Succinylcholine Pharmacodynamics in Peripartum Patients

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Serum cholinesterase activity decreases 30% during pregnancy and remains depressed during the postpartum period. However, succinylcholine recovery is not prolonged in term-pregnant patients. This contrasts with results obtained in other patients with decreased serum cholinesterase activity. To better understand this paradox, the authors compared serum cholinesterase activity and recovery from succinylcholine, 1 mg/kg, in nonpregnant (with and without oral contraceptives) use, in term-pregnant, and in postpartum patients. Serum cholinesterase activity was lower in both term-pregnant (3.66 ± 0.39 U/ml, X ± SE) and postpartum (2.84 ± 0.35 U/ml) patients than in nonpregnant patients not taking oral contraceptives (5.01 ± 0.33 U/ml, P < 0.05). Cholinesterase activity in postpartum patients also was significantly lower than in nonpregnant patients taking oral contraceptives (4.81 ± 0.63, P < 0.05). In contrast, the time to 25% twitch-height recovery did not differ between term-pregnant (470 ± 56 s) and nonpregnant patients (499 ± 29 s) or not taking (501 ± 21 s) oral contraceptives, but was significantly increased in postpartum patients (685 ± 22 s, P < 0.001). The similar duration of action of succinylcholine in term-pregnant patients (with decreased serum cholinesterase activities) and nonpregnant patients may be related to the increased volume of distribution of succinylcholine at term. (Key words: Anesthesia; obstetric. Neuromuscular relaxants: succinylcholine. Pharmacodynamics: succinylcholine.)

HIGH ESTROGEN LEVELS, such as those observed in term-pregnant patients, are associated with a 20–30% decrease in serum cholinesterase activity.1 Despite this, Blitt was unable to demonstrate prolonged recovery from 40 to 80 mg/M² succinylcholine in cesarean section patients compared with patients undergoing interval laparoscopic tubal ligation.2

In the parturient, the extracellular fluid compartment, into which succinylcholine rapidly distributes,3 comprises a larger fraction of the total body mass than in the nonpregnant or postpartum patient.4 Therefore, if succinylcholine is administered on the basis of body weight, increased dilution of succinylcholine by the parturient's increased extracellular fluid volume could offset her decreased serum cholinesterase activity, explaining Blitt's results. Furthermore, the duration of action of succinylcholine should be prolonged in postpartum patients, whose extracellular fluid volume is returning to normal but whose serum cholinesterase activity remains decreased. To test these hypotheses, we measured the duration of action of succinylcholine in nonpregnant, term-pregnant, and postpartum women.

Methods

Thirty-five consenting patients, ASA I or II, participated in this study, which was approved by our Institutional Review Board. Subjects took nothing by mouth for at least 8 h before the study. We gave cesarean-section patients 30 ml of Bicitra® 5 min before induction of anesthesia; other patients received no premedication. After establishing ECG monitoring and obtaining blood for cholinesterase analysis, we placed a blood pressure cuff and inserted an intravenous catheter on the left arm. We gently abraded the skin, attached surface electrodes over the ulnar nerve at the wrist, and placed the patients' right arms in a specially designed armboard. A Grass® FT-10 force transducer aligned with the axis of adductor pollicis muscle action measured twitch strength, which was recorded by a Gilson® M5P polygraph with a CH-CBPP preamplifier. A preload force of 250 g abducted the patients' thumbs.

We administered glycopyrrolate, 3 μg/kg, and fentany, 2.5 μg/kg iv, while the patients took four deep breaths of oxygen from the anesthesia circuit.5 As the patients lost consciousness after thiopental, 5 mg/kg iv, we applied cricoid pressure, stimulated the ulnar nerve at 1 Hz with a Bard® 750 peripheral nerve stimulator (square wave pulse duration = 0.2 ms), and determined that the stimulation was supramaximal by increasing the current output of the stimulator until the twitch height no longer increased. We injected succinylcholine, 1 mg/kg, directly into the intravenous catheter over 3 s and noted the time of administration on the polygraph record. As the twitch disappeared, we intubated the patients' tracheas and maintained anesthesia with 60% nitrous oxide in oxygen and 1 mg/kg increments of thiopental as needed. We gave no additional relaxant until the twitch

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recovered completely, at which time we verified that the preload force on the thumb had not changed. We then added additional relaxants and inhalational anesthetics as clinically indicated.

