CONTINUOUS THORACIC EXTRADURAL 0.5 % BUPIVACAINE WITH OR WITHOUT MORPHINE: EFFECT ON QUALITY OF BLOCKADE, LUNG FUNCTION AND THE SURGICAL STRESS RESPONSE

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The quality of blockade of afferent sensory neurones by local anaesthesia alone and consequent reduction in the surgical stress response is excellent for lower abdominal procedures, but poor for upper abdominal procedures [1–3].

It has been shown that the addition of morphine to a continuous lumbar extradural local anaesthetic infusion prevents the development of acute tolerance or tachyphylaxis [4,5]. This phenomenon occurs also with thoracic extradural anaesthesia, but it is not known if the combination of local anaesthetic and morphine prevents tachyphylaxis during segmental analgesia. By combining morphine with bupivacaine it may be possible to enhance the block and further reduce the stress response.

It is also not known if this combined infusion has a greater beneficial effect on postoperative pulmonary dysfunction than that produced by extradural local anaesthetics alone.

The purpose of this study was to compare the effect of combined thoracic extradural 0.5 % bupivacaine and morphine 5 mg h\(^{-1}\) with thoracic extradural 0.5 % bupivacaine alone on pain, pulmonary function, the stress response and regression of analgesia.

PATIENTS AND METHODS

Twenty patients about to undergo upper abdominal surgery gave informed consent to the study, which was approved by the local Ethics Committee. The patients were randomly allocated to one of two extradural regimens. The extradural infusions were prepared by independent members of the medical or nursing staff and the contents were unknown to the investigators or patients until the study was completed.

Anaesthesia comprised premedication with diazepam 0.2 mg kg\(^{-1}\) by mouth 1 h before operation and induction with thiopentone 2–5 mg kg\(^{-1}\) followed by suxamethonium 1.5 mg kg\(^{-1}\) after precurarization with pancuronium 1 mg. Anaesthesia was maintained using 66 % nitrous oxide and 0.5–1 % halothane in oxygen with pancuronium as required. Before induction of anaesthesia an extradural catheter (Portex) was introduced into the T7–T8 intervertebral space and a test dose of 0.5 % bupivacaine 2 ml was given, followed by 0.5 % bupivacaine 7 ml. Thirty minutes later, a “blind” bolus of saline 4 ml (group B) or morphine 4 ml (4 mg) (group

SUMMARY

Twenty-two patients undergoing upper abdominal surgery were entered into a randomized, double-blind study to receive extradural (T7–T8) 0.5% bupivacaine 9 ml followed by 25 mg h\(^{-1}\) with or without additional extradural morphine (bolus 4 mg plus 0.5 mg h\(^{-1}\)), for 16 h after operation. Addition of morphine was associated with total alleviation of pain, and a stable level of sensory analgesia, but not with changes in blood glucose and cortisol concentrations or postoperative impairment of lung function (PEFR, FEV\(_1\), FVC). Two patients were withdrawn because of hypotension or respiratory depression.
B + M) was given extradurally. The patients then received 0.5% bupivacaine (group B) or 0.5% bupivacaine 25 mg h⁻¹ plus morphine 0.5 mg h⁻¹ (group B + M), to a total volume of 6 ml h⁻¹. Patients with endocrine disease were excluded from the study and the use of carbohydrate infusions was avoided during the period of investigation.

The operations in group B were three cholecystectomy, one choledocholithotomy, two explorative laparotomy, one splenectomy, one partial gastrectomy, one Roux-Y cholecodoenterostomy and one duodenoplasty. In group B + M there were two cholecystectomy, one partial gastrectomy, one gastroentero-anastomosis, three explorative laparotomy, one cystogastrostomy, one jejunal resection and one right hemicolectomy.

**Measurements**

On the day before operation, pulmonary function was assessed by measurement of forced vital capacity (FVC) and forced expiratory volume in the first 1 s (FEV₁) using a Vitalograph. Peak expiratory flow rate (PEFR) was measured using a mini Wright's respirometer. The intra-individual coefficient of variation was less than 10% (unpublished). On the day of surgery, baseline serum glucose and cortisol concentration were measured and the patient instructed on the 5-point scale of pain assessment (0 = no pain; 1 = slight; 2 = moderate; 3 = severe; 4 = unbearable pain). Every 2 h throughout the study period, these variables were measured, together with the dermatomal level of the extradural block, using sensation of pinprick. Pain was determined at rest. Pulmonary function was assessed every 4 h.

If the pain score increased to more than 2 or anaesthesia to pinprick regressed by five or more spinal segments, the extradural infusion was stopped in that patient and no further measurements were made. Otherwise the infusion was continued for 16 h. Two patients entered into the study had to be withdrawn in the early postoperative period. One had hypotension, the other respiratory depression and both required active treatment (vasopressors and naloxone) which might have influenced the results. The infusion regimen used was unknown to the observers and it was therefore justifiable to replace those subjects by two additional patients, still in a blind manner. Both withdrawn patients had been in the B + M group.

