Humidified Compared With Dry, Heated Carbon Dioxide at Laparoscopy to Reduce Pain

Todd M. Beste, MD, James A. Daucher, MD, and Donald Holbert, PhD

OBJECTIVE: To study whether using 95% humidified, heated carbon dioxide (CO_2) at laparoscopy reduces pain compared with dry, heated CO_2.

METHODS: Patients were randomly assigned to either heated, 95% humidified CO_2 (study group) or heated, dry CO_2 (control group) during laparoscopy. Pain control was achieved per standard protocols. Pain scales were administered the first 4 hours and 24 and 48 hours postoperatively.

RESULTS: The 89 patients available in the intent-to-treat model revealed a decrease in total morphine equivalents and a decrease in pain scores at 1, 2, and 24 hours in the study group (directional *P* values < .05). Subgroup analysis in patients without chronic pelvic pain revealed lower mean pain scores at 1, 2, 24, and 48 hours and decreases in postoperative and total morphine equivalents (directional *P* values < .05) in the study group.

CONCLUSION: At laparoscopy, heated, 95% humidified CO_2 effectively decreases postoperative pain and narcotics usage compared with heated, dry CO_2.

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LEVEL OF EVIDENCE: II-2

Carbon dioxide is the distention medium of choice in laparoscopic surgical procedures. Carbon dioxide has the advantages of being quickly absorbed, not supporting combustion, and eliminating the risk of air embolism. It has been shown to decrease inflammatory response compared with air.[1] The most common technique of insufflation is with cold, dry carbon dioxide, which works well for the surgeon, but causes significant pain to the patient. To control postoperative pain, intravenous opioids are effective, but opioids have numerous adverse effects that would be helpful to avoid. This study evaluates 2 different readily available laparoscopic distension media, with the goal of decreasing pain and decreasing narcotic requirements.

In open laparotomy cases, most surgeons attempt to keep tissues moist to avoid damage. This is not routinely done with laparoscopy. The typical amount used during routine laparoscopy is 2,500–3,000 mL to enhance visualization. Conscious patients do not tolerate this well. Demco[2] showed in conscious laparoscopy, patients can only tolerate 500–800 mL of dry carbon dioxide (CO_2). With cold, dry CO_2, patients have problems with hypothermia, postoperative abdominal and shoulder pain theoretically secondary to peritoneal tissue desiccation.[3] Previous attempts by Moore et al[4] to solve the problem of hypothermia using warmed irrigation have failed. Moore also showed with regression analysis the volume of cold dry gas had no effect on hypothermia, but rather only the length of the case affected core temperature.

A warmed CO_2 system was thought to be the solution to help with pain and temperature loss. Our hospital has begun using a warming system in an attempt to solve the heat loss problem caused by the cold dry CO_2. Korell et al[5] showed significantly decreased shoulder pain with warmed, dry CO_2 compared with cold, dry CO_2. However, in a study by Jacobs et al,[6] warmed, dry CO_2 alone was insufficient for keeping patients' body temperature elevated; other devices were required.

The next step was to warm and humidify the CO_2. Whereas patients can only tolerate 500–800 mL of cold, dry CO_2, Demco showed 30% of conscious

From the Division of General Obstetrics and Gynecology, Department of Obstetrics and Gynecology, East Carolina University Brody School of Medicine; Department of Obstetrics and Gynecology, University Health Systems/Pitt County Memorial Hospital, East Carolina University Brody School of Medicine; and Department of Biostatistics, East Carolina University, Greenville, North Carolina.

Corresponding author: Todd M. Beste, MD, Department of Obstetrics and Gynecology, East Carolina University Brody School of Medicine, PCMH TA – 164, Greenville, NC 27834; e-mail: bestet@mail.ecu.edu.

