Randomized Study of Patient Controlled Epidural Analgesia (PCEA) Using Fentanyl and Bupivacaine versus Patient Controlled Analgesia (PCA) With Intravenous (IV) Morphine for Abdominal Surgery

Prerana N. Shah* and Prachi Kapadnis

Department of Anaesthesiology, Seth GSMC & KEM Hospital, Parel, Mumbai 400012, India

Abstract: Randomized Study of Patient Controlled Epidural Analgesia (PCEA) Using Fentanyl and Bupivacaine versus Patient Controlled Analgesia (PCA) With Intravenous (IV) Morphine for Abdominal Surgery

Background: Effective pain relief helps in early mobilization leading to quick recovery and shorter hospital stay.

Materials and Methods: Our aim was to compare, IV PCA and PCEA in terms of analgesic efficacy and side effects after major abdominal surgery. After ethics committee approval, written valid informed consent and sample size calculation, patients were randomly assigned into one of 2 groups of 40 each. Postoperatively, patients in Group A received IV morphine 1mg/ml and patients in Group B received epidural fentanyl 5mcg/ml and bupivacaine 0.125%. PCA pump was programmed to deliver 2ml bolus with a lockout interval of 10 minutes. No background infusion was used. Patients were assessed for pain, sedation, pulse rate, respiratory rate, blood pressure, oxygen saturation and side effects were looked for at 0, 2, 8, 12 and 24 hours. Rescue analgesia was given with IV Tramadol 2mg/kg when VAS > 4 at rest despite three consecutive PCA boluses. All calculations were done at 90% power and 5% significance using two sided tests.

Results: No statistical difference was found in analgesia though quality of analgesia was better with PCEA. Requirement of rescue analgesia and incidence of nausea and vomiting was more with IV PCA though statistically insignificant.

Conclusion: IVPCA using morphine and PCEA using bupivacaine and fentanyl are similar in efficacy. However, PCEA produced better quality of analgesia. Advantages of PCA over conventional pain management include individualization as patients are the best to assess their pain and can get medication as needed by pressing a button.

Keywords: PCA, analgesia, fentanyl, morphine, bupivacaine, epidural.

BRIEF SUMMARY STATEMENT

Pain relief is an important aspect of postoperative management. Patient controlled analgesia (PCA) is a common method employed for the same. PCA can be given either through epidural or intravenous route.

INTRODUCTION

From prehistoric era of ancient civilization, evidence of pain and attempts at its relief has been found throughout history. Effective control of post-operative pain remains one of the integral aspects of anaesthesia [1, 2]. Severe pain can lead to pulmonary, circulatory, gastrointestinal, urinary, muscular dysfunctions and worsening of thromboembolic process [3]. It also adds to adverse psychological and emotional events. Several methods are used to relieve post-operative pain. Opioids are the most commonly used medications for the treatment of post-operative pain. They provide analgesia without loss of touch, proprioception or consciousness. Several studies revealed that most patients received inadequate doses of opioids because of an underestimation of pain or over estimation of risk abuse [4].

It has been shown that after major surgery, equal relief of post-operative pain can be achieved with smaller dose, less respiratory depression and sedation by administering an opioid epidurally rather than administering it intravenously [5]. Epidural co-administration of an opioid and local anaesthetic is a popular method of post-operative pain relief. Theoretically, since the two act by different mechanisms their effects should be additive, leading to decreased requirement for each drug and thereby minimizing their individual side effects. Patient Controlled Analgesia (PCA) allows patient to self-administer small boluses of analgesic, providing better titration and enhancing responsiveness in analgesic requirements.

Morphine is most commonly used drug for Intra Venous (IV) PCA because of its moderate duration of action and is better suited for easy controllability. Fentanyl is used commonly for post-operative analgesia with lower incidence of side effects as compared to morphine [6].

*Address correspondence to this author at the 73B, Varma Villa, Vitthalbhai Road, Vile Parle West, Mumbai 400055, Maharashtra, India;
Tel: 919869117027; Fax: 912224116051;
E-mail: pps@kem.edu

E-ISSN: 2310-9394/14

Current evidence suggest that for patient undergoing major abdominal surgeries, Patient Controlled Epidural Analgesia (PCEA) have lower incidence of post-operative respiratory and cardiovascular complications and lower morbidity and mortality rates [7].

