

## Intrathecal Buprenorphine's Effect on the Hemodynamic Response in Patients Having Laparoscopic Appendicectomy Under General Anaesthesia

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### Abstract

**Aim:** To study the effect of intrathecal buprenorphine on the haemodynamic response in patients undergoing laparoscopic appendicectomy under general anaesthesia.

**Methods:** This comparative observational longitudinal study conducted in the, Department of Anaesthesiology and critical care, Era's Lucknow Medical college and Hospital, Lucknow, Uttar Pardesh, India, for 10 months. 100 patients were divided into two groups of 50 each by random sampling. All of them belonged to Physical Status or as outlined by the American Society of Anaesthesiologists (ASA). Patients were divided into two groups of 50 each by random sampling. The first group was GA group (General anaesthesia group) and the other was GA+SAB group (General anaesthesia with intrathecal buprenorphine group). The principal investigator observed the procedure and had no role in the assignment of cases to different modalities of anaesthesia.

**Results:** In both the groups, drop-in heart rate was noted in patients after pneumoperitonium is achieved. There was no statistically significant difference in the heart rate, systolic and diastolic blood pressure between the GA group and GA+SAB group at preoperative period, after induction, after intubation after pneumoperitonium and after extubation. Percentage change in heart rate, systolic and diastolic from the baseline values showed a similar pattern in both the groups. Oxygen saturation post extubation showed statistically significant difference (p value = 0.027) between GA group and GA+SAB group (98.8± 0.5% versus 98.3± 1.2%). but was clinically insignificant.

**Conclusions:** When compared to general anaesthesia alone, addition of intrathecal buprenorphine provides little advantage in preventing stress response during laparoscopic appendicectomy.

**Keywords:** general anaesthesia, buprenorphine, laparoscopic appendicectomy

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## Introduction

Laparoscopic cholecystectomy (LC) is usually done under general anesthesia (GA) with controlled ventilation to prevent aspiration, abdominal, and respiratory discomfort and to prevent hypercapnia due to carbon-dioxide (CO<sub>2</sub>) pneumoperitoneum.[1] Though regional anesthesia has been used for diagnostic laparoscopy, its use for laparoscopic surgeries is restricted to those patients where administration of GA is hazardous due to respiratory disorders. Both spinal and epidural have been used as an adjunct to GA for LC effectively and safely, and have provided better analgesia.[2,3] Spinal anesthesia (SA), including segmental thoracic SA has been used as a sole anesthetic technique for LC.[4,5] SA offers the advantages of less postoperative pain, less postoperative nausea vomiting, early ambulation and more oriented and awake patient at the end of surgery in comparison to GA.[6-8]

Neuroendocrine stress response is a major event during laparoscopy as tissue manipulation and pneumoperitoneum result in intense stimulation to the nervous system leading to corticosteroid and catecholamine release.[9] This results in hemodynamic surge in the form of raised systemic vascular resistance and hypertension and tachycardia in majority of the cases and raised serum cortisol level. Neuraxial drug administration describes the technique of delivering analgesics and adjuvant drugs in close proximity to the spinal cord with drugs like local anaesthetics, opioids, or adrenergic agonists.[10] Buprenorphine is a long-acting lipid soluble mixed partial agonist  $\mu$  opioid receptor modulator, which can be administered intrathecally.[11] It provides excellent analgesia intraoperatively and post operatively while allowing early ambulation without prolonged motor block and with lesser side effects. It is about 25 times more potent than morphine and has a low level of physical dependence.[12] The study was designed to compare the haemodynamic

response during laparoscopic appendicectomy using combined general anaesthesia with intrathecal buprenorphine and general anaesthesia alone as assessed by changes in heart rate, systolic blood pressure, diastolic blood pressure and oxygen saturation.

## Material and Methods

This comparative observational longitudinal study conducted in the, Department of Anaesthesiology and critical care, Era's Lucknow Medical college and Hospital, Lucknow, Uttar Pradesh, India, for 10 months, after taking the approval of the protocol review committee and institutional ethics committee. According to medical records data in the study hospital regarding the number of laparoscopic appendicectomies done under combined spinal and general anaesthesia in the previous year, a sample size of 100 was arrived. 100 patients were divided into two groups of 50 each by random sampling. All of them belonged to Physical Status or as outlined by the American Society of Anesthesiologist's (ASA). Patients with a body weight less than 40 kg, who refused regional anaesthesia, has known hypersensitivity to opioids and local anaesthetics, pregnant or breast feeding females and those with bleeding disorders were excluded from the study. Patients who participated in the study belonged to the age group of 18–60 years. Pre anaesthetic check-up was done for all patients that included a detailed history, general physical examination and systemic examination. Basic investigations were done which included complete blood count, random blood sugar, serum urea and creatinine, serum electrolytes, electrocardiography (ECG), and chest X-ray. Patients were kept nil per oral overnight.

