

Low-pressure capnoperitoneum reduces stress responses during pediatric laparoscopic high ligation of indirect inguinal hernia sac

A randomized controlled study

Xiaoguang Niu, MM^a, Xubin Song, BD^b, Aiping Su, BD^c, Shanshan Zhao, MM^d, Qinghao Li, BD^{a,*}

Abstract

Background: We aimed to evaluate the effect of different capnoperitoneum pressures on stress responses in pediatric laparoscopic inguinal hernia repair.

Methods: In this prospective randomized controlled study, 68 children with indirect inguinal hernia who underwent high ligation of hernia sac were randomly divided into 3 groups: high-pressure group (12 mm Hg, HP group, n=26); low-pressure group (8 mm Hg, LP group, n=20); open operation group (OP group, n=22). Heart rate (HR), blood pressure, and end-tidal CO₂ (PetCO₂) were recorded, as well as the levels of adrenocorticotrophic hormone (ACTH) and cortisol (COR) were measured by ELISAs before operation, during operation, and after operation, respectively.

Results: After establishing capnoperitoneum, HR, blood pressure, and PetCO₂ were significantly increased in the HP group compared with the OP and LP groups ($P < 0.05$). Comparing the intraoperatively measured ACTH and COR concentrations of the HP group to the LP group, we noted higher values in the first ($P < 0.05$). There was no significant difference in the postoperative concentrations of ACTH and COR among the HP, LP, and OP groups.

Conclusions: Laparoscopic surgery under LP capnoperitoneum or open operation may reduce stress responses and are superior to HP capnoperitoneum.

Abbreviations: ACTH = adrenocorticotrophic hormone, ASA = American Society of Anesthesiologists, COR = cortisol, DBP = diastolic blood pressure, ELISA = enzyme-linked immuno sorbent assay, HP = high-pressure, HR = heart rate, LP = low-pressure, OP = open operation, PetCO₂ = end-tidal CO₂, SBP = systolic blood pressure, SD = standard deviation.

Keywords: child capnoperitoneum, hemodynamic changes, inguinal hernia, laparoscopic surgery, neuroendocrine response

1. Introduction

Pediatric indirect inguinal hernia is a common disorder.^[1] High ligation of the indirect hernia sac and herniorrhaphy are recommended as the effective treatments for pediatric indirect inguinal hernia.^[2] Currently, laparoscopy has flourished worldwide in the diagnosis and treatment of impalpable testes in

children.^[3,4] Due to minimal trauma, less pain, less bleeding, faster recovery and short treatment time, laparoscopic techniques have been demonstrated to be efficient and safe in children.^[5,6] However, the laparoscopic approach may lead to side effects such as pulmonary hypertension, hypercapnia, and acidosis because of the establishment of capnoperitoneum.^[7,8] Moreover, some authors think that the hernia recurrence rate is higher after laparoscopic repair when compared to open operation of indirect hernias in children.^[9–11] Therefore, it is necessary to search for and investigate suitable capnoperitoneum pressures during the laparoscopy.

Although some studies have compared the efficacy and safety of different capnoperitoneum pressures during the laparoscopy in adults,^[12–14] few studies are focused on children. Meanwhile, stress responses in children during surgery are more sensitive than adults.^[15] Thus, the present study analyzed the effects of different capnoperitoneum pressures on stress responses, including heart rate (HR), blood pressure, the levels of adrenocorticotrophic hormone (ACTH) and cortisol (COR) in serum, and aimed to evaluate the suitable capnoperitoneum pressures in pediatric laparoscopic high ligation of the hernia sac.

2. Materials and methods

2.1. Patients

From January 2014 to October 2014, a total of 68 children (44 male and 24 female) who were diagnosed with unilateral indirect

Editor: Somchai Amorniyotin.

Funding: The work was supported by special fund for medical service of Jilin finance department [project number SCZSY201507].

The authors have no conflicts of interest to disclose.

