

Warmed, humidified carbon dioxide insufflation versus standard carbon dioxide in laparoscopic cholecystectomy: a double-blinded randomized controlled trial

Bettina Klugsberger · Markus Schreiner ·
Alexander Rothe · Dietmar Haas · Peter Oppelt ·
Andreas Shamiyeh

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Abstract

Background During laparoscopic cholecystectomy (LCHE), the insufflation with warmed and humidified carbon dioxide (CO₂) may reduce postoperative pain. The aim of the study was to evaluate the positive effects of heated and humidified carbon dioxide gas on patients with regard to postoperative pain after LCHE.

Patients and methods This is a prospective, randomized, double-blinded, controlled clinical trial. 148 patients (female = 98, male = 50) scheduled for elective LCHE were randomized into two groups: receiving either heated humidified carbon dioxide, or standard gas. Intraoperative core temperature was measured. The perioperative management was identical for both groups. Postoperative pain intensity was assessed using a visual analog pain scale, and the amount of analgesic consumption was recorded. The postoperative pain management was also standardized and equal for both groups.

Results 67 out of 148 received standard gas (group A), and 81 received warmed, humidified gas (group B). The groups were comparable demographically. The amount of analgesic consumption was recorded. Intraoperative core temperature was significant higher in group B than in group

A. Pain was significantly less in group B ($p = 0.025$) 6 h postoperatively. On the first postoperative day, no significant difference in pain between the two groups was detectable ($p = 0.437$).

Conclusion The use of warmed and humidified carbon dioxide during LCHE reduces postoperative pain at the day of operation.

Keywords Laparoscopic cholecystectomy · Carbon dioxide insufflation · Postoperative pain · Core temperature

Abbreviations

LCHE	Laparoscopic cholecystectomy
CO ₂	Carbon dioxide
VAS	Visual analog pain scale
°C	Degree Celsius
SD	Standard deviation

The clinical benefits for patients are also contributed through the technical advantages in minimally invasive surgery and also through postoperative pain management, i.e., less postoperative pain, better cosmetic results, shorter hospitalization, and earlier convalescence [1]. The use of fewer and smaller ports reduces incisional morbidity and improves cosmetic outcomes [2].

The current approach for most laparoscopic procedures uses carbon dioxide (CO₂) gas at a temperature of 21 °C and 0 % relative humidity to insufflate the peritoneal cavity for visualization. According to the literature, implantation of heated (to 35 °C) and humidified (95 %) CO₂ for pneumoperitoneum in laparoscopic procedures may be associated with lesser postoperative pain, lower risk of postoperative hypothermia, and lower analgesic requirements [3]. Insufflation with standard

B. Klugsberger (✉) · M. Schreiner · A. Rothe · A. Shamiyeh
2nd Surgical Department, Academic Teaching Hospital, Ludwig Boltzmann Institute for Operative Laparoscopy, Linz General Hospital, Krankenhausstrasse 9, 4021 Linz, Austria
e-mail: bettina.klugsberger@akh.linz.at

D. Haas · P. Oppelt
Department of Obstetrics and Gynecology, Women's General Hospital, Linz, Austria

D. Haas · P. Oppelt
Department of Gynecology, Erlangen University Hospital, Erlangen, Germany

cold-dry CO₂ during laparoscopic surgery has been shown to predispose patients to hypothermia and peritoneal injury [4, 5].

Our department performs a pioneering role in postoperative pain therapy (certified by TÜV Rheinland 2009). A marked improvement in subjective postoperative pain experience of patients in almost all domains was achieved in our clinic by introducing the quality management concept “Pain Free Clinic” [6].

The aim of the study was to evaluate the extent of heat preservation and postoperative pain reduction during laparoscopic cholecystectomy (LCHE) using humidified carbon dioxide (CO₂) gas insufflation instead of standard dry insufflation gas.

Patients and methods

Approval from the local institutional ethics committee was obtained on June 14, 2011 (ref. no. C-31-01). Between July 1 2011, and February 28 2013, a total of 148 patients were scheduled for LCHE at the General Hospital in Linz, Austria. This is a double-blind, prospective, randomized clinical study comparing patients undergoing LCHE with and without warmed humidified CO₂ gas. The patients, surgeons, operative and hospital floor nurses, and study coordinator were masked. Only the secretary was privy to which method of gas was being used. All the operations were carried out by the same team of eight surgeons, in which each surgeon had previously carried out at least 200 laparoscopic cholecystectomies.

