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Efficacy of an intercostal nerve block administered with general anesthesia in elderly patients undergoing distal gastrectomy

Abstract

Purpose: The purpose of this study was to evaluate the efficacy and safety of administration of an intercostal nerve block (INB) with general anesthesia to elderly patients undergoing a distal gastrectomy.

Methods: Elderly patients (>65 years) undergoing selective gastrectomy were randomly assigned to three groups ($n = 80$): general anesthesia (Group A); general + INB anesthesia (Group B); or, general + epidural anesthesia (Group C). General anesthesia was maintained with propofol, remifentanyl and cisatracurium. The mean arterial blood pressure (MAP), heart rate (HR) and C-reactive protein (CRP) levels were determined before anesthesia (T0) and at 5 min after intubation (T1), skin incision (T2), exploration of the peritoneal cavity (T3), gastrointestinal anastomosis (T4), end of operation (T5) and 10 min after extubation (T6).

Results: MAP decreased at T1 in all groups ($P < 0.05$) and at T2, T4 and T5 in Group C ($P < 0.05$) and was lower in Group C than Group B at T2 and T4 ($P < 0.05$). There were no differences in MAP between Groups A and B or between Groups B and C. HR increased at T2 - T6 in Group A ($P < 0.05$) and was higher at T2 - T6 in Group B and Group C ($P < 0.05$). CRP levels decreased at T2 - T5 in Groups B and C ($P < 0.05$) and were lower in Groups B and C compared with Group A ($P < 0.05$). Propofol and remifentanyl doses were lower in Groups B and C ($P < 0.05$ and $P < 0.01$, respectively) and patients recovered faster than in Group A ($P < 0.05$).

Conclusion: Administration of INB with general anesthesia enhanced analgesia, led to stable hemodynamics, and reduced anaesthetic consumption and postoperative stress response.

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As the population ages, new advances in anesthesiology and surgery have been developed to address the unique needs of elderly surgery patients [1]. In these patients, postoperative complications occur with higher frequency because of functional decline in the major organ systems and complications due to comorbid diseases. A combinatorial approach, using an epidural with general anesthesia, has been associated with a lower postoperative stress response, a reduction in the use of general anesthesia, a faster postoperative recovery rate, and optimal analgesia [2]. However, insertion of an epidural catheter is a blind technique that may result in nerve damage, infection, bleeding and other complications, thus limiting its clinical application [1-3]. Intercostal nerve block (INB) has significant advantages as a pain reliever, including the ability to block the production of inflammatory mediators following tissue damage and prevent these chemical mediators from acting on peripheral nerve endings to produce primary and secondary hyperalgesia and the ability to block nociception in the spinal cord [4].

As an intercostal analgesia, INB offers the additional benefits of optimal analgesia, reduced use of perioperative opioid analgesia, improved lung function and decreased occurrence of central nervous system depression. When combined with general anesthesia, INB can substantially reduce the stress response during surgery [5]. A combinatorial approach with INB and general anesthesia has been used primarily for chest surgery [6-9], with only limited use in abdominal surgery. In this study, we improved the efficacy of an intercostal nerve block administered with general anesthesia in elderly patients undergoing distal gastrectomy.

Methods

Participants

The study was reviewed and approved by the Institutional Ethics Committee (Ethics No. ajums.REC.1393.56). All participants, or their legally authorized representatives, provided informed consent. The eligibility criteria for patients included age (65 years or older), weight (≥ 45 kg), pathologically-proven adenocarcinoma and ASA assessment (level II-III). A total of 240 elderly patients with elective radical gastrectomy were enrolled in the study. The patients were randomly divided into three groups ($n = 80$): general anesthesia (Group A), combined INB + general anesthesia (Group B), and combined epidural + general anesthesia (Group C). The following exclusion criteria were used: ASA level $> III$; BMI < 15 kg/m² or BMI > 30 kg/m²; history of allergic reaction to propofol; history of alcohol or narcotic drug addiction; coagulopathy; peripheral neuropathy;

or hindrance to communication. In order to provide a self-assessment of pain severity, all patients were instructed on how to use the visual analogue scale (VAS) to assess their pain degree.