Patients were divided into two groups of 50 each by random sampling. The first group was GA group (General anaesthesia group) and the other was GA+SAB group (General anaesthesia with intrathecal buprenorphine

group). The principal investigator observed the procedure and had no role in the assignment of cases to different modalities of anaesthesia.

Routine monitoring included ECG, pulseoximetry (SpO<sub>2</sub>) and non-invasive blood pressure (NIBP). An intravenous line was secured on the right forearm using an 18 gauge cannula. After shifting the patient to the operation baseline values of heart rate, NIBP and SpO<sub>2</sub> were recorded.

In GA + SAB group the patients were positioned left lateral to perform regional anaesthesia. Under strict aseptic precaution and after injecting 2ml of lignocaine 2% at the site, lumbar subarachnoid space was reached with 25G Quincke needle in L3-L4 intervertebral disc space via median approach. 60µg (0.2ml) of buprenorphine with 1 ml normal saline 0.9% will be injected into the subarachnoid space after confirming the free flow of cerebrospinal fluid through the needle.

After making the patient supine, general anaesthesia was given. Patients were premedicated with midazolam 0.02 mg/kg and glycopyrrolate 0.005 mg/kg. Fentanyl 2µg/kg was given as the analgesic. After preoxygenation with 100% O<sub>2</sub> for 3 minutes, anaesthesia was induced with propofol 2 mg/kg. Neuromuscular blockade to facilitate oral cuffed endotracheal intubation was done with succinylcholine 2mg/kg. Trachea was intubated by the anaesthesiologist in charge of the operation theatre with 6.5mm to 7.5 mm ID cuffed endotracheal tubes in females and 7.5 mm to 8.5 mm ID in males. Bilateral air entry was confirmed by five point auscultation and cuff was inflated to 22cm of H<sub>2</sub>O using

Covidien cuff pressure manometer and endotracheal tube was fixed.

Patients were administered intravenous vecuronium bromide 0.08 mg/kg immediately after tracheal intubation to maintain muscle relaxation. Anaesthesia was maintained with oxygen (FiO<sub>2</sub> – 0.5), nitrous oxide, propofol infusion at 50ug/kg/minute, fentanyl boluses at 1ug/kg/ hour and vecuronium infusion at the rate of 0.05mg/kg/hr. Mechanical ventilation was done with a tidal volume of 8 ml/kg, and a rate between 12 and 16/min to maintain an end tidal CO<sub>2</sub> value between 35 and 45 mmHg. Towards the end of the surgery anaesthetic agents were tapered and cut off. Residual neuromuscular blockade was reversed with intravenous neostigmine 0.05 mg/kg with glycopyrrolate 0.02 mg/kg. Oropharyngeal suction was given and extubation was done once patient opened eyes, obeyed simple commands and breathed regularly with adequate tidal volume. In addition to the baseline parameters the principal investigator also observed the values of heart rate, systolic and diastolic blood pressures and SpO<sub>2</sub> after induction of general anaesthesia, immediately after endotracheal intubation, after creating pneumoperitonium and post extubation.

Statistical analysis was performed using the SPSS 25.0 (Statistical Package for the Social Science for windows; Version 25.0, SPSS Inc., Chicago, USA). Results were analysed using Student's t-test and chi-squared test. Significance level was set at P value < 0.05.

## Results

**Table 1: Demographic profile of the patients**

| Parameter           | G A Group =50 | G A + SAB Group=50 | P value |
|---------------------|---------------|--------------------|---------|
| Age in mean (years) | 26.6 (7.3)    | 27.7 (9.5)         | 0.51    |
| Sex                 |               |                    |         |
| (Male/Female)       | 25/25         | 24/26              | 0.87    |

In both the groups, drop in heart rate was noted in patients after pneumoperitonium is achieved. There was no statistically significant difference in the heart rate, systolic and diastolic blood pressure between the GA group and GA+SAB group at preoperative period, after induction, after intubation after pneumoperitonium and after extubation. Percentage change in heart rate, systolic and diastolic from the baseline values showed a similar pattern in both the groups. Oxygen saturation post extubation showed statistical significant difference (p value = 0.027) between GA group and GA+SAB group ( $98.8 \pm 0.5\%$  versus  $98.3 \pm 1.2\%$ ). but was clinically insignificant.

