

PAIN

Randomized, double-blind comparison of patient-controlled epidural infusion vs nurse-administered epidural infusion for postoperative analgesia in patients undergoing colonic resection

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Background. There is little published evidence of the analgesic efficacy of patient-controlled epidural analgesia (PCEA) for postoperative pain relief. The aim of this study was to compare the analgesic efficacy of epidural infusion of bupivacaine 0.125% and fentanyl 4 µg ml⁻¹ administered by either PCEA with a background infusion or nurse-administered continuous epidural infusion (CEI) after major intra-abdominal surgery.

Methods. In a double-blind, randomized clinical trial, 205 adult patients undergoing colonic resection by laparotomy received either PCEA or CEI. Pain scores were recorded via a four-point verbal rating scale at 1, 2, 3, 4, 8, 12, 24, 48, and 72 h after surgery. The administration of epidural top-ups and systemic analgesia over the same period was also recorded, and patient satisfaction questionnaires completed.

Results. The median area under the curve of pain against time was significantly lower in the PCEA group (2 vs 24, $P < 0.001$) as were median summary pain scores on movement (0.67 vs 1.33, $P < 0.001$). Significantly fewer patients in the PCEA group received one or more epidural top-ups (13 vs 36%, $P = 0.0002$) or any systemic analgesics (41 vs 63%, $P = 0.0021$). Patients in the PCEA group were significantly more likely to be very satisfied than in the CEI group (76 vs 43%, $P < 0.0001$).

Conclusions. PCEA provides greater analgesic efficacy than CEI for postoperative analgesia after major intra-abdominal surgery, and a decreased requirement for physician or nurse intervention.

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The analgesic efficacy and other benefits of epidural infusion for postoperative analgesia are well established.^{1–3} The efficacy of patient-controlled epidural analgesia (PCEA) compared with continuous epidural infusion (CEI) has been studied extensively in obstetrics. A meta-analysis of these trials has shown a decreased requirement for physician-administered epidural top-ups with PCEA, but no demonstrable benefit in terms of pain scores.⁴ There are few published studies comparing PCEA with CEI for postoperative analgesia. Those that

have been published have involved a small number of patients and have not demonstrated a difference in pain scores between treatment modalities.^{5,6} There is no consensus on the benefit of a background infusion as part of a PCEA regimen. One study has shown that a background infusion is of benefit after upper abdominal surgery,⁷ but this has not been shown after gynaecological surgery.⁸ A wide variety of local anaesthetics, opioids, and other drugs has been administered via the epidural route, and although there is evidence that a

combination of local anaesthetic (LA) and opioid has greater efficacy than LA alone,⁹ there is no consensus on the most effective agent or combination of agents, or the most effective concentration.¹⁰

We investigated whether there was a difference in analgesic efficacy between PCEA with a background infusion and nurse-administered epidural infusion, on a general surgical ward in our institution, using the standard epidural infusion mixture adopted by our Acute Pain Service (bupivacaine 0.125% and fentanyl 4 $\mu\text{g ml}^{-1}$) and our standard PCEA regimen of a background infusion of 8 ml h^{-1} , a bolus dose of 3 ml, and a lockout period of 20 min. The primary outcome measure was pain scores during the first 72 h after operation, and secondary outcome measures were the administration of epidural top-ups and systemic analgesia during the same period, and finally patient satisfaction scores.

Patients and methods

As the primary aim of this study was to compare overall pain scores, the sample size calculation assumed a comparison of pain scores using the Mann–Whitney *U*-test and was performed using nQuery Advisor[®]. Assuming one treatment has a 60% or greater chance of producing a more favourable outcome, we required 131 subjects in each treatment group to achieve a power of 80%, assuming a conventional 5% (two tailed) significance level. To allow for incomplete data we aimed at recruiting a total of 290 patients. The Local Research Ethics Committee granted approval for this study.

In the absence of contraindications, epidural analgesia is offered routinely in our hospital for colonic resection by laparotomy, and adult patients judged capable of using PCEA effectively were invited to participate in the study. Patients who regularly took any drug with known analgesic effects were excluded. Patients were recruited on the day before surgery and gave written informed consent. They were randomly allocated at enrolment to receive either CEI or PCEA, using a sequential series of sealed envelopes containing computer-generated random assignments.

A thoracic epidural catheter was inserted in accordance with the usual practice of the individual anaesthetist (i.e. no attempt was made to standardize the interspace used). Intraoperative epidural drugs were administered at the discretion of the anaesthetist, the only stipulation being that each patient received a minimum volume of 10 ml of bupivacaine peroperatively.

