Adriani and Campbell asserted that local anesthetic absorption through mucous membranes could simulate intravenous administration. However, systemic absorption may be slowed through laryngeal and tracheal mucosa, and lidocaine dissolved in secretions lining the upper airway may impede systemic absorption. Indeed, administration of lidocaine resulted in a peak lidocaine concentration within 1 minute, while laryngotracheal administration was associated with later peaks and lower but more sustained arterial-blood lidocaine concentrations.

Mr. J. B. Keenaghan, Astra Pharmaceutical Products, Inc., Worcester, Massachusetts, and Dr. J. F. Nash and Ms. M. K. Brunson, Eli Lilly and Company, Indianapolis, Indiana, performed the arterial lidocaine analyses.

Use of Succinylcholine in the Presence of Atypical Cholinesterase

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Succinylcholine is a short-acting neuromuscular blocking agent because after injection it is rapidly hydrolyzed in the circulation by plasma cholinesterase. Succinylcholine is usually given in doses of 0.5 to 2 mg per kg body weight so that despite metabolism in the circulation, an adequate concentration of drug is achieved at the motor endplate to produce its effect. Atypical cholinesterase is unable to metabolize succinylcholine rapidly. Therefore, in a patient with the atypical enzyme, doses of the order noted comprise an overdose. This is a report of a patient with atypical cholinesterase who required repeated anesthesias for electroconvulsive therapy (ECT), in whom we were able to observe the responses to graded doses of succinylcholine.

REPORT OF A CASE

An 80-year-old man of physical status 2 with depression resulting in severe anorexia and weight loss required anesthesia for ECT. On the first occasion, after atropine premedication and oxygenation, methohexitol sodium, 50 mg, and succinylcholine, 60 mg, were injected intravenously. Following ECT the patient remained apneic and needed assisted respiration for 2 hours. Blood was drawn for measurement of serum electrolyte concentrations and serum cholinesterase levels and for characterization of the cholinesterase. Serum electrolytes were normal. Before the results of the cholinesterase studies were available, anesthesia was given for a second treatment. On this occasion the dose of succinylcholine was reduced to 40

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mg, but prolonged apnea recurred. Assisted respiration was needed for one hour, and again the patient recovered uneventfully. At this stage the plasma cholinesterase level was reported as 1.0 units and the dibucaine number as 23, i.e., the patient was homozygous for atypical cholinesterase. The unit for cholinesterase level was the number of micromoles of benzoylcholine metabolized per hour per ml of plasma at 30°C. The mean value for the laboratory for patients with atypical cholinesterase was 9 units.

For the third ECT treatment, gallamine (80 mg) was used, but the tonic-clonic seizure of ECT was largely unmodified.

At this stage we decided to administer succinylcholine in small doses under carefully controlled conditions. For the fourth and subsequent ten treatments, a nerve stimulator/muscle twitch recorder system was used to monitor neuromuscular blockade. The “Block-Aid” monitor was used for nerve stimulation with a needle electrode inserted subcutaneously over the ulnar nerve at the wrist and the indifferent electrode subcutaneously in the forearm. The arm was strapped to an armboard so that thumb adduction could be measured by attaching the thumb to a Grass force transducer.

Fig. 1. Log dose–response curve for succinylcholine and decamethonium: ordinates = depression of twitch response as a fraction of control value; abscissae = dose of neuromuscular blocking agent expressed in µg/kg body weight: • values for succinylcholine; ○ values for decamethonium.

Twitch response associated with thumb adduction was recorded on a Grass pen recorder.

Anesthesia was induced with thiopental, 150–175 mg, after the patient was given oxygen by mask. A control twitch response was then obtained. Succinylcholine, diluted in 0.9 per cent sodium chloride to a concentration of 1 mg/ml, was given in initial doses ranging from 0.5 mg to 6 mg, and depression of twitch response observed. Increments of 1 mg succinylcholine were given at 1–2-minute intervals, when the twitch response had levelled off, until 90 per cent depression of twitch response occurred. At this stage, the ECT was administered, with suitable modification of the convulsion. Once, 77 per cent depression of the twitch response was present when the ECT was administered, and the modification of the convulsion was unsatisfactory.

Following ECT, the patient resumed spontaneous respiration 1 to 10 minutes after the last dose of succinylcholine. Twitch response returned to 75 per cent of control height 20 to 25 minutes after the last dose of succinylcholine. At this stage the recording had to be discontinued, as the patient had awakened and moved vigorously. After each treatment the patient was returned to a recovery room, where he was observed for several hours. No respiratory or other problem was noted.

On two occasions, decamethonium iodide, 1 mg/ml, was used in the same manner as described

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for succinylcholine. When more than 90 per cent depression of the twitch response occurred, ECT was administered, with good modification of the convolution. On both occasions spontaneous respiration returned within 5 minutes of the last dose of decamethonium. Observations had to be discontinued 30 minutes after the last dose of decamethonium, as the patient moved vigorously although the twitch response had returned to only 44 per cent of control.