AIMS AND OBJECTIVES

This prospective study was designed to compare IV PCA using Morphine versus PCEA using Bupivacaine and Fentanyl for their efficacy on post-operative pain after major abdominal surgeries.

MATERIALS AND METHODS

Sample size calculations were determined using Casagrandes method. According to study done by Behera *et al*. [8] PCEA with fentanyl and bupivacaine provided better analgesia than IV morphine PCA for early thoracotomy pain. The incidence of pain relief in PCEA group was 66%, whereas in the IV PCA it was 20%. The difference of 46% was taken as clinically meaningful for our study. After ethics committee approval and valid informed consent, adult patients undergoing elective major upper abdominal surgery, were randomly assigned into one of 2 groups of 40 each. No epidural catheter was placed in Group A. Preoperatively epidural catheter was inserted at T 11-12 or T12- L1 level only in Group B patients however no drug through epidural catheter was given intra-operatively. Standard technique of general anaesthesia was used in all patients. Postoperatively, patients in Group A received IV morphine 1mg/ml and patients in Group B received epidural fentanyl 5mcg/ml and bupivacaine 0.125% through PCA pump. It was programmed to deliver 2ml bolus with a lockout interval of 10 minutes. On demand patient had to press the button of PCA pump. No background infusion was used.

Patients were assessed for pain, sedation, pulse rate, respiratory rate, blood pressure, oxygen saturation and side effects such as nausea, vomiting, pruritus, hypotension, respiratory depression were looked for at 0 (before starting study drug), 2, 8, 12 and 24 hours.

Analgesic efficacy was described in terms of (Visual Analgesia Scale) VAS score using 0-10cm scale where in 0 cm is no pain and 10 cm is worst pain imaginable. Pain was graded by pain intensity scale as: 0 - No pain, 1 - Mild pain. (Pain reported only in response to questioning without behavioral signs) 2 - Moderate pain. (Pain reported in response to questioning and accompanied by behavioral signs or pain reported spontaneously without questioning) 3 - Severe pain. (Strong vocal response or response accompanied by facial grimacing and arm withdrawal). Rescue analgesia was given with IV Tramadol 2mg/kg when VAS > 4 at rest despite three consecutive PCA boluses.

Sedation was evaluated by a 5-point scoring system: 0-aware, 1-drowsy, 2-asleep or easily respond to verbal command, 3- Asleep or difficulty in responding to verbal commands, 4- Asleep or no response to verbal command.

Hypotension was defined as a drop of systolic blood pressure of more than 20% of preoperative value or less than 90mmHg during the study period. Respiratory depression was defined as respiratory rate of less than 10/min. The primary outcome of the study was: the percentage of patients with analgesia failure defined as Visual analogue scale more than 3 despite three consecutive boluses. The secondary outcomes evaluated were sedation scores and side effects if any.

Statistics

All calculations were done at 90% power and 5% significance using two sided tests. The data obtained was subjected to statistical analysis using Students unpaired t-test (for comparison of mean between two groups – Numerical data included age, weight, heart rate, mean arterial pressure, respiratory rate, SpO_2, sedation score, VAS score) and Chi square test (for comparison of proportions between two groups for categorical data that were included were gender, ASA grade, rescue analgesia, side effects) to find out significant difference between the groups. For statistical comparison, difference was considered significant when the p-value was found to be less than 0.05.

RESULTS

All 80 patients that were enrolled, completed the study.

DISCUSSION

It is challenging to relieve postoperative pain after major surgery because pain relief may be difficult to achieve without simultaneously incurring severe undesirable side effects.

The reasons for inadequate pain relief are numerous. The nature of pain itself is subjective and there is usually no simple test for its quantification. Patient's response to analgesics is also variable and

the efficacies of post-operative pain relief methods are neither uniform nor sufficient.

