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A randomized controlled trial assessing the effect of heated carbon dioxide for insufflation on pain and recovery after laparoscopic fundoplication

V. L. Wills,[1] D. R. Hunt,[1] A. Armstrong[2]

[1] St. George Upper Gastrointestinal Surgical Unit, Level 5, Suite 1, St. George Private Medical Centre, 1 South St, Kogarah, 2217. New South Wales, Australia
[2] Department of Anaesthesia, St. George Hospital, Kogarah, Australia

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Abstract

Background: Insufflation with heated gas for laparoscopy may reduce postoperative pain. This study assessed the effect of heated gas on outcome after fundoplication.

Methods: A blinded, randomized trial compared the effect of heated or standard carbon dioxide (CO_2) on core temperature, postoperative pain, analgesic requirement, and postoperative recovery. Pain scores were assessed with a 100 mm visual analog scale (VAS). Recovery was assessed with a patient diary and clinical follow-up assessment at 8 days and 1 month postoperatively.

Results: For this study, 40 patients were randomized to heated CO_2 (n = 19) and standard CO_2 (control) (n = 21) groups. The heated CO_2 group increased core body temperature from 35.9° to 36.1°C, ($p = 0.008$), whereas the control group maintained core temperature at 35.8°C. The control group had lower analgesic requirements and pain scores, significant at 12 h (VAS: 20 vs 36 mm; $p = 0.04$). There was no difference between the groups in terms of late recovery. The heated CO_2 group showed a significant correlation between operative duration and requirement for postoperative morphine ($p = 0.01$).

Conclusions: Heated gas provides no benefit for patients and may be associated with increased early pain. The elevation of core body temperature observed with heated CO_2 is of little clinical significance.

Key words: Carbon dioxide — Laparoscopic fundoplication — Pneumoperitoneum — Postoperative pain — Temperature

Laparoscopic fundoplication is associated with significantly less pain than open fundoplication [4]. The avoidance of an upper abdominal incision results in earlier discharge from hospital and a more rapid postoperative recovery [4, 7]. Nevertheless, pain persists up to 2 weeks, and patients will require 2 to 3 weeks before returning to work [4, 7]. Pain after laparoscopic procedures arises as a consequence of the port-site wounds, operative dissection, and pneumoperitoneum. The nature, pressure, and temperature of the gas used for pneumoperitoneum may contribute to postoperative pain [17].

Heated gas was used for pneumoperitoneum initially because of concerns that prolonged laparoscopy may contribute to hypothermia [11, 14]. Although hypothermia has not proved to be a significant problem during most laparoscopic procedures with standard gas flow rates, it was observed that the use of heated gas may result in a reduction in postoperative pain [14]. Several studies using dry heated gas [6, 14] or humidified heated gas [8, 12] suggest that heated gas can reduce pain after laparoscopic gynecologic procedures or laparoscopic cholecystectomy.

Laparoscopic fundoplication is of longer operative duration than laparoscopic cholecystectomy, uses larger volumes of insufflated gas, and seemingly results in more postoperative pain. It was felt that fundoplication may provide a better model for evaluating the effect of heated carbon dioxide (CO_2), especially as duration of hospitalization and level of postoperative pain justify the use of a patient-controlled analgesia device. The aim of this double-blind randomized controlled trial was to assess the effect of heated carbon dioxide on postoperative pain and functional recovery after laparoscopic Nissen fundoplication.

Patients and methods

Patients older than 17 years presenting for an elective laparoscopic fundoplication were considered eligible for the trial. Patients were ineligible if they had an allergy to morphine, a large (>6 cm) hiatal hernia, or previous esophageal surgery, or if they required a concomitant procedure such as cholecystectomy, an interpreter for consent, or a postoperative intubation. Patients were to be withdrawn from the trial if they required conversion to

Correspondence to: D. R. Hunt

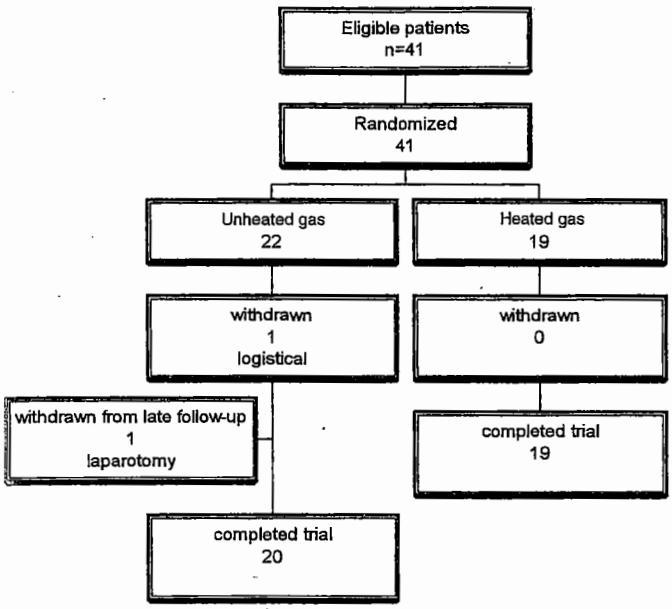


Fig. 1. Patient flow and participation.

