The short duration of effective analgesia produced by intrathecal fentanyl (ITF) at doses ranging from 5 to 25 μg limits the drug's use for the management of labor pain. The understanding of the potential of ITF related to duration of analgesia in the labor patient is derived from studies of and clinical experience with ITF at doses not exceeding 25 μg and less.

We hypothesized that by increasing the dose beyond 25 μg, a prolonged duration of analgesia could be achieved. The purpose of the present study was to compare the difference in duration of effective analgesia and adverse effects produced by 25, 37.5, and 50 μg of ITF.

A sample population of 60 term parturient women with uncomplicated singleton pregnancies who were in active labor and requesting pain control were randomly assigned to 1 of 3 groups: group 1, 25 μg (n = 20); group 2, 37.5 μg (n = 20); and group 3, 50 μg (n = 20). The ITF was then administered by an anesthesia provider blinded to the dose via a combined spinal epidural technique. The time from injection to the time of request for subsequent pain control (considered the duration of effective analgesia), maternal and fetal vital signs, and adverse effects were recorded at specific intervals until the patient requested activation of the epidural catheter or delivery occurred, ending participation in the study.

Statistical analysis using a 1-way analysis of variance and considering a P value of <.05 to be significant revealed no difference in duration of effective analgesia between the groups. Statistical differences in the incidence of adverse effects, particularly uterine hyperstimulation, hypotension, pruritus, nausea, and fetal heart rate decelerations were not evident using the Fisher Irwin test and a significance of P <.05.

The findings of the present study demonstrate that there is no real advantage of using doses of ITF greater than 25 μg in quality and duration of effective labor analgesia.

Key words: Fentanyl, intraspinal narcotics, intrathecal narcotics, labor analgesia, obstetrical analgesia.

Introduction

Intrathecal fentanyl (ITF) in doses of 25 μg and less has been shown to be inadequate for providing effective analgesia required for the duration of labor. Accordingly, a combined technique using lipophilic/hydrophilic opioids and low-concentration local anesthetics may have a greater potential for producing suboptimal conditions inconsistent with effective safe labor. Suboptimal conditions seen more often with the other lipophilic agents, such as meperidine and sufentanil, local anesthetics, and combined morphine solu-
tions, include unwanted motor blockage, maternal hypotension, nausea and vomiting, pruritus, and potential respiratory depression.2,4,5

Studies that have defined dosage recommendations for ITF in the parturient population examined the drug’s effect within very narrow ranges, and none exceeded a ceiling dose of 25 μg.2,5-7 Van Decar et al, in a pilot study of ITF doses ranging from 5 to 25 μg, suggested that effective analgesia could be achieved in 50% of parturients by using 10 μg of ITF for management of labor pain (ED90) and that effective analgesia could be achieved in 95% of parturients by using 15 μg (ED95).7

The duration of action for ITF as determined by the outcomes of the aforementioned studies is considered to be between 0.75 and 1.5 hours. This range is consistent with information given in obstetrical anesthesia texts and with what is seen clinically when ITF is used alone.1,8-10

It is difficult to dispute the accuracy of the studies indicating a range for the duration of analgesia provided by ITF, especially since the clinical experience with the drug also is supportive. However, considering the drug’s pharmacokinetics within the intrathecal space and results of studies in which the ceiling dose of 25 μg was exceeded demonstrating longer durations of action, there is sufficient evidence to suggest that a gap exists in our understanding of the drug’s potential.11-13

Based on the pharmacokinetics of lipophilic opiates in the subarachnoid space, increased concentration of the drug in the cerebrospinal fluid (CSF) would be expected to increase the duration of action and level of analgesia. Cousins et al14 and Chaney15 report that increases in the dose of lipophilic drugs should increase the duration and effect of analgesia. The notion of increasing the duration is supported by the pharmacokinetics that suggest an increase in CSF concentration would permit prolonged equilibrium between opioid receptors and CSF. A larger concentration gradient may provide the driving force necessary to saturate opioid receptors deeper in the dorsal horn where larger wide dynamic range neurons are thought to be located.16-17 Hays et al, in a study of the dose-response effects of ITF in the laboring parturient, demonstrated a statistically significant increase in duration of analgesia as the dose increased.18 Hays et al examined 24 parturient subjects using a range of 5 to 25 μg of ITF.

