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Efficacy and Safety of an Acute Pain Service among 10,760 Postoperative Patients

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ABSTRACT

Introduction. Post-operative pain control improves surgical outcome and many hospitals created multidisciplinary teams, called "Acute Pain Services" (APS). We collected APS data on 10,760 adult patients over a five year period, including complications, side effects and patient satisfaction.

Methods. Data on patients managed by APS in a high surgical-volume university hospital over a 5-year period were collected and analyzed. Data included demographic characteristics, primary analgesic modality, adjuvant analgesic treatment, type of surgical procedure, Visual Analogue Scale, and analgesia-related side-effects and complications.

Results. Patient controlled analgesia with morphine was used in 4,992 surgical patients while epidural analgesia was used in 3,687 surgical patients and 1,670 pregnant women for delivery analgesia. A total of 411 patients received other forms of analgesia. No epidural haematoma was observed. A single case of respiratory depression occurred in an elderly patient using the patient controlled analgesia system. Acetaminophen was the most frequently adjuvant drug prescribed. Postoperative nausea and vomiting was the most frequent analgesia-related side effect. Visual Analogue Scale at rest and on movement was low on day one (0.84±1.15 and 2.05±1.67) and decreased thereafter with epidural analgesia associated with better pain control following hip and liver surgery, and with less postoperative nausea and vomiting (5.0%) when compared to morphine patient controlled analgesia (7.2%).

Conclusions. An APS, with daily postoperative visits, permits adequate post-operative pain control without serious adverse events. Epidural analgesia was associated with less postoperative nausea and vomiting and had at least similar pain control than morphine patient controlled analgesia.

Key words: acute pain service, epidural analgesia, patient controlled analgesia, anesthesia, surgery

INTRODUCTION

The importance of adequate postoperative pain control is widely accepted and its beneficial effects supported by several randomized studies and meta-analyses. (1-4) Pain has to be considered as other vital parameters (e.g. blood pressure, heart rate, breathing and respiratory rate, and diuresis) and has to be monitored at well-defined time intervals and quickly treated if necessary. The need to create a "hospital without pain" is connected to multiple reasons: first of all, pain is probably one of the most disturbing experiences and its treatment is a moral and ethical imperative; furthermore, a painless patient is able to breathe easier, cough efficiently and move sooner; as a direct consequence he/she is less subject to cardiovascular complications, pulmonary infections and thromboembolic events, and definitively presents a better postoperative outcome. (5-8)

Patient-controlled analgesia (PCA) and continuous epidural analgesia are associated with a reduction in postoperative morbidity in defined categories of patients and surgeries. (8) However, these specialized techniques can be associated with serious neurologic, cardiovascular and respiratory complications if used in general wards without particular precautions. (5, 9)

Acute Pain Services (APS) have been instituted in many hospitals to achieve effectiveness and safety of postoperative pain management. A winning strategy is to create a multidisciplinary team involving surgeons, nurses and anesthetists, where the latter assume a leading role thanks to their specific skills. (7, 8, 10) The APS team usually defines protocols to prevent pain in different types of surgery, taking into account the characteristics of specific categories of patients (e.g. the elderly). Moreover the APS should establish organizing models with regular assessment of pain intensity, therapy efficacy, and complications defining how to prevent and treat them as soon as possible. In order to ensure appropriate management of acute postoperative pain, the APS has an important role in train-

ing patients and the medical and nursing staff involved in perioperative care, and in performing audits and clinical research on the efficacy of existing and new methods of treatment. (8, 10)

The aim of our study was to describe the 5-year activities of the APS of a large surgical center focusing on major and minor complications of epidural analgesia and intravenous opiates together with a comparison of postoperative pain management between these two strategies.

MATERIALS AND METHODS

With approval of the local Ethical Committee (San Raffaele Ethical Committee, protocol OSR 33, June 23rd 2014) and patients' written informed consent for the scientific management of their data we collected the 5 year activity data of the APS of San Raffaele Scientific Institute based in Milan, Italy. This is a 1,357 bed referral center (1), with approximately 30,000 major procedures performed each year and with 90 anesthesiologists managing anaesthesia, intensive care, emergency department and APS. An anesthesia fellow is available 24 hour a day and seven days per week, dedicated to the management of postoperative pain and to the prevention and treatment of possible complications. A senior anesthetist can be contacted at every moment for any problem.

The choice of a specific pain management approach starts with a thorough preoperative evaluation that takes into account the characteristics of the single patient (e.g. previous surgery, pre-existing analgesic therapy, psychological attitude, drug allergies/intolerances, etc.) and the specific type of surgery. The anesthetist plays a leading role in a complex team, including surgeons and nurses, and coordinates all the personnel to promote a continuous path of education and improvement of the adopted protocols.

Epidural catheters are placed immediately before surgery while the patient is still awake.

All postoperative patients receive either acetaminophen 1 g or a non-steroidal anti-inflammatory drug (NSAID) at fixed intervals with the possibility of receiving other agents as rescue therapy (table 1). We collected data on patients undergoing major abdominal surgery (e.g. hepatic and gastric surgery, colo-rectal resection, laparoscopic and laparotomic esophagectomy), gynecological (e.g. myomectomy, hysterectomy), orthopedic (e.g. hip and knee replacement), neurosurgical and ear-throat-nose procedures. Due to different databases and organizational issues, we did not collect any data on cardiac surgery patients, only PCA data in vascular, thoracic and urologic operations, and only major complications and post-dural puncture headaches (PDPH) after delivery with epidural analgesia. Therefore, patients receiving epidural analgesia for delivery were excluded from the analysis.

