

## Response of a Patient with Atypical Pseudocholinesterase to Small Intermittent Succinylcholine Doses

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Only one case of controlled administration of succinylcholine (SDC) to a patient with atypical pseudocholinesterase has been reported.<sup>1</sup> The patient, a known homozygote to atypical pseudocholinesterase, was given iv SDC drip on several occasions to attenuate clonic-tonic seizures of electroconvulsive therapy. The following is a report of SDC administration in small intermittent doses to a surgical patient with a similar enzymatic disorder.

### REPORT OF A CASE

The patient, a 63-year-old, 60.6-kg woman, was scheduled for pinning of a fractured head of the left femur. She had a history of mild diabetes mellitus and hypertension, both treated by a diet. About 5 years prior to her present admission, a diagnostic dilatation and curettage was performed under general anesthesia, supplemented by a single dose of SDC, 40 mg, iv. She then sustained prolonged apnea and required ventilatory support for about 3 hours. Dibucaine number was 25. She was instructed to inform her physicians of her abnormal response to SDC in future hospitalizations.

Preoperative physical examination was essentially negative with the exception of signs of a fractured left hip and an arterial blood pressure of 160/90 torr. Routine laboratory data were within normal limits with the exception of the blood glucose level which was 180 mg/dl.

After obtaining an informed consent, meperidine, 50 mg, and atropine, 0.5 mg, were given im about 90 min before surgery. The neuromuscular junction (NMJ) was monitored by inserting her left hand into a "twitch box"<sup>2</sup> which was coupled to an oscilloscope and chart recorder. A Grass 48 nerve stimulator supplied supramaximal stimuli at a frequency of 0.2 Hz and pulse duration of 0.2 ms to the left ulnar nerve at the elbow via two 25-gauge needles.

Thiopental, 200 mg, was administered iv and nerve stimulation initiated. SDC, 2 mg, was then administered iv. Initially a small temporary increase in twitch response was observed and then the response returned to base line without appreciable depression (fig. 1, dose #1). A second 2-mg dose of SDC also increased the twitch response but 64 seconds later, the twitch was depressed by 90 per cent (fig. 1, dose #2), and spontaneous breathing ceased. The trachea was then intubated easily and ventilation controlled.

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Anesthesia was maintained with nitrous oxide 66 per cent and intermittent doses of fentanyl, 0.05 mg, given approximately every 30 min. The twitch response recovered gradually and returned to 10 per cent depression in 4 min 4 s. A third dose of SDC, 2 mg, was then given after which the twitch response almost vanished. It required 6 min 36 s for the twitch response to return to 10 per cent depression (fig. 1, dose #3).

Thirty minutes later, the above sequence of SDC administration was repeated. The twitch responded in a similar fashion as before: a small temporary increase followed the first dose, a temporary increase and then a 90 per cent depression with a 3-min 58-s recovery time to 10 per cent depression followed the second dose, and almost 100 per cent depression with a 6-min 40-s recovery time to 10 per cent depression followed the third dose.

At the conclusion of surgery the trachea was extubated and the patient was transferred to the recovery room with no evidence of neuromuscular compromise.

### Discussion

The normal average adult can metabolize 80 mg of SDC in one minute, mostly by enzymatic breakdown.<sup>3</sup> However, metabolism is not the sole mechanism for clearing the plasma of SDC. The short paralyzing effect of SDC coincides well with a phase of rapid distribution and passage of SDC from the plasma into the extravascular space.<sup>4</sup> In addition, protein binding, urinary excretion, and alkali hydrolysis also contribute to the rate of NMJ recovery from SDC, but these are relatively minor factors.<sup>5</sup> In the final analysis, the duration and intensity of SDC-induced paralysis depends on the total amount of SDC that reaches the NMJ. The slower the enzymatic breakdown of SDC in the plasma, the more SDC reaches the NMJ. Since true cholinesterase, the only esterase at the NMJ, does not metabolize SDC, the recovery from SDC depends on its diffusion from the NMJ into the interstitial fluid.

The lack of twitch depression following the first 2-mg dose of SDC in our patient was probably due to rapid distribution and dilution of this small dose into interstitial fluid. The little SDC that did reach the NMJ caused some increase in the twitch response, probably due to repetitive firing, but the amount was presumably too small to cause paralysis. The second dose caused 90 per cent twitch depression, probably by adding its depolarizing effect to that of the first dose.