Table 1: Demographic Data

Parameters	Group A	Group B	P Value
ASA status I (number)	31	31	1.00
ASA status II (number)	9	9	
Male (number)	20	20	1.00
Female (number)	20	20	
Age (years) Mean ± SD	45.52 ± 10.75	43.1 ± 11.03	0.996
Weight (kg) Mean ± SD	59.45 ± 10.41	58.92 ± 9.9	0.231

As depicted in table 1, the patients were comparable in both groups with respect to demographic data.

Table 2: Heart Rate (Beats Per Minute)

Heart Rate	Group A	Group B	P Value
Baseline	83.72 ± 11.32	82.85 ± 13.37	0.753
0 hr	83.02 ± 9.41	82.70 ± 10.79	0.886
2 hrs	80.90 ± 10.03	81.78 ± 9.60	0.691
8 hrs	79.50 ± 9.22	80.10 ± 9.17	0.771
12 hrs	77.80 ± 10.69	77.55 ± 8.22	0.907
24 hrs	78.22 ± 8.91	78.18 ± 7.86	0.979

Post operatively mean heart rates at all intervals were comparable.

Table 3: Mean Arterial Pressures (mm of Hg)

Mean Arterial Pressure	Group A	Group B	P Value
Baseline	94.52 ± 7.87	91.13 ± 11.52	0.129
0 hr	93.88 ± 7.43	92.25 ± 10.38	0.420
2 hrs	91.48 ± 7.02	87.5 ± 9.37	0.527
8 hrs	88.6 ± 7.77	86.29 ± 9.0	0.223
12 hrs	88.48 ± 7.43	87.75 ± 8.28	0.678
24 hrs	89.17 ± 7.27	87.77 ± 7.44	0.395

The mean arterial pressure was statistically not significant.

Table 4: Respiratory Rate

Respiratory Rate	Group A	Group B	P Value
Baseline	16.68 ± 1.80	17.22 ± 1.67	0.161
0 hr	19.45 ± 15.78	17.08 ± 1.65	0.347
2 hrs	16.35 ± 1.424	15.90 ± 1.58	0.185
8 hrs	15.20 ± 1.77	16.02 ± 1.368	0.422
12 hrs	15.38 ± 1.05	15.20 ± 0.911	0.43
24 hrs	14.28 ± 1.15	14.88 ± 0.911	0.712

The difference in the respiratory rate at all points statistically not significant.

Table 5: Mean VAS Score

VAS Score	Group A	Group B	P value
0 hr	3.05 ± 0.639	2.78 ± 0.80	0.093
2 hrs	2.32 ± 0.73	2.42 ± 0.64	0.515
8 hrs	2.12 ± 0.40	2.32 ± 0.53	0.06
12 hrs	1.28 ± 0.64	1.18 ± 0.39	0.4
24 hrs	0.98 ± 0.357	0.75 ± 0.54	0.072

No statistical difference was found in VAS although lower mean scores were seen in group B. However, VAS grade at 2 hour was between 4-6 in 4 patients in group A and in 2 patients in group B and was 4-6 in one patient in each group at 8 hours.

Table 6: VAS Score Grading

VAS Grade	Group A			Group B		
No of patients	0 - 3	4 - 6	7 - 10	0 - 3	4 - 6	7 - 10
0 hr	31	9	0	32	8	0
2 hrs	36	4	0	38	2	0
8 hrs	39	1	0	39	1	0
12 hrs	40	0	0	40	0	0
24 hrs	40	0	0	40	0	0

Requirement of rescue analgesia was more in group A though it was statistically insignificant.

Table 7: Mean Sedation Score (SS)

Sedation Score	Group A	Group B	P Value
0 hr	0 ± 0	0 ± 0	
2 hrs	0.2 ± 0.61	0.05 ± 0.22	0.146
8 hrs	0.35 ± 0.86	0.10 ± 0.441	0.107
12 hrs	0.4 ± 0.98	0.08 ± 0.35	0.052
24 hrs	0.32 ± 0.83	0.05 ± 0.22	0.-56

All the patients in both the groups were arousable during study period.

