Archives of Anesthesiology and Critical Care (Autumn 2021); 7(4): 227-233.

Available online at http://aacc.tums.ac.ir

Research Article

Effects of Dexmedetomidine on Intraoperative Hemodynamic Responses in Patients Undergoing Laparoscopic Cholecystectomy: A Randomised Double Blind Trial

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ARTICLE INFO

Article history:
Received 28 May 2021
Revised 19 June 2021
Accepted 03 July 2021

Keywords:
Dexmedetomidine;
Hemodynamic responses;
Laparoscopic cholecystectomy

ABSTRACT

Background: Dexmedetomidine is selective alpha 2 agonist with sedative sympatholytic, analgesic properties and is used as an anaesthetic adjuvant. We have evaluated the effect of dexmedetomidine on various hemodynamic responses to incidences such as laryngoscopy, endotracheal intubation, exubation and pneumoperitoneum in patients who were undergoing surgeries like laparoscopic cholecystectomy. We have used loading dose of 0.5mcg/kg of inj. Dexmedetomidine given over 10 minutes followed by infusion of a dose of 0.3mcg/kg/hour for the control of hemodynamic response to laparoscopy.
Methods: Patient of either sex aged between 18-50 yrs, belongs to ASA I and II (AMERICAN SOCIETY OF ANAESTHESIOLOGY) posted for laparoscopic cholecystectomy were included. Institutional ethical committee clearance was obtained prior to study. After enrolment and valid written consent was taken.
60 patients were enrolled written valid informed consent was taken. Patients were divided into two groups 30 each with computerized randomization. Base line parameters were noted. Observer and patient was blinded for the content of syringe. Group A received injection dexmedetomidine and group B received bolus and infusion of normal saline at same rate. Routine general anaesthesia was instituted. Parameters were noted after induction, after intubation, after co2 insufflation, after 20 min, after
40 min, after co2 deflation, after extubation, after 1 and 2 hrs post-extubation.
Results: Group A showed significantly less rise in HR and MAP than Group B. Requirement of intraoperative propofol was more in Group B. There was no significant difference for time taken to awakening in both groups.
Conclusion: We found Injection Dexmedetomidine in given doses gave good hemodynamic control with minimal undesired effects during laparoscopy.

Laparoscopic cholecystectomy is emerging as first choice for surgeries of gall bladder in this era. Control of hemodynamic responses to carbon dioxide (CO2) peumoperitonium is an important concern during laparoscopic cholecystectomy. Increase in HR and MAP occurs due to sympathetic stimulation due to CO2 [1]. In this study we have used inj. Dexmedetomidine to see the effect on intraoperative hemodynamics. Dexmedetomidine is highly selective alpha 2 agonist. It acts on alpha 2 A, alpha 2 B and alpha 2 C receptors which are situated in brain and spinal cord. It produces dose dependent, anxiolysis, sympatholysis, analgesic and sedation effects. Sympatholysis leading to hypotension and bradycardia without respiratory depression [2].

Various doses of dexmedetomidine are studied for different surgical procedures. Bradycardia and excessive sedation are seen with higher doses. Lower doses may not give desired hemodynamic control. Infusion should be titrated depending on type and duration of surgery to achieve minimal undesired effects with good

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hemodynamic control. We have used loading dose of inj dexmedetomidine of
0.5mcg/kg over 10 minutes followed by infusion of dose 0.3mcg/kg/hr for the control of hemodynamic response to laparoscopy.

Primary Objective

Primary objective of our study is to examine effect of inj. Dexmedetomidine on intra-operative hemodynamic response in patients undergoing laparoscopic cholecystectomy.

Secondary Objective

- To study intra-operative requirement of additional injection Propofol.
- To study the effect of dexmedetomidine for the incidence of bradycardia and hypotension requiring intervention.
- To study postoperative sedation score.

Inclusion Criteria

- Patients belonging to either sex and age of between 18 to 60 years.
- Patients of physical status ASA I and II.
- Patients who are posted for elective surgery of laparoscopic cholecystectomy under general anaesthesia.

Exclusion Criteria

- Elderly patients with uncontrolled uncontrolled hypertension.
- Patient not giving consent.
- Pregnant woman or lactating woman.
- Patients with severe bradycardia and heart block.
- Patients having ischemic heart disease, uncontrolled diabetes mellitus, asthma, COPD, renal failure, liver failure.

