J Anesth (2007) 21:1–6
DOI 10.1007/s00540-006-0459-9

Journal of
Anesthesia

Original articles

A comparison of intravenous-based and epidural-based techniques for anesthesia and postoperative analgesia in elderly patients undergoing laparoscopic cholecystectomy

Kohki Nishikawa[1], Saori Kimura[1], Yuki Shimodate[1], Motohiko Igarashi[1], and Akiyoshi Namiki[2]

[1] Department of Anesthesia, Muroran City General Hospital, 3-8-1 Yamate-cho, Muroran 051-8512, Japan
[2] Department of Anesthesiology, Sapporo Medical University School of Medicine, Sapporo, Japan

Abstract
Purpose. We wished to compare the effectiveness of intravenous-based (IV) and epidural-based (EPI) techniques for anesthesia and postoperative analgesia in elderly patients undergoing laparoscopic cholecystectomy. Effectiveness was compared in terms of reduction of postoperative pain and adverse events, and achieving a high level of patient satisfaction.
Methods. Thirty American Society of Anesthesiologists (ASA) physical status I-II patients aged more than 65 years, scheduled for laparoscopic cholecystectomy, were enrolled in this study. The patients in the IV group (n = 15) received modified neurolept anesthesia with droperidol 0.2 mg·kg^{-1} and pentazocine 0.15–0.3 mg·kg^{-1} (maximum dose of 1.0 mg·kg^{-1}) and 60% nitrous oxide in oxygen, followed by postoperative intravenous infusion of 20 μg·ml^{-1} buprenorphine, provided with a patient-controlled analgesia pump programmed to deliver a bolus of 0.5 ml with a lockout interval of 15 min and a background infusion of 0.5 ml·h^{-1}. The patients in the EPI group (n = 15) had combined epidural analgesia and general anesthesia with sevoflurane and 60% nitrous oxide in oxygen, followed by the epidural infusion of a 0.125% bupivacaine and 5 μg · ml^{-1} buprenorphine mixture by means of an on-demand analgesic system (bolus of 2 ml, lockout interval of 60 min, and background infusion of 2 ml·h^{-1}).
Results. The quality of postoperative analgesia was similar in the two groups. The incidences of intraoperative hypotension and bradycardia and postoperative hypotension were significantly lower in the IV group than in the EPI group ($P <$ 0.05). A significantly higher level of patient satisfaction was found in the IV group compared with that in the EPI group ($P < 0.05$). The major contributor to dissatisfaction in the EPI group was anxiety or discomfort associated with the epidural procedures.
Conclusion. Modified neurolept anesthesia with pentazocine and postoperative i.v. analgesia with buprenorphine were superior to epidural-based techniques, in terms of hemodynamic stability and patient satisfaction, in elderly patients undergoing laparoscopic cholecystectomy.

Address correspondence to: K. Nishikawa
Received: May 11, 2006 / Accepted: September 20, 2006

Key words Modified neurolept anesthesia · Intravenous · Epidural · Pentazocine · Buprenorphine · Laparoscopic cholecystectomy · Age factors

Introduction

The laparoscopic surgical approach, in which there is less need for the control of severe pain, requires a broader sensory blockade than does laparotomy, postoperatively, because of the shoulder pain secondary to diaphragmatic irritation as a result of CO_2 pneumoperitoneum, as well as parietal and visceral pain [1]. For pain management after laparoscopic procedures, therefore, the systemic application of opioid analgesics may be more effective than epidural analgesia, which provides pain relief in a limited range.

We performed a prospective randomized study in elderly patients undergoing laparoscopic cholecystectomy to compare the effectiveness of two techniques of anesthesia and analgesia on postoperative pain, side effects, and patient satisfaction.

The two techniques were: general anesthesia using modified neurolept anesthesia (mNLA), followed by postoperative patient-controlled analgesia (PCA) with intravenous (i.v.) buprenorphine; and combined general anesthesia using sevoflurane and epidural analgesia, followed by postoperative epidural PCA, using a mixture of bupivacaine and buprenorphine.

