# Epidural Buprenorphine and Bupivacaine in Major Gynaecological Operations

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## Summary

Eight patients underwent major gynaecological operations. Their post-operative analgesia was provided by epidural buprenorphine 0.15 mg and bupivacaine 0.5%. The efficacy and side-effects of this combination were assessed. All patients had satisfactory analgesia ranging in duration from 10 hours to greater than 36 hours after a single dose injection. No significant side-effect was noted.

*Key words:* Epidural, buprenorphine, bupivacaine, post-operative analgesia.

## Introduction

Since Beher *et al*[1] first used morphine epidurally in man, considerable interest has been generated for other opiates as well, in particular, the agonist-antagonists. Buprenorphine is a potent agonist-antagonist which is 20 to 30 times more potent than morphine[2,3]. It also has a long half-life with relatively little side-effects and is, therefore, a logical choice to be used epidurally. Furthermore, it is prepared in a preservative-free solution. It has high lipid solubility and strong affinity for opiate receptors. Also, it has a low abuse potential and therefore it is not a controlled drug which makes its use easier. Buprenorphine is, therefore, a useful analgesic and it is the intention of this study to evaluate its use epidurally in post-operative patients.

## Patients and Methods

A total of 8 consecutive adult gynaecological patients due to undergo laparotomy for removal of uterus or ovary(ies) were selected. Patients selected were from ASA (American Society of Anaesthesiologists) class I or II. The age of the patients ranged from 28 to 64 years with a mean of 45. The weight of the patients ranged from 45 kg to 63 kg with a mean of 53 kg. All patients were informed of the intended procedure and written consent was taken. The hospital ethical committee approval was not sought because similar studies had been done before[2,5,6] and its safety was established. Each patient was specifically told to ask for analgesic post-operatively when they felt that the incision became uncomfortable.

The patients were all premedicated with diazepam 10 mg, 2 hours before the scheduled operation. An epidural catheter 18 gauge was inserted at the lumbar region between the first and second or the second and third lumbar interspace. The catheter was inserted so that only 3 cm to 4 cm of the catheter remained in the epidural space.

Ten to 20 ml of 0.5% plain bupivacaine and 0.15 mg buprenorphine was injected through the epidural catheter after a test dose of 3 ml of the solution. The establishment of analgesia at the site of incision was tested before the commencement of general anaesthesia. The amount of bupivacaine used was titrated according to the response of each individual patient. The patients' blood pressure and electrocardiogram was continuously monitored and when necessary fluid or intravenous ephedrine was given to maintain the blood pressure at a desired level.

The patients were all induced with thiopentone (dose titrated against response), intubated with the aid of non-depolarising muscle relaxant (alcuronium 0.3 mg/kg or vecuronium 0.1 mg/kg); anæsthesia was maintained with nitrous oxide, oxygen and enflurane 0.5% and muscle paralysis was maintained with either alcuronium or vecuronium. No peripheral nerve stimulator was used and a top-up dose of one-fifth the intubating dose of the muscle relaxant used was given whenever the patients showed signs of inadequate muscle relaxation.

All patients were allowed to recover from anaesthesia in the recovery ward. Before discharge to the general ward, each patient was reminded to ask for analgesic when the pain became uncomfortable or when the analgesia became inadequate. The analgesic given was in the form of intramuscular pethidine 1 mg/kg. The general ward nurses were earlier instructed to give the intramuscular pethidine only when the patients requested for it. The time the analgesic was given was noted down.

Respiratory rate of each patient was recorded every 2 hours for 36 hours and when the respiratory rate fell below 10 per minute, the anaesthesist on call was consulted. The occurrence of emesis, pruritus or other side effects was noted. All patients had continuous bladder drainage, therefore urinary difficulty was not assessed. All patients were reviewed after 24, 36 and 48 hours and the time when the intramuscular pethidine was given was noted.

## Results

Eight patients were involved in the study, 4 of whom underwent Wartheim's hysterectomy, 2 of whom underwent laparotomies for debulking of ovarian tumours, 1 who underwent hysterectomy and 1 who underwent total abdominal hysterectomy (Table I).

All patients received between 10 ml to 15 ml of 0.5% bupivacaine and 0.15 mg of buprenorphine (Table II). The duration of adequate analgesia was taken as the time elapsed between injection of buprenorphine and bupivacaine epidurally and the time the patients requested a second dose of analgesic. It ranged between 10 to 36 hours. Patient number 2 actually had analgesia longer than 13 hours because at the thirteenth hour, intramuscular pethidine 50 mg was given by the night nurse without her asking for it. Patient number 3 actually did not require additional analgesic when reviewed at the 36th hour. Subsequent review of the same patient 2 days later showed that this patient did not require any analgesic after the first dose of buprenorphine and bupivacaine.

