UIJ UroToday International Journal®

www.urotodayinternationaljournal.com
Volume 4 - February 2011

Hemodynamic, Respiratory, and Immunological Effects of Urological Laparoscopic Surgery: A Prospective Study

Mukesh Kumar Vijay, Preeti Vijay, Punit Tiwari, Suresh Kumar, Pramod Kumar Sharma, Amit Goel, Pratim Sengupta, Malay Kumar Bera

Department of Urology, Institute of Post Graduate Medical Education and Research, Seth Sukhlal Karnani Memorial Hospital, Kolkata, West Bengal, India

Submitted November 29, 2010 - Accepted for Publication December 19, 2010

ABSTRACT

INTRODUCTION: Numerous physiological responses as a result of carbon dioxide (CO_2) insufflation occur in almost every organ system. The present study investigated the impact of intraperitoneal or extraperitoneal CO_2 insufflation on cardiopulmonary and immunological variables during urological laparoscopic surgery.

METHODS: From August 2007 to April 2009, we performed 40 laparoscopic urological surgeries (36 transperitoneal; 4 retroperitoneal) on otherwise healthy patients. There were 16 males and 24 females. Their mean age was 39 years. All patients underwent peripheral venous blood sampling preoperatively and 24 hours postoperatively. These were analyzed for C-reactive protein (CRP), white blood cell count, and differential leukocyte count. Arterial blood gas was sampled preoperatively and intraoperatively. Measurements were started when the patient was placed in the lateral decubitus position and continued at 2-minute regular intervals until the time of emergence. End-tidal CO_2 ($ETCO_2$) was measured every 15 minutes during the entire procedure. Outcome measures were surgery duration and mean pH level, partial pressure of oxygen (pO_2), $ETCO_2$, peak airway pressure (PAP), respiratory rate (RR), oxygen (O_2) saturation, mean arterial pressure (MAP), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), C-reactive protein (CRP), and leukocyte levels. Measures before and after CO_2 insufflation were compared with paired *t* tests.

RESULTS: Mean operative time was 3.6 hours. The mean (SD) preoperative pO_2 was 140.28 (25.61) mmHg, which was significantly higher than the mean intraoperative pO_2 of 133.9 (24.43) mmHg ($P < .05$). There was no significant difference in the mean $ETCO_2$ before and after insufflation. However, the mean change in $ETCO_2$ at 15-minute intervals was significantly higher than the $ETCO_2$ before insufflation. There were no significant changes in mean pH, O_2 saturation, MAP, RR, $ETCO_2$, PAP, HR, SBP, DBP, or RR. Inflammatory markers CRP and white blood cell count were statistically similar.

CONCLUSIONS: Physiological changes incurred as a result of CO_2 insufflation have minimal adverse effects in healthy individuals undergoing urological laparoscopic surgery.

KEYWORDS: Intra-abdominal pressure; Mean arterial pressure; Heart rate; pO_2; End-tidal CO_2

CORRESPONDENCE: Mukesh Kumar Vijay, Department of Urology, Institute of Post Graduate Medical Education and Research, Seth Sukhlal Karnani Memorial Hospital, 682 A Newalipore O Block, Kolkata, West Bengal 700020, India (drmukeshpreeti@gmail.com).

CITATION: *UroToday Int J*. 2011 Feb;4(1):art 18. doi:10.3834/uij.1944-5784.2011.02.18

Abbreviations and Acronyms

CO_2, carbon dioxide
CRP, C-reactive protein
DBP, diastolic blood pressure
$ETCO_2$, end-tidal CO_2
HR, heart rate
IAP, intraabdominal pressure
IL-6, interleukin-6
MAP, mean arterial pressure
O_2, oxygen
PAP, peak airway pressure
pCO_2, partial pressure of carbon dioxide
pO_2, partial pressure of oxygen
RR, respiratory rate
SBP, systolic blood pressure

INTRODUCTION

Laparoscopy is now well incorporated into urological surgical practice. Numerous physiological responses as a result of carbon dioxide (CO_2) insufflation occur in almost every organ system. It is thought that increased intraabdominal or retroperitoneal pressure during CO_2 insufflation reduces diaphragm mobility and respiration efficiency. The present study was designed to investigate the impact of intraperitoneal or extraperitoneal CO_2 insufflation and the decubitus lateral position on cardiopulmonary and immunological variables during urological laparoscopic surgery in the adult population.

METHODS

From August 2007 to April 2009, we performed 40 transperitoneal or retroperitoneal laparoscopic urological surgeries in our center. All patients provided informed consent to participate in the investigation.

