

# A study to compare continuous epidural infusion and intermittent bolus of bupivacaine for postoperative analgesia following renal surgery

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## ABSTRACT

**Background:** Extradural administration of local anaesthetics, opioids or a combination of both is now a well-established technique for managing postoperative pain following upper abdominal, pelvic and thoracic procedures or orthopaedic procedures on the lower extremities. There are two techniques of administration of drugs via epidural catheter – one is by continuous infusion and the other is by intermittent boluses. At present there is controversy in the literature regarding the analgesic effects of the techniques.

**Methods:** This study was conducted in a prospective, randomised manner on 60 patients of either sex of ASA class I or II, scheduled to undergo elective renal surgery. The general anaesthetic technique was standardised. The patients were divided randomly into two groups of 30 each. The patients in group 1 received a continuous infusion of 0.166% bupivacaine, while the patients in group 2 received intermittent boluses through epidural catheter. The efficacy of postoperative analgesia was assessed using pulmonary function tests up to 12 hours. The generated data were analysed statistically.

**Results:** There were no significant changes in pulse rate and arterial pressure at different time intervals from the preoperative values. Respiratory rates in both the groups were found to be significantly higher than the preoperative values in the two groups ( $p < 0.05$ ). Forced vital capacity (FVC) and peak expiratory flow rate (PEFR) were significantly lower than the preoperative values at all points in time in both groups, but the drop was greater in group 2 and pain scores on movement were also found to be significantly higher than those in group 1 at the times when the effect of the bupivacaine bolus was wearing off ( $p < 0.05$ ). Pain scores at rest were found to be comparable in both groups postoperatively.

**Conclusions:** We conclude that continuous infusion of bupivacaine (8.3 mg/h) provides better analgesia at rest and on movement than intermittent boluses, and is not associated with fluctuations in the level of analgesia. Incidences of adverse effects are similar and not insignificant with both schedules.

## Introduction

Acute postoperative pain is a manifestation of autonomic, psychological and behavioural responses that result in an unpleasant and unwanted sensory and emotional experience. Patients often perceive postoperative pain as one of the most ominous aspects of surgery. Upper abdominal and thoracic surgery are more painful, and a pain-induced reflex increase in skeletal muscle tension may lead to decreased total thoracic compliance, splinting and hypoventilation.<sup>1</sup> Adequate pain relief benefits the patient not only by reducing the metabolic and endocrine stress response, but also by decreasing the incidence of pulmonary, cardiovascular and thromboembolic complications.<sup>2</sup> The options for the management of postoperative pain include systemic opioids and nonopioids, central neuraxial analgesia, and peripheral nerve blocks. The extradural administration of drugs via continuous infusion or intermittent bolus is a well-established technique.<sup>1</sup>

Continuous infusion not only produces a constant block to maintain analgesia and minimise cardiovascular disturbances,<sup>3</sup> it also reduces the medical and nursing workload.<sup>4</sup> The administration of intermittent epidural boluses of local anaesthetics is technically simple and cheap, as sophisticated, costly infusion devices are not needed, but it is associated with fluctuating levels of analgesia and involves additional work on the part of

nurses to repeatedly inject the local anaesthetic solutions.<sup>1</sup> Some studies report that patients receiving intermittent administration of bolus doses maintain a more extensive block and report marginally better analgesia, and that the requirement for rescue medication decreased.<sup>5</sup> A consensus is yet to evolve over which of the two techniques is better. The few available comparative trials do not help in drawing any definite conclusions.<sup>4-7</sup> Hence, we planned this study to compare the efficacy of pain relief using continuous and intermittent bolus administration of bupivacaine, and the adequacy of analgesia was assessed subjectively (by visual analogue scale) and objectively (using pulmonary function tests). Throughout the study period, the haemodynamic parameters were monitored in both groups and any adverse effects were noted.

## Material and methods

The present study was conducted after obtaining ethical approval from the hospital ethical committee and was undertaken to compare the efficacy of continuous infusion with intermittent epidural boluses of bupivacaine for postoperative analgesia following renal surgery. Sixty patients belonging to ASA class I and II, of either sex and in the age group 20 to 50 years, posted for elective surgery like pyelolithotomy, nephrectomy and pyeloplasty, were included in the study. Patients with a history of hypertension, diabetes, heart disease, and obstructive or

restrictive lung disease, and with hepatic or renal insufficiency, were excluded from the study. Chronic smokers and those on antiplatelet and anticoagulant drugs were also excluded.