Methods

This study was conducted in department of anaesthesiology in surgery operation theater. Ethical committee clearance was obtained prior to study (SKNMC/Ethics/App/2019/566). Total 60 Patients belonging to either sex and age group between 18-60yrs of ASA I and II were enrolled after taking written valid informed consent. Detailed pre- anaesthetic checkup was done. 60 patients were divided by computarized randomization in two groups of 30 each.

1. All equipments and drugs for general anaesthesia and emergency was kept ready. Anaesthesia machine was checked for any leaks and other problems.
2. Resuscitation equipments such as appropriate sized gloves, mask, suction catheter, oropharyngeal airways, self-inflating bag with reservoir, supraglottic airways devices.
3. Appropriate size laryngoscope and endotracheal tubes and connections, oxygen cylinder with oxygen.
4. Monitors such as (NIBP) non invasive blood pressure, continuous electrocardiography, saturation probe and $ETCO_2$ was checked.

Inside the OT, monitors were applied for NIBP, saturation probe and electrocardiography. On operating table 18 or 20 G intracath was secured and ringer lactate 500 ml infusion was given. Base line parameters (HR and MAP) were noted (T0). Dexmedetomidine infusion prepared in 20cc syringe as 4 mcg/ml. Group A received Injection Dexmedetomidine 0.5mcg/kg loading dose given over 10 minutes followed by infusion of 0.3mcg/kg/hr and Group B received bolus and infusion of normal saline (NS) at the same rate. Observer and patients were blinded for contents of the syringe. Patients were pre-oxygenated with 100% oxygen for 3 minutes with face mask and then premedication given with Inj.Midazolam 0.03mg/kg intravenous (IV), Inj. ondansetron 0.08 mg/kg IV, Inj. Glycopyrrolate 0.004mg/kg IV. Induction done with Injection Propofol 2mg/kg intravenously followed by injection succinylcholine 1.5 mg/kg intravenously and intubated with appropriate size cuffed endotracheal tube and maintained on oxygen, nitrous oxide (50:50) and 1 MAC of Sevoflurane and muscle relaxant injection vecuronium bromide. Heart rate, systolic and diastolic blood pressure and MAP (mean arterial pressure) were noted, after induction agent was given (T1), immediatly after intubation (T2), after CO_2 insufflation (T3), after 20 min(T4), after 40 min (T5), after CO_2 deflation (T6), after extubation (T7), after 1 and 2 hrs post-extubation (T8) and (T9). Intra-operative significant bradycardia if any was treated with inj. Atropine 0.6mg/kg and infusion stopped if needed. For hypotension IV fluids and vasopressors as needed. Tachycardia and hypertension was treated with 20 mg Injection Propofol boluses as required. Infusion was stopped after CO_2 deflation. Nitrous oxide and Sevoflurane were stopped after skin closure. Time to extubation was noted after stopping inhalational agents. Sedation score was noted according to Ramsay sedation scale at extubation,1 hour and 2 hours in post-operative period.

Ramsay Sedation Score

Score	Level Of Sedation
0	Patient is awake
1	Patient is agitated and restless
2	Awake and respond to command only
3	Patient is sleeping, but co-operative
4	Patient under deep sedation but quick reaction to pain stimuli.
5	Patient under deep sedation but slow reaction to pain stimuli
6	Patient under deep sedation but no reaction to pain stimuli.

Statistical Analysis

The parameters were recorded and data were entered into Microsoft Excel 2016. In our study Primer of Biostatistics software version 6.0(by santon A. Glanz, © 2005 McGrow-Hill) used for calculation of sample size and analysis of the statistical data obtained from Statistical Package for the Social Sciences Software Version 19 (SPSS Inc., Chicago, Illinois, USA). Statistical significance was accepted as significant at P <0.05. Student's t-test used for the analysis of numerical data. Chi-square test were used for analysis of qualitative data. Sample size was calculated based on study of Manne et al, taking increase in MAP (mean arterial pressure) and HR (heart rate) after carbon dioxide insufflations as the primary parameters. α was taken as 0.01 and β as 0.20 with power as 80 percent.

Results

(Table 1) shows demographic parameters like age, body mass index, M.F (Male to female ratio) of patients and duration of surgery. They were comparable in both the groups.