Patients managed by APS included patients treated with epidural analgesia (with the exceptions described above), through the intravenous administration of morphine by on demand PCA systems or with perineural catheters (in selected orthopedic patients) with specific protocols detailed in table 1. Furthermore, APS also managed patients with inadequate control of pain even seven days after surgery, in which it was necessary to define a therapy regime to be continued at home.

All patients are visited at least once a day, for up to seven days after surgery or referral to APS (more than once in the case of recent APS modifications to pain therapy or if requested by ward staff or physicians) if still in the hospital.

The APS use the Visual Analogue Scale (VAS) at rest (VASr) and during movement (VASm) to standardize pain assessment at each visit and assess the presence of side effects and complications.

The APS is also responsible for the removal of epidural catheters and neurological surveillance in the first 6-8 hours after removal. Removal of the epidural catheter follows the same guidelines as for epidural catheter insertion: platelet count > 100×109/L; International Normalized Ratio < 1.3; no dual antiplatelet therapy; no antiplatelet drugs such as ticlopidine and clopidogrel; no anticoagulants; low molecular weight heparin suspended for at least 10-12 hours. (11)

All the data collected are stored in an electronic database in order to allow quick and efficient communication between different anesthetists involved in pain care on different days and to ensure continuity of care.

We recorded age, sex, type of surgery, ASA score, prescribed therapy, analgesic technique used, daily VASr and VASm, side effects and adverse events: respiratory depression, epidural hematoma, postoperative nausea and vomiting (PONV), paresthesia, itching, hypotension and confusion.

We compared effectiveness of pain control in patients of different ages and in patients with an American Society of Anesthesiologists (ASA) physical status class (ASA score) of 1-2 versus > 2.

STATISTICAL ANALYSIS

Data were stored electronically and analyzed with SAS (release 9.2 by SAS Institute Inc. Cary, NC, USA) and STATA (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Categorical variables are reported as frequencies (percent), whereas continuous variables are expressed as mean ± standard deviation or as median (interquartile range). As for categorical variables, Chi-squared test was used to calculate p-values when two groups were compared, whereas one-way ANOVA was used in comparing more than two groups. A p-value <0.05 was considered statistically significant.

RESULTS

Over a five year period the APS followed 10,760 adult patients for a total of 24,240 visits. The 1,670 women receiving epidural analgesia for delivery had no epidural hematoma and 21 PDPH, and were excluded from analysis. The remaining 9,090 patients were 60±15 years old, equally divided between male and female, and 24.1% were ASA physical status class 3 (table 2).

The APS mainly visited patients admitted to the Division of General Surgery (5,703; 62.7%).

The overall number of patients receiving epidural analgesia alone was 3,687 (40.6%), while 4,992 patients (54.9%) received PCA alone. Combined epidural analgesia plus PCA was used in 58 (0.6%) patients.

In addition, APS followed orthopedic

patients with perineural catheters (298 patients, 3.3%) and patients whose postoperative pain treatment was very difficult even if not requiring a PCA or an epidural infusion (55 patients, 0.6%) (figure 1, these last ones are classified in the figure as "other", including patients undergoing surgery associated with mild or moderate pain, but who presented with difficult pain control according to the standard protocol, requiring specific solutions, e.g. continuous infusion of tramadol or strong oral opiates such as oxycodone). Acetaminophen (4,971 patients, 54.7%), at fixed intervals, was the most frequently prescribed adjuvant drug.

Pain control was excellent on postoperative day 1 (VASr and VASm were 0.84±1.15 and 2.05±1.67 respectively) and decreased day after day. VASr on the 7th post-operative day was 0.581.01 ($p<0.05$, $t=3.595$, $df=8482$) and VASm was 1.561.65 ($p<0.05$, $t=4.6710$, $df= 8471$) (Supplementary table 1 in Supplementary appendix). The number of patients with VAS 0 was significantly ($p<0.05$) higher in the group of patients receiving epidural analgesia for orthopedic surgery on day 3 (79.8% vs 62.1% for VASr) and for hepatic surgery on day 1, day 2 and day 5 when compared to PCA.

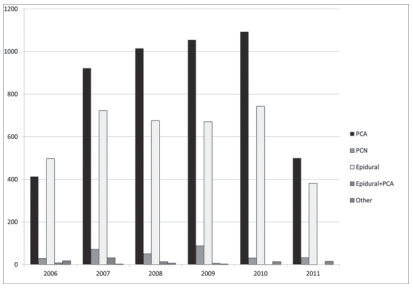

Figure 1. Main analgesic techniques used year by year.
PCA, Patient Controlled Analgesia; PNC, Perineural Catheter.

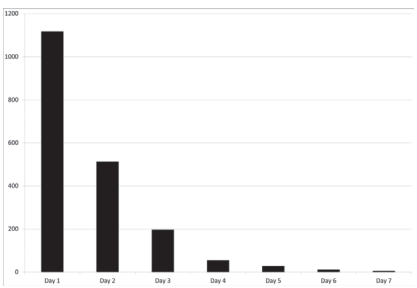

Figure 2. Number of patients experiencing analgesia-related side effects in different postoperative days.