Anesthetic techniques

All patients received 0.1 g luminal sodium through intramuscular administration at 30 min before anesthesia. Electrocardiogram (ECG), blood oxygen saturation (SPO₂), heart rate (HR), respiratory rate (RR) and bispectral index (BIS) were monitored when patients entered the operating room. Under local anesthesia, a catheter was inserted into the left radial artery to measure mean arterial pressure (MAP). Endotracheal intubation was performed using rapid sequence intubation: 0.04 mg/kg midazolam, 3 μ g/kg fentanyl, 0.3 mg/kg etomidate and 0.2 mg/kg cis-atracurium. Group A patients received general anesthesia alone. After endotracheal intubation, the 7–10th pairs of intercostal nerves were blocked in Group B patients through injection of 4.0 ml local anesthetic per block in the mid-axillary line. To accomplish this procedure, patients were positioned with their upper limbs extended. A 22-gauge, short bevel needle was disinfected and inserted at the mid-axillary line and lower border of the ribs. After piercing the rib surface, the needle was lifted slightly and shifted along the surface of the ribs toward the lower border. When the needle reached the lower border, it was inserted 0.3 cm more to reach the intercostal space. At this point, the needle should hit a vacuum/void. The syringe was drawn back, and a mixture of 15 ml 2% lidocaine, 10 ml 0.75% ropivacaine, 10 mg dexamethasone (2 ml), and 8 ml saline was injected if there was no blood or air drawn into the syringe barrel. Patients in Group C received an epidural at the T8-9 interspace before anesthesia induction. After successful catheterization, patients received a test dose of 3 ml of 2% lidocaine and were observed for 5 min for depth of anesthesia, respiratory depression and anesthesia toxicity. A second dose of 0.375% ropivacaine (8 ml) was then injected. The depth of anesthesia was assessed after 10 min and patients with a depth of anesthesia above T4 were excluded from the study group.

If patient MAP values decreased more than 20% of the baseline value, or if HR became less than 50, 5–10 mg of ephedrine or 0.5 mg of atropine was given. On the other hand, if patient MAP increased more than 20% of the baseline value, 10 mg of urapidil was given to control blood pressure. Upon closure of the abdomen, 0.05 mg of fentanyl was given, muscle relaxants were stopped, and all anesthetics were stopped upon skin closure. After the surgery, patients were extubated and

were allowed to recover in the anesthesia recovery room. Patients were sent back to the ward once they were awake and exhibited stable vital signs.

Monitoring signs

MAP, HR, and C-reactive protein (CRP) levels were monitored at the following time points: 5 min before anesthesia (T0), 5 min after intubation (T1), skin incision (T2), exploration of peritoneal cavity (T3), gastrointestinal anastomosis (T4), end of operation (T5) and 10 min after extubation (T6). Data for the following parameters were recorded for all three groups: the duration of surgery; recovery time (time from the end of surgery to when patients awake/extubation); whether patients were consciously aware during surgery; use of vasoactive drugs; and patient score on the VAS (0 is no pain, 10 is unbearable pain) at 10 min, 30 min and 60 min after surgery.

Statistical analysis

Statistical analysis was done using SPSS for Windows 19.0. All data are presented as mean with the standard deviation (mean $\pm$ SD). Group comparisons were done using ANOVA, followed by Student-Newman-Keuls (SNK) method to compare different pairs of means. The Chi Square (X^2) test was used for count data. Statistical significance was set at $P < 0.05$.

Results

No statistically significant differences were detected in age, gender, body weight and surgical duration between the three groups (Table 1).