Table 1- Demographic Table

	GROUP A (n=29)	GROUP B (n=30)	P Value
Age in Years	48.77±10.10	52.97±8.65	0.217(>0.05)
Bmi	22.11±4.38	21.00±4.1	0.277(>0.05)
M/F Ratio	10:20	12:18	0.287(>0.05)
Duration of Surgery in Minutes	110±10.1	118±8.8	0.944(>0.05)

*BMI-Body mass index; M/F-Male to female ratio; HR-Heart rate; MAP-Mean arterial pressure; SD-Standard deviation

Table 2- Changes in HR (mean±SD)

	Group A (N=29)	Group B (N=30)	P Value
Base Line	94±6.1	96±6.4	0.224
After Induction	80±6.1	86±6.2	0.213
After Intubation	70±6.6	84±6.6	<0.001
After Pneumoperitoneum	68±8.2	80±8.6	<0.001
After 20 Minutes	60±6.4	90±8.0	<0.001
After 40 Minutes	62±7.2	86±6.2	<0.001
After Deflaion	60±6.4	88±8.14	<0.001
After Extubation	64±7.1	100±6.4	<0.001
After 1 Hour	70±6.4	90±8.0	<0.001
After 2 Hours	72±8.2	84±8.12	<0.001

Table 3- Changes in Map (mean±SD)

	Group A (N=29)	Group B (N=30)	P Value
Base Line	88±8.21	86±8.26	0.067
After Induction	90±8.11	94±8.13	0.064
After Intubation	90±6.42	100±8.1	<0.001
After Pneumoperitoneum	86±10.41	114±10.14	<0.001
After 20 Minutes	76±8.16	120±8.42	<0.001
After 40 Minutes	74±6.13	108±6.24	<0.001
After Deflation	86±8.14	100±8.26	<0.001
After Extubation	90±10.14	116±10.21	<0.001
After 1 Hour	92±8.61	110±8.24	<0.001
After 2 Hours	90±6.13	100±6.24	<0.001

(Table 2 and 3) show HR and MAP changes. Heart rate and mean arterial pressure were comparable in both the groups after starting infusion. After intubation Dexmedetomidine group show consistently low MAP and HR than control group throughout the procedure till 2 hours in post-operative period. Thus difference in in MAP and HR in both groups was clinically and statistically significant. One patient from group A had significant bradycardia, infusion of injection Dexmedetomidine was stopped and Injection Atropine 0.6mg/kg given and excluded from further observation. He was noted as bradycardia required treatment.

Figure 1- Intraoperative and Postoperative Comparison of Heart Rate in Group A and Group B

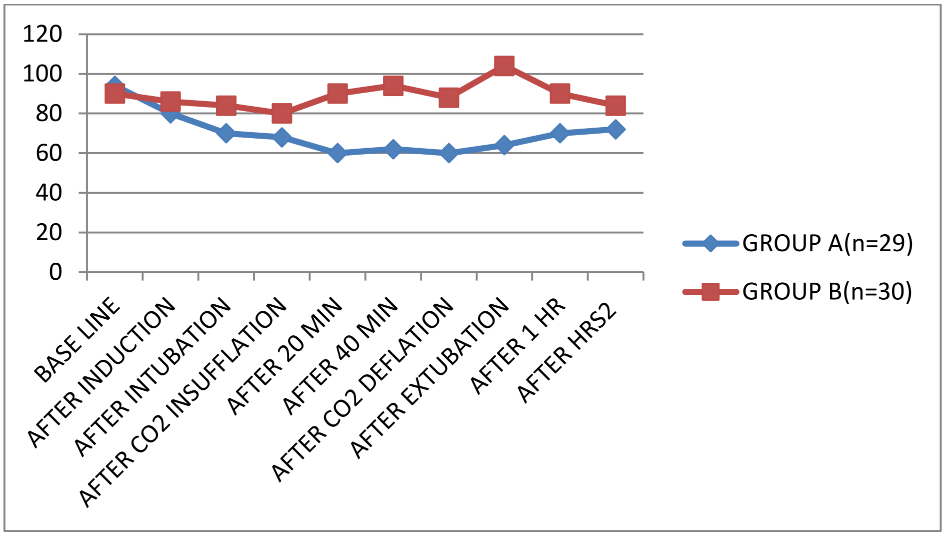


Figure 2- Intraoperative and Postoperative Comparison of Mean Arterial Pressure in Group A and Group B