Methods

Protocol

After obtaining approval from our hospital's ethics committee and informed consent from each patient, 30 American Society of Anesthiologists (ASA) physical status I-II patients, older than 65 years, scheduled for

laparoscopic cholecystectomy, were enrolled in this study. Exclusion criteria were: patients with contraindications for epidural anesthesia, those with previous or current neurologic disease, and those with preoperative abnormal mental status, defined by a modified Abbreviated Mental Test (AMT) score [2] of less than 8. Patients were randomly assigned, using sealed envelopes with a blocked random allocation, to receive either mNLA with droperidol and pentazocine, followed by PCA with i.v. buprenorphine (IV group) or combined epidural analgesia and sevoflurane anesthesia, followed by epidural PCA, using a mixture of bupivacaine and buprenorphine (EPI group).

None of the patients received preoperative medications. Upon their arrival in the operating room, standard monitoring, including continuous electrocardiography and pulse oximetry, were applied, and systolic arterial blood pressure (SAP), mean arterial blood pressure (MAP), heart rate (HR), and peripheral oxygen saturation (S_{PO_2}) were recorded every 5 min intraoperatively. Preanesthetic hemodynamic variables (baseline values) were defined as the average of three independent determinations.

In the IV group, mNLA was induced with droperidol (0.2 mg·kg^{-1}), pentazocine (0.3 mg·kg^{-1}) and thiamylal (2 mg·kg^{-1}), and the trachea was intubated orally with vecuronium (0.1 mg·kg^{-1}) i.v. as required. Anesthesia was maintained with 60% nitrous oxide in oxygen and with a supplemental bolus dose of pentazocine (0.15–0.3 mg·kg^{-1}) i.v., given for clinical signs suggesting inadequate depth of anesthesia such as sweating, tearing, and an increase in MAP exceeding 20% of the baseline values. Supplemental doses of vecuronium were also administered to provide satisfactory muscle relaxation during the surgical procedure. Postoperative analgesia was obtained by i.v. administration of a mixture of buprenorphine (20 μg·ml^{-1}) and droperidol provided with a PCA pump (Baxter Patient Control Module 0.5 ml; Baxter, Deerfield, IL, USA) programmed to deliver a 0.5-ml bolus dose with a lockout interval of 15 min and a background infusion of 0.5 ml·h^{-1}.

In the EPI group, local anesthesia (approximately 5 ml 1% lidocaine) was injected about 1 min before an epidural needle was introduced, and an epidural catheter was placed through the epidural needle at the T7-T9 level. Lidocaine 1.0% solution, containing 1 : 200 000 epinephrine, was injected into the epidural space through the epidural catheter to achieve a bilateral T4 sensory level. General anesthesia was then induced with thiamylal (2 mg·kg^{-1}) i.v. and the trachea was intubated orally with vecuronium (0.1 mg·kg^{-1}) i.v. Maintenance of anesthesia was done with sevoflurane (0.6%–2.0% end-tidal) and 60% nitrous oxide in oxygen. During anesthesia, end-tidal PCO_2 was maintained between 35 and 40 mmHg, using controlled ventilation. Epidural analgesia was obtained by the intermittent intraoperative injection of 1.0% lidocaine with epinephrine (4–8 ml at 45- to 60-min intervals), followed by the postoperative administration of a mixture of 0.125% bupivacaine, buprenorphine (5 μg·ml^{-1}), and droperidol provided with the PCA pump (Baxter Patient Control Module 2 ml; Baxter) programmed to deliver a 2-ml bolus with a lockout interval of 60 min and a background infusion of 2 ml·h^{-1}. All patients were supplied with oxygen at a rate of 3 l·min^{-1}, via a face mask, for 24 h after surgery, and they were monitored for 24 h after surgery with continuous pulse oximetry. In both groups, 50 mg flurbiprofen was intravenously infused on request when pain relief was inadequate.

Intra- and postoperative hemodynamic and respiratory assessments

Lactated Ringer's solution was used as the intraoperative fluid and was run at a rate of 6 ml·kg^{-1} h^{-1} throughout surgery. During anesthesia, an MAP increase of greater than 15% of the baseline value (defined as hypertension), which did not respond to a supplemental bolus dose of pentazocine (0.15–0.3 mg·kg^{-1}, maximum dose of 1.0 mg·kg^{-1}) i.v. in the IV group or to an increase in the level of inspired sevoflurane concentration in the EPI group was treated with incremental 1-mg doses of nicardipine. Hemodynamic responses suggesting hypovolemia, such as a decrease in MAP exceeding 15% of the baseline value (defined as hypotension) and/or HR more than 20% above the baseline value (defined as tachycardia) which did not respond to a preload of 4 ml · kg^{-1} lactated Ringer's solution and a decrease in the inspired concentration of sevoflurane (minimum concentration of 0.6%) were treated with incremental 5-mg doses of i.v. ephedrine and/or 1 mg of i.v. verapamil. Bradycardia (HR < 50 bpm) was managed by 0.5 mg of i.v. atropine. SAP, MAP, and HR were recorded every hour for 24 h postoperatively. Clinically relevant postoperative respiratory depression was defined as a respiratory rate of 8 breaths or less per min and/or oxygen desaturation to 92% or less. No other postoperative sedative or analgesic agents were permitted.