an open procedure, had a postoperative esophageal leak, or required a laparotomy in the postoperative period. Patient flow and participation is shown in Fig. 1. The study was approved by the South Eastern Area Health Service Ethics Committee.

Assignment and masking

A random number table was used for sequence generation, and patient allocations were placed in sequentially numbered opaque, sealed envelopes. Patients were approached on the morning of their operation and enrolled in the trial after providing informed consent. They were instructed in the use of a visual analog scale at this time. The surgeon, anesthetist, data analyst, patient, and ward nurses all were blinded as to the allocated intervention. The operating room nursing staff was responsible for connecting the insufflator to deliver either heated or standard CO_2 as allocated, the connection being concealed from all other staff. The allocation envelope was resealed and remained unopened until the final stage of data analysis.

Operative procedure

All operations were performed by a single surgeon (D.R.H.), using a standard technique. Pneumoperitoneum was established with a Veress needle before the placement of two 10-mm ports and three 5-mm ports. A 360° fundoplication with division of short gastric vessels was performed in each case and fixed to both the esophagus and the right pillar of the hiatus. All patients had a posterior hiatal repair after esophageal mobilization. All patients had lavage with 1,000 ml of warm Hartmann's solution at the completion of the operation. A 5-mm left subphrenic closed suction drain was placed, and wounds were closed with nonabsorbable sutures.

Pneumoperitoneum

A standard insufflator (LINS-2000, Cook Australia, Eight Mile Plains, Qld) was to create the pneumoperitoneum. Stepped insufflation was used after insertion of the Veress needle. Gas flow was begun at a rate of 1 l/min, after a set number of pulses increased to 6 l/min. Maximum flow was set at 12 l/min, and maximum intraperitoneal pressure at 12 mmHg. A standard filtered gas tubing set was used for each case (LINS-CTS-300-LL-HGL, Cook Australia). This tubing contains a heating wire that runs along its length. To provide heated gas, the heating element is plugged into a socket on the insufflator. This region is easily screened from the operating team with a drape. The tube, if heated, becomes warm to the touch, and this was used as a check by the unblinded member of the nursing staff to confirm heating of the gas in allocated cases. Company information suggests that at "standard" flow rates, the gas will be heated to 37°C. An *ex vivo* assessment of the flow in the operating theater demonstrated that at rates of 1 l/min to 6 l/min, the gas was heated from 22° to 30.5°C.

Anesthesia and postoperative analgesia

A standard anesthetic regimen was administered by one of two anesthetists. For premedication, patients received midazolam (0.1 mg/kg) intramuscularly. Rapid sequence induction was performed using propofol 2 to 2.5mg/kg, fentanyl 100 μg, suxamethonium 1.5 to 2 mg/kg, and metoclopramide 10 mg. Anesthesia was maintained with sevoflurane 2% to 3% in nitrous oxide 66% and oxygen 33%, cisatracurium 0.15 mg/kg, and morphine 10 mg. Ondansetron 4 mg and cefotaxime 2 g were given intraoperatively.

At completion of the procedure, patients were administered neostigmine 2.5 mg and atropine 1.2 mg. The operating room temperature was maintained between 20° and 22°C, and a warming device was placed over the upper torso and head (Bair Hugger, Augustine Medical, Eden Prairie, MN, USA). Patient core temperature was measured at the beginning of pneumoperitoneum, at 1 h, and at the completion of pneumoperitoneum using a nasopharyngeal thermistor (Vital Signs, Totowa, NJ, USA).

During recovery, a patient-controlled analgesia device (PCA) was connected, which enabled patients to self-administer 1 mg/ml of morphine every 5 min. In the first postoperative hour, the recovery room staff also could administer bolus doses of morphine in 2-mg increments to a maximum of 10 mg. The PCA device was continued for a minimum of 24 h postoperatively. After the PCA device was removed, patients received a soluble form of paracetamol 1 g combined with codeine 8 mg as necessary. Postoperative nausea was managed with ondansetron in doses of 4 mg. No nonsteroidal anti-inflammatory drugs (NSAIDs) were administered.