A study by Clarke et al observed fetal bradycardia in 9 of 30 subjects who received 50 μg of ITF for labor analgesia.19 The authors theorized that fetal bradycardia may have been related to fentanyl-induced uterine hyperactivity. This study, however, is unique, and this effect has not been reported elsewhere. The cause of the fentanyl-induced uterine tetany remains obscure and certainly deserves formal scientific examination.

The understanding of the duration of action of ITF is limited to the dosages studied. By moving beyond the ceiling dose of 25 μg, a considerable increase in the duration of ITF for management of labor pain may be evidenced. Therefore, we hypothesized that a statistically significant difference in the duration of adequate analgesia provided women in active labor who receive 37.5 and 50 μg of ITF compared with those receiving 25 μg of ITF would be evidenced. The purpose of the present study was to compare the duration of analgesia between 25, 37.5, and 50 μg of ITF for the laboring parturient and study the adverse effects and overall safety of ITF at doses greater than 25 μg.

**Methods**

Approval for the study was given by the scientific review board and human subjects committee at the Naval Medical Center, San Diego, Calif. The general approach was to include 60 women who requested labor analgesia in the study, administer 25, 37.5, or 50 μg of ITF, and then assess the differences in duration of effective analgesia and the adverse effects between the groups. Informed consent was obtained from nulliparous and multiparous women with uncomplicated, term, singleton pregnancies who, after being admitted to the labor ward by the attending obstetrician, requested analgesia for labor pain. Women who had received parenteral narcotics and/or presented with preecampia, eclampsia, gestational diabetes, macrosomia, history of a previous cesarean section, chorioamnionitis, or relative and absolute contraindications to regional anesthetic procedures, were excluded from the study.

After requesting labor analgesia, subjects were randomly assigned by random number generator to receive 25, 37.5, or 50 μg of fentanyl via a combined spinal epidural technique. Following randomization to dose category, patients received a 500-mL bolus of lactated Ringer’s solution, were placed in the sitting position, and prepped to undergo combined spinal epidural technique. The anesthesia provider then accessed the epidural space via the L2-L3 or the L3-L4 interspaces using standard techniques and equipment. The subarachnoid space was entered by passing a 24-gauge Sprotte needle through the epidural needle, puncturing the dura. A randomly determined dose of fentanyl was then administered, an epidural catheter was placed, and the patient was positioned for comfort.

The dose to be administered was prepared
using aseptic technique at the time of the procedure by a second anesthesia provider. The administered dose was determined at the time of the procedure via a sealed envelope. This step was to ensure that a provider was aware of the dose given in the event of an adverse reaction. All 3 dosages were mixed with preservative-free normal saline (0.9%) to achieve a consistent volume of 2 mL. Providers performing the procedure were blinded to the dose they were administering.

Assessment of pain level was performed by using a visual analogue pain scale, a 10-cm line with anchors on each end corresponding to “no pain” and “worst pain.” Pain levels were assessed before the procedure and after administration of the fentanyl at 5 minutes and 15 minutes and every 30 minutes until delivery or until the patient requested additional analgesia.

At each time interval, the presence of adverse effects, including nausea, pruritus, hypotension, respiratory depression, uterine tetany, and fetal heart rate decelerations, also was assessed. The attending obstetrician familiar with the study was consulted immediately for the diagnosis and treatment of malignant decelerations and tetanic contractions.

Definitions used for the purposes of this study were:

1. **Respiratory depression** — Oxygen saturation by pulse oximeter of less than 95%.
2. **Hypotension** — Decrease in systolic blood pressure of greater than 20%.
3. **Uterine hyperstimulation** — Uterine contraction lasting longer than 60 seconds without returning to baseline (diagnosis made by attending obstetrician).
4. **Fetal heart rate decelerations** — Heart rate less than 100 beats per minute and any fetal heart rate pattern determined by the obstetrician to be consistent with morbidity.

Following the procedure, an anesthesia provider remained present in the patient’s room for 30 minutes to assess continuously for adverse reactions and effectiveness of analgesia. Treatment for hypotension, fetal bradycardia, uterine tetany, pruritus, or respiratory depression was immediately available. Treatment for uterine tetany and fetal bradycardia included position changes, cessation of oxytocin infusions, administration of fluid boluses, and subcutaneous administration of terbutaline.

