Original Research Article

Comparison of the efficacy of combined epidural anesthesia with general anaesthesia alone to attenuate hemodynamic responses and perioperative analgesia in laparoscopic cholecystectomy patients

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ABSTRACT

Background: The aim of the study was to compare the efficacy of combined GA-Epidural Anesthesia (CEGA) with GA alone to attenuate hemodynamic responses and perioperative analgesia.

Method: Authors conducted a prospective, randomized, double blind study, in which 60 patients undergoing laparoscopic cholecystectomy. Group A received (n=30) received GA and Group B (n=30) received combined GA and Epidural Anaesthesia (CEGA). Authors analyzed the effect of combined epidural general anaesthesia as compared to plain general anaesthesia with regard to hemodynamic parameters (heart rate, systolic and diastolic blood pressure), intraoperative anaesthetic requirement (intraoperative requirement of propofol), recovery score and postoperative analgesia (VAS score).

Results: Authors found significant decrease in the heart rate, systolic and diastolic blood pressure in response to stress response to pneumoperitoneum in combined epidural general anaesthesia (CEGA) group compared to plain general anaesthesia (GA) group. Total amount of propofol required intraoperatively was less in CEGA group than in GA group. Recovery score and pain score (VAS) score were also compared which were better in CEGA group than in GA group. There were no significant intraoperative and postoperative complications noted in both the groups.

Conclusion: Authors concluded that the use of epidural along with general anaesthesia helps in attenuating hemodynamic changes due to stress response to pneumoperitoneum, which results in maintaining stable intraoperative and postoperative hemodynamics during laparoscopic cholecystectomy surgery. Combining epidural to general anaesthesia results in rapid recovery as compared to plain general anaesthesia and also helps in providing good postoperative analgesia.

Keywords: Combined GA-epidural anesthesia, General anaesthesia, Postoperative analgesia

INTRODUCTION

Laparoscopic cholecystectomy has gained popularity because it offers several advantages compared to open surgical procedures. It is less invasive and allows shorter hospital stays, early ambulation thus reducing hospital costs. Its adverse effects are mainly related to inflation of peritoneal cavity, the use of CO2 and postural changes needed for surgery.1-4 CO2 is a known irritant to peritoneum and its use causes upper abdominal and shoulder pain that also continues in the post-operative period and not relieved by NSAIDS alone. Pneumoperitoneum also affects hemodynamic parameters which are because of increase in systemic vascular
resistance and pain due to stretch, leading to intraoperative tachycardia and hypertension.\textsuperscript{1,3} The ideal anesthesia technique should provide good analgesia and attenuation of these hemodynamic responses. Different modalities were tried to control these responses, for example TIVA, alpha-2 agonist but do not provide postoperative analgesia.\textsuperscript{5,6} Opioids which were found to be effective, caused many adverse side effects like bradycardia, nausea, vomiting, pruritus, sedation etc. NSAIDS alone were found to be inefficient to provide adequate analgesia. GA, by convention, remains the mainstay for all kinds of laparoscopic surgeries.\textsuperscript{7,8}

However, the unopposed increase in systemic vascular resistance (SVR) associated with pneumoperitoneum has to be managed by increasing anesthetic concentrations and, at times, administering vasodilators.\textsuperscript{9} This eventually leads to unnecessary deepening of anesthesia, delayed awakening, and does not prove cost effective. Regional anesthesia combined with GA has been described and successfully used as a technique to attenuate these responses in laparoscopic surgical procedures.\textsuperscript{8,10} Combined GA-Epidural anesthesia (CEGA) could match the benefits of both the techniques without causing any side effects.\textsuperscript{11,12} Adding epidural to general anesthesia can attenuate the haemodynamic changes associated with pneumoinsufflation by decreasing systemic vascular resistance (SVR), decreasing mean arterial blood pressure (MAP) and maintaining cardiac index as well as it will decrease the requirements of various anesthetic agents.\textsuperscript{11-14} The epidural anesthesia can effectively block the nerve conduction pathway of noxious stimulations.\textsuperscript{14} It attenuates the stress response during surgery by depressing the sympathetic response presumably by blocking afferent sympathetic pathways.\textsuperscript{15-18} Thus, general anesthesia combined with preemptive epidural analgesia can provide a lighter stress status for laparoscopic surgeries and provide better hemodynamics.\textsuperscript{14} It also improves surgical field by contraction of bowels due to sympathetic blockade.\textsuperscript{19,20} It can also be used in patients with severe COPD and chronic asthma with uneventful and rapid postoperative recovery.\textsuperscript{21,22} Epidural analgesia in the postoperative period may improve respiratory function, decrease perioperative cardiac complications, improve wellbeing of the patients and facilitate early ambulation as well as return of bowel function.\textsuperscript{23,24} The theoretical advantages of CEGA led us to compare this technique with GA alone with regard to intraoperative hemodynamic stability, requirement of anaesthetic agents, recovery scores and postoperative analgesia. The aim of this study is to compare the efficacy of combined GA-Epidual Anesthesia (CEGA) with GA alone to attenuate hemodynamic responses and perioperative analgesia.