Evaluation of postoperative pain, and delirium, and patient satisfaction

The intensity of postoperative pain at rest was assessed by using both a 100-mm visual analog scale (VAS) and a verbal rating scale (VRS) relief rating [3]. Sleeping patients were not awakened for pain assessment but were assigned VAS score and VRS relief ratings of 0.

Postoperative delirium was evaluated by using the Delirium Rating Scale (DRS) scoring system [4,5] at least two times a day (at 9 a.m. and 9 p.m.) during the first 3 postoperative days, and was considered to have occurred if the total DRS score was over 12 [5]. Patient satisfaction with the anesthetic technique was evaluated at 18 h after surgery by using a scoring system of "poor", "satisfied", or "very satisfied".

Statistical analysis

The VRS relief rating and the DRS scores were expressed as medians and ranges and were compared by using the Mann-Whitney *U*-test. Other data, presented as means ± SD, were compared by using analysis of variance.

Results

The EPI and IV groups were comparable with respect to age, sex, weight, height, ASA physical status (Table 1), duration of anesthesia, and surgery (Table 2), and AMT score. The highest and lowest levels of sensory block at the end of surgery in the EPI group were Th4-Th6 and L1-Th12, respectively.

Table 1. Demographic data

	IV group	EPI group
Number	15	15
Age (years)	71.2 ± 5.3	70.9 ± 6.5
Sex (M/F; *n*)	8/7	9/6
Weight (kg)	61.4 ± 10.5	55.7 ± 9.7
Height (cm)	155.8 ± 4.2	153.2 ± 6.6
ASA physical status (I/II)	3/12	4/11

* $P < 0.05$ compared with the IV group
Values are means ± SD or numbers of patients

During surgery, the incidences of hypotension and bradycardia in the EPI group were significantly higher than those in the IV group. The EPI group also had significantly larger i.v. fluid and ephedrine dose requirements than those in the IV group ($P < 0.01$). On the other hand, the requirement of nicardipine for treating hypertension was similar in the two groups, although the incidence of hypertension was higher in the IV group than in the EPI group ($P < 0.05$; Table 2). No patient in either group experienced intraoperative hypoxemia with an S_{pO_2} of less than 92%.

Postoperative hypotension occurred in three patients in the EPI group. The lowest MAP values in these patients were 72, 73, and 75 mmHg. None of the patients in the IV group experienced hypotension. Decrease in the respiratory rate of less than 8 breaths · min^{-1} occurred in only one patient in the IV group, but no postoperative hypoxemia ($S_{pO_2} < 92\%$) developed in any patient in either group (Table 3). The VAS and VRS relief rating scores for pain at rest and postoperative patient-controlled analgesic consumption are shown in Fig. 1. One patient in the IV group and one in the EPI group required flurbiprofen, at 100 mg and 50 mg, respectively, for rescue analgesic. No difference in postoperative buprenorphine consumption during 18 h after surgery was found between the IV and EPI groups (Fig. 1A). Also the quality of postoperative pain relief did not significantly differ between the two groups, but the EPI group tended to have higher scores on both the VAS and VRS relief ratings compared with the IV group (Fig. 1B,C).