All patients who were enrolled by the study coordinator gave written informed consent scheduled for LCHE on an elective basis. Criteria for inclusion were existence of symptomatic gallstone disease and patients’ age over 18 years. Patients converted intraoperative to open cholecystectomy or those undergoing a concomitant procedure were excluded from the study. Other Criteria for exclusion were irregularities of the study protocol (absence of rectal probe, missing consent form, and conversion to open cholecystectomy) and patients with acute cholecystitis.

Before operation, the secretary opened a sealed opaque envelope to randomly allocate the procedure. The envelopes contained the information to use either standard CO₂ insufflation (group A) or warmed, humidified CO₂ (group B). The randomization list was sealed by our secretary until data queries were resolved, and the database was locked. The following clinical data and clinical findings were noted preoperatively: age, body mass index, diabetes mellitus, arterial hypertension, and degenerative joint disease.

LCHE was performed as per a standardized procedure as usual in our clinic. The access was through the umbilical port (11 mm), and CO₂ gas was established with a pressure at 12 mm mercury. After insertion of the optic (Storz,

Germany) additional ports were placed under direct vision (one epigastric and one or two at the right upper quadrant of the abdomen).

Dissections of the Calot triangle following the “critical view of safety” technique, the cystic artery, and the cystic duct were ligated, each by three titanium clips (two central and one peripheral) and divided. The electro-cautery was used to dissect the gallbladder retrograde from the gallbladder fossa. The specimen was removed through the umbilical incision. The fascia at the umbilical site was closed with non-resorbable suture (Premilene 0[®] Braun, Tuttlingen, Germany). Skin closure was done by the use of single knot suture 4/0. All patients underwent standard general endotracheal anesthesia, which was the same in both groups. Pneumatic sequential compression garments were placed on bilateral lower extremities, and humidified ventilator circuits were used for all patients. In both groups, intraoperative core temperature was measured using a rectal probe (Thermistor zentrale Temperatur sonde 400 Serie[®], Sanitas, Austria). The perioperative management was identical for both groups.

The methodology in the two groups only differed in the use of Optitherm[®] device (Storz, Tuttlingen, Germany) in group B. The Optitherm[®] device was attached to the insufflation equipment in all of the patients but was only activated by the single scrub nurse in those patients randomized to group B.

The Primary Outcome Measure of the study was the postoperative pain intensity, assessed at the day of operation and at the first postoperative day using a visual analog pain scale (VAS) [range 0 (no pain) to 10 (maximum pain)]. All patients were personally reviewed at the operation day 6 h after completion of the operation (VAS₀) and again on the first postoperative day at 7 a.m. and 6 p.m. (VAS₁). VAS₁ was the mean value of both measurements on the first postoperative day. The postoperative pain management was also standardized for both groups using a non-opioid drug as Paracetamol 1,000 mg intravenous up to three times daily or Metamizol[®] 1 g intravenous up to two times daily. The amount of analgesic consumption was recorded. If there was intolerance against Paracetamol or Metamizol[®], then Voltaren[®] 75 mg intravenous up to two times daily was administered. If there was severe pain, Dipidolor[®] 7.5 mg intravenous up to two times was given.

Secondary outcome measures were the intraoperative core temperature, which was taken by using a rectal probe and the point of time of the first bowel movement after operation. After the operation, all patients received a survey with questions about pain and the point of time of the first bowel movement.

The sample size was determined in Cooperation with the Institute for statistic, Johannes Kepler University of Linz,

Austria. Statistical analysis was performed using IBM SPSS Statistics 20 in Cooperation with the Institute for statistic, Johannes Kepler University of Linz, Austria. The analysis included descriptive statistics, and bivariate data were analyzed by a contingency table and Cramer's V.

Correlations between the arithmetical averages of the groups were proved by *t* test, Mann–Whitney *U* test, Kruskal–Wallis test. All the tests were two-tailed, with a confidence level of 95 % ($p < 0.05$).

Results

148 ($w = 103$, $m = 45$) patients were randomized in two groups: 67 receiving standard CO₂ insufflation (group A), and 81 receiving warmed, humidified CO₂ (group B). In group A 21 men and 46 women were included, and in group B 24 men and 57 women were included. There was no statistical difference seen ($p = 0.86$).