No epidural hematoma, epidural abscess or meningitis occurred in the patients receiving an epidural catheter and no permanent alteration in sensitive or motor functions was observed. One episode of respiratory depression occurred among patients managed with morphine PCA. This was due to a pump programming error in a 92 year old ASA 4 patient after an explorative laparotomy for intestinal occlusion. It was promptly treated with naloxone infusion and the patient did not require intensive care unit admission. No cardiac arrest was associated with analgesic protocols in the study period.

The number of patients experiencing analgesia-related side effects was 12.3% on the first postoperative day and rapidly decreased thereafter (figure 2).

The most frequently treated side effects on the first postoperative day were PONV (6.0%), paresthesia (3.7%), itching (1.4%), hypotension (0.5%) and confusion (0.2%). Epidural analgesia was associated with a significant ($2=17.23$, $p<0.05$) reduced incidence of PONV in the first postoperative day as compared with morphine PCA administration (5.0% vs 7.2%).

Table 1. Protocols adopted according to the intensity of pain.

Grade of pain	**Pain management strategy adopted**
Mild pain (e.g. hysteroscopy)	Acetaminophen 1 g x 3/4 iv or NSAID NSAID or acetaminophen 1 g as rescue.
Moderate pain (e.g. Cholecystectomy)	Acetaminophen 1 g x 3/4 iv or NSAID. Weak opiates (e.g. tramadol). NSAID or acetaminophen 1 g as rescue.
Severe pain (e.g. gastrectomy, hepatic resection, etc.) Epidural catheter analgesia	Acetaminophen 1 g x 3/4 iv or NSAID. Epidural catheter or PCA of morphine. NSAID or acetaminophen 1g or weak opiates (e.g. tramadol) as rescue. Position according to the kind of surgery. Intraoperative bolus of sufentanyl 10 mcg at the beginning of surgery in all patients and of local anesthetic at anesthesiologist discretion. Intra- and post-operative infusion of ropivacaine 0.2% 99 ml + sufentanyl 50 mcg/1 ml at 4-6 ml/h
PCA with morphine	Injection dose 1 mg iv Lock out time of 10 minutes Maximum mg for hours: 4 No continuous infusion
Perineural catheter	Infusion of ropivacaine 0.2% 8-10 ml/h Intraoperative bolus of local at anesthesiologist discretion

Severe pain was treated with postoperative epidural analgesia, PCA with morphine or perineural analgesia.
I.v, intravenous; NSAID, non-steroidal anti-inflammatory drug; PCA, patient-controlled analgesia.

Table 2. Characteristics of 9,090 patients visited by the APS during a 5 year period.

Variable	Data
Male, n (%)	4525 (49.8%)
Age, years	60 ± 15
Surgery	
general	5703 (62.7%)
orthopedic	1337 (14.7%)
gynecological	1097 (12.1%)
urology	272 (3.0%)
vascular	196 (2.2%)
neurosurgery	186 (2.0%)
thoracic	133 (1.5%)
ear-throat-nose	84 (0.9%)
plastic	21 (0.2%)
others	61 (0.7%)
ASA status	
ASA 1	1322 (14.5%)
ASA 2	5581 (61.4%)
ASA 3	2107 (23.2%)
ASA 4	77 (0.8%)
ASA 5	3 (0.0%)
Adjuvant drugs	
Acetaminophen 1g	4971 (54.7%)
NSAIDs	4027 (44.3%)
Others	22 (0.24%)
None	70 (0.77%)
Protocol	
Epidural	3687 (40.6%)
PCA	4992 (54.9%)
PNC	298 (3.3%)
Peridural + PCA	58 (0.6%)
Other	55 (0.6%)

Data are expressed as number (%) or mean (standard deviations).
APS, acute pain service; ASA, American Society of Anesthesiologists; NSAIDs, non-steroidal anti-inflammatory drugs; PCA, patient-controlled analgesia; PNC, perineural catheter.

Table 3. The largest studies published on acute pain services.

Authors	N	Journal	Year	Study
Present study	10,760		2016	Epidural analgesia was associated with a reduction in postoperative nausea and vomiting when compared to morphine PCA. A single episode of respiratory depression was reported. No cases of spinal hematoma or bacterial meningitis were reported.
Paul JE et al. (9)	35,384	Anesthesiology	2014	Evaluation of adverse events in three hospitals before and after a formal root cause analysis process. 165 episodes of respiratory depression, 4 epidural abscesses, 2 spinal hematoma and 2 deaths were reported.
Pöpping DM et al. (10)	18,925	British Journal of Anaesthesiology	2008	Epidural analgesia and peripheral nerve block provided superior pain relief than endovenous PCA. 3 cases of epidural hematoma, 2 of epidural abscess, 1 of bacterial meningitis and 1 of respiratory depression were reported.

Schug SA et al. (13)	3,016	Pain	1993	Potentially severe complications without sequelae occurred in 16 patients (0.53%). No trauma to nervous structure, no infections, and no local anesthetic toxicity occurred with continuous regional analgesia (epidural, interpleural and peripheral).
Flisberg P et al. (3)	2,696	Acta Anesthesiologica Scandinavica	2003	Patients with epidural analgesia experienced less pain than those with endovenous PCA. Twenty episodes of respiratory depression and one epidural haematoma were reported.
Syngelin FJ et al. (14)	1,338	Journal of Clinical Anesthesia	1999	Patients undergoing hip surgery. Epidural analgesia, endovenous PCA and "3-in-1" continuous block provided comparable pain relief. No serious adverse events were registered.