Postoperative delirium developed in five patients (17%) during 72 h after surgery. The incidences of postoperative delirium in the two groups were similar

Table 2. Comparison of the two groups during anesthesia

	IV group	EPI group
Duration of surgery (min)	75.8 ± 20.1	71.1 ± 11.9
Duration of anesthesia (min)	128.3 ± 16.2	126.1 ± 13.2
Intravenous fluid (ml)	662.5 ± 113.9	797.3 ± 199.9*
Intraoperative pentazocine (mg)	45.0 ± 7.5	NA
Droperidol (mg)	10.8 ± 2.5	NA
End-tidal sevoflurane (%)	NA	1.0 ± 0.4
Incidence of hypotension (*n*; %)	0 (0)	4 (27)*
Bradycardia (*n*; %)	0 (0)	2 (13)*
Hypertension (*n*; %)	2 (13)	0 (0)*
Tachycardia (*n*; %)	0 (0)	0 (0)
Ephedrine requirement (mg)	0.8 ± 2.9	13.6 ± 5.5*
Atropine requirement (mg)	0 (0)	0.1 ± 0.2
Nicardipine requirement (mg)	0.3 ± 0.6	0 (0)

* $P < 0.05$ compared with the IV group
Values are means ± SD or numbers of patients (%)
NA, not applicable

Table 3. Postoperative adverse events and patient satisfaction

	IV group	EPI group
Postoperative side effects (*n*; %):		
Nausea, vomiting	2 (13)	3 (20)
Headache	1 (7)	0 (0)
Backache	0 (0)	2 (13)*
Shoulder pain	0 (0)	1 (7)
Respiratory depression (*n*; %);		
Hypoxemia (Sp_{O_2} < 92%) 0 (0)	0 (0)	0 (0)
RR ≤ 8·min^{-1}	1 (7)	0 (0)
Hypotension (*n*; %)	0 (0)	3 (20)*
Bradycardia (*n*; %)	0 (0)	0 (0)
Hypertension (*n*; %)	1 (7)	0 (0)
Tachycardia (*n*; %)	0 (0)	0 (0)
DRS score		
1st PO day	3 (0–8)	2 (0–6)
2nd PO day	3 (0–13)	3 (0–10)
3rd PO day	3 (2–13)	4 (1–12)
Incidence of POD (*n*; %)		
1st PO day	0 (0)	0 (0)
2nd PO day	1 (7)	0 (0)
3rd PO day	2 (13)	2 (13)
Total	3 (20)	2 (13)
Patient satisfaction (poor-satisfied-very satisfied)(*n*; %):	0 (0)–6 (27)–9 (73)	0 (0)–9 (60)–6 (40)*

* $P < 0.05$ compared with the IV group
Values are numbers (%) or medians (ranges)
RR, respiratory rate; DRS, delirium rating scale; POD, postoperative delirium; 1st, 2nd, and 3rd PO day, the first, second, and third postoperative day