The patients were subjected to a detailed clinical examination, and routine biochemical investigations were carried out in order to rule out any systemic illness. Basic demographic characters like age, weight and height were also recorded. Baseline readings of pulse rate, respiratory rate, systolic and diastolic blood pressure were recorded. A preoperative reading of the pulmonary function tests (forced vital capacity and peak expiratory flow rate) was taken using the 'micro spirometer' (digital spirometer to measure forced vital capacity and peak expiratory flow rate) after explaining the procedure in detail. All the patients were introduced to the visual analogue scale, with "no pain" and "worst pain ever" labelled at two ends of a 10 cm horizontal or vertical line, and informed consent was obtained from all the patients after explaining the anaesthetic procedure in detail. All the patients included in the study were premedicated with alprazolam 0.5 mg (tablet) the night before surgery and in the morning of surgery, ondansetron 100 µg kg<sup>-1</sup> (injection) and pentazocin 0.5 mg kg<sup>-1</sup> (injection) IV were given 30 minutes before surgery. Selected patients were randomly allocated into two groups, each consisting of 30 patients. Patients in group 1 received continuous epidural infusion at 5 ml h<sup>-1</sup> of 0.166% plain bupivacaine, while patients in group 2 received bolus doses of 15 ml of 0.166% plain bupivacaine three-hourly.

In the operation theatre, a good intravenous line was secured in all the patients after connecting monitors for electrocardiogram, noninvasive blood pressure and pulse oximetry. Under aseptic precautions, epidural anaesthesia was performed using the midline approach; 5 to 6 cm of a 16 G epidural catheter was inserted into the epidural space at the level of the L2–L3 interspinous space and 3 ml of 1.5% lignocaine with adrenaline was injected as a test dose to rule out intravascular and intrathecal placement. This was followed by injection of 15 ml of 0.5% plain bupivacaine in 5 ml increments. All the patients were induced with propofol (2 mg kg<sup>-1</sup>) and vecuronium bromide (0.1 mg kg<sup>-1</sup>), followed by intubation with an appropriately sized cuffed polyvinylchloride tube. Anaesthesia was maintained with the inhalation of 70% nitrous oxide in oxygen, halothane, and intermittent doses of vecuronium bromide. The residual neuromuscular blockade was reversed with neostigmine (injection) and glycopyrrolate (injection), and the patients were extubated fully awake.

Three hours after the initial injection ('zero' hour), all the patients received a bolus of 15 ml of 0.166% plain bupivacaine in 5 ml increments. After that, a continuous infusion of 0.166% plain bupivacaine was started at a fixed rate of 5 ml h<sup>-1</sup> through a disposable infusion pump in group 1, and the patients in group 2 received three-hourly bolus doses of 15 ml of 0.166% plain bupivacaine. Intravenous fluids were continued in the two groups throughout the study period. Follow-up was done for a period of 12 hours. The severity of postoperative pain (at rest and during movement) was assessed using a visual analogue scale (VAS) at zero hour and at hourly intervals thereafter for 12 hours. If any patient complained of pain (VAS ≥ 3 at rest) and requested additional analgesic

supplements, he was obliged and was excluded from the study. For the measurement of pulmonary functions, the patients were instructed to breathe in until their lungs were completely full, to seal their lips around the mouthpiece and to blow out as hard and as fast as possible until no more air could be pushed out. Forced vital capacity (FVC) and peak expiratory flow rate (PEFR) were measured preoperatively, postoperatively at 'zero' hour and at hourly intervals thereafter for 12 hours. Three readi eratively, at 'zero' hour and hourly thereafter for 12 hours in the postoperative period. A close watch was kept on the patient to look for any side effects like nausea, vomiting, dizziness, tinnitus, hypotension and excessive motor weakness. The data were analysed using Student's unpaired and paired 't' test, the chi-square test, the 'Z' test and ridit analysis.<sup>8</sup> In the ridit analysis, a specified series of patients was chosen as a control reference set (identified distribution) and all comparisons were made relative to the identified distribution. The individual scores in the identified distribution were replaced by ridits, which bear a relationship to the incidence of each score in the total series. The mean ridit for the identified distribution was calculated and then the average ridit of the given scores was calculated. If there is no overlap between the 95% confidence limits of the mean scores in any two groups, the difference is considered to be significant.