All epidural infusions were bupivacaine 0.125% with fentanyl 4 $\mu\text{g ml}^{-1}$ and were administered via Graseby 9500 epidural infusion devices configured as PCEA pumps. Continuous epidural infusions were prescribed according to the normal practice of the anaesthetist concerned, usually to a maximum rate of 15 ml h^{-1} , and managed within the prescribed infusion rates by the ward

nurses, in accordance with established Acute Pain Service protocols. The infusion pumps were configured in PCEA mode, but with the bolus dose set to 0.1 ml—the lowest figure allowed by the pump—so as to deliver constant rate infusions with a clinically insignificant bolus dose. Thus, although the ward nursing staff were aware that the patient was in the CEI limb of the study, the patient and the research nurse recording pain scores were not aware of which modality of epidural infusion was received. PCEA was prescribed according to the existing Acute Pain Service protocol of a background infusion of 8 ml h^{-1} , bolus dose of 3 ml, and lockout time of 20 min. Patients were made aware on recruitment that the button may be a dummy and that they should inform the nursing staff if their pain did not improve in response to using it. In response to a complaint of wound pain, the ward staff were trained to assess the extent of epidural block to cold, using ice, and, if the block height was inadequate, to increase the rate of infusion within the prescribed limits. If this did not result in improvement within an hour or the pain was severe, advice was sought from the Acute Pain Service during office hours, or the duty Anaesthetic SpR at other times. They administered an epidural top-up or suggested giving systemic analgesia as appropriate. The number of epidural top-ups and doses of systemic analgesia administered during the study period were recorded, and used as secondary outcome measures. After operation, no regular systemic analgesia was prescribed, as the consumption of such drugs was to be used as an outcome measure: systemic rescue analgesia was prescribed as required, again according to the preference of the anaesthetist.

Postoperative pain was assessed using a four-point verbal rating scale (VRS), which has been used by the Acute Pain Service in Portsmouth for a decade, is in use throughout Wessex, and forms part of the minimum data set developed by the Wessex acute pain group. The scores are 0, 1, 2, 3 for no pain or asleep, mild pain, moderate pain, or severe pain, respectively.

Pain scores were recorded at 1, 2, 3, 4, 8, 12, 24, 48, and 72 h after operation, at rest and on taking a deep breath. Patients who were asleep at any given time point were allocated a score of zero for pain at rest, but no score was recorded for pain on movement, as this could not be tested without waking them up. The number of epidural top-up doses administered during the first 72 h after operation and the use of all systemic analgesic drugs during this period were also recorded. Patients completed questionnaires on their satisfaction with their pain management on the third day after surgery and again on the day of discharge. No attempt was made to record differences in either consumption of epidural analgesic solutions or side-effects.

For pain scores at rest, the mean pain scores for each treatment group were calculated at each time point, and the area under the curve of pain score against time (AUC)

for the first 72 h after operation was computed, using the trapezoidal rule, to provide a single summary measure. Pain scores on movement were recorded only for patients who were awake at any given time point, so the number of scores varies at different times. Most patients were awake at 24, 48 and 72 h, and mean pain scores for these time points are presented. The mean of these three scores was taken to provide a single summary measure.

The four-point VRS scores might be expected to produce non-parametric data, and these data were therefore analysed by Mann–Whitney *U*-test. Chi-square tests were applied to the number of epidural top-ups and consumption of systemic analgesia. The patient satisfaction data were analysed using Fisher’s exact test. All statistical calculations were performed using the Minitab computer package.

Results

A total of 290 patients were recruited into the study between July 2001 and May 2005, of whom 85 were subsequently excluded. The commonest reason for this was that they did not undergo the planned surgery, in most cases this was because of a decision being made subsequent to their recruitment to perform a laparoscopic-assisted procedure in place of the originally planned laparotomy, as a result of the appointment of a laparoscopic surgeon during the study. Of the 290 patients who consented to participate, 205 (101 in the CEI group and