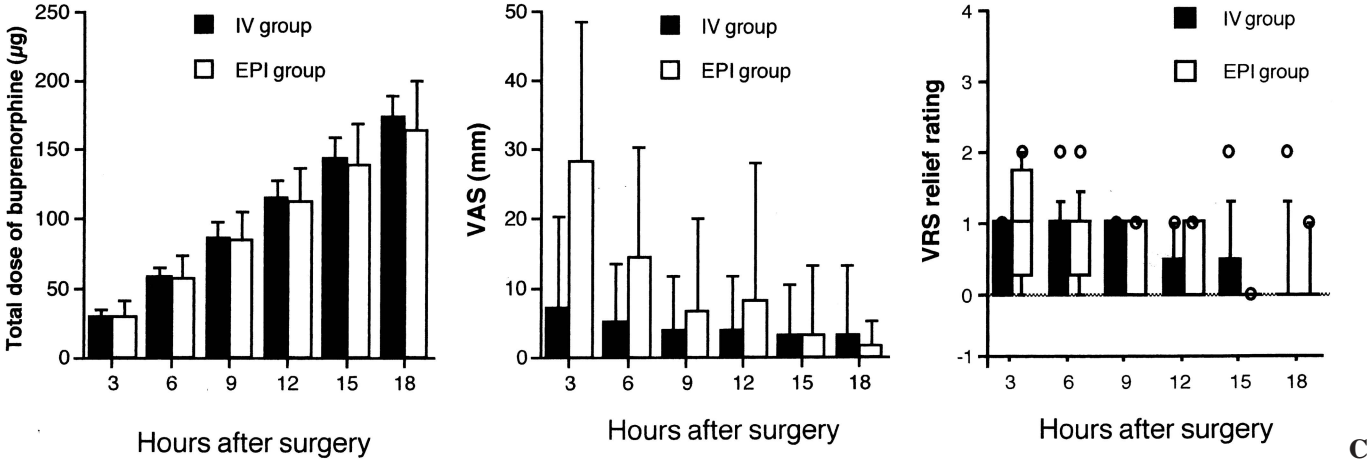

Fig. 1. Cumulative doses of buprenorphine. **B**, **C** Total pain after laparoscopic cholecystectomy, evaluated at rest using a 100-mm visual analog scale (*VAS*; **B**) and verbal rating scale (*VRS*) relief rating (**C**) in the intravenous-based (*IV*) and the epidural-based (*EPI*) groups. Values for doses of buprenorphine and VAS are presented as means ± SD. *Box plots* are shown of diferent levels of pain relief by the VRS relief rating (*0*, none; *1*, a little; *2*, some; *3*, a lot; and *4*, complete). The *heavy lines* indicate *medians*, the *box boundaries*, 25th–75th percentiles, and the *whiskers*, 10th–90th percentiles. *Outliers* beyond 10%–90% are shown as *individual data points*

(Table 3). As for patient satisfaction, though none of the patients in either group reported a score of "poor", the use of an i.v. route for pain relief was associated with significantly higher patient satisfaction scores compared with epidural analgesia ($P = 0.024$; Table 3).

Discussion

This study demonstrated that in laparoscopic cholecystectomy for elderly patients, mNLA with pentazocine and postoperative i.v. analgesia with buprenorphine re-

sulted in significantly higher patient satisfaction and a lower incidence of perioperative hypotension than did sevoflurane anesthesia combined with epidural analgesia and postoperative epidural analgesia. The incidence of postoperative complications and quality of pain relief were similar for the two anesthetic and analgesic techniques.

It has been reported that epidural analgesia was superior to i.v. analgesia with respect to pain relief, patient satisfaction [6], and incidence of pulmonary complications [7], and that epidural analgesia was similar to i.v. analgesia in terms of mortality, incidence of major morbidity, hospital stay, and total costs [7,8]. However, these studies were all performed for patients scheduled for major abdominal surgeries, and there have been few studies in less invasive procedures, such as a laparoscopic approach. This study was therefore designed to compare the effects of epidural and i.v. analgesic techniques on pain relief, postoperative complications, and patient satisfaction in elderly patients undergoing laparoscopic cholecystectomy.

Postoperative buprenorphine and flurbiprofen requirement and postoperative VAS and VRS relief rating scores did not significantly differ between our two groups. Laparoscopic procedures using CO_2 pneumoperitoneum have been reported to be associated with a high incidence (35% to 60%) of shoulder pain [1,9], which remains at a relatively high intensity [10] after laparoscopy, because of residual carbon dioxide inside the abdominal cavity. In the present study, because few of the patients in either group complained of shoulder pain, epidural and i.v. analgesia may have had comparable analgesic efficacy for postoperative pain management. However, in the EPI group, pain management during the early postoperative period appeared to be poor. The epidural block in the limited range used may have been insufficient to produce adequate analgesia, because analgesia after laparoscopy requires a relatively broad sensory blockade. On the other hand, patients in the IV group seemed to have relatively adequate postoperative analgesia. Pentazocine and buprenorphine, which were administered intra-, and postoperatively via the i.v. route, are opioid analgesics with an agonist-antagonist profile, a k-agonist and a partial μ-agonist, respectively. The results of a previous study [11] suggesting synergism between the analgesic actions of morphine (μ-agonist) and pentazocine (k-agonist) may also explain the synergistic effects of pentazocine and buprenorphine in this study. However, the total number of patients was too small to compare the efficacy of the epidural and i.v. analgesic approaches. A large-scale study is needed to confirm these analgesic effects.

As for adverse events, the incidences of postoperative delirium and pulmonary complications did not differ significantly between the two groups. This may have been to a small effect on mental and respiratory functions, because of the use of smaller cumulative doses of buprenorphine in the two groups, compared with the doses used in previous trials [12,13]. On the other hand, the incidence of intra- and postoperative hypotensive and bradycardiac episodes was significantly higher in the EPI group than in the IV group. Hemodynamic instability during general anesthesia has been reported to greatly increase the risk of myocardial infarction or stroke, especially in patients with a labile cardiovascular system [14]. Special attention should therefore be paid to perioperative hypotension in elderly patients, who may have a latent attenuated physiological reserve.

