

## *Original Articles*

# The Usefulness of Postoperative Continuous Epidural Morphine in Abdominal Surgery

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**Abstract:** The influence of continuous epidural morphine on the recovery course of intestinal activity, urinary function, and ambulation after surgery was studied in 40 patients who underwent either gastrectomy for gastric cancer or cholecystectomy for cholelithiasis. Compared with a control group of patients whose postoperative pain was managed by pentazocine or hydroxyzine as before, the length of time before passing flatus or faeces was significantly shortened in the morphine groups ( $P < 0.05$ ). Following gastrectomy, the urinary catheter was able to be removed significantly earlier in the morphine group ( $P < 0.05$ ) although there was no statistical difference between both cholecystectomy groups. The morphine group experienced no difficulty with postoperative ambulation and exercise, although the difference in time before ambulation between the two groups was not considered significant. The results of this study led us to conclude that the postoperative continuous epidural infusion of morphine would be more beneficial following major abdominal surgery than the conventionally used methods of administering postoperative analgesia.

**Key Words:** epidural morphine, postoperative, pain relief, gut motility, abdominal surgery

## Introduction

A surgeon should not only be concerned with the progress of a surgical procedure, but also about the control of pain in patients throughout the term of their hospitalization. Since the first report by Behar et al. in 1979,<sup>1</sup> the epidural administration of narcotics, particularly morphine, for pain relief after various kinds of surgery has spread around the world.<sup>2–6</sup> However, although effective analgesia can be achieved, there

exists a risk of possible associated systemic side effects which are life-threatening in some patients.<sup>4,5</sup> To reduce such major systemic side effects, El-Baz et al.<sup>7</sup> reported a technique for the continuous epidural infusion of low dose morphine; but does this procedure always act beneficially throughout the postoperative course? Morphine is a drug known to induce gastrointestinal inhibition when administered systematically,<sup>8</sup> and urinary dysfunction when used intrathecally or epidurally.<sup>6</sup> Thus, there should be some fear of it being a disturbing factor which might induce a risk of such unpleasant postoperative complications as postoperative paralytic ileus due to the inhibition of gastrointestinal motility, urinary infection due to the prolonged presence of a urinary catheter and delayed ambulation due to its sedative effects.

Although many case reports have already been published, most were presented by anesthesiologists discussing subjects related to its analgesic potency and the effects or side effects on major systems such as the respiratory or circulatory systems. We, on the other hand, report our observations on the influence of continuous epidural morphine on the recovery course of intestinal activity, urinary function and ambulation after abdominal surgery which is of greater clinical importance from the viewpoint of surgeons.

## Patients and Methods

From among a number of patients in whom epidural catheters had been inserted and intraoperative anesthesia maintained by an experienced anesthetist, 20 patients who had undergone either gastrectomy for gastric cancer or cholecystectomy for cholelithiasis and received continuous epidural morphine after the operation, were selected randomly as the subjects for this investigation, being the morphine group. Another 20 patients, who had also undergone gastrectomy or

cholecystectomy but who had not been given any kind of drug after surgery through an epidural catheter were selected randomly as the control group. The clinical details of all patients are summarized in Table 1.

An epidural catheter was inserted in all patients preoperatively in order to obtain an epidural anesthesia level from T2-4 to S3-5. In the morphine group, 0.01% morphine-HCL solution was infused continuously at a rate of 2 ml/h by an autoinfusion pump for a period of 48 h, commencing immediately after they arrived in the recovery room. To manage post-operative pain relief, when a patient from either group complained of severe pain, an intramuscular injection of pentazocine or hydroxyzine was offered as often as needed to keep them comfortable during the entire postoperative period. The time when patients indicated they had first passed flatus or faeces, or when bowel sounds were confirmed by auscultation, was recorded as an indicator of the return of propulsive activity in the gastrointestinal tract after surgery, and compared within each group. Similarly, the time of removal of the urinary catheter after certification of sufficient recovery of urinary function was compared as an indicator of the recovery from urinary retention. Finally, the time when the patients began to ambulate freely was compared as an indicator of vivid body movement.

For statistical calculations, the Wilcoxon rank-sum test was used for comparison of the two groups, with  $P < 0.05$  being considered significant.

## Results

Results are expressed as the mean  $\pm$  SEM.