Participants

The 40 participants were otherwise healthy patients in whom laparoscopic intervention was successfully completed. There were 16 males and 24 females. Their mean age was 39 years (range, 32-43 years). Out of the 40 patients, 36 had transperitoneal and 4 had retroperitoneal laparoscopic urological surgeries. The surgeries were further classified as nephrectomies (n = 12), donor nephrectomies (n = 13), pyeloplasty (n = 6), adrenelectomy (n = 3), ureterolithotomy (n = 4), and ureteric reimplantation (n = 2).

Procedures

All patients underwent peripheral venous blood sampling twice: preoperatively on the day of surgery and 24 hours postoperatively. The blood was analyzed for C-reactive protein (CRP), white blood cell count, and differential leukocyte count. All patients also underwent arterial blood gas analysis sampling twice: preoperatively on the day of surgery and intraoperatively.

The participants were supine for induction and emergence from anesthesia. They remained in a flexed lateral decubitus position during intervention. Measurements were started when the patient was placed in the lateral decubitus position and continued at 2-minute regular intervals until the time of emergence. End-tidal CO_2 ($ETCO_2$) was measured every 15 minutes during the entire procedure. The time intervals for assessment of the physiological parameters were selected based on discussions with the anesthesiologist; they were kept constant for all patients.

Data Analysis

Variables included age, sex, and type of surgery. Outcome measures were surgery duration, pH level, partial pressure of oxygen (pO_2), $ETCO_2$, peak airway pressure (PAP), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), oxygen (O_2) saturation, mean arterial pressure (MAP), CRP, and leukocyte levels. For each patient, the mean value of each variable was calculated before and after CO_2 insufflation.

Results were expressed as means and standard deviations. Statistical analysis was done with SPSS (IBM Corp, Somers, NY) v-11.01. Paired *t* tests were used to determine statistically significant differences between comparisons, using a probability cutoff of $P < .05$.

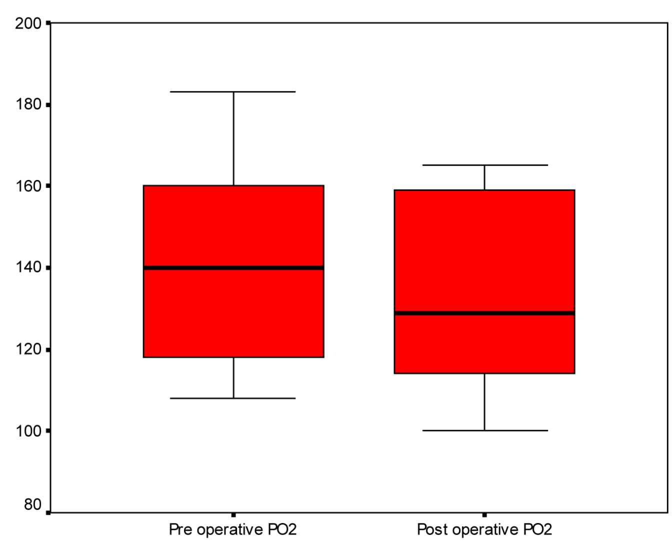
RESULTS

The mean operative time was 3.6 Hours. The CO_2 insufflation pressure was 15 mm Hg.

The means and standard deviations for all outcome measures before and after CO_2 insufflation and the probability of significant differences are contained in Table 1. There was no significant difference in the mean pH levels before and after insufflation. The mean (standard deviation) preoperative pO_2 was 140.28 (25.61) mmHg, which was significantly higher than the mean intraoperative pO_2 of 133.9 (24.43) mmHg ($P = .015$) (see Figure 1). There was no significant difference in respiratory rate or oxygen saturation levels before and after insufflation.

Figure 1. The Dispersion of Partial Pressure of Oxygen (pO_2) on the Y axis (in mm of Hg) Before and After Insufflation ($P = .015$).

doi: 10.3834/uij.1944-5784.2011.02.18f1



UIJ UroToday International Journal®
original study
Mukesh Kumar Vijay, Preeti Vijay, Punit Tiwari, Suresh Kumar, Pramod Kumar Sharma, Amit Goel, Pratim Sengupta, Malay Kumar Bera
www.urotodayinternationaljournal.com