We determined serum cholinesterase activities and dibucaine and succinylcholine numbers by the butryrlthiocholine method of Das and Liddell. Normal serum cholinesterase activity in our laboratory is 3.68 ± 1.37 U/ml (X ± SD); serum cholinesterase was considered atypical if both dibucaine and succinylcholine numbers were below 80. An investigator who was unaware of the patients’ pregnancy status measured the time from succinylcholine injection to 25 and 75% recovery of baseline twitch height and calculated the 25–75% twitch-height recovery time. One-way analysis of variance and the protected least-significant-difference test determined the significance of differences in these variables among groups, P < 0.05 indicated significance.

Results

We studied 35 patients: six term-pregnant patients (37–41 wk gestation) undergoing cesarean section, eight patients undergoing tubal ligation 33 ± 5 h (mean ± SE) postpartum, seven women taking oral contraceptives containing 41 ± 4 µg ethinyl estradiol, and 14 nonpregnant women not taking oral contraceptives (controls). One term-pregnant patient was heterozygous for atypical serum cholinesterase; therefore, we excluded her data a priori from analysis. Table 1 summarizes demographic information for the remaining patients. Ages and heights did not differ among the groups studied. The term-pregnant patients weighed significantly more than the control patients (P < 0.05); other differences in weights were insignificant.

Table 2 contains data on twitch-height recovery and serum cholinesterase activity. The time from succinylcholine injection to 25% twitch-height recovery was significantly longer in postpartum patients than in any other group (P < 0.001). This variable did not differ among term-pregnant patients, nonpregnant women taking oral contraceptives, and control patients. Twenty-five to 75% recovery times did not differ among any of the groups studied.

Cholinesterase activities in term-pregnant and postpartum patients were significantly less (P < 0.05) than in control patients. However, there was no significant difference between the serum cholinesterase activities of term-pregnant and postpartum patients.

Discussion

Peripartum patients have delayed gastric emptying. The increased risk of regurgitation and aspiration of gastric contents during induction of general anesthesia in this population can be decreased by rapid sequence induction with cricoid pressure. Succinylcholine has been the most widely used muscle relaxant in this situation, as it rapidly provides good conditions for intubation with minimal adverse fetal effects.

Because of its rapid hydrolysis in normal plasma, no assay is available for plasma succinylcholine. However, Levy developed a model applicable to a drug, like succinylcholine, whose elimination appears to follow first-order kinetics, and for which quantitative pharmacodynamic data (muscle-twitch recovery) are available. In a first-order system, the duration (t) of a given effect of an administered dose of a drug (Ao) depends on the elimination rate constant (k) and the minimum dose capable of causing the effect (Amin) according to the equation:

\[ t = 2.3(\log Ao - \log A_{min})/k \]

We found that the duration of action of succinylcholine 1 mg/kg is prolonged in postpartum as compared with term-pregnant patients. This could be caused by a decrease in either the minimum effective dose (Amin) or the elimination-rate constant (k) for succinylcholine in the postpartum state. However, the elimination-rate constant is unlikely to differ, because we found similar serum cholinesterase activities and 25–75% recovery times in these two patient groups. Therefore, a decrease in the minimum effective dose is more likely to be responsible for the observed difference in succinylcholine’s duration of action between term-pregnant and postpartum patients.

Such a decrease may be related to changes in the volume of distribution of succinylcholine in the postpartum state. Succinylcholine rapidly distributes into the extracellular fluid compartment. Chesley showed that extracellular fluid, as a fraction of body mass, decreases appreciably within the first postpartum week; much of this change occurs at the time of delivery.

### Table 1. Demographic Data for Subjects in Succinylcholine Pharmacodynamics Study

<table>
<thead>
<tr>
<th></th>
<th>Age (yr)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>28 ± 2</td>
<td>163 ± 3</td>
<td>59 ± 2</td>
<td>14</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>24 ± 2</td>
<td>166 ± 2</td>
<td>60 ± 5</td>
<td>7</td>
</tr>
<tr>
<td>Term-pregnant</td>
<td>28 ± 2</td>
<td>160 ± 1</td>
<td>78 ± 4*</td>
<td>5</td>
</tr>
<tr>
<td>Postpartum</td>
<td>29 ± 2</td>
<td>164 ± 1</td>
<td>71 ± 8</td>
<td>8</td>
</tr>
</tbody>
</table>

Values are mean ± SE.

* P < 0.05, compared with controls.

† Excludes one patient heterozygous for atypical cholinesterase.
of succinylcholine at the neuromuscular junction, decreasing the minimum effective dose (in mg/kg) and prolonging the relaxation from a given dose of succinylcholine.