Table 8: Side Effects

Side Effects	Group A	Group B	P Value
Nausea	7 (17.5%)	3 (7.5%)	0.310
Vomiting	4 (10.0%)	3 (7.5%)	1.000
Pruritus	0	0	------
Respiratory depression	0	0	------

Side effects like nausea, vomiting, pruritus and respiratory depression were looked for. Incidence of nausea and vomiting was more in group B though it was statistically insignificant. No patient developed pruritus or respiratory depression.

Recent advances in the treatment of pain are the use of patient controlled analgesia (PCA). This can be used either intravenously (IVPCA) or epidurally (PCEA). Advantages of PCA over conventional pain

management are that the therapy is individualized to the patient. Patients are the best to assess their pain and they can get medication as and when required by pressing a button of PCA pump. Thus it avoids overdose and. Usually epidural catheter is inserted for major abdominal surgeries. However, if epidural catheter cannot be inserted successfully, PCA can be used via IV route.

After PCA pumps were available in our department, this prospective open blind randomized study was done to compare and evaluate the efficacy and safety of patient controlled analgesia using intravenous morphine (group A) versus patient controlled epidural analgesia using fentanyl and bupivacaine (group B) for post-operative pain relief in patients undergoing major abdominal surgery.

With respect to demographic variables both the groups were comparable. The importance of the variation being non-significant for age, gender, weight and ASA grading is that a random distribution of patients was confirmed to and there were no confounding factors which would later interfere with the postoperative assessment.

In our study we also monitored vital parameters of both groups for 24 hours postoperatively at 0 hour, 2 hours, 8hours, 12 hours and 24 hours.

In our study, we found that there was no statistically significant difference in post-operative analgesia as assessed by VAS score over a period of 24 hours,

In the similar study done by Behera *et al*. [8] in 2008, comparison between IVPCA with morphine and PCEA with fentanyl and bupivacaine was done after thoracotomy procedures. They found that PCEA using fentanyl and bupivacaine provided better pain relief both at rest and during coughing and was associated with fewer side effects as compared to IV PCA using morphine. Neal Badner *et al*. [9] in 1992 showed that 0.1% bupivacaine epidurally did not improve the quality of analgesia alone. But if it was combined with fentanyl, it definitely improved the quality of analgesia and decreased pain score. Epidural infusions of fentanyl, in a 10 mcg/ml concentration, combined with bupivacaine 0.1% were compared with epidural infusions of fentanyl alone for postoperative analgesia following abdominal or thoracic surgery. There were no detectable differences between the two groups in analgesia, no difference in postoperative pulmonary function or bowel function.

Cooper *et al*. [10] in 1993 showed that 0.125% bupivacaine with fentanyl 5 mcg/ml when delivered by PCA pump via epidural catheter decreased the requirement of one another. Pain score over 24 hour period in their study was less than 3 and incidence of side effects was also less. In the study by Claude Mann *et al*. [11], pain relief was better at rest and after coughing in the PCEA group and the satisfaction scores were significantly greater in the PCEA group.

In the study conducted by Saito *et al*. [12], the efficacy and safety of postoperative analgesia with continuous epidural infusion of either morphine or fentanyl in combination with bupivacaine were evaluated. They found that 18% patients developed significant hypotension in morphine bupivacaine group as compared to fentanyl bupivacaine group. In the study conducted by Cooper *et al*. [10] hypotension occurred in two patients in the fentanyl group, compared with eight in the bupivacaine group and 10 in the combined fentanyl and bupivacaine group.

In our study, not a single patient developed hypotension. In the study conducted by Mann *et al*. [11] five episodes of postoperative hypotension occurred in the PCEA group versus none in the PCA group. The patients were treated by simple fluid loading.

In our study, there was no episode of respiratory depression.

Saito *et al*. [12] in 1994 and Cooper *et al*. [10] found no respiratory depression in their study. In both studies bupivacaine with fentanyl was used via the epidural route.

Similar to the study conducted by Cooper *et al.* [10], in our study all the patients were arousable.