In the present study, the level of patient satisfaction was significantly higher in the IV group than in the EPI group. It has been suggested that patient satisfaction is dependent on the quality of postoperative pain relief and the incidence of postoperative side effects [15,16]. In this study, the quality of postoperative pain relief did not differ significantly between the two groups, but the i.v. analgesia tended to be more effective than epidural analgesia, especially in the early postoperative period. In addition, two patients in the EPI group experienced back pain postoperatively (Table 3), and some patients in the EPI group, including these two patients, complained of discomfort during insertion of the epidural catheter when they were asked to rate the anesthetic experience after surgery. The major contributor to the suppression of patient satisfaction, therefore, may have been discomfort or anxiety during the epidural procedures and, probably, the intensity of postoperative pain. For the future, an adequate depth of sedation for elderly patients, achieved by premedication, may have to be considered for the introduction of epidural procedures.

In conclusion, modified neurolept anesthesia with pentazocine and postoperative i.v. analgesia with buprenorphine is superior to sevoflurane anesthesia and postoperative epidural analgesia with buprenorphine, in terms of hemodynamic stability and patient satisfaction, in laparoscopic cholecystectomy for elderly patients.

References

1. Edwards ND, Barclay K, Catling SJ, Martin DG, Morgan RH (1991) Day case laparoscopy: a survey of postoperative pain and an assessment of the value of diclofenac. Anaesthesia 46:1077–1080
2. Jitapunkul S, Pillay I, Ebrahim S (1991) The abbreviated mental test: its use and validity. Age Ageing 20:332–336
3. Jensen MP, Chen C, Brugger AM (2002) Postsurgical pain outcome assessment. Pain 99:101–109
4. Trzepacz PT, Baker RW, Greenhouse J (1988) A symptom rating scale for delirium. Psychiatry Res 23:89–97

5. Nishikawa K, Nakayama M, Omote K, Namiki A (2004) Recovery characteristics and post-operative delirium after long-duration laparoscope-assisted surgery in elderly patients: propofol-based vs sevoflurane-based anesthesia. Acta Anaesthesiol Scand 48:162–168
6. Mann C, Pouzeratte Y, Boccara G, Peccoux C, Vergne C, Brunat G, Domergue J, Millat B, Colson P (2000) Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. Anesthesiology 92:433–441
7. Peyton PJ, Myles PS, Silbert BS, Rigg JA, Jamrozik K, Parsons R (2003) Perioperative epidural analgesia and outcome after major abdominal surgery in high-risk patients. Anesth Analg 96:548–554
8. Norris EJ, Beattie C, Perler BA, Martinez EA, Meinert CL, Anderson GF, Grass JA, Sakima NT, Gorman R, Achuff SC, Martin BK, Minken SL, Williams GM, Traystman RJ (2001) Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. Anesthesiology 95:1054–1067
9. Collins KM, Docherty PW, Plantevin OM (1984) Postoperative morbidity following gynaecological outpatient laparoscopy. A reappraisal of the service. Anaesthesia 39:819–822
10. Narchi P, Benhamou D, Fernandez H (1991) Intraperitoneal local anaesthetic for shoulder pain after day-case laparoscopy. Lancet 338:1569–1570
11. Levine JD, Gordon NC (1988) Synergism between analgesic actions of morphine and pentazocine. Pain 33:369–372
12. Lehmann KA, Grond S, Freier J, Zech D (1991) Postoperative pain management and respiratory depression after thoracotomy: a comparison of intramuscular piritramide and intravenous patient-controlled analgesia using fentanyl or buprenorphine. J Clin Anesth 3:194–201
13. Lehmann KA, Reichling U, Wirtz R (1988) Influence of naloxone on the postoperative analgesic and respiratory effects of buprenorphine. Eur J Clin Pharmacol 34:343–352
14. Goldman L, Caldera DL (1979) Risks of general anesthesia and elective operation in the hypertensive patients. Anesthesiology 50:285–292
15. Li S, Coloma M, White PF, Watcha MF, Chiu JW, Li H, Huber, Jr. PJ (2000) Comparison of the costs and recovery profiles of three anesthetic techniques for ambulatory anorectal surgery. Anesthesiology 93:1225–1230
16. Song D, Greilich NB, White PF, Watcha MF, Tongier WK (2000) Recovery profiles and costs of anesthesia for outpatient unilateral inguinal herniorrhaphy. Anesth Analg 91:876–881