The duration of action of succinylcholine also is longer in postpartum than in nonpregnant women, despite the fact that their extracellular fluid volumes, as a fraction of body mass, are similar.4 This may be related to the decreased serum cholinesterase activity13 and the resulting slower succinylcholine elimination in these patients. Viby-Mogensen found a prolonged duration of action of succinylcholine in other patients with decreased activity of genotypically normal cholinesterase.14

It appears, therefore, that the similarity of the duration of action of succinylcholine in term-pregnant and nonpregnant women probably is related to two offsetting factors: a decrease in the elimination-rate constant secondary to decreased serum cholinesterase activity,15 and an increase in the minimum effective dose related to parturients’ increased extracellular fluid volume. Our findings may help to explain previous reports of prolonged duration of succinylcholine’s action in cesarean section patients.16-18 In most of these cases, patients received appreciably more than 1 mg/kg of succinylcholine. According to the equation, if Ao ≫ Amin, the effect of an increase in Amin becomes negligible compared with the effect of a decrease in k. Therefore, comparable increases in succinylcholine dose should prolong paralysis more in term-pregnant than in nonpregnant patients. The fact that both Blitt and we found no prolongation of succinylcholine’s action in term-pregnant patients is probably related to the fortuitous choice of a relatively low succinylcholine dose.

Ganga et al. also demonstrated that the duration of action of succinylcholine is longer in postpartum than in nonpregnant patients.19 However, their succinylcholine dose, 20 mg, may be inadequate to provide complete relaxation. It is apparent from the equation that, when the administered dose (Ao) approximates the minimum effective dose (Amin), the effect of a small change in either the minimum effective dose or the elimination rate constant may be unduly magnified. Our results confirm that when clinically relevant doses of succinylcholine are administered, paralysis lasts significantly longer in postpartum than in either nonpregnant or term-pregnant women. While a 3-min prolongation of succinylcholine paralysis may be of little significance in most cases, it could be important if airway difficulties occur.

We found that oral contraceptives did not significantly affect serum cholinesterase activity or succinylcholine recovery times. This contrasts with earlier findings of Robertson, who showed a 20% decrease in serum cholinesterase activity accompanying oral contraceptive use. He did not measure succinylcholine recovery times.20 This discrepancy may be related to our patients’ use of oral contraceptives with lower ethinyl estradiol content (41 ± 4 μg) than those used by Robertson’s patients (50–100 μg range, mean not reported).

In summary, we have shown that the duration of action of succinylcholine, 1 mg/kg, is approximately 3 min longer in postpartum patients than in normal controls; this is probably secondary to a decrease in the rate of elimination. On the other hand, the effect of the same succinylcholine dose is not prolonged in term-pregnant patients. In this case, the decreased rate of elimination probably is offset by an increase in the volume of distribution of succinylcholine and the resulting increase in the minimum effective dose of the drug.

References


Table 2. Recovery and Cholinesterase Data for Succinylcholine (1 mg/kg)

<table>
<thead>
<tr>
<th></th>
<th>Injection-25% Recovery Time (s)</th>
<th>25–75% Recovery Time (s)</th>
<th>Cholinesterase Activity (U/ml)</th>
<th>Dibucaine Number</th>
<th>Succinylcholine Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 14)</td>
<td>501 ± 21</td>
<td>102 ± 6</td>
<td>5.01 ± 0.33</td>
<td>82.5 ± 0.4</td>
<td>82.5 ± 0.4</td>
</tr>
<tr>
<td>Oral contraceptives (n = 7)</td>
<td>499 ± 29</td>
<td>104 ± 8</td>
<td>4.81 ± 0.65</td>
<td>80.7 ± 0.8</td>
<td>80.3 ± 1.0</td>
</tr>
<tr>
<td>Term-pregnant (n = 5)</td>
<td>470 ± 56</td>
<td>83 ± 6</td>
<td>3.66 ± 0.39†</td>
<td>82.4 ± 1.0</td>
<td>83.6 ± 1.4</td>
</tr>
<tr>
<td>Postpartum (n = 8)</td>
<td>685 ± 22*</td>
<td>95 ± 11</td>
<td>2.84 ± 0.35‡</td>
<td>82.7 ± 0.9</td>
<td>83.0 ± 0.7</td>
</tr>
</tbody>
</table>

Values are means ± SE.
* P < 0.001, compared with all other groups.
† P < 0.05, compared with controls.
‡ P < 0.05, compared with controls and oral contraceptive patients.