The mean age of all patients was 55.7 years (SD \pm 15.14). In group A, the mean age was 55.87 years (SD \pm 14.44), and in group B the mean age was 55.68 years (SD \pm 16.93). There was no statistical difference seen ($p = 0.76$). The mean body mass indexes of patients were 28.56 and 28.74 in group A 28.34 and in group B, respectively ($p = 0.64$).

There were 18 patients with diabetes mellitus, 49 patients with arterial hypertension, and 20 patients with degenerative joints disease. In group A, there were 6 patients with diabetes mellitus, 20 patients with arterial hypertension, and 7 patients with degenerative joints disease. There were 12 patients with diabetes mellitus, 29 patients with arterial hypertension, and 13 patients with degenerative joints disease in group B. The demographic and clinical characteristics of patients in both groups are described in Table 1.

Table 1 Demographic and clinical characteristics of 148 patients

Characteristics	Group A ($n = 67$)	Group B ($n = 81$)	<i>p</i>
Gender			0.86
Female	46 (68.7 %)	57 (70.4 %)	
Male	21 (31.3 %)	24 (29.6 %)	
Age (years)	55.87 (14.44)	55.68 (16.93)	0.76
BMI	28.34 (5.22)	28.74 (5.40)	0.88
Arterial hypertonia	20	29	
Diabetes mellitus	6	12	
Degenerative joint disease	7	13	

BMI Body mass index

Data are presented as mean \pm standard deviation or *n* (%)

Table 2 Mean amounts of medication used in group A and in group B at the operation day

Analgesic drug	Group A	Group B	Total	<i>p</i>
Metamizol® 1 g	0.866	0.802	0.831	0.753
Paracetamol 1,000 mg	0.821	0.753	0.784	0.765
Voltaren® 75 mg	0	0.037	0.020	0.501
Dipidolor® 7.5 mg	0.07	0.012	0.010	1

Data are presented as mean

Table 3 Mean amounts of medication used in group A and in group B at the first postoperative day

Analgesic drug	Group A	Group B	Total	<i>p</i>
Metamizol® 1 g	0.821	0.864	0.845	0.768
Paracetamol 1,000 mg	0.716	0.728	0.728	0.969
Voltaren® 75 mg	0	0.037	0.020	1
Dipidolor® 7.5 mg	0.037	0.012	0.024	0.751

Data are presented as mean

The mean operative time of all patients was 63.88 min (SD \pm 23.47). In group A, the mean operative time was 59.27 min (SD \pm 19.74), and in group B the mean operative time was 67.41 min (SD \pm 25.72) ($p = 0.34$).

Mean intraoperative core temperature of all patients was 36.97 °C (range 35.0 and 38.1 °C, SD \pm 0.41). Mean intraoperative core temperature in group A was 36.85 °C (SD \pm 0.46), and in group B, it was 37.07 °C (SD \pm 0.35). A statistical difference was seen between both groups ($p = 0.01$).

No adverse effects of insufflation of warmed and humidified gas were observed. There were no perioperative deaths.

The amounts of analgesic consumption at the day of operation and first postoperative day are illustrated in Tables 2 and 3. There was no significant difference seen in both groups in the mean amounts of medication used at the operation day and at the first postoperative day.

Pain, as assessed by a VAS, was measured 6 h postoperatively (VAS_0) and at the first postoperative day at 7 a.m. and 6 p.m., the mean value was taken. The mean VAS_0 in group A was 2.22 (SD \pm 0.97), and in group B was 1.92 (SD \pm 0.84). There was a statistical difference between pain at the operation day (VAS_0) ($p = 0.025$) (Fig. 1).

The mean VAS_1 in group A was 1.97 (SD \pm 0.78), and in group B was 1.92 (SD \pm 0.86). At the first postoperative day, there was no statistical difference ($p = 0.437$) in pain detectable (Fig. 2; Table 4).