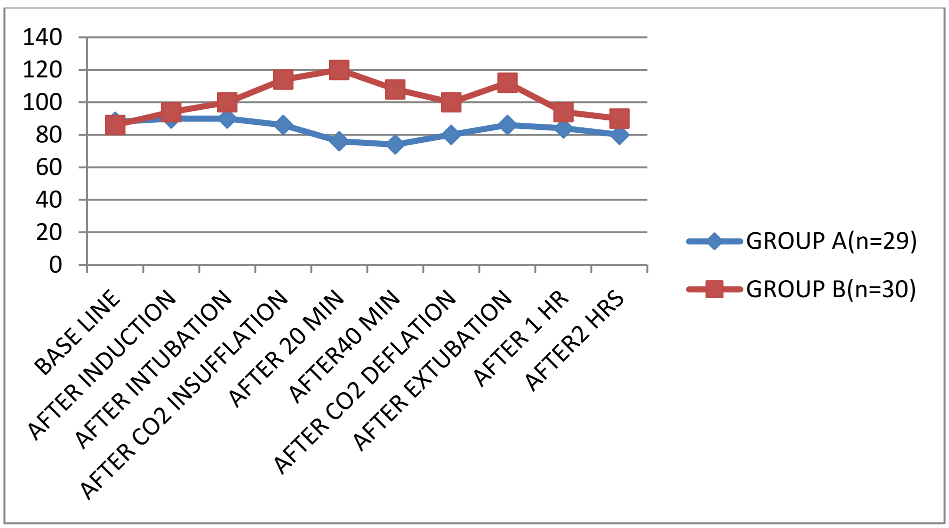


Figure 3- Comparison in Group A And Group B For Intraop Requirement of Propofol and Intraop Bradycardia Requiring Treatment.

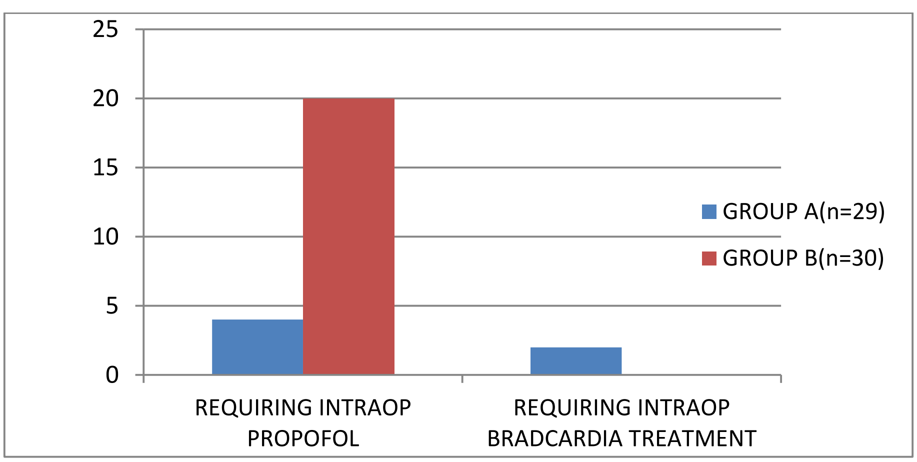


Figure 4- Comparison in Group A and Group B for Postop Sedation and Nausea/Vomiting