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patients were able to tolerate 3,000 mL of warmed, humidified CO_2 or when 15 mm Hg of pressure was achieved with warmed, humidified CO_2 with no intravenous sedation.[2] A randomized, controlled trial by Mouton et al[7] showed a decrease in loss of body temperature with warming and humidifying the CO_2 compared with cold, dry CO_2. With electron microscopy, Mouton was also able to show less structural injury with the warmed, humidified CO_2. Prior studies have shown a reduction in postoperative hypothermia, a shortened recovery room stay, and reduced postoperative pain with warmed, humidified CO_2.[2,8] Although warmed, humidified CO_2 has been shown to be superior to cold, dry CO_2, the use of warmed, humidified CO_2 has not been compared with warmed, dry CO_2. Further evaluation of these techniques was necessary to determine whether humidification provides benefit.

Based on the above studies, our hypothesis was that patients will have decreased pain and will decrease narcotic usage with warmed, humidified CO_2 compared with warmed, dry CO_2. This study compares subjects exposed to warmed, dry CO_2 to warmed, 95% humidified CO_2 during laparoscopic surgery as measured by postoperative pain control, pain medication usage, and required length of stay postoperatively.

MATERIALS AND METHODS

A randomized, controlled clinical trial was performed. Institutional review board approval was obtained from the University and Medical Center Institutional Review Board. The study was performed at Pitt County Memorial Hospital, a teaching hospital associated with East Carolina University Brody School of Medicine. Patients who were candidates for same-day outpatient laparoscopy for any diagnosis were considered eligible candidates. Patients who were at high risk for conversion to exploratory laparotomy were excluded before consent. Informed consent was obtained. Patients who agreed to participate were randomly assigned to the study or control group in advance. The SAS procedure PROC PLAN (*SAS II. SAS/STAT User's Guide.* Fourth, Version 6 ed. Cary (NC): SAS Institute Inc.; 1989.) was used to generate random assignment of 90 subjects to 2 treatments. The assignments were placed by the investigators in sequentially numbered, opaque sealed envelopes, which were opened by the operating surgeon in the operating room after the patient was well under general anesthesia to blind the patients.

The patients underwent the laparoscopic procedure determined by the surgeon with either the warmed, dry CO_2 or the warmed, humidified CO_2 for the entire case. The Insuflow device (Lexion Medical, St. Paul, MN), which is an Food and Drug Administration–approved device, was used to provide warmed, 95% humidified CO_2. The cost of this device is approximately $90.00. The decision of which medications to give in both groups was made by the anesthesiologist in the operating room and in the postanesthesia care unit (PACU) for the first hour. The nurses dispensing these medications were blinded as to the patients' study group. The narcotics given were a combination of fentanyl, hydromorphone, morphine, and meperidine. Pain medications given in the ambulatory surgical unit and at discharge were by surgeon preference. The narcotics given were a combination of morphine, meperidine, oxycodone, and propoxyphene, with acetaminophen as needed. All narcotics given were recorded and converted to morphine equivalents to perform calculations. Ketorolac tromethamine was also given on an as-needed basis. The nurses dispensing the medications and collecting the pain scores were blinded to the patient's study group. The medications were given on an as-needed basis and based on the nurse's assessment of patients' pain levels. After surgery, the patients were given a visual analog scale[9] to be filled out at 1, 2, 3, and 4 hours and on postoperative days 1 and 2. The patients were also blinded to study group until all pain scores were recorded.

Using power calculations, with a visual analog pain scale greater than 5 in 50% of patients in the control group compared with 20% in the study group, a study population of 90 patients was required to achieve power of 80% with a significance level of .05. Other data included operating room time, type of procedure, preoperative and postoperative temperatures, estimated blood loss, CO_2 volume, pain medications, length of time until the patient is ready for discharge from the PACU and actual time of departure, length of time until the patient is ready for discharge from the hospital and actual time of departure.

Because the variables were not normally distributed (Kolmogorov-Smirnov test), the nonparametric Mann-Whitney U test was used. For proportions, Fisher exact test or the χ^2 test was used, depending on whether tables were or were not sparse. Because the research hypothesis was that humidified CO_2 would improve outcomes, directional P values from 1-tailed tests were used to compare hypothesis-related outcomes in the 2 treatment groups. Differences were considered statistically significant if $P < .05$.