Data collection

Patient age, weight, and height were recorded preoperatively. Intraoperative data, recorded by the anesthetist, included duration of pneumoperitoneum, core body temperature, volume of CO_2 used for insufflation, volume of irrigation, and the occurrence of an upper pole splenic infarct. Postoperatively, the ward nurses asked the patients to record a pain score on a 100 mm visual analog scale (VAS) at 6, 12, 24, 48, and 72 postoperatively. Morphine consumption at 12 and 24 h postoperatively and overall also was recorded. Patients were discharged when they were able to walk unaided and swallow soft food, and when they no longer required parenteral narcotics or antiemetics.

Patients were seen on day 8 postoperatively and had their skin sutures removed. Pain was measured with a VAS, and patients were instructed to complete a simple diary recording time until return to work, "normal activity" and "normal energy level." All the patients were then seen 1 month postoperatively.

Data analysis

The calculated sample size required to demonstrate a reduction in postoperative morphine consumption by 30% ($\alpha = 0.05$, $\beta = 0.1$) was 40 patients, and the size required to demonstrate a 50% reduction in VAS at 12 and 24 h was 30 patients. Body temperature, presented as mean value with associated standard deviation, was analyzed using paired t-tests. Pain scores are presented as median values with interquartile ranges, as are times to discharge and return of function. The Mann-Whitney *U* test was used for statistical analysis. Linear regression was used to explore the association between postoperative pain and gas volume, and between pain and operative duration. A p value less than 0.05 was considered significant.

Results

This study was conducted over a 1-year period (May 1999 to April 2000). Initially, 41 patients were enrolled. One

Table 1. Patient details

	Heated gas	Control
n	19	21
Gender M:F	12:7	10:11
Mean age (range)	47.5 (21–71)	52.2 (28–74)
BMI (kg/m^2)	27.0	29.2
Indication		
Achalasia	3	2
Gastroesophageal reflux	16	19

BMI, body mass index

Table 2. Operative variables

	Heated gas	Control	*p*
Pneumoperitoneum duration (min)	69 ± 18	72 ± 24	0.64
Volume carbon dioxide (l)	96 ± 43	116 ± 66	0.26
Volume irrigation (l)	1.35 ± 0.31	1.51 ± 0.86	0.45
Splenic infarct	6	6	
Myotomy	5	7	
No myotomy	14	14	
Hiatal hernia	10	6	
Adhesions divided	0	1	
Postoperative complication	3	3	

patient was excluded because postoperative pain scores were not completed as a result of logistical problems. One patient in the control group underwent laparotomy on day 7 postoperatively for cecal volvulus and therefore was not included in follow-up evaluation after day 3. Preoperative variables and indications for operation are shown in Table 1. Operative variables are shown in Table 2. Both groups were similar in these attributes. There was no difference in early pain scores (2.1 vs 2.7) or day 8 pain scores (1.2 vs 2) between patients with an upper pole splenic infarct and those without a splenic infarct. Patients undergoing a myotomy had early pain scores (2.6 vs 2.6) and day 8 scores (1 vs 1.6) similar to those of patients not undergoing a myotomy.

Body temperature

Body temperature increased significantly at 1 h in the patients receiving warmed gas from a mean preoperative level of 35.9 ± 0.4°C to 36.1 ± 0.5°C ($p = 0.008$). Temperature remained unchanged in the control group, with a temperature of 35.8° ± 0.3°C before surgery and 35.8 ± 0.6°C at 1 h ($p = 0.8$). Because most procedures required nearly 60 min, there was no further change in temperature at completion of pneumoperitoneum, as compared with temperature at 1 h.

Pain

There was no statistical difference in postoperative pain after 12 h. At 12 h, patients in the control group had significantly lower VAS scores (Fig. 2). Morphine consumption also was lower in the control group at 12 and 24 h, but this difference did not reach statistical significance. Requirements for supplementary opiates, oral analgesia, and antiemetics were similar between groups (Table 3). As a secondary outcome, the association among pain, duration of pneumoperitoneum, and volume of CO_2 was assessed using linear regression. For both the control group and the heated gas group, pain scores at 12 h and analgesic consumption at 24 h were used as two measures of pain (Table 4). The control group had no association between pain and gas volume or between pain and operative duration. Gas volume and duration of pneumoperitoneum were correlated positively in this group ($t = 5.4$; $r = 0.78$; $p < 0.001$). In the heated CO_2 group, there was a weak correlation between gas volume and duration of pneumoperitoneum ($t = 1.85$; $r = 0.41$; $p = 0.08$). Gas volume was not associated with postoperative pain, but duration of pneumoperitoneum was (Fig. 3).