When subsequent analgesia was requested by the patient, the existing epidural catheter was tested and activated by using standard techniques. The treatment of the patient was then managed according to existing epidural analgesia protocols.

Data obtained for subjects included maternal age, gravidity and parity, membrane status, height, weight, fetal heart tones, vaginal examination results, monitoring type, augmentation, and whether the patient had received previous epidural or subarachnoid narcotics. Study data included visual analogue scale scores for the aforementioned intervals; time of injection; time of request for additional analgesia; and the presence of pruritus, nausea, respiratory depression, hypotension, hypoxemia, uterine tetany, or threatening fetal heart rate decelerations. The use of the combined spinal epidural technique and the means by which adverse effects and duration of effective analgesia were assessed were consistent with similar studies that have evaluated the use of intrathecal opiates in the laboring parturient.

A power analysis based on similar studies found in the literature with a $P$ value of 5% and a power of 80% indicated that a difference of 25 minutes could be discerned with sample sizes of 20 patients per group. To determine the significance of differences in the duration of analgesia produced by the 3 study dosages, a 1-way analysis of variance was performed. A Fisher Irwin test was used to determine the significant differences in adverse effects produced.

**Results**

Sixty subjects consented to participate. Four patients were excluded due to accidental administration of a dose differing from the group assigned, the administration of a local anesthetic rather than fentanyl, and failure to follow the designated protocol for monitoring and documentation. The exclusion of the 4 patients resulted in the following sample sizes on which statistical analysis were based: group 1, 21; group 2, 18; and group 3, 17.

No significant differences in patient demographics or the obstetrical history were evident in the groups (Table 1). There was no significant difference in the mean effective duration of analgesia in the groups (Table 2). The mean $\pm$ SD duration of effective analgesia was 95.62 $\pm$ 43.3 minutes for group 1, 105.78 $\pm$ 46.8 minutes for group 2, and 99.24 $\pm$ 42.6 minutes for group 3. The mean visual analogue scale score at the time additional pain relief was requested (epidural activation) and the number of patients in each group delivering without the need for additional pain control did not differ (Figures 1 and 2).

Adverse effects noted in the groups were not significantly different (Table 3). The incidence of pruritus among the groups was 100%, with only 1 patient in each group requiring treatment. Five patients from all 3 groups experienced nausea, 1 of...
Table 1. Demographics*

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (y)</th>
<th>Gravida</th>
<th>Parity</th>
<th>Dilation</th>
<th>Oxytocin (%)</th>
<th>Oxytocin (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (25 µg)</td>
<td>24.42 ± 4.2</td>
<td>1.95 ± 0.97</td>
<td>0.48 ± 0.87</td>
<td>4.40 ± 1.4</td>
<td>57</td>
<td>21</td>
</tr>
<tr>
<td>2 (37.5 µg)</td>
<td>24.72 ± 4.2</td>
<td>2.33 ± 1.8</td>
<td>0.72 ± 1.0</td>
<td>4.50 ± 1.3</td>
<td>61</td>
<td>18</td>
</tr>
<tr>
<td>3 (50 µg)</td>
<td>23.51 ± 3.3</td>
<td>1.76 ± 1.3</td>
<td>0.58 ± 0.87</td>
<td>4.70 ± 0.83</td>
<td>70</td>
<td>17</td>
</tr>
</tbody>
</table>

* Data are given as ± SD unless otherwise indicated. $P \geq .05$

Table 2. Mean effective duration of labor analgesia in minutes*

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SD</th>
<th>Minimum duration</th>
<th>Maximum duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (25 µg)</td>
<td>95.62 ± 43.3</td>
<td>19</td>
<td>169</td>
</tr>
<tr>
<td>2 (37.5 µg)</td>
<td>105.78 ± 46.8</td>
<td>26</td>
<td>209</td>
</tr>
<tr>
<td>3 (50 µg)</td>
<td>99.24 ± 42.6</td>
<td>23</td>
<td>180</td>
</tr>
</tbody>
</table>

