. *Anesthesiology* 1991; 74: 1151–3.
- 5 Beck DH, McQuillan PJ. Fatal carbon dioxide embolism and severe haemorrhage during laparoscopic salpingectomy. *Br J Anaesth* 1994; 72: 243–5.
- 6 Phillips J, Keith D, Hulka J, Hulka B, Keith L. Gynecologic laparoscopy in 1975. *J Reprod Med* 1976; 16: 105–17.
- 7 Derouin M, Couture P, Boudreau D, Girard D, Gravel D. Detection of gas embolism by transesophageal echocardiography during laparoscopic cholecystectomy. *Anesth Analg* 1996; 82: 119–24.
- 8 Thio JM, Reichert CLA. Transesophageal echocardiographic assessment of venous carbon dioxide embolism during laparoscopic cholecystectomy. *Anesthesiology* 1994; 81: A112.

- 9 *Agresti A.* Categorical Data Analysis. Wiley Series in Probability and Mathematical Statistics. New York: John Wiley & Sons, 1990: 64–5.
- 10 *Southern DA, Mapleson WW.* Which insufflation gas for laparoscopy? (Letter) *BMJ* 1993; 307: 1424.
- 11 *Gevantman LH.* Solubility of selected gases in water. In: Lide DR (Ed.). *CRC Handbook of Chemistry and Physics*. Boston: CRC Press, 1991–1992, 6–3, 6–4.
- 12 *Mintz M.* Risks and prophylaxis in laparoscopy: a survey of 100,000 cases. *J Reprod Med* 1977; 18: 269–72.
- 13 *Wahba RWM, Tessler MJ, Kleiman SJ.* Acute ventilatory complications during laparoscopic upper abdominal surgery. *Can J Anaesth* 1996; 43: 77–83.
- 14 *Couture P, Boudreault D, Derouin M, et al.* Venous carbon dioxide embolism in pigs: an evaluation of end-tidal carbon dioxide, transesophageal echocardiography, pulmonary artery pressure, and precordial auscultation as monitoring modalities. *Anesth Analg* 1994; 79: 867–73.