The mean VAS_0 in women was 2.13 (SD \pm 0.94), and in men was 1.87 (SD \pm 0.82). The mean VAS_1 in women

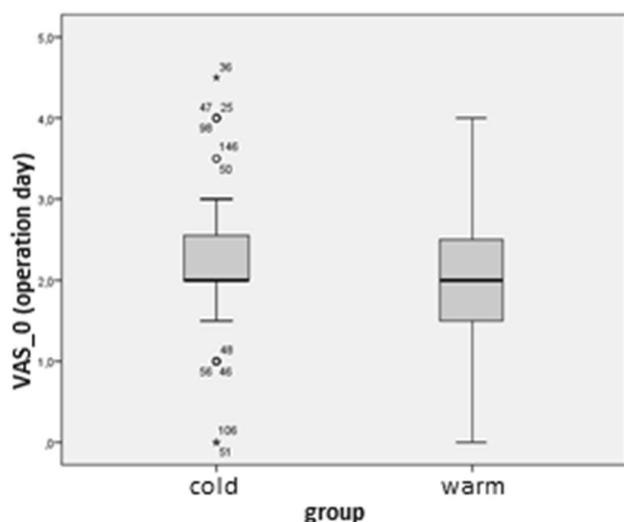


Fig. 1 VAS for patients receiving standard CO₂ gas (cold: group A) and warmed and humidified CO₂ gas (warm: group B) 6 h postoperatively

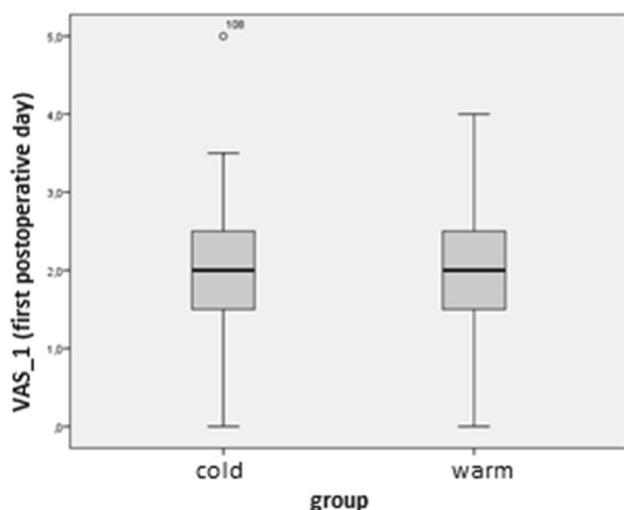


Fig. 2 VAS for patients receiving standard CO₂ gas (cold: group A) and warmed and humidified CO₂ gas (warm: group B) at first postoperative day

was 2 (SD \pm 0.81), and in men was 1.80 (SD \pm 0.81). Women had higher VAS scores, but there was no statistical difference between men and women in VAS₀ ($p = 0.21$) and VAS₁ ($p = 0.4$).

There was no difference between both groups in view of bowel movement after the operation ($p = 0.52$).

Discussion

Our results have shown that the use of warmed and humidified CO₂ during LCHE has positive effects on pain.

Table 4 Postoperative pain according to VAS

Time	Mean of VAS Group A	Group B	p
Operation day VAS ₀	2.22 (SD 0.97)	1.92 (SD 0.84)	0.025
First postoperative day VAS ₁	1.97 (SD 0.78)	1.92 (SD 0.86)	0.437

VAS₀: pain at the operation day; VAS₁: pain at the first postoperative day

VAS Visual analog scale, SD standard deviation

Insufflation with warmed and humidified carbon dioxide reduces pain significantly at the operation day. It was surprising that at the first postoperative day no statistical difference in pain was measurable. Referring to the literature, there is correlation between the degree of hypothermia and pain detectable. In our study, intraoperative core temperature was significantly decreased in group A (cold gas), whereas it was increased in group B (warmed gas). Insufflation with standard cold-dry CO₂ during laparoscopic surgery has been shown to predispose patients to hypothermia and peritoneal injury [7], and warmed, humidified carbon dioxide led to less postoperative pain [8].

A clinically interesting and important finding was the number of comorbidities in group B. In group B, there were 13 patients with degenerative joints disease in comparison with 7 Patients in group A with the same disease. Anyway, in group B, pain 6 h postoperatively was significantly less than in group A.

We recorded the amount of analgesic consumption. There is no significant difference in the amounts of used analgetic medication in both groups detectable. There was no correlation between the point of time of the first bowel movement after operation and the use of warmed and humidified gas.

There are inconclusive data in the literature referring to the effect of warmed and humidified gas in laparoscopic surgery. Slim et al. [9] did not determine a difference in intra-abdominal temperature in 100 patients who underwent laparoscopic operations. Saad et al. [10] analyzed 20 patients and determined no significant difference in pain intensity or postoperative consumption of analgesics between patients receiving standard CO₂ gas and patients receiving heated gas. The ability of humidified gas insufflation to provide a physiologically thermoneutral pneumoperitoneum has been proven under exaggerated conditions in an animal study [11], but the practical merit of this facility under normal clinical conditions has been questioned.