DOSE–RESPONSE RELATIONSHIP

While careful monitoring was instituted to provide safer anesthesia, valuable information about the dose-response relation of succinylcholine and decamethonium was also derived in this case of a patient with atypical cholinesterase, particularly since the patient's depression involved repeated therapy under similar conditions. Dose–response curves in which fractional depression of the control twitch response was plotted against dose of neuromuscular blocking agent expressed in \( \mu g/\text{kg} \) body weight were constructed (fig. 1). The dose–response curves were sigmoid-shaped and were fitted by the maximum-likelihood method\(^1\) to a logistic function \( Y = D^p/(D^p + K^p) \), where \( Y \) is fractional depression of twitch response; \( D \), the dose of neuromuscular blocking agent; \( K \), the \( ED_{50} \); and \( P \), the slope of the dose–response curve. \( P \) is numerically equal to the Hill coefficient.\(^2\)

The results are shown in table 1. The slopes of the dose–response curves for succinylcholine and decamethonium were 2.7 and 3.8, respectively. The \( ED_{50} \)'s for succinylcholine and decamethonium were 67.5 \( \mu g/\text{kg} \) body weight and 49.0 \( \mu g/\text{kg} \) body weight, respectively. Cumulative doses of 6 to 8 mg succinylcholine were necessary to yield greater than 90 per cent depression of twitch response. Doses of 4 to 6 mg decamethonium were needed to produce a similar effect. Although there were not enough observations available to make a statistically meaningful kinetic comparison, our clinical impression was that the duration of action of decamethonium was similar to that of succinylcholine in this patient.

**Table 1.**

<table>
<thead>
<tr>
<th></th>
<th>Succinylcholine</th>
<th>Decamethonium</th>
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<tbody>
<tr>
<td>Slope of dose–response</td>
<td>2.7 ± 0.4 SE</td>
<td>3.8 ± 1.3 SE</td>
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<tr>
<td>response curve</td>
<td></td>
<td></td>
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<tr>
<td>( ED_{50} ) (( \mu g/\text{kg} ) body weight)</td>
<td>67.5 ± 4.2 SE</td>
<td>49 ± 5.2 SE</td>
</tr>
<tr>
<td>Cumulative dose for</td>
<td>6–8 mg</td>
<td>4–6 mg</td>
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<tr>
<td>90 per cent depression</td>
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<td>of twitch response</td>
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**DISCUSSION**

While the presence of atypical cholinesterase would be expected to lead to a longer duration of action of succinylcholine, the action of this drug might still be appreciably shorter than actions of the more stable non-depolarizing neuromuscular blocking agents. In a patient with abnormal pseudocholinesterase (\( E_1, E_2 \)) Cohen et al.\(^3\) found that 1 mg succinylcholine reduced twitch tension and resulted in apnea, both lasting 5 minutes. These observations argue for the use of succinylcholine in small doses under closely controlled conditions. On the other hand, the action of succinylcholine might be so prolonged that decamethonium might prove more convenient. Kalow and Gunn\(^4\) reported that patients with low dibucaine numbers reacted normally to decamethonium in doses of 3 to 7 mg.

The dose–response relationships we obtained reflect three processes: 1) access of the drug to the receptor; 2) reaction of the drug with the receptor; 3) production of a response as a result of reaction with the receptor. Decamethonium is a straight-chain carbon compound of \( (\text{CH}_2)_{10} \) separating the two quaternary nitrogen atoms, and is not metabolized. The two quaternary nitrogen atoms of succinylcholine are separated by the chain -\( \text{CH}_2 - \text{CH}_2 - \text{O - CO - CH}_2 - \text{CH}_2 - \text{CO - O - CH}_2 - \text{CH}_2 \) with two labile ester bonds. Because of its rapid hydrolysis by normal plasma cholinesterase, metabolism of the drug is a major factor affecting access of the succinylcholine to the motor endplate. However, in the presence of atypical cholinesterase this backbone would behave more like that of decamethonium. Thus, it was interesting to compare the dose–response curves of succinylcholine and decamethonium in the presence of atypical cholinesterase. Since at concentra-
tions of atypical cholinesterase usually found in individuals with this genetic defect, little or no hydrolysis of succinylcholine takes place, the dose–response relationships we obtained should reflect the reaction of succinylcholine or decamethonium with the receptor at the motor endplate and the result of this reaction. Typically, dose–response curves show a slope parameter (P) of about unity. The values of 2.7 and 3.8 observed here are thus much higher than usual. However, these high values are consistent with the steep dose–response relationship between concentration of succinylcholine and depolarization found in vitro by Waud and Waud. Furthermore, presumably the slope also reflects the relationship between depolarization and twitch height. This relationship between the electrical and mechanical effects has been reported by Waud and Waud, who found that the rate of change of twitch height with depolarization was also steep.

In the presence of the atypical enzyme, the pharmacokinetics of succinylcholine and decamethonium should be similar, so the ED₅₀'s should reflect the relative activities of succinylcholine and decamethonium at the receptor of the motor endplate. The roughly equal potencies of the two agents suggest that the quaternary heads contribute most to the activity and the backbone very little.

**Summary**

The use of succinylcholine and decamethonium in a patient with homozygous atypical cholinesterase has been described. Much smaller doses of succinylcholine were needed than in patients with normal cholinesterase.

Analysis of the dose–response relationships showed: 1) ED₅₀’s of 67.5 μg/kg body weight for succinylcholine and 49 μg/kg body weight for decamethonium; 2) the dose–response curves for succinylcholine and decamethonium are steeper than most.

Rational management of this patient with inadequate cholinesterase activity was facilitated by a reasonably precise titration of the drug against the patient’s responses.

The authors thank Dr. D. R. Waud for his assistance and for the statistical analyses.

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