Ventilatory rates were recorded every 2 hours. None of the patients in the study had a ventilatory rate of less than 10 per minute. Two patients complained of mild nausea (patient numbers 5 and 9) in the recovery room. No patient had any vomiting or pruritus.

**Table I**
**Types of gynaecological operations**

| Operations | No of patients |
|---|---|
| Total abdominal hysterectomy | 1 |
| Extended hysterectomy | 1 |
| Wertheim's hysterectomy | 4 |
| Laparotomy — ovarian tumour | 2 |
| Total | 8 |

## Discussion

Many different methods have been used to measure pain objectively. One of the most commonly used is the linear VISUAL ANALOGUE SCALE (VAS)[4]. Others divide pain simply as 'none', 'mild', 'moderate', 'severe' and 'very severe'. The VAS is attractive in theory but difficult in practice, especially with our Malaysian population. Many patients find it difficult to grasp the principle behind it and therefore a value in VAS is no more sensitive or accurate as simply asking the patient whether the pain is mild, moderate or severe.

In this study, the author decided to let the patients decide their analgesic requirements. Obviously, it is the patients themselves who are the best judge of the adequacy of the analgesia in themselves. When analgesia becomes inadequate, they request for additional doses of analgesic. Therefore, the time between injection of the drug and the subsequent dose represents fairly accurately the duration of clinical effect of epidural buprenorphine.

In the above study, the results confirmed our initial expectation of buprenorphine when used epidurally. The results also correlated fairly well with other studies in Western populations[5,6]. There was a wide interpatient variation in the duration of analgesia. It ranged from 10 hours to greater than 36 hours. This is in keeping with other studies[5,6]. This is hardly surprising, given the strong bond between buprenorphine and its receptors (50 times more than morphine). This prolonged duration of analgesia is advantageous in that a single injection ensures long duration of comfort for patients even after major abdominal operations and obviously makes frequent top-ups unnecessary.

**Table II**
**Types of operations, dosages of buprenorphine and bupivacaine and the duration of analgesia**

| Patient no | Operations | Drugs used | Duration of analgesia |
|---|---|---|---|
| 1 | Wertheim's hysterectomy | 10 ml 0.5% bupivacaine + 0.15 mg buprenorphine | 21 hours |
| 2 | Extended hysterectomy | 15 ml 0.5% bupivacaine +0.15 mg buprenorphine | >13 hours |
| 3 | Wertheim's hysterectomy | 15 ml 0.5% bupivacaine +0.15 mg buprenorphine | >36 hours |
| 4 | Laparotomy ovarian tumour | 15 ml 0.5% bupivacaine +0.15 mg buprenorphine | 12 hours |
| 5 | Laparotomy ovarian tumour | 10 ml 0.5% bupivacaine +0.15 mg buprenorphine | 23 hours |
| 6 | Total abdominal hysterectomy | 20 ml 0.5% bupivacaine +0.15 mg buprenorphine | 10 hours |
| 7 | Wertheim's hysterectomy | 15 ml 0.5% bupivacaine +0.15 mg buprenorphine | 16 hours |
| 8 | Wertheim's hysterectomy | 15 ml 0.5% bupivacaine +0.15 mg buprenorphine | 18 hours |

No systemic side-effects were noted except for mild nausea. The respiratory rates remained normal in all patients. Respiratory depression has been one of the most feared complications of spinal or epidural opiates, ever since Scott and McClure[7] reported their 2 cases of severe respiratory depression with epidural pethidine barely 4 months after Wang *et al*[8] published the use of intrathecal morphine in 1979. The mechanism of respiratory depression is complex. Several subclasses of opioid receptors exist in the spinal cord. Mu receptors mediate analgesia and respiratory depression and kappa receptors mediate analgesia and sedation[9] and there is evidence to show the existence of large numbers of kappa receptors in the spinal cord. Buprenorphine is believed to be a mu receptor antagonist but a potent kappa agonist, hence its lack or respiratory depression effect. Besides, buprenorphine is very lipophilic and lipophilicity is a major determinant of cephalad spread in the cerebrospinal fluid, preventing its action on the respiratory centre.

The method of detecting respiratory depression appeared simplistic. Although Jordan[10] gave an almost exhaustive list of methods of detecting respiratory depression, the author felt that measuring the respiratory rate alone was adequate to detect significant respiratory depression as it is practical without resorting to complicated devices.

In conclusion, epidural buprenorphine at a dose of 0.15 mg in combination with bupivacaine provides good and prolonged pain relief in major abdominal operations. There was no significant side-effect demonstrable in these 8 patients. However, a larger number of patients need to be investigated in order to ascertain its efficacy in our local population.

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