### Observations and results

Age, weight, sex, height, physical status and duration of anaesthesia were statistically comparable between the two groups ( $p > 0.05$ ) (Table D). The two groups were comparable with regard to the type of surgical procedure ( $p > 0.05$ ). The preoperative haemodynamic and respiratory parameters were comparable in both groups. The mean postoperative pulse rates, mean arterial pressures and respiratory rates in the two treatment groups were statistically comparable ( $p > 0.05$ ) at all points in time. At all points in time, the mean respiratory rate in the two groups was found to be significantly higher compared to the corresponding preoperative values ( $p < 0.001$ ).

At all points in time, the mean FVC values in the two treatment groups were found to be significantly lower than the corresponding preoperative values ( $p < 0.001$ ). In group 1, the preoperative mean FVC was  $3.13 \pm 0.83$  L and the minimum mean FVC reading was  $2.02 \pm 0.52$  L at 'zero' postoperative hour, but in group 2, decrements from the preoperative values were greater at the third, sixth, ninth and twelfth hours of study postoperative. Preoperatively, the mean FVC of the group 2 patients was  $3.28 \pm 0.74$  L, and it dropped to  $1.12 \pm 0.23$ ,  $1.16 \pm 0.25$ ,  $1.17 \pm 0.25$  and  $1.2 \pm 0.29$  L at the third, sixth, ninth and twelfth hour of study postoperative (Table II).

**Table I:** Demographic data (mean SD)

Parameters	Group 1 (n = 30)	Group 2 (n = 30)
Age (years) (mean ± SD)	37.75 ± 9.30	38.45 ± 9.51
Weight (kg) (mean ± SD)	59.3 ± 7.95	60.55 ± 8.15
Height (inches) (mean ± SD)	63.8 ± 3.19	64.05 ± 2.87
Gender (M:F)	10 : 10	8 : 12
Physical status (ASA I : ASA II)	16 : 4	15 : 5
Anaesthesia duration (min) (mean ± SD)	135.5 ± 18.73	138.2 ± 19.8

$p > 0.05$  (no significant difference)

**Table II:** Mean forced vital capacity (L) in the two groups at stated time intervals (mean ± SD)

Time interval (hr)	Group 1 (n = 30)	Group 2 (n = 30)
0	2.02 ± 0.52	2.16 ± 0.49
1	2.16 ± 0.53	2.28 ± 0.48
2	2.19 ± 0.56	2.30 ± 0.50
3	2.16 ± 0.53	1.12 ± 0.23*
4	2.19 ± 0.58	2.30 ± 0.46
5	2.15 ± 0.53	2.3 ± 0.46
6	2.19 ± 0.59	1.16 ± 0.25*
7	2.17 ± 0.56	2.35 ± 0.51
8	2.19 ± 0.58	2.35 ± 0.47
9	2.17 ± 0.57	1.17 ± 0.25*
10	2.16 ± 0.53	2.29 ± 0.46
11	2.22 ± 0.58	2.33 ± 0.48
12	2.22 ± 0.62	1.2 ± 0.29*

\* p &lt; 0.05 – significant

In group 1, the mean preoperative PEFR (L min<sup>-1</sup>) was 413 ± 81.6, decreasing to 208.7 ± 27 (L min<sup>-1</sup>) at 'zero' hour postoperative. In group 2, the mean PEFR in the preoperative period was 410 ± 76.3 L min<sup>-1</sup>, and it dropped to 188.4 ± 35.54, 191.15 ± 35.31, 187 ± 31.57 and 188.25 ± 36.44 L min<sup>-1</sup> at the third, sixth, ninth and twelfth hour of the study (Table III).

**Table III:** Mean peak expiratory flow rate (L/min) in the two groups at stated time intervals (mean ± SD)

Time interval (hr)	Group 1 (n = 30)	Group 2 (n = 30)
0	208.7 ± 27	195.05 ± 38.47
1	262.25 ± 48.29	275.3 ± 49.51
2	262.65 ± 50.2	275.3 ± 49.51
3	262.5 ± 49.85	188.4 ± 35.54*
4	264.85 ± 53.34	274 ± 49.74
5	265.95 ± 49.24	276.75 ± 48.29
6	266.05 ± 51.29	191.15 ± 35.31*
7	268.5 ± 51.85	276.15 ± 48.66
8	267.35 ± 54.03	280.7 ± 48.37
9	268.75 ± 51.37	187 ± 31.57*
10	267.65 ± 50.91	280.55 ± 49.59
11	267.05 ± 52.63	283.9 ± 48.25
12	268.15 ± 51.97	188.25 ± 36.44*