### Discussion

The present study was designed to compare the haemodynamic response in combined general anaesthesia with intrathecal buprenorphine and general anaesthesia alone in patients undergoing elective laparoscopic appendectomy, the response was studied in terms of changes in heart rate, systolic blood pressure, diastolic blood pressure and oxygen saturation. Various drugs along with local anaesthetics have been used as adjuvants for intrathecal placement along with general anaesthesia to obtund the neuroendocrine response and for perioperative analgesia but with avarying success. The introduction of intrathecal opioids into clinical practice has been very beneficial. Drugs such as morphine, pethidine, phenylephrine, neostigmine, ketamine, buprenorphine, fentanyl, and many others have been used, but not a single adjuvant can be considered as an ideal drug for such purpose.

In this study we used injection buprenorphine as the intrathecal opioid. It provides excellent analgesia intraoperatively and post operatively while allowing early ambulation without prolonged motor block.[13] Opioid receptors are present in throughout the nervous system. Buprenorphine a lipid soluble opioid and when administered intrathecally it is rapidly soaked up in the

lipid tissue of spinal cord with affinity 50 times more than that of morphine thus having faster onset and greater duration of analgesia and lesser concentration of drug remains in CSF and hence less respiratory depression. Blunting of neuroendocrine response during pneumoperitonium is a challenge for anesthesiologist's. In an attempt to blunt this response, various regional anaesthetic techniques were experimented along with general anaesthesia so that use of vasoactive drugs and deeper plane of general anaesthesia can be avoided. Poonam

S. Ghodki et al. compared the effect of 10mg bupivacaine heavy intrathecally along with general anaesthesia alone for laparoscopic hysterectomy. It was found that a statistically significant rise in mean arterial blood pressure ( $113.40 \pm 4.06$  v/s  $92.42 \pm 2.72$ ,  $p=0.001$ ).[14] continued throughout pneumoperitonium when general anaesthesia only was given. After the release of pneumoperitonium, the difference was not statistically significant and blood pressure values were within 22% of baseline. In the present study intrathecal buprenorphine failed to blunt the neuroendocrine stress as the hypertensive response persisted throughout pneumoperitonium.

P Calvo Soto et al. in 2011 compared the effect of 10 to 15 mg of bupivacaine 0.5% and 20 mcg of fentanyl given intrathecally along with general anaesthesia during laparoscopic cholecystectomy in 40 patients.[15] Systolic and diastolic arterial pressures were lower in the combined spinal and general anaesthesia group ( $95 \pm 16$  vs  $111 \pm 18$

mmHg ;  $p < 0.01$  and  $58 \pm 8$  vs  $68 \pm 12$  mmHg;  $p < 0.01$ , respectively) but a similar heart rate and oxygen saturation in both groups. Also a similar randomized prospective trial by Writuparna Das et al compared the effect of 0.5% hyperbaric bupivacaine and 25  $\mu$ g fentanyl along with general anaesthesia in attenuation of stress response in laparoscopic

cholecystectomy.[16] None of the patients experienced hypertension during pneumoperitoneum. Heart rate was found to be lower in the spinal anaesthesia group. In the present study we used only intrathecal buprenorphine. Systolic and diastolic blood pressure, heart rate and oxygen saturation followed almost the same pattern in both GA group and GA+SAB group following pneumoperitoneum.

Intrathecal administration of local anaesthetic produces sympathetic block which compensates for the increased sympathetic tone resulting from pneumoperitoneum and offsets the vasomotor constriction of splanchnic organs and leg muscles. Vasodilatation due to this sympathetic blockade lessens the hemodynamic perturbations due to pneumoperitoneum.[16] This probably explain the pattern of hemodynamic changes seen in the present study. This points towards the fact that intrathecal opioid like buprenorphine couldn't provide the adequate sympathetic blockade needed to attenuate the stress responses.

In the present study comparison of post extubation hemodynamic parameters like heart rate, blood pressure showed clinically significant reduction in patients who were given intrathecal buprenorphine when compared to general anaesthesia alone. This may be attributed to the additional analgesia provided by intrathecal buprenorphine.

Side effects of buprenorphine like sedation, respiratory depression, postoperative nausea and vomiting and pruritus which can be attributed to general anaesthesia drugs also was monitored in the present study. None of the patients in either group had any of the side effects except for mild sedation.

### Conclusions

When compared to general anaesthesia alone, addition of intrathecal buprenorphine provides little advantage in preventing stress response during laparoscopic appendectomy. Combining general

anaesthesia with intrathecal buprenorphine offers a more stable postextubation haemodynamics in laparoscopic appendectomies thus providing a platform for a stable postoperative course.

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