Following completion of the dose-response studies, anesthesia was maintained with isoflurane and it was, therefore, not possible to adequately study recovery from succinylcholine. This is because myasthenic patients are sensitive to the neuromuscular depressant effects of the potent inhaled anesthetics, which cause decreases in T1/ control and T4/T1 ratios, at reduced dosages.10

In summary, we have shown that myasthenic patients are resistant to succinylcholine and that the ED20 and ED95 in these patients are 2.0 and 2.6 times normal, respectively. Because the doses in common clinical use (1.0–1.5 mg/kg) represent three to five times the ED95 in normals, adequate intubating conditions should be achieved in myasthenic patients using these doses. If a rapid sequence tracheal intubation is required, however, our results suggest that a succinylcholine dose of at least 1.5–2.0 mg/kg may be needed to produce rapid onset of excellent intubating conditions. The mechanism whereby patients with myasthenia gravis are resistant to succinylcholine is unknown, although the decreased number of acetylcholine receptors at the motor end plate may serve as a possible explanation.10

REFERENCES


A Blinded Study Using Nalbuphine for Prevention of Pruritus Induced by Epidural Fentanyl

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Epidural fentanyl is frequently used and has been found effective for treatment of postsurgical and labor pain.1

Pruritus, although seemingly trivial, is a common side effect occurring in 13–63% of patients.2 Methods of detection of pruritus have a great bearing on its reported incidence,1 and in our experience most patients admit to some degree of pruritus after effective pain relief from a variety of epidural narcotics.

Treatment of pruritus after intrathecal opiates has generally involved use of antihistamines or naloxone. Antihistamines have been largely ineffective and are reported to cause sedation.1 Naloxone may reverse analgesia and because of its short duration of action has generally re-

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**TABLE 1. Demographics and Operative Characteristics of Saline-treated and Nalbuphine-treated Groups**

<table>
<thead>
<tr>
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<th>Saline-treated Group</th>
<th>Nalbuphine-treated Group</th>
<th>P</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>54.6 ± 6.4</td>
<td>50.5 ± 4.5</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.1 ± 2.3</td>
<td>172.0 ± 2.2</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.2 ± 5.3</td>
<td>75.7 ± 2.7</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index*</td>
<td>27.2 ± 1.6</td>
<td>25.8 ± 1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Length of procedure</td>
<td>29.4 ± 7.5</td>
<td>26.4 ± 4.7</td>
<td>NS</td>
</tr>
<tr>
<td>Number of shocks</td>
<td>1,441.0 ± 356.1</td>
<td>1,550.0 ± 230.1</td>
<td>NS</td>
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</tbody>
</table>

Data are mean ± SEM.

<table>
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<tr>
<th>Weight kg</th>
<th>Height M²</th>
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Required continuous infusion. Nalbuphine is effective in reversing side effects after systemic fentanyl administration, such as respiratory depression, nausea, and vomiting. There are reports regarding nalbuphine’s ability to reverse pruritus after epidural morphine and hydrocortisone. In patients having extracorporeal shock wave lithotripsy (ESWL) with epidural fentanyl analgesia, we have found 2.5 mg of intravenous nalbuphine totally effective in eliminating troublesome pruritus. This project was undertaken to document this favorable clinical impression using a randomized double-blind design comparing subcutaneous injection of nalbuphine 10 mg with placebo.

**METHOD**

The study was carried out on 24 patients scheduled for ESWL. Study protocol was approved by the Human Subjects Review Committee. All patients gave informed consent. In the ESWL suite, an infusion of Ringer’s lactate solution was started through a peripheral intravenous catheter. Peripheral blood pressure and ECG were continuously monitored. An epidural catheter was inserted through a 17-gauge Hustead needle placed at the L1–2 interspace and passed 5–6 cm cephalad. Patients were then placed in the supine position and, after a negative aspiration test for cerebrospinal fluid or blood, 3 mL lidocaine (1.5% solution, with 1:200,000 epinephrine) was injected. Three minutes later, fentanyl 100 μg, mixed with 5 mL normal saline, was administered by the epidural catheter. Patients were then positioned in the frame and ESWL commenced. While in the water bath, patients received midazolam through the intravenous catheter as required for sedation. Additional local anesthetic was also given, if needed, via the epidural catheter and titrated to relieve patient discomfort during ESWL. Before commencement of the study, 24 unmarked envelopes were prepared; 12 contained written orders for administration of nalbuphine, whereas 12 contained orders for saline. After ESWL, patients were transported to the postanesthesia recovery area (PAR), where a nurse randomly selected one of the envelopes and administered either nalbuphine 10 mg (1 ml) or saline (1 ml) subcutaneously with the use of a 25-gauge needle. Neither patient nor investigator was aware of treatment given. Assessment of pruritus, pain, sedation, dysphoria, urinary retention, nausea/vomiting, and respiratory depression took place before injection and subsequently at 15 min, 30 min, and hourly for up to 5 h if symptoms continued. Pruritus and pain were assessed in a similar manner. Each patient was asked to indicate on a 0–10 cm visual analog scale: 1) pruritus (0 = no pruritus, 10 = worst possible pruritus); 2) pain (0 = no pain, 10 = worst possible pain).