Compared with Group A, doses of propofol and remifentanyl were reduced in Groups B and C ($P < 0.05$ and $P < 0.01$,

TABLE 1. Demographic characteristics

	Group A (n = 80)	Group B (n = 80)	Group C (n = 80)
Age (years)	71 $\pm$ 9	72 $\pm$ 7	72 $\pm$ 8
Gender (male/female)	53/27	49/31	52/28
Body weight (kg)	66 $\pm$ 7	63 $\pm$ 8	65 $\pm$ 8
Surgical duration (min)	185 $\pm$ 13	187 $\pm$ 11	188 $\pm$ 12

Group A, general anesthesia; Group B, general + intercostal nerve block anesthesia; Group C, general + epidural anesthesia

TABLE 2. Dosage of propofol and remifentanyl administered, with associated recovery times

	Group A	Group B	Group C
Propofol (mg)	1462 $\pm$ 21	772 $\pm$ 13*	747 $\pm$ 12*
Remifentanyl (mg)	2.01 $\pm$ 3.4	0.9 $\pm$ 0.02**	0.8 $\pm$ 0.03**
Recovery time (min)	16.5 $\pm$ 3.4	5.2 $\pm$ 2.1*	5.4 $\pm$ 2.2*

Mean $\pm$ SD

Group A, general anesthesia; Group B, general + intercostal nerve block anesthesia; Group C, general + epidural anesthesia

* $p < 0.05$ vs Group A, ** $p < 0.01$ vs Group A

TABLE 3. VAS score at 10 min, 30 min and 60 min after surgery in the three groups

	Group A	Group B	Group C
10 min after surgery	6.5 $\pm$ 1.1	0.5 $\pm$ 0.1	0.3 $\pm$ 0.1
30 min after surgery	7.8 $\pm$ 1.3	0.7 $\pm$ 0.2	0.5 $\pm$ 0.2
60 min after surgery	8.1 $\pm$ 1.4	1.1 $\pm$ 0.5	0.8 $\pm$ 0.4

Group A, general anesthesia; Group B, general + intercostal nerve block anesthesia; Group C, general + epidural anesthesia

FIGURE 1. Alteration in MAP in three groups. T0 = before anesthesia, T1 = intubation, T2 = skin incision, T3 = exploration of peritoneal cavity, T4 = gastrointestinal anastomosis, T5 = end of operation, T6 = 10 min after extubation. $\Delta^{* \#}$ $P < 0.05$ compared to respective baseline. $\dagger P < 0.05$ between Group A and Group C; Values are presented as the mean $\pm$ SE.

Group A, general anesthesia; Group B, general + intercostal nerve block anesthesia; Group C, general + epidural anesthesia

FIGURE 2. Changes in HR in three groups. T0 = before anesthesia, T1 = intubation, T2 = skin incision, T3 = exploration of peritoneal cavity, T4 = gastrointestinal anastomosis, T5 = end of operation, T6 = 10 min after extubation. $*$ $P < 0.05$ compared to baseline in Group A. $\dagger P < 0.05$ between Group A and Group B or C; Values are presented as the mean $\pm$ SE. Group A, general anesthesia; Group B, general + intercostal nerve block anesthesia; Group C, general + epidural anesthesia

FIGURE 3. Changes in serum CRP levels in three groups. T0 = before anesthesia, T1 = intubation, T2 = skin incision, T3 = exploration of peritoneal cavity, T4 = gastrointestinal anastomosis, T5 = end of operation, T6 = 10 min after extubation. # $P < 0.05$ compared to baseline in Group B. ▲ $P < 0.05$ compared to baseline in Group C. ‡ $P < 0.05$ between Group A and Group B or C; Values are presented as the mean $\pm$ SE. Group A, general anesthesia; Group B, general + intercostal nerve block anesthesia; Group C, general + epidural anesthesia

respectively). Patients in Group B and Group C recovered significantly faster than Group A ($P < 0.05$) (Table 2). Compared with preoperative respective values, MAP decreased at T1 in all three groups ($P < 0.05$) and at T2, T4 and T5 in Group C ($P < 0.05$). MAP was reduced in Group C compared with Group B at T2 and T4 ($P < 0.05$). MAP was not significantly different between Group A and Group B and between Group B and Group C. Sixteen patients in Group A received urapidil to lower their blood pressure, and 11 patients in Group B and 36 patients in Group C received ephedrine to raise their blood pressure. HR increased at T2, T3, T4, T5 and T6 in Group A compared with value at T0 ($P < 0.05$). HR increased at T2, T3, T4, T5 and T6 in Group B and Group C compared with Group A, ($P < 0.05$) (Fig. 1, 2).