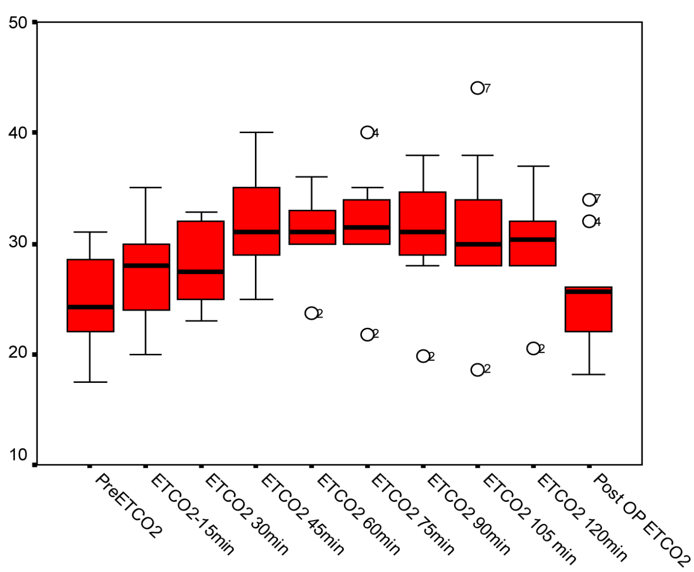
Table 1. Means and Standard Deviations (SD) for Outcome Measures Before and After Insufflation; Probability of Significant Differences (N = 40).

doi: 10.3834/uij.1944-5784.2011.02.18t1

Outcome Measure	Before Insufflation		After Insufflation		*P*
	Mean	SD	Mean	SD	
pH	7.43	0.09	7.41	0.07	.99
pO_2, mmHg	140.28	25.61	133.9	24.43	.015
Oxygen saturation (%)	98	1	96	1.4	.60
Respiratory rate, breaths/min	19	2.5	22	2.6	.80
$ETCO_2$, mmHg	24.75	4.57	25.29	4.92	.40
Peak airway pressure, cmH_2O	19.4	1.57	19.7	1.25	.40
Heart rate, beats/min	73.7	9.68	69.8	4.83	.09
Mean arterial pressure, mmHg	85.9	8.5	87.6	8.3	.65
Blood pressure, mmHg					
Systolic	114.0	14.49	118	12.86	.50
Diastolic	71.8	5.5	72.4	6.02	.80
C-reactive protein, mg/dL	6.69	6.01	6.63	6.17	.40
Leukocyte, mm^3	9536	1917.61	9930	2243.03	.13

Figure 2. Box Plot Showing the Pattern of End-Tidal Carbon Dioxide ($ETCO_2$) in 15-Minute Intervals During the Laparoscopy.

doi: 10.3834/uij.1944-5784.2011.02.18f2



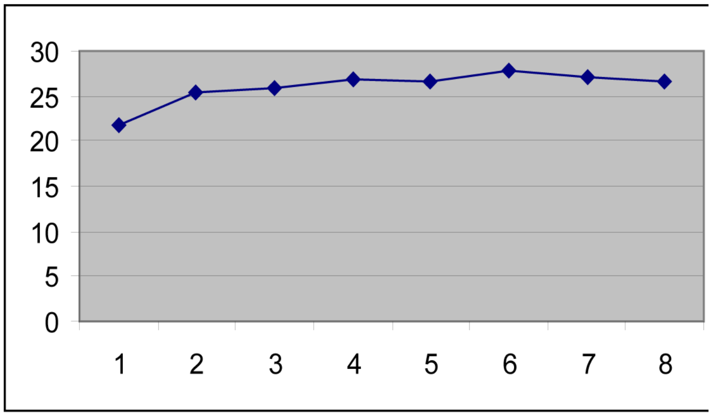
Y axis presents $ETCO_2$ in mm of Hg; X-Axis presents the sequential timeframe.

There was no significant difference in the mean $ETCO_2$ before and after insufflation. However, the mean change in $ETCO_2$ at every 15-minute interval was significantly higher than the $ETCO_2$ before insufflation (Figure 2). There was no significant difference in the mean PAP before and during CO_2 insufflation (Figure 3).

There was no significant difference in the mean HR before and after insufflation. Figure 4 is a line diagram showing that there was a substantial drop in mean HR at about 90-minutes. This may have been due to decreased pH (hypercarbia or other cause) that is associated with myocardial depression and may have manifested as decreased heart rate. There were no significant differences in mean arterial pressure, SBP, or DBP before and during surgery.