METHODS

After approval by hospital research ethics committee, informed written parental consent for anaesthesia was taken. 60 patients aged between 18 years and 55 years of either sex belonging to ASA class I and class II posted for laparoscopic cholecystectomy were enrolled for the study.

The study was carried out from Aug 2014 to Oct 2016, at Mahatma Gandhi Mission Medical College and Hospital, Kamathe, Navi Mumbai. The patients were randomly divided into 2 groups Group A (n=30) received GA. Group B (n=30) received combined GA and Epidural Anaesthesia (CEGA). Patient of both sexes aged and belonging to ASA Class I and II between 18-55 yrs and weighing between 50-60 kg posted for elective laparoscopic cholecystectomy were included in the study. Patients with hypertension, cardiac, renal, hepatic and cerebral diseases, difficult airway and obese patients, endocrinial diseases like hyperthyroidism, hypothyroidism and diabetes mellitus, history of Chronic pain or daily intake of analgesics and any contraindications to NSAIDS or to insertion of an epidural catheter like Local sepsis, anti-platelet/anti-coagulant therapy were excluded from the study. After obtaining approval by ethical committee and written informed patient consent, 30 ASA grade I or II patients in each group were enrolled for the study. Appropriate patients were selected after preoperative assessment by eliciting proper history and physical examination. Thorough investigations included hemoglobin, complete blood count, bleeding time, clotting time, fasting blood sugar level, urine Routine and microscopy, chest x-ray, ECG (age >35 years), renal function tests, liver function tests. Patients were premedicated on the night before surgery with Tablet Ranitidine (150 mg) and Tablet Alprazolam (0.5 mg). The patients were divided into two groups as designated above and demographic data was noted. Baseline measurements of SBP, DBP, MAP, HR and O₂ saturation were taken in operating room. Group A patients were premedicated with Inj. glycopyrolate (0.004 mg/kg), Inj. midazolam (0.02 mg/kg), Inj. fentanyl (2 µg/kg) and induced with Inj. propofol (2 mg/kg). Inj. Vecuronium (0.1 mg/kg). Patients were intubated with appropriate sized cuffed endotracheal tube and mechanically ventilated with N₂O with 50% O₂ and titrated doses of Isoflurane and boluses of 1mg Inj. Vecuronium every 30 minutes to maintain EtCO₂ between 30-35 mmHg. Intraoperatively patients were maintained with 1-2mg/kg/hr inj. propofol infusion and supplemented with Inj. paracetamol IV (15 mg/kg) for adequate analgesia.

Group B patients were premedicated with Inj. Glycopyrolate (0.004 mg/kg). Patient were given sitting position, the epidural catheter was inserted at T12-L1 level under due aseptic precautions. The epidural catheter was cranially directed for about 5 cms. Test dose was given with 3 cc of Inj. Lignocaine 2% with Adrenaline (1:200000). After 10 minutes, 8 cc of Inj. Bupivacaine 0.25% was given, followed by 1 ml increments until the attainment of a T6 level sensory block. Blood pressure and heart rate was monitored during and after the epidural procedure. Hypotension (decrease in systolic
arterial pressure greater than 20% of the baseline value) was treated with infusion of ringer’s lactate solution and Inj. ephedrine (5 mg increments). Bradycardia (HR <60BPM) was treated with Inj. Atropine (0.01 mg/kg). After that, patient was induced and mechanically ventilated as mentioned in group A. Patient was maintained with 1-2 mg/kg inj propofol infusion and 8 ml of 0.25% Inj Bupivacaine will given as epidural supplements every 1 hourly. In both the groups, Insufflation pressure of the peritoneal cavity was maintained at 12 mmHg. A moderate reverse Trendelenburg position with left lateral tilt was used when requested by the surgeons. Inj propofol and Epidural top ups were stopped before desufflation. At the end of the surgical procedure, patients were reversed with Inj. neostigmine (0.05 mg/kg)+Inj glycopyrolate (0.008 mg/kg) intravenously. Postoperatively patients were managed by giving Inj diclofenac 75 mg every 8 hourly in group A and by epidural bolus of 8 ml 0.125% bupivacaine every 8 hourly in group B.