The two groups were comparable with regard to clinical data (Table 1). Following gastrectomy, the total dose of pentazocine and hydroxyzine given within 48 h after surgery were  $51.0 \pm 15.3$  mg and  $75.0 \pm 25.0$  mg, respectively, in the control group, while only three patients in the morphine group required intramuscular injections of 15 mg of pentazocine and 50 mg of hydroxyzine for pain relief. Following cholecystectomy, the total doses of pentazocine and hydroxyzine were  $40.5 \pm 16.5$  mg and  $55.6 \pm 15.7$  mg respectively, while only one patient required 15 mg of pentazocine and 50 mg of hydroxyzine in the morphine group.

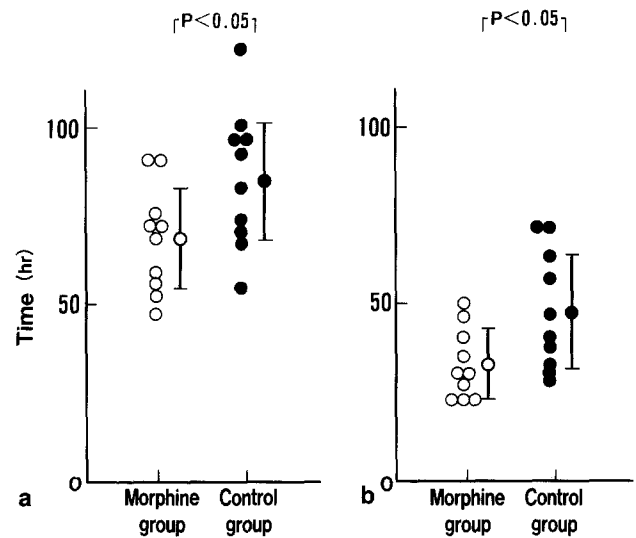
### Effect on Motility of the Intestine

The time before the first passing of flatus or faeces was  $68.1 \pm 13.9$  h in the morphine group following gastrectomy and  $84.3 \pm 16.8$  h in the control group (Fig. 1a). Following cholecystectomy, the time was  $33.5 \pm 9.3$  h in the morphine group and  $48.9 \pm 15.7$  h in the control group (Fig. 1b). The shorter times of the

**Table 1.** Clinical data of the patients

Diagnosis	Morphine group	Control group
Gastric cancer		
Age	$60.5 \pm 14.7$	$60.3 \pm 10.5$
M/F	3/7	2/8
Operation		
TG + Ly	3	2
SG + Ly	7	8
Duration of surgery (min)	$196 \pm 47.2$	$186.7 \pm 53.3$
Total blood loss (ml)	$820 \pm 330$	$808 \pm 654$
Cholelithiasis		
Age	$58.0 \pm 9.2$	$51.3 \pm 13.7$
M/F	4/6	3/7
Operation		
Ch	7	8
Ch + T	3	2
Duration of surgery (min)	$80 \pm 38.7$	$83.9 \pm 24.7$
Total blood loss (ml)	$182 \pm 150$	$196 \pm 141$

TG, total gastrectomy; Ly, lymphnode dissection; SG, subtotal gastrectomy; Ch, cholecystectomy; T, T-tube drainage

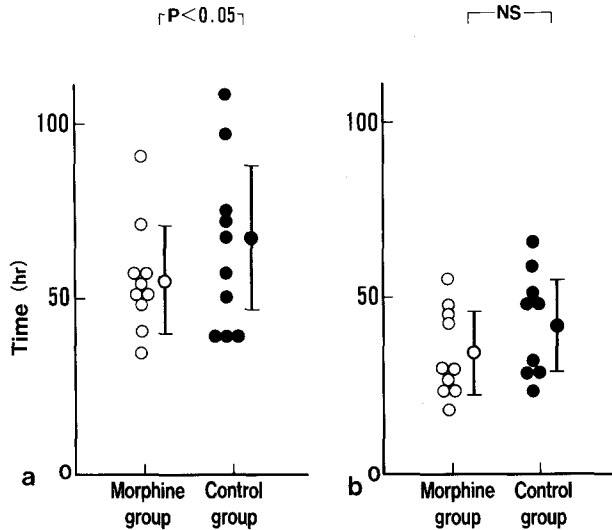


**Fig. 1a,b.** The time taken before flatus or faeces were passed postoperatively. **a**  $Wt = 79.5$ ,  $P(Wt < 79.5) = 0.0315$ . **b**  $Wt = 75.0$ ,  $P(Wt < 75.0) = 0.0116$ . Significant differences were observed between the 2 groups ( $P < 0.05$ ) as determined by the Wilcoxon rank-sum test

morphine groups were statistically significant ( $P < 0.05$ ).