* $P \geq .05$

Table 3. Adverse effect profile*

<table>
<thead>
<tr>
<th>Group 1 versus 2 and 3</th>
<th>Group 3 versus 1 and 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nausea</strong></td>
<td>.640</td>
</tr>
<tr>
<td><strong>Pruritus</strong></td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Hyperstimulation</strong></td>
<td>.596</td>
</tr>
<tr>
<td><strong>Fetal heart rate deceleration</strong></td>
<td>.579</td>
</tr>
<tr>
<td><strong>Hypotension</strong></td>
<td>.432</td>
</tr>
<tr>
<td><strong>Respiratory depression</strong></td>
<td>None</td>
</tr>
</tbody>
</table>

*The significance of comparisons made between the control group (25 µg) labeled as group 1, and the 2 higher doses studied (37.5 µg and 50 µg), labeled as group 2 and group 3, respectively, in regard to the incidence of adverse effects. The table also demonstrates comparisons made between the highest dose (group 3) and the 2 lower doses (groups 1 and 2). The P values are given to demonstrate their relationship to the level of significance ($P < .05$).

Figure 1. Patients who required no additional pain control

The percentage of subjects in each group who did not require activation of the existing epidural catheter before delivery to manage labor pain. These subjects were satisfied with analgesia produced by intrathecal fentanyl alone. No statistically significant difference existed between the groups. For all data, $P \geq .05$.

Figure 2. Mean visual analogue scale (VAS) scores

The average VAS score given at the time subjects were no longer satisfied with analgesia produced by intrathecal fentanyl and requested activation of epidural catheter. The mean VAS score for each group is given, as well as the SD. No statistically significant difference was evident between the groups. For all data, $P \geq .05$.

whom required treatment. No patients in the present study experienced respiratory depression ($\text{SpO}_2 < 95\%$). One patient in group 1, 3 patients in group 2, and 1 patient in group 3 demonstrated a drop in blood pressure of more than 20% after injection of the drug and required treatment consisting of 5 to 10 mg of ephedrine and repeated fluid boluses. The incidence of uterine hyperstimula-
The percentage of subjects in each group who required treatment for uterine hyperstimulation following administration of intrathecal fentanyl. No statistically significant difference existed between the groups when the incidence of hyperstimulation requiring treatment was compared. For all data, $P \geq .05$.

No difference among the groups and the incidence of fetal heart rate decelerations requiring treatment was evident (Figure 3 and Table 3). Patients in each of the groups receiving oxytocin at the time of ITF injection were compared for the incidence of uterine hyperstimulation and fetal heart rate decelerations with patients not receiving oxytocin. No significant relationship between oxytocin augmentation and these adverse effects was evident.

No difference among the groups and the incidence of fetal heart rate decelerations requiring treatment was evident (Figure 4). All cases of fetal bradycardia with the exception of 1 patient in group 1 were associated with ongoing hyperstimulation and resolved with administration of subcutaneous terbutaline. For the patient in group 1, hyperstimulation was not diagnosed, and treatment consisting of patient position changes, oxygen administration, and increased fluid administration resolved the bradycardia. No patients in the study required cesarean section for delivery.

**Discussion**

We hypothesized that by increasing the dose of ITF, a prolonged duration of analgesia could be achieved, as was evidenced in similar studies.\textsuperscript{11-13} The methods chosen to test the hypotheses were designed to examine the pure effects of ITF without the influences of local anesthetics or other pharmacological analgesics.

The results of the present study revealed that fentanyl doses of 37.5 and 50 $\mu$g provided no increase in duration of effective analgesia. A possible explanation for the lack or increase in effective duration seen with higher doses of fentanyl is the extreme lipophilic nature of the drug and the large number of lipophilic structures that exist beyond the arachnoid membrane. The lipid structures, including blood vessels, white matter surrounding the dorsal horn and non–analgesic-producing opioid receptors, deal with ITF similar to the way in which abundant enzymes in the liver manifest first-order kinetic metabolism. Regardless of the dose administered, the ITF is absorbed into the multiple lipid structures leaving only a fraction of the dose available to analgesia-producing receptors. Rather than equilibrating with CSF and providing for a sustained release of drug from these lipophilic structures as we suspected was the case, the drug most likely is redistributed to the bloodstream and removed from the site of action. There also is a possibility that the pharmacokinetics of fentanyl in the intrathecal space could be like zero-order kinetics.