\* p &lt; 0.05 – significant

The severity of postoperative pain (if present) was assessed using a visual analogue scale, both at rest and during efforts to move. The VAS scores were analysed using riddit analysis. There was overlapping between the mean riddits of the pain scores of group 1 and group 2 at rest (Table IV). On movement, there

was no overlapping between the mean riddits of group 1 and group 2 at the third, sixth, ninth and twelfth hour of the study (Table V). The difference was thus significant at the 5% level at the abovementioned times, since there was no overlap of the 95% confidence limits of the two corresponding means. The 'Z' test was used to compare the incidences of adverse effects in the two groups. In group 1, one patient complained of nausea and one had excessive sweating, while two patients in group 2 complained of nausea.

**Table IV:** Mean riddits (95% confidence limits) of pain scores in the two groups (at rest)

Time (hr)	Group 1 (n = 30)	Group 2 (n = 30)
0	0.5 ± 0.13	0.38 ± 0.13
1	0.5 ± 0.13	0.41 ± 0.13
2	0.5 ± 0.13	0.34 ± 0.13
3	0.5 ± 0.13	0.7 ± 0.13
4	0.5 ± 0.13	0.4 ± 0.13
5	0.5 ± 0.13	0.44 ± 0.13
6	0.5 ± 0.13	0.7 ± 0.13
7	0.5 ± 0.13	0.38 ± 0.13
8	0.5 ± 0.13	0.39 ± 0.13
9	0.5 ± 0.13	0.66 ± 0.13
10	0.5 ± 0.13	0.33 ± 0.13
11	0.5 ± 0.13	0.40 ± 0.13
12	0.5 ± 0.13	0.68 ± 0.13

**Table V:** Mean riddits (95% confidence limits) of pain scores in the two groups (on movement)

Time (hr)	Group 1 (n = 30)	Group 2 (n = 30)
0	0.5 ± 0.13	0.53 ± 0.13
1	0.5 ± 0.13	0.44 ± 0.13
2	0.5 ± 0.13	0.39 ± 0.13
3	0.5 ± 0.13	0.80 ± 0.13*
4	0.5 ± 0.13	0.36 ± 0.13
5	0.5 ± 0.13	0.39 ± 0.13
6	0.5 ± 0.13	0.84 ± 0.13*
7	0.5 ± 0.13	0.36 ± 0.13
8	0.5 ± 0.13	0.39 ± 0.13
9	0.5 ± 0.13	0.81 ± 0.13*
10	0.5 ± 0.13	0.41 ± 0.13
11	0.5 ± 0.13	0.43 ± 0.13
12	0.5 ± 0.13	0.77 ± 0.13*

## Discussion

Acute postoperative pain is associated with adverse physiological sequelae on multiple organ systems. Respiratory dysfunction is the most commonly associated with upper abdominal surgery, and there is a fall in tidal volume and an

increase in respiratory frequency. Pain results in the voluntary reduction of muscle movement in the thorax and abdominal area, leading to 'muscle splinting', which is often associated with partial closure of the glottis. Acute pain is therefore associated with decreased tidal volume, decreased forced vital capacity (VC) and PEF<sub>R</sub>.<sup>9</sup> Epidural analgesia incorporating the use of local anaesthetics alone or in combination with opioids provides better pain control during activity, improves pulmonary function,<sup>11,12,13</sup> decreases side-effects, and helps in faster recovery of bowel function.<sup>14,15</sup> Its use is also associated with a lower incidence of postoperative myocardial ischaemia.<sup>10</sup> Cleland was the first to describe the use of an epidural catheter for postoperative analgesia with intermittent doses of local anaesthetic solutions. As this technique was associated with fluctuating levels of analgesia and significant sympathetic blockade, continuous infusion of local anaesthetic was subsequently recommended as an alternative.<sup>1</sup> In this study we compared the two techniques and pain relief was assessed objectively using lung function tests.