RESULTS

A total of 90 women were randomized. One patient withdrew before completing the study. After consent, patients were taken to the operating room and placed under general anesthesia. The envelope was then opened and the appropriate equipment used. The procedure was performed as seen below. Postoperatively, patients were treated in the PACU followed by ambulatory surgical unit, then discharged to home. Patients filled out pain questionnaires the for first 4 hours until they were discharged and then called for postoperative days 1 and 2 pain levels.

Data were available on 89 patients. Subject accrual commenced on August 16, 2002, and concluded on April 29, 2004. Twelve of the patients had surgery for chronic pelvic pain. Because this was an intent-to-treat study, the data were analyzed first with the chronic pelvic pain patients included. Patient demographics, including age, height, weight, body mass index, ethnicity, and operative characteristics, including postoperative temperature, estimated blood loss, carbon dioxide gas used, number of incisions, and times in the operating room, PACU, and ambulatory surgical unit are shown. There were no significant differences between the 2 groups as seen in Table 1.

There were no significant differences in past surgical history. Diagnoses for the groups were voluntary sterilization, pelvic mass, infertility, and pelvic pain. In each group, 6 patients were operated on for pelvic pain. In the study group, 35 had a bilateral tubal ligation; the other 12 either had a salpingo-oophorectomy, cystectomy, ablation of endometriosis, lysis of adhesions or chromopertubation. In the control group, 34 had a bilateral tubal ligation; the other 8 either had a salpingo-oophorectomy, cystectomy, ablation of endometriosis, lysis of adhesions or chromopertubation. There was no significant difference between the groups as seen in Table 2 (Fisher exact test for diagnosis: $P = .46$; Fisher exact test for procedure: $P = .81$).

Variations in laparoscopic port size were associated with changes in pain scores. Patients who had a 10-mm trocar had significantly higher pain scores at 24 and 48 hours postoperatively (directional $P = .024$ and .015, respectively). In each group there were 9 patients who had 10-mm ports, as seen in Table 1.

When including all patients who completed the study, there was a statistically significant difference in total morphine equivalents, with a median of 146 in the study group compared with 162 in the control group. Chronic pelvic pain was noted to be a confounder. The data were subsequently analyzed without chronic pelvic pain patients. This further stratified the differences between the groups. The patient demographics and operative characteristics were analyzed and no significant differences were found. In the nonpelvic pain patient group, there were 77 patients, 41 patients in the humidified CO_2 group and 36

Table 1. Demographics, Operative Characteristics, and Postoperative Times in Patients Randomly Assigned to Receive Warmed, Humidified CO_2 or Warmed, Dry CO_2 at Laparoscopy

Characteristics	Humidified Group (n = 47)	Dry Group (n = 42)	P
Age (y)	29.0 (25.0, 36.0)	28.5 (25.0, 35.0)	.76
Height (m)	1.61 (1.57, 1.68)	1.65 (1.60, 1.68)	.73
Weight (kg)	79.38 (62.71, 93.55)	74.84 (63.96, 88.45)	.73
Body mass index (kg/m^2)	28.6 (24.3, 32.9)	27.9 (24.5, 34.6)	.34
Postoperative temperature (°C)	35.7 (35.5, 36.0)	35.8 (35.4, 36.2)	.33
Estimated blood loss (mL)	10.0 (5.0, 25.0)	5.0 (5.0, 25.0)	.52
CO_2 Volume (L)	16.9 (10.7, 27.5)	13.2 (9.6, 28.6)	.16
Operating room time (min)	38.0 (29.0, 54.0)	35.5 (29.8, 50.3)	.30
PACU time (min)	55.0 (45.0, 60.0)	55.0 (45.0, 60.0)	.80
ASU time (min)	120.0 (90.0, 180.0)	127.5 (103.8, 157.5)	.72
≥ 1 10-mm trocar (n)	9	9	–
2 incisions (n)	37	34	
3 incisions (n)	8	7	
4 incisions (n)	1	1	.99
Ethnicity (n)			
African American	26	28	
White	20	12	
Latino	1	1	.49

PACU, postanesthesia care unit; ASU, ambulatory surgical unit.