RESULTS

Intraoperative heart rates in both the groups were comparable till pneumoperitoneum. Postpneumoperitoneum until the completion of surgery, HR in group B was lower as compared to group A. Authors found that HR following pneumoperitoneum were significantly increased from 78±2 per min to 86±8 per min in A group as compared to 78±2 per min to 80±4 per min in B group, which was statistically significant (p <0.01). Postoperatively, HR in group B (78±4 per min) was more stable as compared to group A (86±4 per min), which was statistically significant (p <0.01). While analyzing the changes in systolic blood pressure in this study it was seen that the preoperative baseline SBP were comparable in both the groups (p value >0.05). It was observed that systolic blood pressures were comparable in both the groups till pneumoperitoneum.

Post-pneumoperitoneum until the completion of surgery, SBP in Group B was lower as compared to Group A. Which was statistically significant. Authors found that SBP following pneumoperitoneum were significantly increased from 110±4 mm of Hg to 118±8 mm of Hg in A group as compared to 112±5 mm of Hg to 114±6 mm of Hg in B group, which are statistically significant (p <0.01). Postoperatively, SBP in group B 112±6 mm of Hg was more stable as compared to group A 120±8 mm of Hg, which was statistically significant (p <0.01). Postoperative diastolic BP is significantly lower in Group B as compared to Group A.

While analyzing the changes in diastolic blood pressure in our study it was seen that the preoperative baseline DBP were comparable in both the groups till pneumoperitoneum (p value >0.05) .Post-pneumoperitoneum until the completion of surgery, DBP in Group B was lower as compared to Group A. Which was statistically significant. Authors found that DBP following pneumoperitoneum were significantly increased from 78±3 mm of Hg to 86±6 mm of Hg in A group as compared to 78±2 mm of Hg to 76±5 mm of Hg in B group, which are statistically significant (p <0.01). Postoperatively, DBP in group B 72±3 mm of Hg was more stable as compared to group A 84±4 mm of Hg, which was statistically significant (p <0.01).

Total amount of propofol required in group A is significantly higher than in group B (P value <0.01). We studied the total amount of propofol required intraoperatively in each group. In group A mean dose was 1.717 mg/kg and in group B mean dose was 0.503 mg/kg showing reduction in the total dose of propofol required after induction in group B which was statistically highly significant (p <0.01) (Figure 1).

Recovery score in group A are significantly lower than for group B at 2, 4, 6 and 8 minutes. However, the recovery scores are same for both the groups at 0, 10 and 12 minutes. Recovery was evaluated beginning with extubation by steward’s test and we observed that all patients had rapid recovery (steward score of 6 within 10 minutes for both groups). Group B showed significantly better recovery score as compared to group A at 4 minutes with mean of A=2.47 and B=4, (P value <0.01). And at 6 minutes with A=3.5 and B=5.07 (P value <0.01) with a complete recovery attained at 8 minutes in group B and at 10 minutes in group A.

Pain Score is significantly less in Group B as compared to Group A. We studied pain score (VAS) for postoperative 24 hours and found that postoperative pain was well controlled in both groups; the VAS score was never above 4.1. But Group B (used epidural analgesia for postoperative pain management) exhibited significantly better scores as compared to group A (used inj diclofenac as postoperative analgesia). We found that VAS score in group A was 3.4±0.6 and in group B was 1.7±0.5 which was statistically significant with (P value <0.01) (Figure 2).
DISCUSSION

Laparoscopy is a minimally invasive procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO₂) to create space between the anterior abdominal wall and the viscera. This space is necessary for the safe manipulation of instruments and organs. The three major forces that uniquely alter patient’s physiology during laparoscopy are; the increase in intra-abdominal pressure and volume which are transmitted to the thorax, the effects of patient positioning and lateral position and carbon dioxide pneumoinsufflation which is not inert.