CRP levels decreased at T2, T3, T4 and T5 in Group B or C, compared with levels at T0 ($P < 0.05$). CRP levels at T2, T3, T4 and T5 were reduced in Group B and Group C compared with Group A ($P < 0.05$) (Fig. 3).

VAS scores

At 10 min, 30 min and 60 min after surgery VAS scores in Group A patients were higher than those in Group B and

Group C ($P < 0.01$); thus, 73 patients in Group A required analgesia drugs in the recovery room whereas patients in Groups B and C did not. No reports of intraoperative awareness were made in any of the three groups.

Discussion

Detterbeck *et al.* demonstrated the analgesic effectiveness and improved postoperative recovery of INB during and following chest surgery [12]. No study on the effects of INB on elderly patients undergoing abdominal surgery has been performed. Continuous epidural anesthesia in combination with general anesthesia is recognized as an efficient approach for major abdominal surgery [13]. In this study, we found that epidural anesthesia in combination with general anesthesia provides better postoperative analgesia (in patients undergoing distal gastrectomy) as well. This supports the findings of previous studies [14, 15].

At the same time, we found that combining INB with general anesthesia could also provide better postoperative analgesia as epidural anesthesia with general anesthesia. INB was found to be as efficient as epidural analgesia for elderly patients undergoing abdominal surgery.

Intercostal nerves are the anterior rami of spinal nerves T1-12. After exiting the intervertebral foramen, each pair of intercostal nerves runs anteriorly with intercostal vessels in the subcostal groove along the lower border of the ribs and around the trunk. They branch at the anterior axillary line as a lateral cutaneous branch, or at the sternum as anterior cutaneous branches to innervate the intercostal and abdominal wall muscle and supply the skin. For these reasons, INB can offer optimal analgesia.

The epidural technique is often difficult to perform, and the success of entry into the epidural space is lower in elderly patients than in other populations [16]. In addition, side effects and complications, such as a substantial perioperative drop in blood pressure, occur frequently [17, 18]. In the present study, hypotension occurred in more patients who received combined epidural and general anesthesia than those who received combined INB with general anesthesia. This suggests that INB might have more stable hemodynamics and be safer than epidural analgesia.

There are currently no uniform standards for assessing intensity of the stress response, other than measuring changes in stress hormones and immune factors as an overall evaluation. Changes in serum CRP and other cytokines are not only directly stimulated by stress factors, but they are also affected by the neuroendocrine system. As a result, changes in serum CRP levels are delayed but may provide an overall reflection of the intensity of the stress response [19]. Here, we utilized changes of serum CRP levels to assess the intensity of the stress response in elderly stomach cancer patients. The results of our study showed that combined epidural anesthesia or INB with general anesthesia noticeably reduced the stress response of elderly patients during surgery. On the other hand, general anesthesia could not completely eliminate the patient stress response, similar to the results observed by Fares *et al.* [20].

Despite the beneficial findings of our study, there are some limitations. First, the widespread use of ultrasound in the field of anesthesia has enabled more accurate positioning in INB, achieving greater anesthetic efficacy. Second, we only observed short-term postoperative VAS scores. In addition, serum CRP was used to assess stress responses. In future studies, additional markers will be chosen to further assess effects of INB on stress responses. In conclusion, combined intercostal nerve block with general anesthesia demonstrated stable hemodynamics, reduced anesthetic consumption and reduced the postoperative stress response.