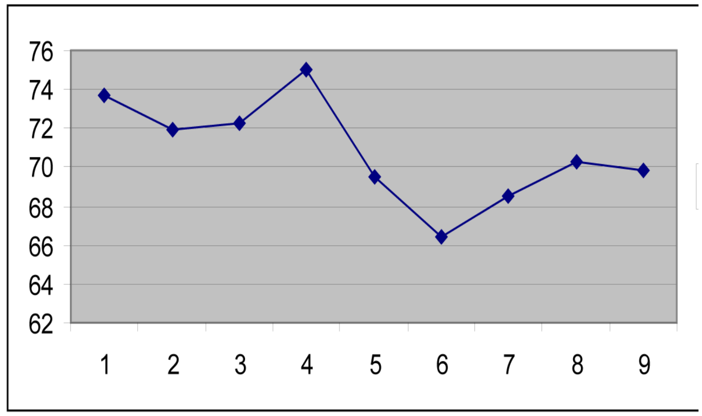
There was no significant difference in the mean CRP levels before and after insufflation (it should be noted that the standard deviations were very large). As an immunological stress response (along with CRP), the total leukocyte count was also followed before and after surgery. There was no significant difference in the mean leukocyte levels.

Figure 3. Line Diagram of Mean Peak Airway Pressure (PAP) During Surgery.
doi: 10.3834/uij.1944-5784.2011.02.18f3



Y- Axis represents the mean PAP in mm of Hg; X axis represents the value at every 15-minute interval during the surgery (1 = 15 minutes; 2 = 30 minutes, etc).

Figure 4. Line Diagram of Heart Rate During Surgery.
doi: 10.3834/uij.1944-5784.2011.02.18f4



Y axis shows the heart rate per minute; X axis shows the value at every 15-minute interval during the surgery (1 = 15 minutes; 2 = 30 minutes, etc).

DISCUSSION

In the drive to master laparoscopic technique and application we must be reminded of the basic physiological changes that accompany laparoscopic procedures in order to maximize preoperative, intraoperative, and postoperative patient care. Physiological changes as a result of CO_2 insufflation occur in every organ system of the human body in time-dependent and pressure-dependent manners. Clinically, the degree to which various vascular and cardiac parameters change during surgery is a function of several factors, including intraabdominal pressure, patient position, CO_2 absorption, intravascular volume, preexisting cardiopulmonary status, and current medications.

Changes in cardiovascular physiology during CO_2 insufflation mainly result from increases in intraabdominal pressure (IAP). Generated IAP may secondarily affect hemodynamic status via vagal reflexes and neurohumoral responses of the renin-angiotensin-aldosterone system. The general trend in studies of cardiovascular changes associated with laparoscopic surgery has indicated an increase in systemic vascular resistance, mean arterial pressure (MAP), and myocardial filling pressure, accompanied by a decrease in cardiac index with little change in heart rate. These are ideal responses at pressures of 12-15 mm Hg. Two recent randomized studies comparing CO_2-based laparoscopic cholecystectomy vs gasless abdominal wall lift laparoscopic cholecystectomy measured cardiac function and found dramatically different results. Larsen et al [1] reported no difference in cardiac output between study groups; Alijani et al [2] noted a significant decrease in cardiac output in the positive pressure capnoperitoneum group. Animal studies suggest that elevated intraabdominal pressure leads to an increase in total peripheral vascular resistance, which negatively influences cardiac function. Likewise, as intraabdominal pressure increases, mean systemic pressure increases as a result of compression of the small capacitance vessels and augmented venous return. Our study showed no differences in MAP or heart rate after CO_2 insufflation when compared with baseline. We also found that these values normalized after completion of the laparoscopic intervention. Kashtan and colleagues [3] demonstrated that increased mean systemic pressure enhanced venous return and right atrial pressure in hypervolemic animals. The Association for Endoscopic Surgery practice guidelines consensus [4] summarized that, at intraabdominal pressures up to 15 mm Hg, the decrease in venous return and cardiac output is minimal and without consequences in healthy patients. Marshall and colleagues [5] also found no change in cardiac output in 7 young women undergoing laparoscopic tubal ablation, but they found that significant increases in central venous pressure, mean arterial pressure, and HR occurred with insufflation to between 15 and 21 mm Hg. Likewise, in our study we used intraabdominal pressure up to 15 mm Hg and found no change in MAP or HR.