^a Department of Pediatric Surgery, ^b Department of Pharmacy, Taian City Central Hospital, ^c Department of Surgery, Taishan Hospital of Shandong Province, ^d Department of Reproductive Genetics Center, Taian City Central Hospital, Taian, China.

* Correspondence: Qinghao Li, Department of Pediatric Surgery, Taian City Central Hospital, Taian, Shandong, China (e-mail: qingdaoli_1506@hotmail.com).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medicine (2017) 96:14(e6563)

Received: 5 January 2017 / Received in final form: 7 March 2017 / Accepted: 10 March 2017

<http://dx.doi.org/10.1097/MD.0000000000006563>

inguinal hernia at the Department of Pediatric surgery, Taian City Central Hospital, were included in this prospective study. Patients were included according to the following criteria: (1) patients with American Society of Anesthesiologists (ASA) grade 2 that patients had slight systemic diseases and mild lesions of important organs, but normal compensatory function,^[16] and (2) aged 4 to 9 years old. Patients with cardiopulmonary anomaly and other serious systemic diseases were excluded from this study. Approval from the Ethics Committee of Taian City Central Hospital was obtained and informed consents were signed by legal guardians of all patients prior to operation.

All the patients were randomly divided into 3 groups in accordance with the random number table: high-pressure group (HP group, $n=26$), patients received laparoscopic high ligation of the hernia sac, and a pressure of the capnoperitoneum of 12 mm Hg was used; low-pressure group (LP group, $n=20$), patients received laparoscopic high ligation of the hernia sac with a pressure of the capnoperitoneum of 8 mm Hg; open operation group (OP group, $n=22$), patients received high ligation of hernia sac by open operation.

2.2. Anesthesia and surgery method

HR, blood pressure, and blood oxygen saturation were monitored regularly when children entered the operation room. Anesthesia was induced by intravenous atropine (0.02 mg/kg) with 100% oxygen at 8 L/min for 3 minutes, followed by fentanyl (2 μ g/kg), midazolam (0.05 mg/kg), etomidate (0.2 mg/kg) and cis-atracurium (0.15 mg/kg). After intubation, patients received an aerosol solution of 1% isoflurane and continuous intravenous injection of 15 mL/h mixture composed of 50 mL propofol + 1 mg remifentanyl during operation. Meanwhile, capnoperitoneum pressure was controlled using the capnoperitoneum apparatus. All the operations were performed by the same team of surgeons. After satisfactory anesthesia, patients in HP and LP groups were maintained in the supine position. Open laparoscopy was performed using an 1 cm arc incision at the umbilicus of patients, and then the high ligation of the hernia sac was performed at a 2 mm abdominal transverse cleavage line incision on the affected side with the stable capnoperitoneum pressure of either 12 mm Hg (HP group) or 8 mm Hg (LP group). Residual CO₂ was evacuated at the end of operation by compressing the abdomen. For patients in the OP group, the high ligation of the hernia sac was performed through a 2 cm abdominal transverse cleavage line incision on the affected side by open operation.^[17]

2.3. Monitoring index

The values of HR, systolic blood pressure (SBP), and diastolic blood pressure (DBP), as well as end-tidal CO₂ (PetCO₂) were recorded at 5 minutes before operation and 20 minutes after establishing capnoperitoneum, respectively. Operative time and length of postoperative stay were also recorded. In addition, venous blood of all patients was collected at 30 minutes before operation, 20 minutes after establishing capnoperitoneum, and 12 h after operation, respectively. Then, the levels of ACTH and COR in serum were measured by enzyme-linked immunosorbent assays (ELISAs) kits (ADL) according to the manufacturer's instructions.

2.4. Statistical analysis

Statistical analysis was performed by SPSS 13.0 statistical analysis software (IBM Corporation, New York). Data were

expressed as mean \pm standard deviation (SD) and analyzed by analysis of variance followed by least significant difference test. A value of $P < 0.05$ was considered significant.