The inability to increase duration by increasing dose may be due the fact that a dose necessary to saturate lipid structures has not yet been established. The lipophilic nature of fentanyl always has been considered the primary attribute limiting its ability to provide the duration of analgesia seen with hydrophilic morphine.\textsuperscript{4,22} This also is the most likely explanation for the fact that no difference in adverse effects was evident.

Uterine hyperstimulation leading to fetal bradycardia following the administration of 50 $\mu$g ITF to laboring women was described by Clarke et
al, who reported that 9 of 30 subjects (30%) experienced fetal bradycardia within 30 minutes after the administration of ITF. They believed fetal bradycardia was secondary to ITF-induced tetanic contractions. Clarke et al proposed that the rapid profound analgesia created by ITF causes an equally profound decrease in circulating catecholamine, particularly epinephrine. The decrease in circulating epinephrine may be associated with the relaxation of uterine smooth muscle (β-receptors), leaving the uterus vulnerable to unopposed contracting effects of oxytocin, which theoretically could cause a tetanic uterine contraction and associated sequelae, such as fetal bradycardia.

To date, no formal study of the phenomenon described by Clarke et al or others has been conducted. The present study was designed to examine whether the phenomenon of ITF-associated uterine hyperstimulation could be reproduced at lower doses. Our findings suggest that ITF-induced hyperstimulation can occur at doses as low as 25 μg. The uterine hyperstimulation in the present study occurred within 5 to 10 minutes after injection of ITF and led to profound fetal bradycardia, with heart rates falling below 80 beats per minute. The tetanic uterus and associated fetal bradycardia responded in all cases to 1 or 2 subcutaneous injections of 0.25 mg of terbutaline. Conservative measures, including oxygen, fluid bolus, and position changes, also were used. In all cases, the fetal heart rate returned to baseline without complications in variability, following resolution of the tetanic uterine contractions. The mean duration of uterine tetany was approximately 2.5 to 3 minutes.

Clarke et al suggested a possible relationship between oxytocin augmentation at time of ITF injection and the observed phenomenon. We found no difference in the incidence of ITF-induced uterine hyperstimulation between women receiving oxytocin at the time of ITF injection and those not receiving it. Based on the potential for sustained morbidity associated with uterine hyperstimulation when administering ITF, further studies are necessary. These studies should focus on identifying the mechanism for the ITF-induced hyperstimulation and discovering whether the phenomenon is unique to fentanyl.

The findings in the present study suggest that it may be in the best interest of patients when using ITF to educate them about the possibility of ITF-induced hyperstimulation, be able to treat it if it occurs, and use lower, equally efficacious doses of the drug.

REFERENCES


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† At higher dosage range (0.6 mg/kg to 1.2 mg/kg) in most patients who are appropriately premedicated and adequately anesthetized.

‡ ZEMURON® is not recommended for rapid-sequence induction in cesarean section patients.

§ Clinically significant changes in heart rate or blood pressure unlikely; heart rate changes (≥30%) occurred in 0% to 2% of geriatric and other adult patients. Tachycardia (≥30%) occurred in 12 of 127 children. Since ZEMURON® may be associated with increased pulmonary vascular resistance, caution is appropriate in patients with pulmonary hypertension or valvular heart disease.

†† Histamine release unlikely at doses up to 4 x ED₅₀.

† Signs of histamine release were observed in 0.8% of 1137 patients in clinical trials.

** It is strongly recommended that, during long-term use in the ICU, neuromuscular transmission be monitored continuously during administration and recovery with the help of a nerve stimulator. Additional doses of ZEMURON® or any other neuromuscular blocking agent should not be given until there is a definite response (one twitch of the train-of-four) to nerve stimulation. Prolonged paralysis and/or skeletal muscle weakness may be noted during initial attempts to wean from the ventilator patients who have chronically received neuromuscular blocking drugs in the ICU.

†† Since ZEMURON® is primarily excreted by the liver, caution should be taken in patients with clinically significant hepatic disease as prolonged clinical duration can occur.

Please see following page for brief summary of full prescribing information.
Injection
ZEMURON
(rocuronium bromide)

Before prescribing, please consult full prescribing information, a summary of which follows:

INDICATIONS AND USAGE
ZEMURON (rocuronium bromide) Injection is a non-depolarizing neuromuscular blocking agent with a rapid onset and duration of action comparable to that of succinylcholine, and is intended for use in the pre- and postoperative period for surgical or diagnostic procedures requiring skeletal muscle relaxation, to facilitate endotracheal intubation, and to provide skeletal muscle relaxation during general or regional anesthesia.