### Effects on Urinary Function

Following gastrectomy, the detention period of the urinary catheter was  $50.0 \pm 13.0$  h in the morphine group and  $70.6 \pm 28.6$  h in the control group (Fig. 2a), while following cholecystectomy, it was  $33.0 \pm 11.7$  h and  $36.8 \pm 10.9$  h, respectively (Fig. 2b). Following



**Fig. 2a,b.** The time to removal of the urinary catheter. **a** Wt = 77.5,  $P(Wt < 77.5) = 0.0216 (<0.05)$ . **b** Wt = 94.5,  $P(Wt < 94.5) = 0.2406 (>0.05)$ . NS, not significant

gastrectomy, the shorter time of the morphine group was considered statistically significant at  $P < 0.05$ , although there was no statistical difference between the groups following cholecystectomy.

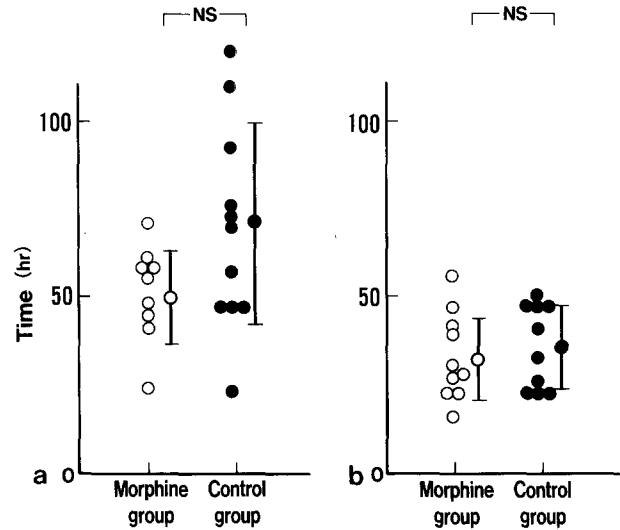
#### Effects on Ambulation

Following gastrectomy, the time taken to ambulate freely was  $54.0 \pm 14.9$  h in the morphine group and  $66.6 \pm 20.2$  h in the control group (Fig. 3a), while following cholecystectomy, it was  $34.7 \pm 11.2$  h and  $41.3 \pm 13.5$  h, respectively (Fig. 3b). Statistically, the difference between the groups was not considered significant ( $P > 0.05$ ).

All patients in the present study underwent an elective procedure. In the morphine group, two patients complained of systemic pruritus, but it was mild enough to permit continuation of the epidural infusion of morphine. Depression of the ST wave in an ECG was observed in one of the patients, but this did not require any treatment except for the inhalation of oxygen. No patient in either group showed any other clinical side effect.

#### Discussion

The discovery of opiate receptors in the spinal cord,<sup>9</sup> as well as in the brain,<sup>10</sup> has led to the use of intrathecal or epidural opiates in the management of acute or chronic pain. Following the epidural injection, the opiate binds directly to nociceptive receptors in the posterior spinal gray matter by penetrating the dura or sinking into the



**Fig. 3a,b.** The time taken for patients to be able to ambulate freely. **a** Wt = 89.5,  $P(Wt < 89.5) = 0.1399$ . **b** Wt = 88.0,  $P(Wt < 88.0) = 0.1088$ . There was no difference between the 2 groups statistically ( $P > 0.05$ ).

spinal radicular arteries which supply the dorsal horn region of the spinal cord, thereby inhibiting the pain pathways selectively without interference to the sensory or motor functions of the spinal cord and nerves.<sup>11</sup> Thus, touch and proprioception are not impaired and patients can ambulate normally, whereas the epidural administration of local anesthetics such as lidocaine increase the total spinal blockade. On the other hand, a portion of the epidural opiate spreads rostrally to the brain stem carried by the spinal CSF flow. Thus, a large dose of an opiate is thought to cause respiratory depression, life threatening central depression of consciousness, urinary dysfunction, and systemic pruritus.<sup>11</sup>

To avoid these effects, El-Baz et al.<sup>7</sup> reported a technique of administering the continuous low-dose epidural infusion of morphine. Excellent analgesia was noted in the patients with a low incidence of systemic side effects. From our bedside observation of the continuous low-dose epidural infusion of morphine, the patients had an undistressed look on their faces and seldom required another anodyne. In the most effective case, the patient could comfortably read in a sitting position on the night of their operation. Furthermore, our study showed that the postoperative continuous epidural infusion of morphine allowed early restoration of normal gut motility and urination, and easier ambulation which is beneficial following major abdominal surgery.