PCA, patient-controlled analgesia.

The Visual Analogue Scale at rest and during movement was significantly lower in elderly patients compared with young patients on treatment day 1 and this difference persisted until day 5. In addition, older patients reported significantly lower incidence of PONV and paresthesia (Supplementary tables 2, 3 in Supplementary appendix).

We found that VASm was higher in patients with an ASA score >2 compared with patients with an ASA 1-2 on treatment days 1 to 4, while no difference was reported for VASr. However, patients with an ASA score 1-2 had a higher incidence of PONV, paresthesias and itching (Supplementary tables 4-7 in Supplementary appendix).

When analyzing the subgroups of patients receiving epidural analgesia or PCA alone, data confirmed that VASr and VASm were higher in youngest patients in the first treatment days. Incidence of PONV was significantly lower in older patients, both in the subgroups receiving epidural analgesia and PCA, while a significant difference in incidence of paresthesia was found only in the epidural subgroup (Supplementary tables 8-19 in Supplementary appendix).

DISCUSSION

We present one of the largest case series of APS ever reported, confirming that the use of epidural analgesia and intravenous PCA with morphine in surgical wards is effective and safe with no major complications and a reasonable number of minor side effects. This was the second largest single center experience ever reported in the medical literature describing both epidural and intravenous PCA analgesia technique.

Although the risk of related adverse effects initially limited the use these analgesic techniques outside "safe settings" such as intensive care units, studies and surveys have shown that continuous epidural and patient-controlled intravenous analgesia greatly improve postoperative pain relief with a low rate of complications. (5,9)

We also found a very low incidence of side effects, which were quickly detected and resolved without affecting the postoperative course. Unlike other studies, we did not observe any case of spinal hematoma. A possible explanation is that, in our hospital, epidural catheter placement and removal follows very strict criteria. Our data also showed that epidural analgesia provides slightly superior pain relief with less PONV when compared to intravenous opiates PCA. These results are consistent with the literature, and the lower incidence of PONV in our setting can be explained by the use of small doses of neuraxial opioids. (5,9)

An extensive literature review confirmed that our case series is one of the largest (5, 9, 12-14) ever reported on APS and the second largest single center case series comparing epidural and PCA analgesia. In table 3, we summarized the largest published studies on this topic and report the most commonly reported complications.

The reduced incidence of severe side effects observed in our study is in line with other excellent perioperative results (15) reported by our group in other settings and cannot be easily explained.

To ensure a "pain and risk free" postoperative course, close supervision of patients treated with these specialized pain relief methods by an APS is mandatory. The protocols and the organization we described in the methods allowed us to obtain such excellent results.

As previously reported in the literature, we found in our study that older patients had better pain control and a reduced incidence of side effects when compared to younger patients. (16) This might be due to the fact that elderly people frequently suffer from chronic pain, and therefore consider pain as part of the ageing process. (17) Presence of cognitive impairment has also been associated with reduced analgesic prescription in the elderly. (18)

Another interesting finding of our study is that both the incidence of pain and analgesia-related side effects is different in patients with a different ASA physical status class. Patients with higher ASA class had less satisfactory pain control compared to those of ASA class 1-2. This might be explained by the fact that patients with higher ASA class > 2 have chronic systemic diseases associated with pain, or that they lead physicians to reduce analgesics doses to avoid possible complications (e.g. NSAIDs in patients with chronic kidney disease, or opioids in patients with chronic pulmonary diseases). This might also explain the lower incidence of side effects reported by these patients.

STUDY LIMITATIONS

Our study has some limitations. First of all, it is an observational study. Furthermore,

we excluded from the data collection some settings (e.g. vascular surgery) that take great advantage of epidural analgesia but are prone to develop epidural haematoma because of preoperative antiplatelet therapy and intraoperative systemic heparinization. Another limitation is the lack of information regarding the postoperative course, in particular the length of hospital stay, the recovery of intestinal function and the rate of respiratory complications even if our hospital is known to perform well when comparing these outcomes with other centers worldwide. (15) Attention is now being directed toward the introduction of new approaches to perioperative care aimed at improving outcome and shortening recovery after surgery. Effective treatment of postoperative pain certainly contributes to achieving this goal, and, in addition to providing a direct benefit to the patient, it could also be profitable for the health care system. Cost-effectiveness analysis, in fact, must consider both direct costs associated with analgesic drugs, devices, nursing and physician time, length of stay in the intensive care unit or surgical ward, and postoperative morbidity, and the indirect costs of improved analgesia and patient satisfaction. In our study, these aspects have not been taken into account but are important to ensure better use of hospital resources and improve the quality of care. Furthermore, adjusted p-value for multiple comparison tests was not taken into account.

The strengths of this study are that it has a very low incidence of severe analgesia-related complications and that it includes a very large number of patients.

CONCLUSIONS

Our large study demonstrates that an APS, with daily postoperative visits, is effective in providing adequate post-operative pain control without serious adverse events. Compared with PCA with morphine, epidural analgesia was associated with a lower incidence of postoperative nausea and vomiting with a similar effectiveness in pain control.