Discharge and recovery

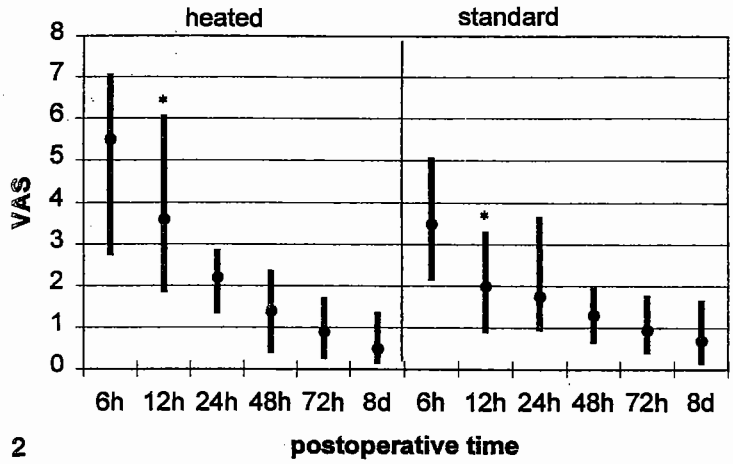
Three patients in the control group had postoperative complications. One patient had a cecal volvulus on day 7 and required laparotomy. One patient developed self-limiting gastroenteritis on day 6 postoperatively, and one noticed a painful port-site hematoma on day 4 postoperatively. These latter two patients are included in follow-up data. Three patients in the heated gas group also experienced postoperative complications. In one patient atrial fibrillation developed intraoperatively, requiring medical therapy for reversion to sinus rhythm. One patient was treated for a postoperative respiratory tract infection, and one patient had persistent nausea, delaying discharge.

Median time to discharge in each group was 3 days (range, 2–4 days). When the heated CO_2 group was compared with the control group, no difference was found in median time until return to work at 12 days (range, 9–22 days) vs 14 days (range, 7–20 days), return to normal activity at 19 days (range, 11–24 days) vs 17.5 days (range, 14–21 days), or return to a normal sense of well-being at 29.5 days (range, 21–35 days) vs 25 days (range, 20–32 days).

Discussion

The findings from this study demonstrate that dry heated CO_2 used for laparoscopic insufflation does not improve pain or postoperative recovery after laparoscopic fundoplication. In fact, during the first 12 h postoperatively, the control group experienced less pain and required less analgesia than the group receiving heated intraperitoneal CO_2. The use of heated gas did increase core body temperature, a change not seen in the control group. Both of these findings contradict previous reports in the literature.

Early reports suggest that laparoscopic insufflation results in intraoperative hypothermia, and that this could be prevented with the use of heated insufflation gas. However, these reports describe nonrandomized studies that used inappropriate statistical analysis and nonstandard operative conditions [10, 11]. Theoretically and in experimental situations, it has been demonstrated that heating cool insufflated gas to body temperature intraperitoneally requires little energy [3, 5]. The latent heat required to humidify this



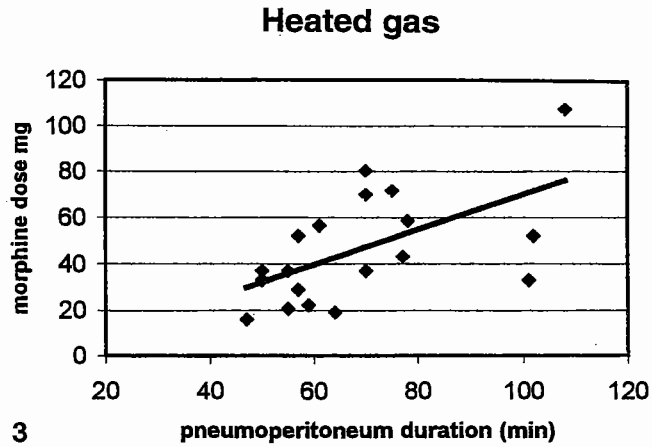


Fig. 2. Postoperative visual analog scale scores. •, median value; ▬, interquartile range; *, $p = 0.04$

Fig. 3. Association between postoperative consumption of morphine and duration of pneumoperitoneum.