General anesthesia combined with preemptive epidural analgesia can provide a good surgical environment and a lighter stress status for retroperitoneal laparoscopic surgeries. Q DM et al and Vera Von Dossow et al, showed that combined general anaesthesia and epidural anaesthesia blunts the stress response during thoracic surgery. Q DM et al, also reported that the cortisol concentration in combined epidural general anaesthesia (CEGA) group was significantly lower as compared to in plain general anaesthesia (GA) group and it is the main steroid hormone responsible for stress response. Luchetti M et al, showed combined epidural general anaesthesia (CEGA) can control pain due to CO₂ induced peritoneal irritation, providing intra and postoperative analgesia and pain free and rapid recovery in laparoscopic cholecystectomy. Hence, part from maintaining stable haemodynamics one of the added advantages of epidural anaesthesia is providing intraoperative and prolonged postoperative analgesia and a rapid recovery. Yun-song et al, used epidural anaesthesia as preemptive analgesia in retroperitoneal laparoscopic adrenalectomy and they found decreased in requirement of anaesthetic agents and other vasoactive drugs which results in rapid recovery.

Comparison of heart rate

While analyzing the changes in heart rate in our study it was seen that the preoperative baseline heart rates were comparable in both the groups (p value >0.05). It was observed that heart rates were comparable in both the groups till pneumoperitoneum. Post-pneumoperitoneum until the completion of surgery, HR in Group B was lower as compared to Group A, which was statistically significant. We found that HR following pneumoperitoneum were significantly increased from 78 ±2 per min to 86±8 per min in A group as compared to 78 ±2 per min to 80±4 per min in B group, which was statistically significant (p <0.01). Postoperatively HR in group B (78±4) was more stable as compared to group A (86±4 per min), which was statistically significant (p<0.01). The epidural anesthesia can effectively block the nerve conduction pathway of noxious stimulations. Thus, general anesthesia combined with preemptive epidural analgesia can provide a lighter stress status for laparoscopic surgeries and helps in attenuating hemodynamic responses. Suryavanshi et al, studied hemodynamic responses in gynecological laparoscopic surgery and found that HR following pneumoperitoneum was significantly increased from 83 ± 12 per min to 94 ± 9 per min in general anesthesia (GA) group as compared to 80±10 per min to 83±11 per min in combined epidural general anesthesia (CEGA) group. They found that combined epidural and general anesthesia successfully attenuated stress response to pneumoperitoneum while in general anesthesia group (GA), plain GA failed to attenuate stress response to pneumoperitoneum as HR increased by 12%, which was statistically very significant with P value <0.03.

Pan YS et al, studied hemodynamic responses in retroperitoneal laparoscopic adrenalectomy surgery and found that intraoperatively HR in the combined general epidural anaesthesia group was reduced compared with that of the general anaesthesia group. Tekelioglu UY et, studied haemodynamic responses in gynaecological laparoscopic surgery under plain general anaesthesia and found that HR were significantly increased from 76.9±9.43 per min to 95.2±12.1 per min (p <0.05) respectively during pneumoperitoneum. Therefore, we can state that epidural anaesthesia helps to provide stable haemodynamics in laparoscopic surgeries along with general anesthesia by attenuating stress responses to pneumoperitoneum.

Comparison of systolic and diastolic Blood pressure

While analyzing the changes in systolic blood pressure in our study it was seen that the preoperative baseline SBP were comparable in both the groups(p value>0.05). It was observed that systolic blood pressure was comparable in both the groups till pneumoperitoneum. Post-pneumoperitoneum until the completion of surgery, SBP in Group B was lower as compared to Group A, which was statistically significant. We found that SBP following pneumoperitoneum were significantly increased from 110 ±4 mm of Hg to 118 ± 8 mm of Hg in A group as compared to 112 ± 5 to 114±6 in B group, which was statistically significant(p<0.01). Postoperatively, SBP in group B 112±6 mm of Hg was more stable as compared to group A 120±8 mm of Hg, which was statistically
significant (p<0.01). The use of other vasoactive drugs is also reduced in presence of epidural anaesthesia such as esmolol, metoprolol, nicardipin for attenuating the stress response.\(^\text{28}\) Calvo et al observed post pneumoperitoneum in GE group SBP and DBP were reduced to 6-8% from base line and stable throughout the surgery.\(^\text{28}\) Pan YS et al, had observed that intraoperatively mean arterial pressure was significantly lower in the combined general epidural group than that in the plain general anaesthesia group and the difference was statistically significant (P < 0.05).\(^\text{16}\)