REFERENCES

1. Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, Chalmers TC, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. Anesth Analg 1998;86:598-612.
2. Beattie WS, Badner NH, Choi P. Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis. Anesth Analg 2001;93:853-8.
3. Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. Br J Anaesth 2001;87:62-72.
4. Rodgers A, Walker N, Schug S, McKee A, Kehlet H, van Zundert A, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. BMJ 2000;321:1493.
5. Flisberg P, Rudin A, Linnér R, Lundberg CJ. Pain relief and safety after major surgery. A prospective study of epidural and intravenous analgesia in 2696 patients. Acta Anaesthesiol Scand 2003;47:457-65.
6. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. Am J Surg 2002;183:630-41.
7. Miaskowski C, Crews J, Ready LB, Paul SM, Ginsberg B. Anesthesia-based pain services improve the quality of postoperative pain management. Pain 1999;80:23-9.
8. Werner MU, Søholm L, Rotbøll-Nielsen P, Kehlet H. Does an acute pain service improve postoperative outcome? Anesth Analg 2002;95:1361-72.
9. Pöpping DM, Zahn PK, Van Aken HK, Dasch B, Boche R, Pogatzki-Zahn EM. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. Br J Anaesth 2008;101:832-40.
10. Rawal N. Organization, function, and implementation of acute pain service. Anesthesiol Clin North America 2005;23:211-25.
11. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK, Kopp SL, Benzon HT, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). Reg Anesth Pain Med 2010;35:64-101.
12. Paul JE, Buckley N, McLean RF, Antoni K, Musson D, Kampf M, et al. Hamilton acute pain service safety study: using root cause analysis to reduce the incidence of adverse events. Anesthesiology 2014;120:97-109.
13. Schug SA, Torrie JJ. Safety assessment of postoperative pain management by an acute pain service. Pain 1993;55:387-91.
14. Singelyn FJ, Gouverneur JM. Postoperative analgesia after total hip arthroplasty: i.v. PCA with morphine, patient-controlled epidural analgesia, or continuous "3-in-1" block?: a prospective evaluation by our acute pain service in more than 1,300 patients. J Clin Anesth 1999;11:550-4.
15. Landoni G, Pasin L, Monti G, Cabrini L, Beretta L, Zangrillo A. Towards zero perioperative mortality. Heart Lung Vessel 2013;5:133-6.
16. Koh JC, Lee J, Kim SY, Choi S, Han DW. Postoperative Pain and Intravenous Patient-Controlled Analgesia-Related Adverse Effects in Young and Elderly Patients: A Retrospective Analysis of 10,575 Patients. Medicine (Baltimore) 2015;94:2008.
17. Ferrell BA. Pain evaluation and management in the nursing home. Ann Intern Med 1995;123:681-7.
18. Closs SJ, Barr B, Briggs M. Cognitive status and analgesic provision in nursing home residents.
19. Br J Gen Pract 2004;54:919-21.

SUPPLEMENTARY APPENDIX

Table 1. Visual Analogue Scale (VAS) at rest (VASr) and during movement (VASm).
SD, standard deviation.

	VASr	VASm
> Day 1		
Mean ± SD	0.84 ± 1.147	2.05 ± 1.674
> Day 2		
Mean ± SD	0.65 ± 0.983	1.93 ± 1.514
> Day 3		
Mean ± SD	0.48 ± 0.865	1.67 ± 1.526
> Day 4		
Mean ± SD	0.47 ± 0.915	1.62 ± 1.564
> Day 5		
Mean ± SD	0.55 ± 1.019	1.67 ± 1.653
> Day 6		
Mean ± SD	0.65 ± 1.220	1.73 ± 1.725
> Day 7		
Mean ± SD	0.58 ± 1.014	1.56 ± 1.654

Table 2. Visual Analogue Scale at rest (VASr) per age.
SD, standard deviation.

VASr	**<45**	**45-64**	**65-79**	**>79**	**p-value**
> Day 1					
Mean ± SD	0.99 ± 1.324	0.85 ± 1.125	0.78 ± 1.079	0.78 ± 1.119	<0.001*
> Day 2					
Mean ± SD	0.78 ± 1.146	0.67 ± 0.990	0.59 ± 0.906	0.56 ± 0.858	<0.001*
> Day 3					
Mean ± SD	0.57 ± 0.981	0.48 ± 0.869	0.47 ± 0.831	0.34 ± 0.671	<0.001*
> Day 4					
Mean ± SD	0.55 ± 0.965	0.51 ± 0.965	0.42 ± 0.842	0.39 ± 0.938	0.037 *
> Day 5					
Mean ± SD	0.72 ± 1.111	0.57 ± 1.065	0.47 ± 0.935	0.55 ± 1.062	0.042*
> Day 6					
Mean ± SD	0.79 ± 1.123	0.66 ± 1.119	0.62 ± 1.384	0.37 ± 1.033	0.39
> Day 7					
Mean ± SD	0.75 ± 1.055	0.66 ± 1.005	0.46 ± 1.041	–	0.078

Table 3. Visual Analogue Scale during movement (VASm) per age.
SD, standard deviation.