**Statistics**

Data were analysed using Fisher's exact test or Student's $t$ test, as appropriate. $P < 0.05$ was taken as significant.

**RESULTS**

Groups B and B + M were comparable with regard to age (53 (SD) 6 and 63 (5) yr, respectively), sex (M:F, 4:6 and 5:5), body weight (61 (4) and 64 (3) kg) and duration of operation (118 (43) and 167 (26) min). All patients had a sensory level of analgesia from at least T4 to T10. Both regimens provided excellent analgesia with low pain scores and stable sensory analgesia to pinprick in the initial postoperative period (fig. 1). However, with the bupivacaine infusion only four patients remained pain free and with a stable block for the entire study period, compared with all 10 patients who received the bupivacaine and morphine infusion ($P < 0.05$).

Both groups were free from lower limb paralysis after initial recovery from general anaesthesia. There was an increase in plasma concentrations of cortisol and glucose in the postoperative period, but no significant difference between the two

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**Fig. 1.** Pain scores and level of sensory analgesia in patients receiving extradural bupivacaine ($n = 10$) (---) or extradural bupivacaine plus morphine ($n = 10$) (—) during upper abdominal surgery.
groups (fig. 2). PEFR, FVC and FEV₁ were all reduced ($P < 0.05$) by 40–50% throughout the study (fig. 3), but there was no significant difference between the two groups.

DISCUSSION

Our data demonstrate that the use of a continuous infusion of bupivacaine at a constant rate provides excellent analgesia. However, there was a considerable attenuation of effect with time. In only four of 10 patients did analgesia last 16 h. When morphine was added to the infusion, analgesia continued for at least 16 h in all patients in the group.

Previous studies also have demonstrated that morphine enhances and prolongs the block achieved by bupivacaine [4,5], but the mechanism of this effect is unknown. Recent experimental studies have suggested one possible explanation. Injury leads to a state of pain hypersensitivity by decreasing nociceptive thresholds peripherally and in the spinal cord [6] and the spinal dorsal column receptive fields enlarge with time [7]. It seems reasonable to deduce that spinal nerve blockade diminishes with time in the presence of unaltered local anaesthetic doses because of the resulting competitive increase in afferent input. Morphine is known to activate descending inhibitory pathways and is also effective within the dorsal horn. The resulting inhibition of nociceptive transmission may therefore restore and maintain sensory levels of analgesia, as shown in this and our previous study [5].

We failed to demonstrate any significant reduction in the glucose and cortisol responses using extradural analgesia, which is consistent with most other studies on upper abdominal surgery [1]. However, in many of the other studies, details of both the spread and duration of anaesthesia are incomplete, and very few studies document the degree of pain relief by subjective assessment. As pain is believed to contribute to, but not to precipitate, the metabolic response, such details should be documented to allow uniform interpretation of results.

There are two possible explanations of the
failure to block stress responses. First, the anatomy and physiology of intraperitoneal afferent pathways are too diffuse, and afferents in the sympathetic chain synapse throughout its length before passing to the spinal cord [8], allowing stimuli to pass above and below a segmental blockade to the spinal cord. In addition, the relative extent of sympathetic block and somatosensory block during spinal and extradural analgesia with local anaesthetics is controversial [1,9]. Second, our combined regimen may not cause total afferent somatic block. Neither thoracic extradural 0.5% bupivacaine [2] nor extradural morphine [10] provides a total block of fast-conducting nerve fibres, but no studies are available for a combined regimen.

The pathophysiology of postoperative pulmonary dysfunction is complex and multifactorial [11]. The finding that near-total analgesia with extradural morphine has no effect on several tests of pulmonary function after surgery has suggested a mechanism which is not dependent on pain [12,13]. Whilst mechanical factors are clearly important [14], there may also be a neurohumoral component. Thus extradural local anaesthesia significantly improves pulmonary dysfunction [15–18]. However, our study has shown a greater than expected decrease in respiratory variables in the bupivacaine-alone group compared with other studies, and no benefit from total pain relief provided by the combined regimen. It may be that diaphragmatic and intercostal muscle paralysis was greater with the high concentrations we used, although it has been found that a sensory block from T1 to T5 with 0.5% bupivacaine 5 ml in normal individuals had little effect on lung function [19].

Two patients who received morphine extradurally were removed from the study because of hypotension and respiratory depression. We consider that the dose of morphine we used was too great to be recommended treatment. However, a low-dose regimen with approximately 4 ml h⁻¹ of 0.1% bupivacaine and morphine 0.1 mg ml⁻¹ did not provide total pain relief after thoracotomy [20]. Recent studies suggest that a combination of a non-steroid anti-inflammatory agent (indo-methacin) with an intermediate dose regimen of extradural morphine and bupivacaine may be very effective for post-cholecystectomy pain [21].

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