Following laparotomy, gut peristalsis becomes diminished, which may lead to paralysis, the magnitude and duration of which is directly proportional to the

invasiveness of the surgical procedure.<sup>12</sup> Although there are conflicting opinions on the mechanism of gastrointestinal paralysis after surgery, it has been believed for many years that this inhibition of motility is partially due to the activation of spinal reflexes which involve sympathetic efferent nerves to the gut elicited by operative intervention or direct damage to the serosal surface.<sup>13</sup>

There are several possibilities to explain the early restoration of normal gut motility caused by epidural morphine. Firstly, it could be due to the relative predominance of parasympathetic nerves caused by a blocking of sympathetic efferent nerves. Greene<sup>14</sup> and Aitkenhead et al.<sup>15</sup> suggested that a subarachnoid or extradural spinal block might produce sympathetic denervation of the small and large bowel, thereby increasing the propulsive force of peristalsis and tone of the bowel wall. Johansson et al.<sup>16</sup> reported that epidural anesthesia increased intestinal microcirculation due to a decreased mesenteric vascular resistance secondary to a sympathetic nerve blockade, which restored bowel function, while Breslow et al.<sup>17</sup> reported that epidural morphine appeared to attenuate increased postoperative sympathetic nervous system activity and decrease the incidence of postoperative hypertension. Ahn et al.<sup>18</sup> reported that postoperative epidural bupivacaine shortened the duration of intestinal paralysis, although they reported that epidural morphine did not shorten the transit time of barium through the intestinal tract. On the other hand, Wallin et al.<sup>19</sup> asserted that continuous epidural anesthesia did not prevent postoperative paralytic ileus and suggested that a mechanism other than one involving spinal reflexes plays a major part in the development and maintenance of intestinal paralysis. They used bupivacaine for epidural anesthesia during the first 24 h postoperatively, and studied the transit time in the colon with radio-opaque markers. In our opinion, there may be a refractory period within the first 24 h until the restoration of intestinal motility, because the intestine should restore its normal motility around 48 h after the operation. In their study, the transit time of the marker from ileum to cecum was in fact far beyond 24 h after surgery, which poses an objection that the first passing of flatus or faeces is not a valid indicator of measuring bowel motility. A surgeon, however, usually decides the timing of enteral or oral nutrition according to this sign, which suffices as a clinical indicator. Secondly, it could be due to pentazocine, which was administered in a large quantity in the control group, and is known to prevent normal gut motility.<sup>20</sup> Thirdly, easy exercise caused by epidural morphine is good for the early restoration of gut motility.

Many reports have mentioned urinary dysfunction as the major problem of epidural morphine.<sup>5</sup> Bromage

et al.<sup>6</sup> described that it was related to a partial loss of bladder sensation caused by the cephalad spread of morphine to partial deafferentation when used in large quantities. Chrubasik et al.<sup>21</sup> studied the continuous-plus-on-demand epidural infusion of morphine for postoperative pain relief in 50 patients, and reported that although 9 complained of urinary retention, none required catheterization. Torda et al.<sup>22</sup> reported that the extradural injection of morphine caused difficulty in micturition, although following i.m. administration, no urogenital side effects were noted. He mentioned, however, that this autonomic disturbance, which is probably caused by parasympathetic inhibition, is transient and self-limiting in duration despite the continuation of extradural analgesia. We observed a significant shortening of the detention period of the urinary catheter in the gastrectomy group patients compared with the control group patients ( $P < 0.05$ ). Although the mechanism of urinary dysfunction after laparotomy is not clear, pain-relief by epidural morphine in the positioning for urination should be linked to the early removal of a urinary catheter. Thus, there should be little possibility of epidural morphine causing any trouble in the removal of a urinary catheter after major abdominal surgery.

The results of our study showed that there was no significant difference between the two groups with respect to the time taken to ambulate after the operation. Many authors have reported that the epidural administration of opiates relieved postoperative pain and permitted early ambulation.<sup>22</sup> There could be various policies as to ambulation in accordance with the respective system, but in our hospital, ambulation proceeds according to the appropriate protocol with the management of drains and nasogastric tubes, or the prevention of such complications such as respiratory failure. Thus, some artificial elements would be contained in this study, although there was a marked difference in the quality of pain relief between the two groups.