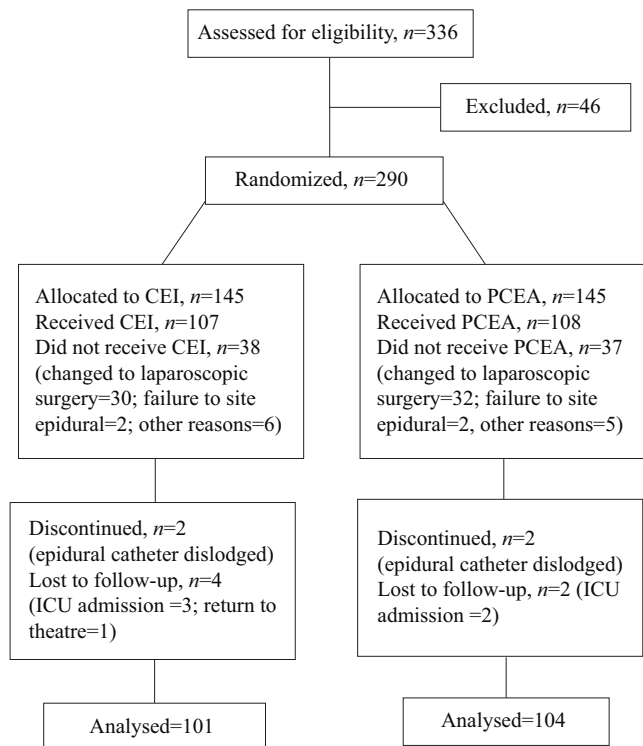


Fig 1 Flow diagram: no. of participants in each stage of the study.

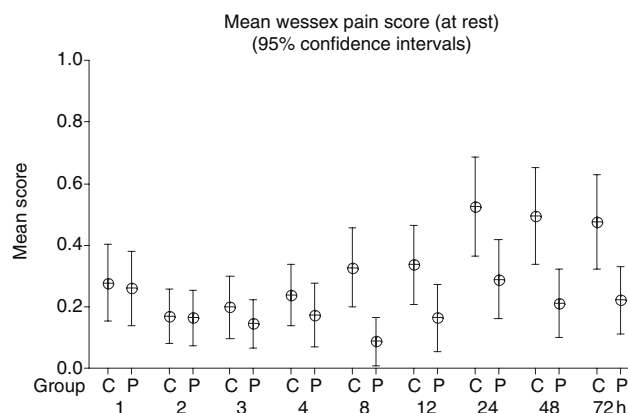


Fig 2 Mean VRS scores at rest by treatment group and assessment time: C, CEI; P, PCEA.

104 in the PCEA group) provided evaluable data. Figure 1 shows a participant flow diagram.

The median age of patients in the CEI group was 68.8 yr (range 21–88 yr) and in the PCEA group 68.4 yr (range 18–82 yr). The male to female ratio was 57:44 in the CEI group and 63:41 in the PCEA group. The two intervention groups were thus similar with regards to both age and gender ratio.

Mean VRS scores at rest for the first 72 h after operation showed little difference between groups in the first 2 h after surgery, but a widening difference over the next 6 h (Fig. 2). Median AUC is 24 (range 0–138.0) in the CEI group and 2 (range 0–120.5) in the PCEA group. The mean (sd) values are 32.2 (34.7) and 15.6 (24.0), respectively ($P<0.001$). Mean VRS scores on movement at 24, 48, and 72 h had data missing for seven patients asleep at 24 h, eight patients asleep at 48 h, and six patients asleep at 72 h (Fig. 3). The scores decrease over time in both groups; the trend is more pronounced in the PCEA group, such that the difference between groups is significant at 48 and 72 h. The mean of these three scores was taken to provide a single summary measure for each patient. The median score for the CEI group is 1.33 (range 0–2.67)

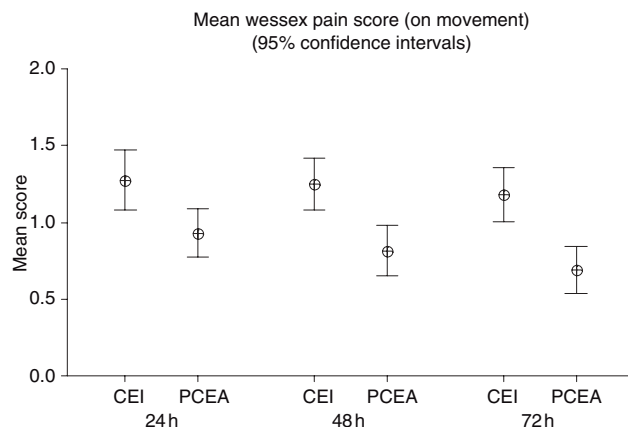


Fig 3 Mean pain scores on movement by treatment group and time.

Table 1 Number of epidural top-ups administered

No. of top-ups	CEI (n=101)	PCEA (n=104)
0	65	90
1	19	8
2	12	3
3	5	1
4	0	2

and for the PCEA group 0.67 (range 0–2.67). The mean (SD) is 1.23 (0.68) and 0.81 (0.62), respectively ($P<0.001$).

The mean (SD) of top-ups per patient in the CEI group was 0.58 (0.89) compared with 0.24 (0.73) in the PCEA group (Table 1). Patients in the CEI group were significantly more likely to require one or more top-ups compared with the PCEA group (relative risk 2.65, $P=0.0002$, 95% CI 1.15–4.61).