Values are median (25th percentile, 75th percentile) unless otherwise specified, with *P* values based on 2-tailed Mann-Whitney *U*; Fisher exact test used on categorical outcomes.

Table 2. Preoperative Diagnosis and Procedures Done in Women Randomly Assigned to Receive Warmed, Humidified CO_2or Warmed, Dry CO_2 at Laparoscopy

	Humidified Group (n = 47)	Dry Group (n = 42)	P*
Diagnosis			
Voluntary sterilization	35	34	.46
Pelvic pain	6	6	
Other	6	2	
Procedure			
Bilateral tubal ligation	35	34	.81
Salpingo-oophorectomy/cystectomy	7	5	
Other	5	3	

Values are n.
* *P* value computed using Fisher exact test.

patients in the dry CO_2 group. Because 10 subjects had no pain data for hours 24 and 48, pain scores for hours 1–4 were analyzed with a nonparametric repeated measures analysis, which indicated both a main effect of group ($P = .012$) and a group-by-hour interaction effect ($P = .003$). Because this interaction effect suggests that the shapes of the time profiles differ significantly between groups, groups were compared at each hour as shown in Table 3. There was a significant difference at 1, 2, 24, and 48 hours postoperatively, with directional $P = .001$, .024, .029, and .032, respectively. There was not a significant difference at 3 and 4 hours postoperatively. There was a greater difference in analgesic use in patients undergoing surgery for indications other than pelvic pain than in the total study population as seen in Table 4.

There was a statistically significant decrease in postoperative (PACU and ambulatory surgical unit) pain medication usage and a decrease in total (intraoperative and postoperative) pain medication usage, with total morphine equivalents of 146 in the study group compared with 162 in the control group. Although the PACU and ambulatory surgical unit pain medication usage differences did not meet the 0.05 threshold, they were close to being statistically significant ($P = .053$ and $P = .064$, respectively).

DISCUSSION

The primary finding in this study is that the use of heated, 95% humidified CO_2 at laparoscopy reduces narcotic usage in patients compared with heated, dry CO_2. Total pain medication usage was lower in this population. A patient would use on average the equivalent of 16 mg less of morphine in a 4-to-6-hour period of time, which may help in avoiding the side effects of narcotics. Despite lower narcotics use, patients who had warmed, humidified CO_2 had decreased pain scores at 1, 2, and 24 hours postoperatively.

A limitation of our study was including chronic pelvic pain patients in the study originally because the primary outcome variables were pain and pain medication usage. These variables are sure to be influenced by the chronic condition. There are at least 2 possibilities which would cause study problems: 1) marked pain relief and 2) no pain relief. In either case, the result would depend on preexisting pain states or surgical outcomes that were unrelated to the type of

Table 3. Pain Medication Usage and Pain Levels in all Patients Randomly Assigned to Receive Warmed, Humidified CO_2 or Warmed, Dry CO_2 at Laparoscopy

Characteristics	Humidified Group (n = 47)	Dry Group (n = 42)	P
Total morphine sulfate equivalent	146 (120, 192)	162 (130, 218)	.048
Pain, hour			
1	4 (1, 7)	7 (5, 8)	.002
2	3 (1, 5)	4 (3, 6)	.024
3	2 (1, 4)	3 (2, 4)	.237
4	3 (1, 5)	3 (2, 3)	.240
24	3 (1, 7)	5 (4, 6)	.046
48	3 (1, 5)	4 (2.5, 5)	.100

Values are median (25th percentile, 75th percentile), with *P* values based on 1-tailed Mann-Whitney *U*.