VASm	**<45**	**45-64**	**65-79**	**>79**	**p-value**
> Day 1					
Mean ± SD	2.22 ± 1.793	2.07 ± 1.633	1.94 ± 1.560	1.98 ± 1.602	<0.001*
> Day 2					
Mean ± SD	2.04 ± 1.620	1.96 ± 1.532	1.86 ± 1.457	1.84 ± 1.454	0.0045*
> Day 3					
Mean ± SD	1.90 ± 1.646	1.68 ± 1.530	1.60 ± 1.496	1.45 ± 1.369	<0.001*

> Day 4					
Mean ± SD	1.89 ± 1.513	1.69 ± 1.594	1.54 ± 1.546	1.37 ± 1.541	<0.001*
> Day 5					
Mean ± SD	1.97 ± 1.725	1.65 ± 1.662	1.56 ± 1.610	1.65 ± 1.692	0.044*
> Day 6					
Mean ± SD	2.04 ± 1.716	1.73 ± 1.638	1.64 ± 1.847	1.47 ± 1.525	0.22
> Day 7					
Mean ± SD	1.78 ± 1.706	1.61 ± 1.609	1.30 ± 1.581	1.73 ± 1.902	0.36

Table 4. Visual Analogue Scale at rest (VASr) per ASA score.
ASA, American Society of Anesthesiologists score; SD, standard deviation.

VASr	ASA 1-2	ASA >2	p-value
> Day 1			
Mean ± SD	0.83 ± 1.129	0.85 ± 1.170	0.44
> Day 2			
Mean ± SD	0.64 ± 0.971	0.69 ± 1.016	0.059
> Day 3			
Mean ± SD	0.46 ± 0.845	0.52 ± 0.908	0.056
> Day 4			
Mean ± SD	0.45 ± 0.907	0.52 ± 0.930	0.076
> Day 5			
Mean ± SD	0.53 ± 1.020	0.56 ± 0.991	0.66
> Day 6			
Mean ± SD	0.65 ± 1.264	0.64 ± 1.100	0.99
> Day 7			
Mean ± SD	0.52 ± 0.897	0.65 ± 1.202	0.34

Table 5. Visual Analogue Scale during movement (VASm) per ASA score.
ASA, American Society of Anesthesiologists score; SD, standard deviation.

VASm	ASA 1-2	ASA >2	p-value
> Day 1			
Mean ± SD	2.01 ± 1.638	2.14 ± 1.654	0.003*
> Day 2			
Mean ± SD	1.88 ± 1.505	2.08 ± 1.535	<0.001*
> Day 3			
Mean ± SD	1.60 ± 1.511	1.86 ± 1.549	<0.001*
> Day 4			
Mean ± SD	1.59 ± 1.571	1.74 ± 1.531	0.032*
> Day 5			
Mean ± SD	1.65 ± 1.698	1.71 ± 1.518	0.57
> Day 6			
Mean ± SD	1.74 ± 1.807	1.70 ± 1.729	0.80
> Day 7			
Mean ± SD	1.48 ± 1.613	1.61 ± 1.662	0.58

Table 6. Distribution of treated side effects per age.
PONV, post-operative nausea and vomiting.

	Age				
Treated side effects	**<45**	**45-64**	**65-79**	**>79**	**p-value**
PONV	138 (9.2)	208 (6.1)	176 (5.0)	24 (3.7)	<0.001*
paresthesia	87 (5.8)	141 (4.1)	95 (2.7)	15 (2.3)	<0.001*
itching	21 (1.4)	46 (1.4)	51 (1.4)	5 (0.8)	0.61
confusion	2 (0.1)	8 (0.2)	7 (0.2)	3 (0.5)	0.49
hypotension	2 (0.1)	17 (0.5)	18 (0.5)	6 (0.9)	0.08

Table 7. Distribution of Treated side effects per ASA score.
ASA, American Society of Anesthesiologists; PONV, post-operative nausea and vomiting.

	ASA		
Treated side effects	**1-2**	**>2**	**p-value**
PONV	464 (6.7)	82 (3.8)	<0.001*
paresthesia	313 (4.5)	25 (1.1)	<0.001*
itching	106 (1.5)	17 (0.8)	0.007*
confusion	13 (0.2)	7 (0.3)	0.25
hypotension	35 (0.5)	8 (0.4)	0.40

Table 8. Visual Analogic Scale at rest (VASr) per age – Subanalysis for Epidural group.
SD, standard deviation.

VASr	**<45**	**45-64**	**65-79**	**>79**	**p-value**
> Day 1					
Mean ± SD	0.98 ± 1.405	0.77 ± 1.050	0.74 ± 1.109	0.74 ± 1.044	0.0017*
> Day 2					
Mean ± SD	0.78 ± 1.189	0.62 ± 0.953	0.56 ± 0.903	0.53 ± 0.842	<0.001*
> Day 3					
Mean ± SD	0.55 ± 0.988	0.50 ± 0.902	0.46 ± 0.839	0.32 ± 0.638	0.026*
> Day 4					
Mean ± SD	0.49 ± 0.896	0.52 ± 0.980	0.43 ± 0.859	0.33 ± 0.800	0.12
> Day 5					
Mean ± SD	0.61 ± 1.032	0.53 ± 1.097	0.49 ± 1.001	0.53 ± 1.026	0.86
> Day 6					
Mean ± SD	0.65 ± 1.075	0.64 ± 1.175	0.63 ± 1.495	0.12 ± 0.440	0.30
> Day 7					
Mean ± SD	0.56 ± 0.922	0.60 ± 0.935	0.38 ± 0.991	–	0.25

Table 9. Visual Analogue Scale during movement (VASm) per age – Subanalysis for Epidural group. SD, standard deviation.