As pain scores at rest remained low throughout the study, there was minimal sympathetic over-activity and thus no significant changes were seen in haemodynamic parameters during the study. Besides, the concentration and volume of bupivacaine used by us were not high enough to cause a significant fall in blood pressure. Aribogan et al<sup>16</sup> used 8 ml/h of 0.125% bupivacaine (10 mg/hr) for postoperative analgesia after major urological surgery and found insignificant haemodynamic changes when compared to the group that was given only tramadol. Duncan et al<sup>7</sup> compared intermittent bolus of 5 ml of 0.375% (18.75 mg/h) bupivacaine with continuous infusion of the same dose. They found no difference in the cardiovascular variables between the groups and no episodes of hypotension were documented, which again coincides with the findings of our study. The respiratory rate was comparable in both groups at all points in time, although it was found to be significantly higher ( $p < 0.001$ ) than the preoperative value. In this particular study, very high respiratory rates were not observed and this was also found in the study conducted by Spence and Smith.<sup>17</sup>

Yushang et al also found that post-thoracotomy pulmonary function was severely lowered to about 40% of the baseline on the first day, and rehabilitated to 60% of the baseline on the eighth day.<sup>18</sup> They found that epidural analgesia was able to improve pain relief and pulmonary function to some extent. Ioti et al studied the effect of epidural morphine on post-thoracotomy respiratory function and found that the group that had been injected with morphine had significantly better VC and FEV<sub>1</sub> values in the first two days postoperative, although it was still significantly less than the preoperative value.<sup>19</sup> We also observed a significant fall in postoperative FVC and PEF<sub>R</sub> from the preoperative values despite adequate analgesia. Spence and Smith compared lung function and postoperative analgesia in 21 patients posted for upper abdominal surgery.<sup>17</sup> The patients were allocated randomly to receive either morphine by injection or continuous extradural block with 5 to 7 ml of 0.5% bupivacaine, and they found a marked reduction in forced vital capacity and PEF<sub>R</sub> in both groups, which did not return to normal until the fifth postoperative day. This could be explained by the partial loss of motor function in the lower intercostal and upper abdominal muscles due to the high concentration of bupivacaine used. Despite adequate analgesia, postoperative pulmonary function may not return to baseline values and mechanisms other than pain may also contribute to the fall in postoperative pulmonary function. Although postoperative pulmonary function improves after good epidural analgesia, it may not return to normal due to persisting diaphragmatic dysfunction and basal atelectasis. The fall in FVC and PEF<sub>R</sub> was more in group 2 at the third, sixth, ninth and twelfth hour of the study when compared to the corresponding values in group 1 because of inadequate analgesia, as the patients in group 2 had significantly higher pain scores (on movement) at these time points.

Pain scores at rest in the two groups in this study were comparable at all points in time, although the pain scores on movement (dynamic pain scores) were significantly higher in group 2 at the third, sixth, ninth and twelfth hour of assessment, probably due to the level of analgesia having receded; the boluses of the drug in group 2 were being given at three-hourly intervals. Bupivacaine at 0.125% and 0.25% produces adequate analgesia with minimal motor deficit.<sup>54</sup> In this study we wanted to use a concentration that was effective yet produced minimal motor weakness so that the patients could perform pulmonary function tests with their full effort. In a pilot evaluation we found that 0.166% bupivacaine (8.3 mg/hr) provided better analgesia compared to 0.125%, with minimal increase in motor weakness. Aribogan et al used 10 mg/h of bupivacaine to provide adequate analgesia after major urological surgery.<sup>16</sup>

No significant differences were found in the incidence of adverse effects in the two groups. Nausea was noticed in one patient in group 1 and in two patients of group 2. A significant fall in blood pressure was not observed, probably due to the low concentration of bupivacaine, and continuous infusion of intravenous fluids was given throughout the study period. Olivas Mendoza et al<sup>6</sup> compared continuous and intermittent epidural analgesia for postoperative pain relief following caesarean section and found the former to be the better alternative.<sup>6</sup> Lamont et al compared continuous and intermittent epidural analgesia for the relief of labour pain and concluded that the maintenance of epidural analgesia by continuous infusion is less labour-intensive.<sup>4</sup> Duncan et al reported that the intermittent administration technique maintained a more extensive sensory block and better analgesia and was not associated with an increase in the incidence of side-effects.<sup>5</sup> This could be explained due to the preset hourly bolus of 5 ml of 0.375% bupivacaine, which was administered with the help of a special infusion pump – the hourly bolus might have prevented any regression in the level of analgesia. In the absence of such devices, as in our setting, this method was not feasible.

We conclude that continuous infusion of 0.166% bupivacaine produces better analgesia at rest and on movement than intermittent epidural bolus, as the former contributes to the better preservation of pulmonary function.

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