Systemic and epidural administration of opioids are often associated with side effects like respiratory depression, nausea, vomiting, pruritus, urinary retention whereas epidural administration of local anaesthetics is associated with side effects like postural hypotension due to sympathetic blockade. Earlier studies found to have similar incidences of nausea and vomiting in patients who received fentanyl alone. In the study conducted by Cooper *et al*. [10] and Mann *et al*. [11], nausea and vomiting was seen.

Saito *et al.* 1994 reported 10% incidence of pruritus in Bupivacaine and fentanyl group. Cooper also reported 16% incidence of pruritus in Bupivacaine Fentanyl group [12].

CONCLUSIONS

Although both IVPCA using morphine and PCEA using bupivacaine and fentanyl were similar in efficacy to relieve post-operative pain following major abdominal surgeries, PCEA using bupivacaine and fentanyl can be considered as an effective alternative for the management of post-operative pain as compared to conventional IVPCA if epidural is possible or vice versa.

REFERENCES

[1] Chapman CR, Syrjala KL. Measurement of Pain. In Bonica JJ (Ed) The management of pain. 2nd Ed, Vol 1: Philadelphia; Lea and Febiger: 1990; 580-594

[2] Bonica JJ. Anatomic and physiologic basis of nociception and pain. In Bonica JJ (Ed). The management of Pain. 2nd Ed, Vol 1 Philadelphia; Lea and Febiger: 1990; 28- 94.

[3] Harrison principle of internal medicine. Pain pathophysiology and management.14th Edition: 53-58; 1998.

[4] Crews JC. Epidural opioid analgesia. Crit Care Clin. 1990; 6: 315-42.

[5] Chaney MA: Side effects of intrathecal and epidural opioids. Can J Anaesth. 1995; 42: 891-903. http://dx.doi.org/10.1007/BF03011037

[6] Glass PS, Estok P, Ginsberg B, Goldberg JS, Sladen RN. Use of patient controlled analgesia to compare the efficacy of epidural to intravenous fentanyl administration. Anesth Analg. 1992; 74: 345-51.

[7] Gambling DR Christopher JH, Johnathan B, Paul H, Jean ES, Peggy LER, Chantal TC. Timothy J.G. Pavy TJ, Patient Controlled Epidural Analgesia in labour: varying bolus dose and lockout interval. Can J Anaesth. 1993; 40: 211-7. http://dx.doi.org/10.1007/BF03037032

[8] Behera BK, Puri GD, Ghai B. Patient controlled epidural analgesia with fentanyl and bupivacaine provides better analgesia than Intravenous morphine patient controlled analgesia for early thoracotomy pain. J Postgrad Med. 2008; 54: 86-90. http://dx.doi.org/10.4103/0022-3859.40772

[9] Badner NH, Komar WE. Bupivacaine 0.1% does not improve postoperative epidural fentanyl analgesia after abdominal or thoracic surgery. Can J Anaesth. 1992; 39: 330-6. http://dx.doi.org/10.1007/BF03009042

[10] Cooper DW, Turner G. Patient-controlled extradural analgesia to compare bupivacaine, fentanyl and bupivacaine with fentanyl in the treatment of postoperative pain. Br J Anaesth. 1993; 70: 503-7. http://dx.doi.org/10.1093/bja/70.5.503

[11] Mann C, Pouzeratte Y, Boccara G, Peccoux C, Vergne C, Brunat G, Domergue J, Millat B, Colson P. Comparison of Intravenous or Epidural Patient controlled Analgesia in the Elderly after Major Abdominal Surgery. Anesthesiology. 2000; 92: 433-41. http://dx.doi.org/10.1097/00000542-200002000-00025

[12] Saito, Y., Uchida, H., Kaneko, M., Nakatani, T. and Kosaka, Y. Comparison of continuous epidural infusion of morphine/bupivacaine with fentanyl/ bupivacaine for postoperative pain relief. Acta Anaesthesiol Scand, 1994; 38: 398-401. http://dx.doi.org/10.1111/j.1399-6576.1994.tb03915.x

Received on 08-07-2014 Accepted on 20-08-2014 Published on 05-09-2014

DOI: http://dx.doi.org/10.14205/2310-9394.2014.02.01.4