Mathematical expressions of drug kinetics developed by Levy in recent years,<sup>6</sup> allow analysis and com-

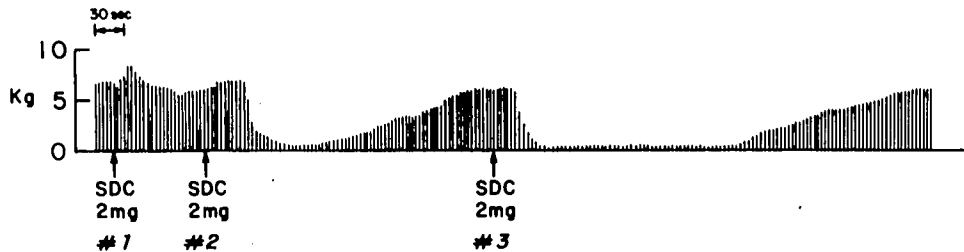


FIG. 1. Twitch response of a patient with an homozygote atypical pseudocholinesterase to small intermittent doses of SDC.

parison of our patient's response to SDC to that of normal patients. Levy has shown that the equation

$$tR = m(\log A^{\circ} - \log A_{min})$$

where  $t$  is duration of effect to a certain end point,  $R$  = rate of decline of the effect,  $A^{\circ}$  = total dose, and  $A_{min}$  = minimal effective dose, is valid for drugs that are eliminated by first order kinetics, such as SDC. The product  $tR$  remains constant as long as the metabolic and excretion rates of the drug, as well as the sensitivity to the drug do not change. Levy analyzed data from clinical reports of SDC kinetics<sup>7,8</sup> and showed that  $R$  and  $tR$  values were similar in adults<sup>9</sup> and neonates.<sup>10</sup> We compared our patient to normal patients (fig. 2) and found a similar  $R$  (30 per cent/

min) but a shorter  $t$ . The similar  $R$  indicates that recovery of the twitch from 90 per cent to 10 per cent depression is independent of pseudocholinesterase activity and is probably due to passive diffusion of SDC out from the NMJ. The shorter  $t$  in our patient was probably due to the vast dilution and redistribution of the small SDC dose and the minimal amounts that reached the NMJ. Repeated doses, however, would probably raise the plasma level of SDC, slow down its diffusion rate from the NMJ, and delay recovery of the twitch response. This presumption is supported by our observation of a longer  $t$  value following the third dose of SDC.

#### REFERENCES

1. Lee-Son S, Pilon RN, Nahon A, et al: Use of succinylcholine in the presence of atypical cholinesterase. *ANESTHESIOLOGY* 43:493-496, 1975
2. Azar I, Wu W, Turndorf H: Twitch box: a new device to monitor neuromuscular blockade. *Medical Instrumentation* 12:92, 1978
3. Kalow W: *Relaxants, Uptake and Distribution of Anesthetic Agents*, Edited by Papper EM, Kitz, RJ. New York, Blakiston Division, McGraw-Hill, 1963, p 302
4. Dal Santo G: Kinetics of distribution of radioactive labeled muscle relaxants: III. Investigations with <sup>14</sup>C-succinylcholine and <sup>14</sup>C-succinylmonocholine during controlled conditions. *ANESTHESIOLOGY* 29:435-443, 1968
5. Miller RD, Stevens WC: Antagonism of succinylcholine paralysis in a patient with atypical pseudocholinesterase. *ANESTHESIOLOGY* 36:511-513, 1972
6. Levy G: Kinetics of pharmacologic effects. *Clin Pharmacol Ther* 7:362-372, 1966
7. Walts LF, Dillon JB: Clinical studies on succinylcholine chloride. *ANESTHESIOLOGY* 28:372-376, 1967
8. Walts LF, Dillon JD: The response of newborn to succinylcholine and *d*-tubocurarine. *ANESTHESIOLOGY* 31:35-38, 1969
9. Levy G: Kinetics of pharmacologic activity to succinylcholine in man. *J Pharmacol Sci* 56:1687-1688, 1967
10. Levy G: Pharmacokinetics of succinylcholine in newborns. *ANESTHESIOLOGY* 32:551-552, 1970.

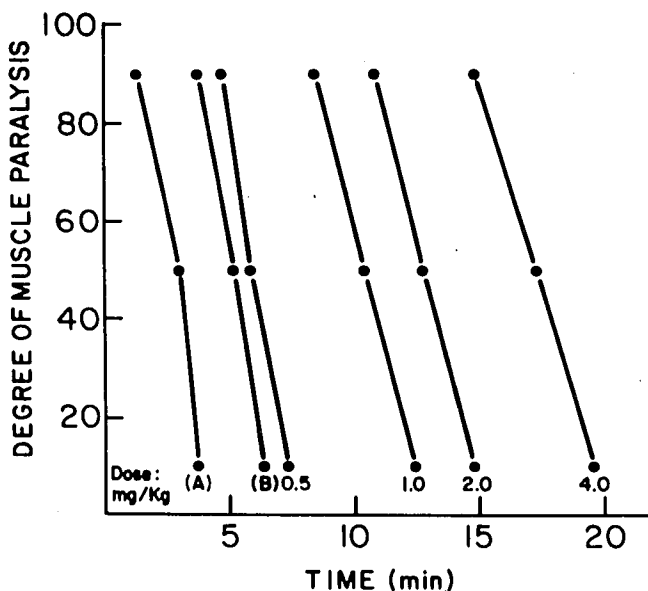


FIG. 2. Degree of muscle paralysis as a function of time after iv administration of 0.5-4.0 mg/kg SDC in normal human subjects<sup>9</sup> and after iv administration of: (A) 0.066 mg/kg, and (B) 0.099 mg/kg of SDC, to a patient with atypical pseudocholinesterase.