Table 4. Pain Medication Usage in Nonchronic Pelvic Pain Patients Randomly Assigned to Receive Warmed, Humidified CO_2 or Warmed, Dry CO_2 at Laparoscopy

Characteristics	Humidified Group (n = 41)	Dry Group (n = 36)	*P*
MSO_4 equivalents			
PACU	60 (0, 60)	60 (30, 79)	.053
ASU MSO	0 (0, 7.5)	5 (0, 10)	.064
Postoperative MSO	60 (7.5, 75)	68 (36, 86)	.046
Total (including intraoperative)	146 (120, 188)	162 (130, 215)	.030

PACU, postanesthesia care unit; MSO_4, morphine sulfate; ASU, ambulatory surgical unit.
Values are median (25th percentile, 75th percentile), with *P* values based on 1-tailed Mann-Whitney *U*.

distension media used during surgery. Either way could produce outliers, making data interpretation more difficult. A study by Kissler et al[10] illustrates this. They showed no difference in pain levels comparing humidified, warmed CO_2 to dry, warmed CO_2 to dry, cold CO_2. In their article, they did not specify diagnosis, which could have been chronic pelvic pain in the procedures they describe, leading to difficulty finding pain differences among the groups. In our study, when patients were included with chronic pelvic pain, there was a statistically significant difference between the study and the control groups. However, this difference was emphasized when pelvic pain patients were removed from the analysis. Another recent study by Einarsson et al[11] controlled for this by having patients be their own controls, with local injection of bupivacaine. Unless we did a second surgery on the same patient, however, this would not be an option for a distension medium study.

Another limitation in our study was not blinding the surgeons to whether the CO_2 was humidified. We tried to minimize the effect of not blinding the surgeons by having standard postoperative orders, similar procedures, and having multiple different surgeons, so as to not allow 1 individual's surgical style, opinion, or ability to influence the study. The patients were blinded to study group, as were the nurses dispensing the medications and collecting the pain scores, so as to decrease potential bias in reporting pain levels or the administration of pain medications.

Another limitation in our study was that the procedures performed in our study were relatively simple and in general completed in less than 1 hour. Our goal was to pick uncomplicated cases so that the case itself would not greatly influence the pain levels postoperatively. As mentioned above, we wish that we had excluded chronic pelvic pain patients. Otherwise, the procedures were very similar, which accomplished our goal. Certainly another study looking at longer, more technical cases would be beneficial to assess the usefulness of heated, humidified gas in that setting.

A factor that increased pain levels at 24 and 48 hours postoperatively was port size. Patients who had a 10-mm trocar site had higher pain levels than those with 8-mm or 5-mm sites. This may in part be due to our institutional practice of fascial closure in the 10-mm port site. Whether it is wound size or fascial closure, this would suggest surgeons should use smaller ports whenever feasible. Among the non–chronic pelvic pain patients, there were 7 in each group that had 10-mm ports; consequently, port size was not a confounding variable in group comparisons.

A previous study has shown decreased postoperative recovery times for the heated, humidified gas group.[8] We did not find a difference in postoperative recovery times between the groups. We were also unable to show a difference in postoperative temperature between the groups. However, as Moore et al[4] pointed out, longer cases were the main variable in causing temperature loss, and the cases in this study were of relatively short duration.

An area of concern is the pain levels on postoperative day 1 and 2. Patients are typically seen a few weeks after surgery, at which point they have minimal or no pain. Yet the pain levels given by the subjects are as high on postoperative day 1 as they are at the second hour after surgery, and day 2 is only slightly better. It is unclear why these levels are so high. The standard at our institution is Darvocet (Eli Lilly and Company, Indianapolis, IN) and ibuprofen. It is possible that this is inadequate. It is also possible that pain levels of that magnitude are acceptable to patients, knowing it will get better shortly. Whatever the reason, it seems better pain relief postoperatively does not end when the patient leaves the hospital.

The device used in this study is approved by the Food and Drug Administration and readily available. The cost of the device is approximately $90.00, as compared with the standard insufflation tubing which costs approximately $6.00. A cost comparison would

have to include surgeon's preference, patient satisfaction, additional pain medications, and dispensing those medications postoperatively.

Using warmed, humidified CO_2 at laparoscopy reduces pain postoperatively compared with warmed, dry CO_2. Total narcotic usage is also lower, which may help in avoiding the adverse effects of narcotics. This is another tool for the surgeon in helping reduce pain after surgery.

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