**Dose of propofol required intraoperatively**

We studied the total amount of propofol required intraoperatively in each group. In group A mean dose was 1.717 mg/kg and in group B mean dose required was 0.503 mg/kg showing reduction in the total dose of propofol required after induction in group B which was statistically highly significant (p<0.01). Agarwal A et al in their study found that the requirement of propofol for induction and maintenance of anaesthesia in the combined epidural GA group was 1.3 +/- 0.3 mg/kg and 2.4 +/- 0.9 mg/kg/hr, respectively, compared with 2.4 +/- 0.6 mg/kg and 4.4 +/- 1.6 mg/kg/hr observed in the general anaesthesia group (P <0.05).

They conclude that epidural anaesthesia given before induction of anaesthesia reduces the requirement of propofol.\(^\text{31}\) Yun-song et al, used epidural analgesia as preemptive analgesia in retroperitoneal laparoscopic adrenalectomy and they found decreased in requirement of anaesthetic agents and other vasoactive drugs to blunt the stress response.\(^\text{27}\) Therefore, we can state that in presence of epidural anaesthesia as requirement of anaesthetic drugs is decreased thus resulting in quick awakening and extubation at the end of the surgery.

**Comparison of recovery scores**

Recovery was evaluated beginning with extubation by steward’s test and we observed that all patients had rapid recovery (steward score of 6 within 10 minutes for both groups). Group B showed significantly better recovery score as compared to group A at 4 minutes with mean of A=2.47 and B=4, P<0.01, and at 6 minutes with A=3.5 and B=5.07, P<0.01 with a complete recovery attained at 8 minutes in group B and at 10 minutes in group A.

Luchetti et al, also compared recovery score in patients undergoing laparoscopic cholecystectomy and found that all patients had rapid recovery (steward score of 6 within 12 minutes for both groups). Group B (CEGA) showed significantly better recovery score at 4 minutes (A=2.8±0.4 and B=4.5±0.6, P<0.05) and 6 minutes (A=4.1±0.5 vs B=5.7±0.2, P<0.05) with a complete recovery attained at 8 minutes.\(^\text{4}\) Thus we can state that in patients undergoing combined general anaesthesia, recovery was usually pain free and rapid.

**Comparison of VAS score**

In our study, we studied pain score for postoperative 24 hours and found that postoperative pain was well controlled in both groups; the VAS score was never above 4.1. But Group B (used epidural analgesia for postoperative pain management) exhibited significantly better scores as compared to group A (used injection diclofenac as postoperative analgesia). We found that VAS score in group A was 3.4±0.6 and in group B was 1.7± 0.5 which was statistically significant with P<0.01. Luchetti et al also compared VAS score for first four hours in patients undergoing laparoscopic cholecystectomy and found that that postoperative pain was well controlled in both groups; the VAS score was never above 4.2. Group combined GA epidural exhibited significantly better scores at the second (A=3.2±0.5 vs B=1.8±0.3, P<0.05), the third (A=3.7±0.4 vs B=1.5±0.4, P<0.05), and the fourth postoperative hour(A=4.2±0.6 vs B=1.7±0.3, P<0.05).\(^\text{4}\) Thus we can state that the use of an epidural catheter permitted us to adequately control pain secondary to peritoneal irritation, resulting in excellent intra and postoperative analgesia. This was achieved without administering intravenous opioids and with no increase of adverse effects or alteration of the hemodynamics and respiratory stability. The patients recovery was usually pain free and rapid.

**CONCLUSION**

Authors concluded that the use of epidural along with general anaesthesia helps in attenuating hemodynamic changes due to stress response to pneumoperitoneum, which results in maintaining stable intraoperative and postoperative hemodynamics during laparoscopic cholecystectomy surgery. It can effectively reduce the requirement of anesthetic agents (total intraoperative requirement of propofol). Combining epidural to general anaesthesia results in rapid recovery as compared to plain general anaesthesia and also helps in providing good postoperative analgesia (VAS score is better in combined epidural general anaesthesia group as compared to plain general anaesthesia group. There were no significant intraoperative and postoperative complications noted in both the groups.

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