VASm	**<45**	**45-64**	**65-79**	**>79**	**p-value**
> Day 1					
Mean ± SD	2.15 ± 1.895	1.88 ± 1.567	1.77 ± 1.593	1.90 ± 1.564	<0.001*
> Day 2					
Mean ± SD	1.93 ± 1.661	1.80 ± 1.488	1.73 ± 1.446	1.77 ± 1.484	0.18
> Day 3					
Mean ± SD	1.68 ± 1.653	1.56 ± 1.527	1.50 ± 1.451	1.43 ± 1.332	0.22

> Day 4					
Mean ± SD	1.84 ± 1.544	1.54 ± 1.622	1.44 ± 1.563	1.40 ± 1.514	0.041*
> Day 5					
Mean ± SD	1.81 ± 1.620	1.55 ± 1.641	1.54 ± 1.701	1.68 ± 1.666	0.60
> Day 6					
Mean ± SD	2.03 ± 1.672	1.67 ± 1.667	1.69 ± 1.965	1.28 ± 1.308	0.44
> Day 7					
Mean ± SD	1.56 ± 1.723	1.34 ± 1.593	1.30 ± 1.520	2.00 ± 2.000	0.63

Table 10. Visual Analogue Scale at rest (VASr) per ASA score – Subanalysis for Epidural group.
ASA, American Society of Anesthesiologists score; SD, standard deviation.

VASr	ASA 1-2	ASA >2	p-value
> Day 1			
Mean ± SD	0.78 ± 1.107	0.78 ± 1.172	0.99
> Day 2			
Mean ± SD	0.60 ± 0.938	0.62 ± 1.047	0.65
> Day 3			
Mean ± SD	0.47 ± 0.861	0.51 ± 0.888	0.43
> Day 4			
Mean ± SD	0.45 ± 0.892	0.52 ± 0.996	0.23
> Day 5			
Mean ± SD	0.52 ± 1.042	0.53 ± 1.031	0.85
> Day 6			
Mean ± SD	0.62 ± 1.341	0.51 ± 1.073	0.50
> Day 7			
Mean ± SD	0.41 ± 0.793	0.63 ± 1.234	0.21

Table 11. Visual Analogic Scale during movement (VASm) per ASA score – Subanalysis for Epidural group.
ASA, American Society of Anesthesiologists score; SD, standard deviation.

VASm	ASA 1-2	ASA >2	p-value
> Day 1			
Mean ± SD	1.86 ± 1.617	1.91 ± 1.626	0.56
> Day 2			
Mean ± SD	1.76 ± 1.464	1.91 ± 1.630	0.054
> Day 3			
Mean ± SD	1.50 ± 1.486	1.72 ± 1.502	0.006*
> Day 4			
Mean ± SD	1.48 ± 1.570	1.70 ± 1.641	0.039*
> Day 5			
Mean ± SD	1.58 ± 1.691	1.61 ± 1.537	0.81
> Day 6			
Mean ± SD	1.71 ± 1.850	1.62 ± 1.538	0.70
> Day 7			
Mean ± SD	1.33 ± 1.563	1.63 ± 1.705	0.32

Table 12. Distribution of Treated side effects per age – Subanalysis for Epidural group.
PONV, post-operative nausea and vomiting.

Age					
Treated side effects	**<45**	**45-64**	**65-79**	**>79**	**p-value**
PONV	35 (7.8)	74 (5.3)	65 (4.2)	10 (3.3)	0.01*
paresthesia	80 (18)	130 (9.3)	87 (5.7)	14 (4.6)	<0.001*
itching	12 (2.7)	37 (2.7)	44 (2.9)	3 (1.0)	0.32
confusion	0 (0.0)	1 (0.1)	2 (0.1)	1 (0.3)	0.55
hypotension	1 (0.2)	15 (1.1)	17 (1.1)	5 (1.7)	0.25

Table 13. Distribution of Treated side effects per ASA score – Subanalysis for Epidural group.
ASA, American Society of Anesthesiologists score; PONV, post-operative nausea and vomiting.

ASA			
Treated side effects	1-2	>2	p-value
PONV	170 (5.5)	14 (2.3)	0.001*
paresthesia	286 (9.3)	25 (4.2)	<0.001*
itching	86 (2.8)	10 (1.7)	0.12
confusion	3 (0.1)	1 (0.2)	0.51
hypotension	31 (1.0)	7 (1.2)	0.72

Table 14. Visual Analogue Scale at rest (VASr) per age – Subanalysis for PCA group.
PCA, patient control analgesia; SD, standard deviation.