CONTRAINDICATIONS
ZEMURON (rocuronium bromide) injection is contraindicated in patients known to have hypersensitivity to rocuronium or any of its components.

WARNINGS
Rocuronium bromide (rocuronium bromide) injection should be administered in carefully adjusted dosages by physicians experienced in the use of neuromuscular blocking agents. ZEMURON is associated with the risk of malignant hyperthermia. ZEMURON has not been studied in patients with known susceptibility to malignant hyperthermia.

Pregnancy Category B: A teratogenicity study has been conducted in rats using intravenously administered doses of ZEMURON (rocuronium bromide) injection approximating the clinical dose in humans (0.3 mg/kg). No teratogenic effects were observed in this study. There are no adequate and well-controlled studies in pregnant women. ZEMURON should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

PRECAUTIONS

Long-term Use in I.C.U.: ZEMURON (rocuronium bromide) injection has not been studied for long-term use in the I.C.U. As with other nondepolarizing blocking agents, an occasional patient may develop myalgia or arthralgia after prolonged treatment. The development of these events should be monitored, and the patient should be monitored for the development of myasthenia gravis or other autoimmune neuromuscular conditions. If a patient who has received ZEMURON has developed any of these symptoms, the administration of ZEMURON should be discontinued and evaluated for other causes of the symptom before rechallenge with ZEMURON is attempted.

Possible Induction of Malignant Hyperthermia: ZEMURON has not been studied in patients with known susceptibility to malignant hyperthermia. ROCURON (rocuronium bromide) has been reported to trigger malignant hyperthermia. Due to the limited oral toxicity of the inhibitor of renal blood flow or the volume of distribution of ZEMURON, it is always used with other agents, and the occurrence of malignant hyperthermia is considered uncommon.

The use of ZEMURON should be monitored for the development of any of the symptoms of malignant hyperthermia, including hypertension, tachycardia, and acidosis. If any of these symptoms develop, the infusion should be stopped and a non-depolarizing neuromuscular blocking agent should be administered. Patients with known or suspected susceptibility to malignant hyperthermia should not receive ZEMURON. ZEMURON should be used only by physicians who are experienced in monitoring patients for malignant hyperthermia.

Labor and Delivery: The use of ZEMURON (rocuronium bromide) injection in caesarean section has been studied in a limited number of patients. ZEMURON is not recommended for rapid sequence induction in caesarean section patients (see Clinical Trials subsection). In an aortic clamp study in rabbits, the administration of ZEMURON (rocuronium bromide) injection did not appear to trigger malignant hyperthermia.

Hepatic Disease: Since ZEMURON (rocuronium bromide) injection is primarily excreted by the liver it should be used with caution in patients with clinically significant hepatic disease. ZEMURON (0.6 mg/kg) has been studied in a limited number of patients with impaired hepatic function. After administration of 0.6 mg/kg, the mean (range) clinical duration of 0.05 (0.03–0.16) minutes was moderately prolonged compared to 42 minutes in patients with normal hepatic function. The median recovery time of 53 minutes was also prolonged compared to 20 minutes in patients with normal hepatic function.

In one study, use of enflurane in 10 patients resulted in a 20% increase in mean clinical duration of ZEMURON (rocuronium bromide) injection. In one study, patients with cirrhosis who received ZEMURON (0.6 mg/kg) opioid/nitrous oxide/oxygen anesthesia, did not achieve THR 100% and a 37% increase in the duration of subsequent maintenance doses, when compared to normal hepatic function.

Skin and Appendages: No rash, urticaria, or other skin reactions have been reported.

OVERDOSAGE
In the event of an overdose, supportive care and ventilatory assistance may be necessary. Laboratory tests such as serum creatine kinase and complete blood count should be performed since rhabdomyolysis and hemolytic anemia have been reported with other nondepolarizing neuromuscular blocking agents.

ADDITIONAL INFORMATION
Injection strengths of 5 and 10 mg/ml are available for use.

REFERENCES
2. ZEMURON (rocuronium bromide) Injection prescribing information.