3. Results

Demographic data of the children are shown in Table 1. No significant difference was found in sex, age, and weight among the HP, LP, and OP groups. Compared with OP group (22.55 ± 4.60 min), operative time in the HP (30.95 ± 4.75 min) and LP (28.04 ± 4.44 min) groups was increased ($P < 0.001$). Length of postoperative stay was shortened in the HP (3.46 ± 0.65 day) and LP (3.35 ± 0.49 day) groups when compared to the OP group (4.55 ± 0.51 day) ($P < 0.001$). All children recovered well and no intraoperative complications were found in these 3 groups.

Preoperative circulatory system indexes, including HR, SBP, and DBP, were similar in the HP, LP, and OP groups (Table 2). After establishing capnoperitoneum for 20 minutes, HR and SBP were higher in the HP group than those in the OP ($P < 0.001$ and $P < 0.001$) and LP ($P < 0.001$ and $P = 0.001$) groups, whereas no significant difference was found between the OP and LP groups (Table 2). In addition, DBP was higher in the HP group than that in the OP group ($P = 0.008$), whereas no significant difference was found between the OP and LP groups or LP and HP groups (Table 2). Preoperative respiratory system index PETCO₂ also had no significant difference among the HP, LP, and OP groups (Table 2). During the operation under capnoperitoneum for 20 minutes, PetCO₂ in the HP group was increased compared with the OP ($P < 0.001$) and LP ($P < 0.001$) groups, and PetCO₂ was higher in the LP group than that in the OP group ($P = 0.001$, Table 2).

Furthermore, neuroendocrine system indexes (ACTH and COR) in the HP, LP, and OP groups were detected by ELISA and the results are shown in Table 3. During operation, the concentrations of ACTH and COR were higher than those before operation ($P < 0.001$). Perioperative ACTH content was significantly increased in the LP group compared with the HP ($P = 0.021$) and OP ($P < 0.001$) groups. In addition, during operation, the concentration of ACTH in the HP group was higher than that in the OP group ($P < 0.001$). In the HP group, perioperative concentration of COR was higher than that in the OP ($P < 0.001$) and LP ($P = 0.001$) groups, and the concentration of COR in the LP group was increased compared with the OP group ($P = 0.02$). Twelve hours after the operation, the concentration of ACTH in the HP group and the concentration of COR in the HP, LP, and OP groups were all increased compared with before operation, while no significant difference was found among the HP, LP, and OP groups.

4. Discussion

Although capnoperitoneum had been widely applied in laparoscopy due to the low cost, the nonflammable nature of the gas,

Table 1
Demographic data of patients in the OP, LP, and HP groups.

	OP group (n=22)	LP group (n=20)	HP group (n=26)	P
Sex, male/female, n	15/7	14/6	15/11	0.631
Age, mean \pm SD, years	5.36 \pm 1.00	5.80 \pm 1.54	6.00 \pm 0.98	0.177
Weight, mean \pm SD, kg	19.34 \pm 1.95	20.13 \pm 2.77	20.02 \pm 1.73	0.429

HP = high-pressure, LP = low-pressure, OP = open operation.

Table 2
Circulatory and respiratory systems indexes of patients in the OP, LP, and HP groups.

	OP group		LP group		HP group	
	Before operation	During operation	Before operation	During operation	Before operation	During operation
HR, beats/min	86.82 ± 4.96	96.09 ± 3.29	87.80 ± 4.85	97.60 ± 4.66	88.85 ± 4.97	103.38 ± 5.65* [#]
SBP, mm Hg	90.73 ± 9.12	94.36 ± 4.96	91.15 ± 8.44	95.80 ± 4.66	92.62 ± 7.75	101.46 ± 6.31* [#]
DBP, mm Hg	57.82 ± 5.63	65.68 ± 5.41	57.10 ± 5.86	67.50 ± 5.50	58.35 ± 5.56	70.04 ± 5.55*
PETCO ₂ , mm Hg	39.68 ± 1.39	46.14 ± 4.13	39.70 ± 1.42	49.95 ± 3.59	39.73 ± 1.43	55.42 ± 3.37* [#]

DBP = diastolic blood pressure, HP = high-pressure, HR = heart rate, LP = low-pressure, OP = open operation, PETCO₂ = end-tidal CO₂, SBP = systolic blood pressure.