Table 3. Requirement for analgesia and antiemetics

	Heated gas	Control	*p*
Morphine (mean dose, mg)			
Total at 12 h	27.8 ± 13.5	20.8 ± 11.4	0.12
Total at 24 h	46.0 ± 23.8	32.9 ± 23.5	0.07
After 24 h	8.2	8.2	
Number of patients requiring supplemental morphine	9	9	
Ondansetron			
Mean dose (mg)	7.1 ± 9.1	3.8 ± 5.9	0.24
Number of patients requiring antiemetics	11	10	
Mean doses of oral analgesia	7.5	7.6	

Table 4. Association among postoperative pain, operative duration, and gas volume

Group	Dependent variable	Independent variable	*t*	*p*	95% Confidence interval
Heated gas	VAS	Duration	0.98	0.34	−0.02–0.08
Heated gas	Morphine	Duration	2.9	0.01	0.2–1.3
Heated gas	VAS	Gas volume	0.59	0.56	−0.17–0.03
Heated gas	Morphine	Gas volume	0.2	0.84	−0.2–0.31
Control	VAS	Duration	−1.65	0.11	−0.07–0.008
Control	Morphine	Duration	−0.13	0.89	−0.2–0.15
Control	VAS	Gas volume	0.02	0.98	−0.02–0.01
Control	Morphine	Gas volume	−0.13	0.89	−0.2–0.15

VAS, visual analog scale gas volume

dry gas is a significantly greater source of energy loss [3] but gas volumes far in excess of those used intraoperatively are required for this to be a clinical problem [2, 3, 5]. For instance, the energy loss from heating and humidifying a cool gas volume of 840 l would result in a fall in body temperature of 0.39°C if no intrinsic or extrinsic warming occured [5]. However, in the clinical setting, the current study and other randomized studies have been able to demonstrate small increases in core temperature from the use of dry heated gas for insufflation [1, 13]. Although a statistical improvement in core temperature was seen, a 0.2°C elevation of core temperature is of little clinical significance. As demonstrated by the control group in the current study, body temperature can be maintained using other warming devices during anesthesia.

Heated gas also is thought to provide a measure of postoperative pain relief. Semm [14] in a randomized trial claimed a reduction in shoulder tip pain and analgesic requirements associated with the use of dry heated gas, although only descriptive statistics were used for interpretation of data. Similarly, a "randomized" study assessing heated and humidified gas during miscellaneous gynecologic procedures reported reduced postoperative pain, but provided minimal data for analysis, failed to use interpretative statistics, and read more like an advertisement than like a scientific study [12]. Heated and humidified gas also was used in a randomized trial by Mouton et al. [8] in patients undergoing laparoscopic cholecystectomy. Pain reduced to 10 days postoperatively and earlier return to activity was demonstrated in the group receiving heated and humidified gas. However, the study was not double-blinded; multiple surgeons and anesthetists were involved in the operative procedures; only inpatients were assessed for pain scores during early follow-up assessment; 20% of cases were excluded; and parametric tests were used for analysis of VAS scores. Korell et al. [6] demonstrated a reduction in abdominal and shoulder tip pain lasting up to 3 days postoperatively in 103 patients randomized to dry heated gas or normal gas and undergoing various gynecologic laparoscopic procedures. Although anesthesia was standardized, little information is provided concerning standardization of operations, operating room conditions, and the provision of postoperative analgesia.

Despite these studies supporting the use of heated gas [6], methodologic deficiencies make interpretation of results difficult. Additionally, two of the studies [8, 12] are reported by groups directly involved in the development of a heated insufflation. Two smaller studies examining the effect heated gas on temperature, intraperitoneal immunology, and renal function have not demonstrated a benefit for heated gas in terms of pain reduction [1, 13]. The current study also fails to support the use of heated gas in the context of laparoscopic fundoplication. This lack of benefit may arise because fundoplication is of longer duration and

requires greater operative dissection than cholecystectomy or most gynecologic procedures. Additionally, many patients experience temporary dysphagia and dietary restriction after fundoplication that influences postoperative recovery. Alternatively, the use of warm saline lavage [15, 16], administered to all patients in the current study, may obviate any benefit of heated gas.

However this study demonstrated that patients receiving heated gas had more early postoperative pain than the control group, suggesting that heated gas has no benefit in terms of pain reduction, and may in fact be a stimulus to early pain. It is difficult to provide a hypothesis to explain this. Although warm gas diffuses more readily, and although increased absorption of CO_2 into the bloodstream may affect central sensitization [9], the difference in intraperitoneal temperature between warm and standard gas would have minimal effect on transperitoneal gas diffusibility [13]. Postoperative pain in the heated gas group was associated with operative duration rather than with gas volume. Therefore, the drying effect of the gas is unlikely to be a cause.

The results of the current carefully controlled study do not demonstrate any clinically useful benefit in the use of heated gas for laparoscopic insufflation. Body temperature can be maintained with the use of other anesthetic interventions. The use of insufflators with heating capability in the context of prolonged laparoscopic procedures cannot be supported.

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