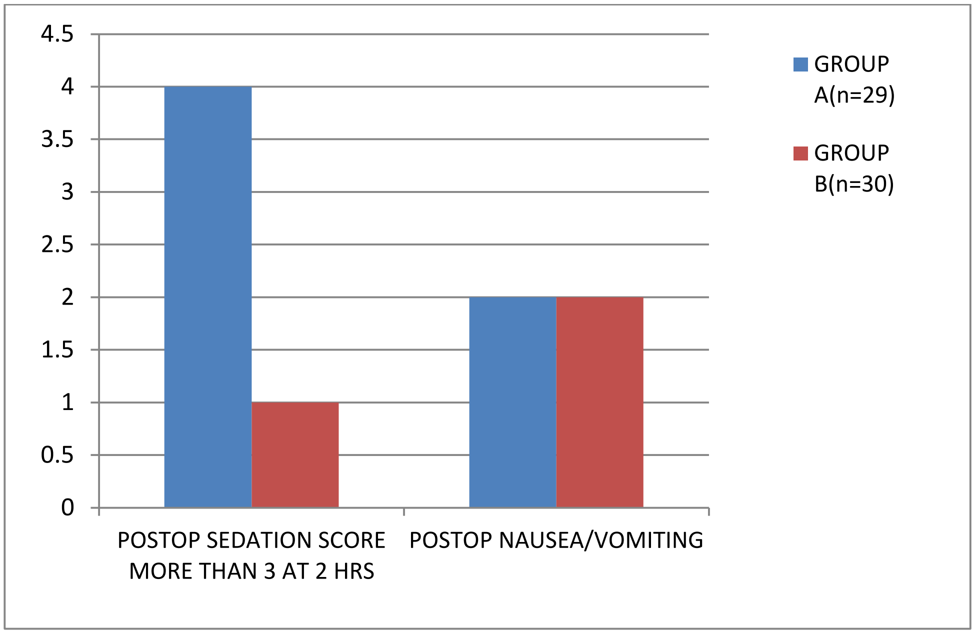
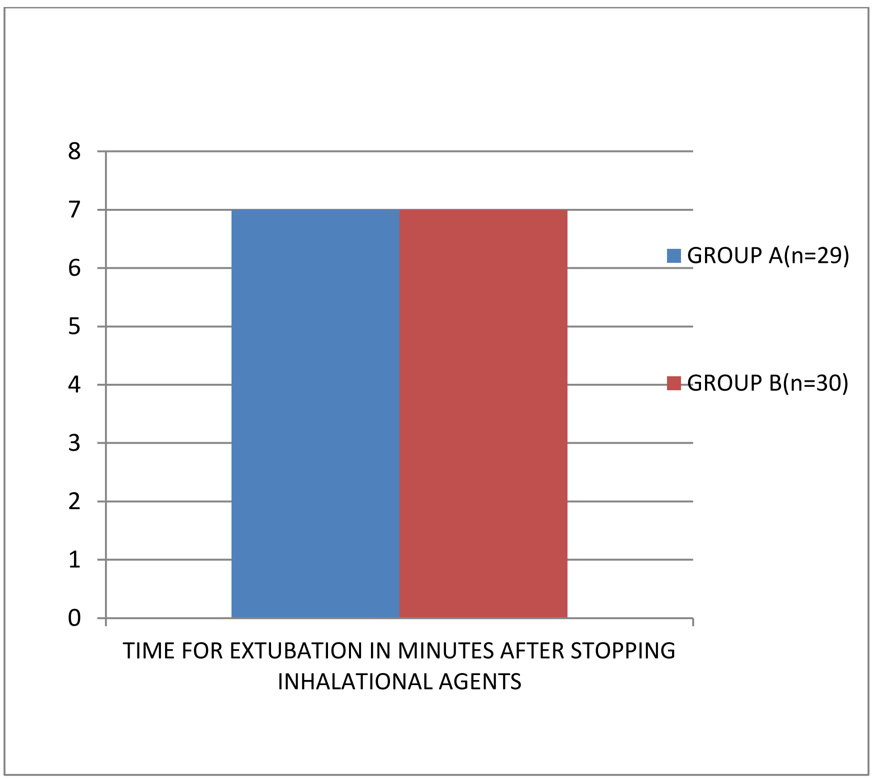


Figure 5- Comparison Between Group A and Group B. Time for Extubation in Minutes after Stopping Inhalational Agents.



(Figure 1) shows significant rise in heart rate at 20 minutes of pneumoperitonium and after extubation in control group as compaired to dexmedetomidine group.

(Figure 2) shows significant rise in mean arterial pressure at 40 minutes of pneumoperitoneum and after extubation in control group as compared to dexmedetomidine group.

(Figure 3) shows only 4 patients out of 30 in dexmedetomidine group required intraoperative boluses of propofol for control of sympathetic response to pneumoperitoneum as compared to 20 patients out of 30 in control group.

(Figure 4) shows 4 patients in dexmedetomidine group had Ramsay sedation score more than 3 at 2 hours of post operative period as as compared with score of 1 patient in control group receiving normal saline.