When CO_2 is used, hypercarbia with subsequent acidosis may additionally affect cardiovascular status through sympathoadrenal stimulation. The hemodynamic consequences of hypercarbia have been well described. Price [6] divided the effects of hypercarbia into direct and indirect types. In isolated animal hearts, decreased pH (whether due to hypercarbia or other causes) is associated with myocardial depression, which is manifested by decreased heart rate and force of contraction. Isolated blood vessels respond to a low pH by vasodilatation. In contrast, CO_2 directly enhances sympathetic activity, which promotes cardiac contraction and induces peripheral vasoconstriction. The cardiovascular effects of hypercarbia are difficult to distinguish from the effects of increased intraabdominal pressure during laparoscopy. According to our study, there was no significant change in HR.

Regarding respiratory function, alterations in pulmonary physiology are primarily mechanical with increased intraabdominal pressure. The increase in intraabdominal volume and pressure impedes diaphragmatic excursion and increases intrathoracic pressure. This causes a increase in peak airway pressures and a decrease in vitals. Motew and colleagues [7] noted that the average peak airway pressure that was required to maintain a constant tidal volume in 10 women undergoing laparoscopy increased from 17.9 mm Hg at 0 mm Hg intraabdominal pressure to 25.9 mm Hg at 20 mm Hg intraabdominal pressure. Likewise, Alexander and colleagues [8] evaluated 24 patients undergoing laparoscopy and found that significantly increased airway pressure was required to maintain adequate ventilation during insufflation to 20 mm Hg intraabdominal pressure. The overall effect of these variables in our study showed that there were significant differences in average $ETCO_2$ at 15-minute intervals but no significant differences in average PAP after CO_2 insufflation (at 15 mm of Hg intraabdominal pressure) when compared with baseline values.

Metabolic changes associated with CO_2 insufflation include development of systemic acidosis and hypercapnia secondary to absorption of CO_2 across the peritoneal surface. After peritoneal absorption, CO_2 is transported to the lungs where it is eliminated via ventilation. In patients under controlled ventilation, significant hypercarbia and acidosis require ventilatory changes. Alexander and colleagues [8] evaluated 24 healthy patients undergoing laparoscopy with 20 mm Hg CO_2. Arterial blood gases were obtained before insufflation and during laparoscopy. A significant increase in pCO_2 by 8.6 mm Hg and decrease in arterial pH by 0.082 pH units were measured after insufflations; pO_2 remained constant. Alexander and Brown [9] subsequently showed that the effect occurred only with CO_2 insufflation and not nitrous oxide insufflation, thereby implicating CO_2 absorption from the peritoneal cavity (rather than hypoventilation) as the etiology of the hypercarbia and acidosis. Seed and colleagues [10] also measured a significant increase in $ETCO_2$ concentration after insufflations.

Although hypercarbia associated with CO_2 insufflation is well recognized, the choice of an appropriate monitoring technique is controversial. Liu and colleagues [11] prospectively evaluated 16 healthy patients undergoing laparoscopy using CO_2 pneumoperitoneum. Capnography was used to measure $ETCO_2$ during insufflation; arterial blood gases were obtained intermittently to simultaneously assess arterial pCO_2. Good correlation was found between 2 measurements during the procedure: $ETCO_2$ increased from 31 to 42 mm Hg and pCO_2 increased from 33 to 44 mm Hg. Because of its noninvasive nature, capnography was recommended for monitoring healthy patients during laparoscopy (as we used it in our series). Halachmi and colleagues [12] also noted a significant increase in RR, PAP, and $ETCO_2$ after CO_2 insufflation and a decrease pO2 in the extraperitoneal group, which could be attributed to several factors. For example, the increased retroperitoneal pressure will increase intrathoracic pressure that leads to reduction in chest wall compliance and increased dead space. These physiological changes may result in increased ventilation perfusion mismatch and elevation of $ETCO_2$. Our study showed that $ETCO_2$ elevated but pO_2 decreased; however, pH was not changed.

The exact systemic immune responses to pneumoperitoneum have not been completely defined. The majority of studies that have been done in animal models have yielded mixed results. Similarly there have been few clinical studies in humans examining the immunological and stress responses during urological laparoscopic procedures. Laparoscopic surgery induces less abdominal wall trauma and, therefore, elicits less of an acute systemic stress response [13]. Alterations in the stress and immune response correlate with the severity or extent of injury; as such, the physiologic response to laparoscopic surgery may differ from that of open surgery. The primary mediators of the acute-phase response are the inflammatory cytokines interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor (TNF), which are released from peritoneal macrophages. The hepatic component of the acute phase response is regulated by IL-6. This stimulates production of acute-phase response proteins including CRP, which is the primary marker [14]. A number of investigators have compared IL-6 and CRP levels after laparoscopic and corresponding open operations, for which cholecystectomy is the best studied. Numerous series have demonstrated increased levels of IL-6 and white blood cell count in patients having both open and laparoscopic procedures, but the levels are significantly higher with open when compared with laparoscopic cholecystectomy [15,16]. Conversely, Stage and colleagues [17] measured higher levels of IL-6 and CRP in patients having laparoscopy than in those having laparoscopic-assisted or open colectomy. The effect of laparoscopic surgery on CRP has also been investigated. Although most studies demonstrated more modest increases in CRP with laparoscopy when compared with open cholecystectomy, a few demonstrated no difference in acute-phase response proteins between the 2 groups. Our prospective study clearly showed that inflammatory markers (CRP, white blood cell count, and differential leukocyte count) were statistically similar.