The difference between groups in numbers of patients receiving systemic analgesia did not reach significance for any single class of analgesic, but when all systemic analgesics are aggregated, a difference is apparent between groups, with significantly more patients in the CEI group receiving systemic analgesics than in the PCEA group (relative risk 1.5, $P=0.0021$, 95% CI 1.17–2.03) (Table 2).

The degree of satisfaction reported by the patients at 72 h was significantly associated with their treatment ($P=0.0002$) (Table 3). In the PCEA group, 84% patients were very satisfied compared with 57% in the CEI group ($P<0.0001$). The degree of satisfaction reported by the patients at discharge was also significantly associated with their treatment, with 76% in the PCEA group reporting to be very satisfied compared with 43% in the CEI group ($P<0.0001$). Three patients in each group were lost to follow-up at discharge.

Discussion

PCEA has previously been shown to have advantages over CEI in the management of postoperative pain, including lower consumption of local anaesthetic and decreased incidence of motor block,⁴ but has not been demonstrated to provide superior analgesic efficacy. Furthermore, there is little evidence as to whether a background infusion is beneficial. We therefore set out to investigate solely the

Table 2 Consumption of systemic analgesia. *Fisher's exact test

Analgesic	Number (%) of patients receiving analgesic		
	CEI (n=101)	PCEA (n=104)	P-value*
Opioids	6 (5.9)	4 (3.8)	0.5336
NSAIDs	8 (7.9)	6 (5.8)	0.5898
Others	60 (59.4)	41 (39.4)	0.0052
Any	64 (63.4)	43 (41.3)	0.0021

Table 3 Satisfaction at 72 h and on discharge

Satisfaction at 72 h (discharge)	CEI	PCEA	Total
Very satisfied	58 (42)	87 (77)	145 (119)
Satisfied	33 (50)	13 (20)	46 (70)
Dissatisfied	8 (5)	4 (4)	12 (9)
Very dissatisfied	2 (1)	0 (0)	2 (1)
Total	101 (98)	104 (101)	205 (199)

analgesic efficacy of a PCEA regimen including a background infusion, which has been in use for several years by the Portsmouth Acute Pain Service.

The primary outcome measure was a summary pain score. Administration of epidural top-ups, consumption of systemic analgesia, and patient satisfaction scores provided the secondary outcome measures. Overall pain scores in both groups were low, providing further evidence for the efficacy of epidural analgesia for the treatment of postoperative pain. Summary measures of pain at rest and on movement for the first 72 h post-surgery show highly significant differences between groups, with lower pain scores in the PCEA group: the difference increases with time. The secondary outcome measures also show significant differences between groups, with significantly fewer patients in the PCEA group receiving epidural top-ups or systemic analgesia during the first 72 h after operation. Patient satisfaction scores were also higher in the PCEA group.

In the context of relatively low pain scores in both groups, the clinical significance of this difference is not clear. There is currently no evidence as to what constitutes a significant difference in VRS scores in postoperative pain. However, acute pain data from a study of cancer-related breakthrough pain using a 10-point numerical rating scale (NRS) suggest that a reduction in pain scores of 33% represents a clinically important outcome,¹² and Rowbotham¹³ suggests that, for the purposes of clinical trials, a reduction of 30% in NRS represents a clinically meaningful improvement. Caution should be exercised in the application of these criteria to postoperative VRS scores. However, the mean summary pain scores are lower in the PCEA group by more than 50% at rest and more than 33% on movement. These data may therefore be interpreted as suggesting that PCEA offers a clinically significant improvement in analgesic efficacy over epidural infusions controlled by the nursing staff on a general surgical ward. The widening difference in mean VRS scores seen during the first 8 h of the study confirms a clinically observed phenomenon, which the authors attribute to the postoperative recovery of psychomotor function required for effective use of PCEA.

We have confirmed the efficacy of postoperative epidural analgesia and conclude that, on a general surgical ward, PCEA with a background infusion provides greater analgesic efficacy than CEI for postoperative analgesia after major intra-abdominal surgery. We have confirmed the

conclusion of Mann and colleagues¹¹ that PCEA is effective after major abdominal surgery in the elderly. Our findings agree with those of van der Vyver and colleagues⁴ that PCEA decreases the requirement for epidural top-ups, and we have also demonstrated a reduction in the consumption of systemic rescue analgesia, with a consequent reduction in the requirement for intervention by ward nurses, physicians, and the Acute Pain Service. These may be significant advantages on a busy surgical ward.

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