* P < 0.05 compared with the OP group.

[#] P < 0.05 compared with the LP group.

high diffusion capacity and rapid absorption, high absorption of CO₂ causes changes of the internal environment and increase stress response.^[18] Thus, the present study evaluated the influence of different capnoperitoneum pressures on stress responses in children. The results showed that compared with OP and LP groups, circulatory system indexes, including HR, SBP, and DBP, as well as respiratory system index PetCO₂ were increased after establishing capnoperitoneum for 20 minutes. In addition, the concentrations of ACTH and COR were higher after operation than those before operation. Compared with the OP group, perioperative concentrations of ACTH and COR were significantly increased in the LP and HP groups, and the concentration of ACTH in the LP group was higher, while perioperative concentration of COR was lower than those in the HP group. Twelve hours after the operation, no significant difference was found in the concentration of ACTH or COR among the HP, LP, and OP groups.

The side effects of high-pressure capnoperitoneum with CO₂ on circulatory, respiratory and neuroendocrine systems had been reported during laparoscopy.^[19,20] A previous study showed that HR and blood pressure significantly increased after the induction of capnoperitoneum.^[21] Similarly, the present study found that capnoperitoneum increased HR and blood pressure. This might be explained that: (1) the establishment of capnoperitoneum induced an increase of the intra-abdominal pressure and the change in position, which led to the elevated blood pressure and increased peripheral vascular resistance, thereby increasing cardiac afterload; (2) high diffusion of CO₂ into blood induced hypercapnia and the productions of adrenaline, norepinephrine, or dopamine, which resulted in capillary contraction and raised blood pressure; (3) increased HR and blood pressure were caused by reduced coronary perfusion pressure and decreased aortic compliance due to reduced chest volume and increased pulmonary pressure after the induction of capnoperitoneum; (4) due to incomplete development of the cardiac muscle in children, the side effects of capnoperitoneum on HR and blood pressure may be more significant.^[22–25] Thus, the endotracheal intubation and high-

concentration oxygen inhalation were provided in children during operation. In addition to HR and blood pressure, PETCO₂ was also increased due to the establishment of capnoperitoneum in our study, which was consistent with the study of Pan et al.^[26] It had been demonstrated that increased PetCO₂ was induced because of the transperitoneal absorption of CO₂ and reduced lung function.^[27] Our study also found that HP capnoperitoneum induced higher HR, blood pressure, and PetCO₂ than LP and OP. Consistent with our study, Khan et al.^[28] suggested that HR, mean arterial blood pressure, and PETCO₂ were elevated with increased pressure of the capnoperitoneum. These results can be interpreted that LP capnoperitoneum had less intraoperative hemodynamic changes than HP capnoperitoneum in pediatric laparoscopic surgery.

Furthermore, this study found that compared with the OP group, neuroendocrine changes of children had obvious difference in laparoscopy. However, Reith et al.^[29] reported that cytokine response in open cholecystectomy was less pronounced when compared to laparoscopic cholecystectomy in adult. The contradiction might be caused by different types of surgery and a more sensitive neuroendocrine stress response in children. We found that the establishment of capnoperitoneum induced different alterations in influences in the concentrations of ACTH and COR dependent on the discretion of the capnoperitoneum pressures. When the body suffered sudden intense stimulation, both ACTH and COR levels were significantly increased because of stress reaction. Watanabe et al.^[30] also demonstrated that plasma concentrations of ACTH and COR were both increased during capnoperitoneum. We speculate that the reasons may be: (1) increased intra-abdominal pressure resulted in reduced renal perfusion and then activated the vascular control center of the medulla oblongata, which enhanced sympathetic activation; (2) pain caused by surgical trauma activated the hypothalamus-adenohypophysis-adrenocortical system, which induced elevated ACTH and COR.^[31,32] These results indicated that LP capnoperitoneum might have lower neuroendocrine response than HP capnoperitoneum in pediatric laparoscopic surgery.