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References

1. Holt NF. Trends in healthcare and the role of the anesthesiologist in the perioperative surgical home – the US perspective. *Curr Opin Anaesthesiol*, 2014, 27: 371-376.
2. Chen WK, Ren L, Wei Y, Zhu DX, Miao CH, Xu JM. General anesthesia combined with epidural anesthesia ameliorates the effect of fast-track surgery by mitigating immunosuppression and facilitating intestinal functional recovery in colon cancer patients. *Int J Colorectal Dis*, 2015, 30: 475-481.
3. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. *Anesthesiology*, 2004, 101: 950–959.
4. Brull R, McCartney CJ, Chan VW, El Beheiry H. Neurological complications after regional anesthesia: contemporary estimates of risk. *Anesth Analg*, 2007, 104: 965–974.
5. Cook TM, Counsell D, Wildsmith JA. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth*, 2009, 102: 179–190.
6. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth*, 1997, 78: 606-617.
7. Chen J, Li X, Li K. Effects of different methods of anesthesia on serum prolactin, growth hormone and cortisol in patients with esophageal cancer surgery. *J Practical Med*, 2012, 28 : 1827-1829.
8. Concha M, Dagnino J, Cariaga M, Aguilera J, Aparicio R, Guerrero M. Analgesia after thoracotomy: epidural fentanyl/bupivacaine compared with intercostal nerve block plus intravenous morphine. *J Cardiothorac Vasc Anesth*, 2004, 18: 322–326.
9. Osinowo OA, Zahrani M, Softah A. Effect of intercostal nerve block with 0.5% bupivacaine on peak expiratory flow rate and arterial oxygen saturation in rib fractures. *J Trauma*, 2004, 56: 345-347.

10. Takamori S, Yoshida S, Hayashi A, Matsuo T, Mitsuoka M, Shirouzu K. Intraoperative intercostal nerve blockade for post-thoracotomy pain. *Ann Thorac Surg*, 2002, 74: 338–341.
11. Liu M, Rock P, Grass JA, Heitmiller RF, Parker SJ, Sakima NT, Webb MD, Gorman RB, Beattie C. Double-blind randomized evaluation of intercostal nerve blocks as an adjuvant to subarachnoid administered morphine for post-thoracotomy analgesia. *Reg Anesth*, 1995, 20: 418–425.
12. Dettlerbeck FC. Efficacy of methods of intercostal nerve blockade for pain relief after thoracotomy. *Ann Thorac Surg*, 2005, 80: 1550- 1559.
13. Zabolotskikh I, Trembach N. Safety and efficacy of combined epidural/general anesthesia during major abdominal surgery in patients with increased intracranial pressure: a cohort study. *BMC Anesthesiol*, 2015, 15, 15:76. doi: 10.1186/s12871-015-0056-2.
14. Ventham NT, Hughes M, O'Neill S, Johns N, Brady RR, Wigmore SJ. Systematic review and meta-analysis of continuous local anaesthetic wound infiltration versus epidural analgesia for post-operative pain following abdominal surgery. *Br J Surg*, 2013, 100: 1280-1289.
15. Kato A, Koitabashi T, Masuda S, Masuda Y, Ouchi T, Serita R. Comparison of the efficacy of ropivacaine and that of levobupivacaine for postoperative epidural analgesia in patients undergoing gynecological open abdominal surgery. *Masui*, 2013, 62: 1160-1165.
16. Heinink TP, Baker BG, Yates VF, Addison DC, Williams JP. The effect of anaesthetist grade and frequency of insertion on epidural failure: a service evaluation in a United Kingdom teaching hospital. *BMC Anesthesiol*, 2015, 21: 15:5. doi: 10.1186/1471-2253-15-5.
17. Fares KM, Mohamed SA, Hamza HM, Sayed DM, Hetta DF. Effect of thoracic epidural analgesia on pro-inflammatory cytokines in patients subjected to protective lung ventilation during Ivor Lewis esophagectomy. *Pain Physician*, 2014, 17: 305-315.
18. Gramigni E1, Bracco D, Carli F. Epidural analgesia and postoperative orthostatic haemodynamic changes: observational study. *Eur J Anaesthesiol*, 2013, 30: :398-404.
19. 19. Kenny GN, Sutcliffe NP. Target-controlled infusions: stress free anesthesia? *J Clin Anesth*, 1996, 8: 15S-20S.
20. Fares KM, Mohamed SA, Hamza HM, Sayed DM, Hetta DF. Effect of thoracic epidural analgesia on pro-inflammatory cytokines in patients subjected to protective lung ventilation during Ivor Lewis esophagectomy. *Pain Physician*, 2014, 17: 305-315.