There is nothing to prove that epidural morphine directly improves intestinal activity or urinary function after abdominal surgery. However, although insufficient numbers were used in this study to reach a definite conclusion, we believe that the postoperative continuous epidural infusion of morphine would be more beneficial following major abdominal surgery than past methods which need anodynes such as pentazocine.

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## References

1. Behar M, Olshwang D, Magora F, Davidson JT (1979) Epidural morphine in treatment of pain. *Lancet* 1:527-9
2. Reiz S, Ahlin J, Ahrenfeldt B, Andersson M, Andersson S (1981) Epidural morphine for postoperative pain relief. *Acta Anaesthesiol Scand* 25:111-4
3. Martin R, Salbaing J, Blaise G, Tetrault JP, Tetreault L (1982) Epidural morphine for postoperative pain relief: A dose-response curve. *Anesthesiology* 56:423-6
4. Gustafsson LL, Schildt B, Jacobsen K (1982) Adverse effects of extradural and intrathecal opiates: Report of a nationwide survey in Sweden. *Br J Anaesth* 54:479-86
5. Rawal N, Wattwil M (1984) Respiratory depression after epidural morphine — An experimental and clinical study. *Anesth Analg* 63:8-14
6. Bromage PR, Camporesi EM, Durant PAC, Nielsen CH (1982) Nonrespiratory side effects of epidural morphine. *Anesth Analg* 61:490-5
7. El-Baz NMI, Faber LP, Jendik RJ (1984) Continuous epidural infusion of morphine for treatment of pain after thoracic surgery. *Anesth Analg* 63:757-64
8. Todd JG, Nimmo WS (1983) Effect of premedication on drug absorption and gastric emptying. *Br J Anaesth* 55:1189-93
9. LaMotte C, Pert CB, Snyder SH (1976) Opiate receptor binding in primate spinal cord: Distribution and changes after dorsal root section. *Brain Res* 112:407-12
10. Pert CB, Kuhar MJ, Snyder SH (1976) Opiate receptor: Autoradiographic localization in rat brain. *Proc Natl Acad Sci USA* 73:3729-33
11. Cousins MJ, Mather LE (1984) Intrathecal and epidural administration of opioids. *Anesthesiology* 61:276-310
12. Wilson JP (1975) Postoperative motility of the large intestine in man. *Gut* 16:689-92
13. Dubois A, Kopin IJ, Pettigrew KD, Jacobowitz DM (1974) Chemical and histochemical studies of postoperative sympathetic activity in the digestive tract in rats. *Gastroenterology* 66:403-7
14. Greene NM (1969) *Physiology of spinal anesthesia*, 2nd edn. Williams and Wilkins, Baltimore, p 219
15. Aitkenhead AR, Wishart HY, Brow DAP (1978) High spinal nerve block for large bowel anastomosis. *Br J Anaesth* 50:177-83
16. Johansson K, Ahn H, Lindhagen J, Tryselius U (1982) Effect of epidural anaesthesia on intestinal blood flow. *Br J Surg* 75:73-6
17. Breslow MJ, Jordan DA, Christopherson R (1989) Epidural morphine decreases postoperative hypertension by attenuating sympathetic nervous system hyperactivity. *JAMA* 261:3577-81
18. Ahn H, Brouget A, Johansson K, Ygge H, Lindhagen J (1988) Effect of continuous postoperative epidural analgesia on intestinal motility. *Br J Surg* 75:1176-78
19. Wallin G, Cassuto J, Hogstrom S, Rimback G, Faxen A, Tolleson PO (1967) Failure of epidural anesthesia to prevent postoperative paralytic ileus. *Anesthesiology* 65:292-7
20. Danhof IE (1967) Pentazocine effects on gastrointestinal motor functions in man. *Am J Gastroenterol* 48:295-310
21. Chrubasik J, Wiemers K (1985) Continuous-plus-on-demand epidural infusion of morphine for postoperative pain relief by means of a small, externally worn infusion device. *Anesthesiology* 62:263-67
22. Torda TA, Pybus DA, Liberman H, Clark M, Crawford M (1980) Experimental comparison of extradural and i.m. morphine. *Br J Anaesth* 52:939-43