Table 3
The concentrations of ACTH and COR in serum of patients in the OP, LP, and HP groups.

	ACTH (pmol/L)			COR (nmol/L)		
	OP group	LP group	HP group	OP group	LP group	HP group
Before operation	2.48 ± 0.89	2.55 ± 0.49	2.28 ± 0.92	331.09 ± 90.66	353.25 ± 78.06	344.81 ± 84.06
During operation	2.40 ± 0.67	3.56 ± 0.51*	3.10 ± 0.74* [#]	359.27 ± 83.13	424.25 ± 71.45*	512.35 ± 102.56* [#]
After operation	2.39 ± 0.75	2.57 ± 0.56	2.47 ± 0.86	349.09 ± 76.92	369.10 ± 60.88	364.19 ± 97.42

ACTH = adrenocorticotropic hormone, COR = cortisol, HP = high-pressure, LP = low-pressure, OP = open operation.

* P < 0.05 compared with the OP group.

[#] P < 0.05 compared with the LP group.

However, this study has some limitations. First, the sample size is small, which may cause the result bias. Thus, a larger sample study should be performed to confirm our results. Second, the supplements of some clinically relevant data may increase the more clinical significance. Even so, the current data also can illustrate the effect of different capnoperitoneum pressures on stress responses.

5. Conclusions

Our results indicate that LP capnoperitoneum may reduce intraoperative hemodynamic changes and neuroendocrine stress reaction. We hypothesize that laparoscopic surgery under LP capnoperitoneum may be superior to HP capnoperitoneum.