(Figure 5) shows patients in both groups had no significant difference for time to extubation after stopping inhalational agents.

Discussion

Laparoscopic cholecystectomy the commonly practiced surgeries for gall bladder diseases due to its advantages such as less chances post-operative pain, short hospital stay and faster recovery. However, laparoscopy poses challenges to anaesthesia. Important ones being haemodynamic responses secondary to CO2 pneumoperitonium and other issues include increase in peak airway pressure, decreased functional residual capacity (FRC), decreased renal blood flow.
Hemodynamic responses are because of systemic absorption of CO2 causing sympathetic stimulation.

Cardiovascular responses characterized by increase myocardial oxygen requirement due to tachycardia and hypertension. Reverse Trendelenburg position which required for this surgery may leads to diminished venous return and reduction in cardiac output may occur [3].

Various agents like opioid, benzodiazepines, beta blockers and calcium channel blockers have been used to prevent sympathetic discharge and provide hemodynamic stability in perioperative period.

Injection dexmedetomidine is a highly selective alpha2 agonist have 8 times more affinity for alpha 2 adrenergic receptors as compared to injection clonidine. Giving inj.Dexmedetomidine intravenously in the perioperative period was found to decrease catecholamine levels [4], which causes blunting of the haemodynamic response to laryngoscopy, endotracheal intubation reflex, pneumoperitoneum and extubation reflex [5] and provide analgesia and sedation without respiratory depression.

Various authors have used various loading and infusion doses of Injection Dexmedetomidine. Some authors have used only infusion of Injection Dexmedetomidine 1mcg/kg/hr and found it to be associated with intra-operative and postoperative bradycardia, hypotension requiring treatment and postoperative sedation [6].

Very low dose of only infusion of injection Dexmedetomidine of 0.2mcg/kg/hr may not give desired hemodynamic control in laparoscopic surgeries [7]. Some authors also found only single loading dose of inj. Dexmedetomidine of 1mcg/kg during induction were showed significant bradycardia [8-9]. Dexmedetomidine has to be titrated based on surgical stimulus and type of surgery. Hence we find many different doses for studies of various surgeries in literature.

We found that the loading dose of injection Dexmedetomidine 0.5mcg/kg followed by infusion of 0.3mcg/kg/hr gives good hemodynamic response to laparoscopic cholecystectomy without significant bradycardia or sedation in ASA physical status I and II. Maximum increase in mean arterial pressure and heart rate was seen from 20 to 40 minutes after pneumoperitoneum and at extubation in control group as compaired to dexmedetomidine group.

Infusion rates of varying dose from 0.1 to 10 mcg/kg/hr [10-11] have been studied by various authors. Giving loading dose very slowly is important to prevent transient hypertension with dexmedetomidine [12]. In our study we have not found any patient with transient hypertension as our loading dose was very low and given over 10 minutes. With higher loading dose of dexmedetomidine, higher incidence of intraoperative bradycardia was observed in some studies [13]. However our infusion dose was lower than the above study and we have found only 1 patient with significant bradycardia requiring treatment.

In our study 4 no of patients in dexmedetomidine group required bolus doses of propofol as compaired to control group 20 no.of patients in which bolus dose of propofol required to control the intra- operative response to pneumoperitoneum [14].

In some studies it was found because of sedative effect of dexmedetomidine, verbal command response and time of extubation was delayed. Bhattacharjee et al [15]. also observed that there was no significant effect of dexmedetomidine on response to verbal command and time to extubation. In our study also we found no difference in time to extubation in both the groups.

In our study we found minimal postoperative sedation. In dexmedetomidine group 25 patients showed sedation score less than 3 at 2 hours

Limitation:

In our study we have included only ASA I and II patients. We did not study the effects of Dexmedetomidine on patients with uncontrolled hypertension and other co-morbidities.

Conclusion

In our study we found that bolus dose of injection Dexmedetomidine 0.5mcg/kg followed by infusion of 0.3mcg/kg/hr served as a useful means for controlingl haemodyanamic stress response to intubation reflex, pneumoperitoneum and extubation reflex in patients who were undergoing laparoscopic cholecystectomy surgery. It also provides sedation with minimal undesired effects during laparoscopy.

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