CONCLUSIONS

Physiological changes incurred as a result of CO_2 insufflation have minimal adverse effects in healthy individuals undergoing urological laparoscopic surgery. In different fraternity, studies showed no significant impact of CO_2 insufflation in adults; however, in urology more prospective studies are required to confirm these conclusions.

Conflict of Interest: none declared.

REFERENCES

1. Larsen JF, Svendsen FM, Pedersen V. Randomized clinical trial of the effect of pneumoperitoneum on cardiac function and haemodynamics during laparoscopic cholecystectomy. *Br J Surg*. 2004;91(7):848-854.
2. Alijani A, Hanna GB, Cuschieri A. Abdominal wall lift versus positive-pressure capnoperitoneum for laparoscopic cholecystectomy: randomized controlled trial. *Ann Surg*. 2004;239(3):388-394.
3. Kashtan J, Green JF, Parsons EQ, Holcroft JW. Hemodynamic effect of increased abdominal pressure. *J Surg Res.* 1981;30(3):249-255.
4. Neudecker J, Sauerland S, Neugebauer E, et al. The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. *Surg Endosc*. 2002;16(7):1121-1143.
5. Marshall RL, Jebson PJ, Davie IT, Scott DB. Circulatory effects of carbon dioxide insufflation of the peritoneal cavity for laparoscopy. *Br J Anaesth*. 1972;44(7):680-684.
6. Price HL. Effects of carbon dioxide on the cardiovascular system. *Anesthesiology.* 1960;21(6):652-663.
7. Motew M, Ivankovich AD, Bieniarz J, Albrecht RF, Zahed B, Scommegna A. Cardiovascular effects and acid-base and blood gas changes during laparoscopy. *Am J Obstet Gynecol*. 1973;115(7):1002-1012.
8. Alexander GD, Noe FE, Brown EM. Anesthesia for pelvic laparoscopy. *Anesth Analg*. 1969;48(1):14-18.
9. Alexander GD, Brown EM. Physiologic alterations during pelvic laparoscopy. *Am J Obstet Gynecol*. 1969;105(7):1078-1081.
10. Seed RF, Shakespeare TF, Muldoon MJ. Carbon dioxide homeostasis during anaesthesia for laparoscopy. *Anaesthesia*. 1970;25(2), 223-231.
11. Liu SY, Leighton T, Davis I, Klein S, Lippmann M, Bongard F. Prospective analysis of cardiopulmonary responses to laparoscopic cholecystectomy. *J Laparoendosc Surg.* 1991;1(5):241-246.
12. Halachmi S, El-Ghoneimi A, Bissonnette B, et al. Hemodynamic and respiratory effect of pediatric urological laparoscopic surgery: a retrospective study. *J Urol*. 2003;170(4 Pt 2):1651-1654.
13. Grande M, Tucci GF, Adorisio O, et al. Systemic acute-phase response after laparoscopic and open cholecystectomy. *Surg Endosc*. 2002;16(2):313-316.
14. Baumann H, Gauldie J. Regulation of hepatic acute phase plasma protein genes by hepatocyte stimulating factors and other mediators of inflammation. *Mol Biol Med*. 1990;7(2):147-159.
15. Glaser F, Sannwald GA, Buhr HJ, et al. General stress response to conventional and laparoscopic cholecystectomy. *Ann Surg*. 1995;221(4):372-380.
16. Chaudhary D, Verma GR, Gupta R, Bose SM, Ganguly NK. Comparative evaluation of the inflammatory mediators in patients undergoing laparoscopic versus conventional cholecystectomy. *Aust N Z J Surg*. 1999;69(5):369-372.
17. Stage JG, Schulze S, Møller P, et al. Prospective randomized study of laparoscopic versus open colonic resection for adenocarcinoma. *Br J Surg*. 1997;84(3):391-396.