References

- [1] Shalaby A, Curry J. Inguinal hernias in children. Management of Abdominal. Hernias Berlin: Springer; 2013:185–99.
- [2] Ziegler M, Azizkhan RG, von Allmen D, et al. Operative pediatric surgery. New York: McGraw-Hill Professional; 2014:613–31.
- [3] Scott JE. Laparoscopy as an aid in the diagnosis and management of the impalpable testis. *J Pediatr Surg* 1982;17:14–6.
- [4] Chan KWE, Lee KH, Wong HYV, et al. Use of laparoscopy as the initial surgical approach of impalpable testes: 10-year experience. *World J Clin Pediatr* 2015;4:155.
- [5] Peters CA. Laparoscopy in pediatric urology. *Urology* 1993;41:33–7.
- [6] Harrington S, Simmons K, Thomas C, et al. Pediatric laparoscopy. *AORN J* 2008;88:211–40.
- [7] Karapolat S, Gezer S, Yildirim U, et al. Prevention of pulmonary complications of pneumoperitoneum in rats. *J Cardiothorac Surg* 2011;6:1–7.
- [8] Hasukić Š. Co₂-pneumoperitoneum in laparoscopic surgery: pathophysiological effects and clinical significance. *World* 2014;7:33–40.
- [9] Rosenberg J. Pediatric inguinal hernia repair—a critical appraisal. *Hernia* 2008;12:113–5.
- [10] Schier F, Montupet P, Eposito C. Laparoscopic inguinal herniorrhaphy in children: a three-center experience with 933 repairs. *J Pediatr Surg* 2002;37:395–7.
- [11] Schier F. Laparoscopic inguinal hernia repair—a prospective personal series of 542 children. *J Pediatr Surg* 2006;41:1081–4.
- [12] Sandhu T, Yamada S, Ariyakachon V, et al. Low-pressure pneumoperitoneum versus standard pneumoperitoneum in laparoscopic cholecystectomy, a prospective randomized clinical trial. *Surg Endosc* 2009;23:1044–7.
- [13] Gurusamy K, Vaughan J, Davidson B. Low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy. *Aorn J* 2014;3: CD006930.
- [14] Bogani G, Uccella S, Cromi A, et al. Low vs standard pneumoperitoneum pressure during laparoscopic hysterectomy: prospective randomized trial. *J Minim Invasive Gynecol* 2014;21:466–71.
- [15] Dingemann J, Kuebler J, Ure B. Laparoscopic and computer-assisted surgery in children. *Scand J Surg* 2011;100:236–42.
- [16] Sankar A, Johnson SR, Beattie WS, et al. Reliability of the American Society of Anesthesiologists physical status scale in clinical practice. *Brit J Anaesth* 2015;113:424–32.
- [17] Chan KL, Hui WC, Tam PK. Prospective randomized single-center, single-blind comparison of laparoscopic vs open repair of pediatric inguinal hernia. *Surg Endosc* 2005;19:927–32.
- [18] Matsuzaki S, Jardon K, Maleysson E, et al. Impact of intraperitoneal pressure of a CO₂ pneumoperitoneum on the surgical peritoneal environment. *Hum Reprod* 2012;27:1613–23.
- [19] Dexter S, Vucevic M, Gibson J, et al. Hemodynamic consequences of high-and low-pressure capnoperitoneum during laparoscopic cholecystectomy. *Surg Endosc* 1999;13:376–81.
- [20] Stuttmann R, Vogt C, Eypasch E, et al. Haemodynamic changes during laparoscopic cholecystectomy in the high-risk patient. *Endosc Surg Allied Technol* 1995;3:174–9.
- [21] Neudecker J, Sauerland S, Neugebauer E, et al. The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. *Surg Endoscopy Other Interv Tech* 2002;16:1121–43.
- [22] Kadono Y, Yaegashi H, Machioka K, et al. Cardiovascular and respiratory effects of the degree of head-down angle during robot-assisted laparoscopic radical prostatectomy. *Int J Med Robot Comput Assist Surg* 2013;9:17–22.
- [23] Bhangu A, Morton D. Is this laparoscopic technique study the perfect surgical trial? *Lancet* 2016;387:1351–2.
- [24] Sajid MS, Khawaja AH, Sains P, et al. A systematic review comparing laparoscopic vs open adhesiolysis in patients with adhesional small bowel obstruction. *Am J Surg* 2016;212:138–50.
- [25] Iwasaka H, Miyakawa H, Yamamoto H, et al. Respiratory mechanics and arterial blood gases during and after laparoscopic cholecystectomy. *Canad J Anaesth* 1996;43:129–33.
- [26] Pan Y-S, Hu Y-F, Tian F-B, et al. Effects of epidural preemptive analgesia on stress reaction in retroperitoneal laparoscopic adrenalectomy surgery: a randomized controlled study. *Int J Clin Exp Med* 2015;8:9862.
- [27] Truchon R. Anaesthetic considerations for laparoscopic surgery in neonates and infants: a practical review. *Best Pract Res Clin Anaesthesiol* 2004;18:343–55.
- [28] Khan F, Manzoor A, Jamal S. Low pressure pneumoperitoneum laparoscopic cholecystectomy: a comparison of intra-operative hemodynamic stability and physiological changes with standard pressure pneumoperitoneum laparoscopic cholecystectomy. *Rawal Med J* 2015;40:299–302.
- [29] Reith H, Kaman S, Mittelkötter O, et al. Cytokine activation in patients undergoing open or laparoscopic cholecystectomy. *Int Surg* 1996;82: 389–93.
- [30] Watanabe K, Kashiwagi K, Kamiyama T, et al. High-dose remifentanyl suppresses stress response associated with pneumoperitoneum during laparoscopic colectomy. *J Anesth* 2014;28:334–40.
- [31] Schuetz M, Gockel I, Beard J, et al. Three different types of surgeon-specific stress reactions identified by laparoscopic simulation in a virtual scenario. *Surg Endosc* 2008;22:1263–7.
- [32] Ozawa A, Konishi F, Nagai H, et al. Cytokine and hormonal responses in laparoscopic-assisted colectomy and conventional open colectomy. *Surg Today* 2000;30:107–11.