On the other hand, it has been shown that the insufflation of warmed and humidified CO₂ gas during LCHE may

reduce postoperative pain in comparison with standard CO₂ gas [12]. A meta-analysis [3] of ten randomized controlled trials on 565 patients showed that the use of heated and humidified CO₂ for pneumoperitoneum in laparoscopic procedures is associated with less postoperative pain, lower risk of postoperative hypothermia, and lower analgesic requirements. The mechanisms mediating postoperative pain after laparoscopy are contemplated to be multifactorial [7]. Insufflation with standard cold-dry CO₂ during laparoscopic surgery has been shown to predispose patients to hypothermia and peritoneal injury [13].

Conclusion

On the basis of this study, the use of warmed and humidified carbon dioxide during LCHE reduces postoperative pain significantly at the operation day.

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References

- Hünerbein M, Gretschel S, Rau B, Schlag PM (2003) Reducing trauma with minimally invasive surgery: evidence and new strategies. *Chirurg* 74:282–289
- Hong TH, You YK, Lee KH (2009) Transumbilical single-port laparoscopic cholecystectomy: scarless cholecystectomy. *Surg Endosc* 23:1393–1397
- Sajid MS, Mallick AS, Rimpel J, Bokari SA, Cheek E, Baig MK (2008) Effect of heated and humidified carbon dioxide on patients after laparoscopic procedures: a meta-analysis. *Surg Laparosc Endosc Percutan Tech* 18:539–546
- Peng Y, Zheng M, Ye Q, Chen X, Yu B, Liu B (2009) Heated and humidified CO₂ prevents hypothermia, peritoneal injury, and intra-abdominal adhesions during prolonged laparoscopic insufflations. *J Surg Res* 151:40–47
- Mouton WG, Naef M, Bessell JR, Otten KT, Wagner HE, Maddern GJ (2001) A randomized controlled trial to determine the effect of humidified carbon dioxide (CO₂) insufflation on postoperative pain following thoracoscopic procedures. *Surg Endosc* 15:579–581
- Pilz M, Shamiyeh A, Hörmandinger K, Gombotz J, Neugebauer EAM, Wayand W (2010) Die Implementierung der S3-Leitlinie Akutschmerztherapie über die „Initiative Schmerzfreie Klinik“—Verbesserung der Ergebnisqualität in einer Viszeralchirurgischen Klinik. *Perioperative Medizin* 2:50–56
- Pier A, Benedic M, Mann B, Buck V (1994) Das postlaparoskopische Schmerzsyndrom. *Chirurg* 65:200–208
- Sammour T, Kahokehr A, Hill AG (2008) Meta-analysis of the effect of warm humidified insufflation on pain after laparoscopy. *Br J Surg* 95:950–956
- Slim K, Bousquet J, Kwiatkowski F, Lescure G, Pezet D, Chipponi J (1999) Effect of CO₂ gas warming on pain after laparoscopic surgery: a randomized double-blind controlled trial. *Surg Endosc* 13:1110–1114
- Saad S, Minor I, Mohri T, Nagelschmidt M (2000) The clinical impact of warmed insufflation carbon dioxide gas for laparoscopic cholecystectomy. *Surg Endosc* 14:787–790
- Bessell JR, Ludbrook G, Millard SH, Baxter PS, Ubhi SS, Maddern GJ (1999) Humidified gas prevents hypothermia induced by laparoscopic insufflation: a randomized controlled study in a pig model. *Surg Endosc* 13:101–105
- Ott DE, Reich H, Love B, McCorvey R, Toledo A, Liu CY, Syed R, Kumar K (1998) Reduction of laparoscopic-induced hypothermia, postoperative pain and recovery room length of stay by pre-conditioning gas with the Insuflow device: a prospective randomized controlled multi-center study. *JSLS* 2:321–329
- Bessell JR, Karatassas A, Patterson JR, Jamieson GG, Maddern GJ (1996) The influence of insufflated gas on temperature balance during laparoscopy. In: Rosenthal RJ, Friedman RL, Philips EH (eds) *The pathophysiology of pneumoperitoneum*. Springer, Los Angeles, pp 18–27