Sedation was assessed with the use of a 0–3 scale: 0 = unresponsive, 1 = responds/noxious, 2 = responds/verbal, 3 = awake. Respiratory rate was monitored. Patients were questioned regarding dysphoria, urinary retention, and nausea. Incidence of vomiting was recorded.

Demographic and operative characteristics were compared between groups with the use of unpaired t tests. Time-related change in drug effect was assessed by two-way repeated-measures analysis of variance and Dunnnett’s test. P < 0.05 was considered significant.

**RESULTS**

There was no difference in patient demographics, length of procedure, or number of shock waves between the two groups of patients (Table 1). Two patients, one in each group, were given an additional 5 mL of 1% xylocaine during stone disintegration because of discomfort. Pruritus scores were not different during initial evaluation in the PAR.

All patients in the saline-treated group experienced some degree of pruritus after injection. After a slight decrease in pruritus with injection of placebo, pruritus remained largely unchanged between 1 and 2 h after operation. Pruritus scores were significantly less in patients in the nalbuphine-treated group after injection (Fig. 1).

**FIG. 1. Assessment of pruritus by visual analog scoring. Mean values ± SEM. *P < 0.05 denotes values significantly different from pre-injection.**
At the fourth postoperative hour, pruritus was undetectable in patients in both saline-treated and nalbuphine-treated groups. In both groups of patients, pain scores were zero until the fourth postoperative hour, when four patients (two in each group) experienced renal colic. Patients in both groups were judged to be “awake” (i.e., 3 on the 0–3 scale used for sedation assessment) at all observation periods. No patient became dysphoric. Only one patient in the saline-treated group, an 84-year-old man with prostatism, had urinary retention. Two patients in the control group complained of nausea. Clinically significant respiratory depression was not seen in either group of patients.

**DISCUSSION**

After epidural fentanyl, the incidence of pruritus in our control group of patients was 100%. This is not surprising in view of our direct questioning and use of a scale providing opportunity to grade even the mildest subjective experience of pruritus. Use of a visual analog scale to assess pruritus contrasts with assessment of pruritus by Shipston, who used a simpler three-level scale. The visual analog scale detected a high incidence of pruritus of mild intensity. Bias introduced using this scale would be true of both saline-treated and nalbuphine-treated groups.

Results of this study are limited to a specific group of patients with no continuing postsurgical pain other than renal colic. Pruritus was overall regarded as mild, as judged by the highest mean score of 2.7 in controls, although in some patients it remained a significant and troublesome complaint. This is consistent with work done by Bromage et al., who reported pruritus, after epidural morphine, that was occasionally severe, in nine of 10 healthy volunteers who had not had surgery.

Naulity et al. have shown that analgesia from epidural fentanyl 100 μg diminishes after 200–300 min. Our data suggest that pruritus diminishes after 180 min and is absent after 300 min following epidural fentanyl 100 μg. Other reported complications of epidural opiates, such as nausea, sedation, dysphoria, or clinically significant respiratory depression, were absent in both groups.

In this study, we chose a subcutaneous rather than intramuscular injection of nalbuphine because of the likelihood of a more prolonged duration of action and decreased pain and hematoma associated with a 25-gauge needle. Also, we wanted a relatively painless route of administration that could be used on the ward on a time-contingent basis to counter pruritus associated with longer-acting opiates.

An additional potential benefit from nalbuphine is that it might also be effective in preventing the late respiratory depression associated with epidural morphine. In the study of Doran et al., clinical respiratory depression was produced by a large dose (0.15 mg/kg) of epidural morphine; significant reduction in an already elevated Paco2 was achieved with an intravenous loading dose of 0.2 mg/kg and an infusion of 0.05 mg·kg⁻¹·h⁻¹ of nalbuphine; 0.1 mg/kg and 0.025 mg·kg⁻¹·h⁻¹ produced a less significant decrease in Paco2.

An important practical consideration in the management of patients with epidural opiates is breakthrough pain that commonly occurs as the effect of epidural opiates is wearing off. There is a natural reluctance to use pure agonist narcotics because of possible compounding effects increasing the likelihood of respiratory depression. Breakthrough pain may be treated safely with additional nalbuphine injections as required.

In summary, nalbuphine 10 mg subcutaneously resulted in significantly less intense pruritus after epidural fentanyl. The relief was evident within 15 min, and pruritus did not recur.

**REFERENCES**