VASr	**<45**	**45-64**	**65-79**	**>79**	**p-value**
> Day 1					
Mean ± SD	1.00 ± 1.282	0.91 ± 1.165	0.79 ± 1.032	0.81 ± 1.193	<0.001*
> Day 2					
Mean ± SD	0.79 ± 1.115	0.72 ± 1.011	0.62 ± 0.913	0.58 ± 0.880	0.0017*
> Day 3					
Mean ± SD	0.58 ± 0.979	0.46 ± 0.815	0.48 ± 0.819	0.36 ± 0.710	0.035*
> Day 4					
Mean ± SD	0.60 ± 1.015	0.48 ± 0.931	0.42 ± 0.820	0.49 ± 1.197	0.20
> Day 5					
Mean ± SD	0.86 ± 1.211	0.60 ± 0.992	0.39 ± 0.756	0.69 ± 1.250	0.0037*
> Day 6					
Mean ± SD	0.89 ± 1.153	0.71 ± 1.054	0.53 ± 0.981	2.00 ± 2.160	0.049*
> Day 7					
Mean ± SD	0.85 ± 1.099	0.73 ± 1.071	0.63 ± 1.212	–	0.83

Table 15. Visual Analogue Scale during movement (VASm) per age – Subanalysis for PCA group.
PCA, patient control analgesia; SD, standard deviation.

VASm	**<45**	**45-64**	**65-79**	**>79**	**p-value**
> Day 1					
Mean ± SD	2.27 ± 1.734	2.22 ± 1.650	2.07 ± 1.567	2.07 ± 1.690	0.013*
> Day 2					
Mean ± SD	2.14 ± 1.584	2.13 ± 1.550	1.99 ± 1.459	1.91 ± 1.430	0.036*
> Day 3					

Mean ± SD	2.04 ± 1.619	1.82 ± 1.512	1.73 ± 1.522	1.47 ± 1.432	<0.001*
> Day 4					
Mean ± SD	1.93 ± 1.472	1.88 ± 1.525	1.69 ± 1.511	1.33 ± 1.651	0.023*
> Day 5					
Mean ± SD	2.14 ± 1.833	1.82 ± 1.693	1.59 ± 1.402	1.50 ± 1.897	0.072
> Day 6					
Mean ± SD	2.04 ± 1.758	1.79 ± 1.519	1.43 ± 1.443	2.75 ± 2.500	0.17
> Day 7					
Mean ± SD	1.96 ± 1.675	1.97 ± 1.518	1.22 ± 1.865	–	0.26

Table 16. Visual Analogue Scale at rest (VASr) per ASA score – Subanalysis for PCA group. ASA, American Society of Anesthesiologists score; PCA, patient control analgesia; SD, standard deviation.

VASr	**ASA 1-2**	**ASA >2**	**p-value**
> Day 1			
Mean ± SD	0.87 ± 1.127	0.88 ± 1.168	0.78
> Day 2			
Mean ± SD	0.67 ± 1.000	0.72 ± 1.002	0.20
> Day 3			
Mean ± SD	0.46 ± 0.822	0.52 ± 0.912	0.087
> Day 4			
Mean ± SD	0.45 ± 0.939	0.51 ± 0.869	0.29
> Day 5			
Mean ± SD	0.55 ± 0.975	0.59 ± 0.956	0.70
> Day 6			
Mean ± SD	0.70 ± 1.079	0.80 ± 1.132	0.56
> Day 7			
Mean ± SD	0.71 ± 0.997	0.65 ± 1.199	0.79

Table 17. Visual Analogue Scale during movement (VASm) per ASA score – Subanalysis for PCA group.
ASA, American Society of Anesthesiologists score; PCA, patient control analgesia; SD, standard deviation.

VASm	**ASA 1-2**	**ASA >2**	**p-value**
> Day 1			
Mean ± SD	2.13 ± 1.622	2.24 ± 1.657	0.052
> Day 2			
Mean ± SD	2.02 ± 1.534	2.16 ± 1.485	0.013*
> Day 3			
Mean ± SD	1.72 ± 1.523	1.94 ± 1.567	0.002*
> Day 4			
Mean ± SD	1.77 ± 1.561	1.76 ± 1.437	0.91
> Day 5			
Mean ± SD	1.78 ± 1.726	1.82 ± 1.505	0.80
> Day 6			
Mean ± SD	1.75 ± 1.663	1.79 ± 1.520	0.84
> Day 7			
Mean ± SD	1.77 ± 1.628	1.60 ± 1.694	0.66

Table 18. Distribution of Treated side effects per age – Subanalysis for PCA group.
PCA, patient control analgesia; PONV, post-operative nausea and vomiting.

Age					
Treated side effects	**<45**	**45-64**	**65-79**	**>79**	**p-value**
PONV, n (%)	102 (11)	132 (7.1)	110 (5.9)	14 (4.5)	<0.001*
paresthesia, n (%)	2 (0.2)	3 (0.2)	2 (0.1)	0 (0.0)	0.81
itching, n (%)	10 (1.1)	9 (0.5)	6 (0.3)	2 (0.6)	0.089
confusion, n (%)	2 (0.2)	7 (0.4)	5 (0.3)	2 (0.6)	0.64
hypotension, n (%)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.3)	0.45

Table 19. Distribution of Treated side effects per ASA score – Subanalysis for PCA group. ASA, American Society of Anesthesiologists score; PCA, patient control analgesia; PONV, post-operative nausea and vomiting.

ASA			
Treated side effects	**1-2**	**>2**	**p-value**
PONV	290 (8.4)	68 (4.4)	<0.001*
paresthesia	7 (0.2)	0 (0.0)	0.11
itching	20 (0.6)	7 (0.5)	0.57
confusion	10 (0.3)	6 (0.4)	0.57
hypotension	3 (0.1)	1 (0.1)	0.99