The Myth of the Phase I Block After Succinylcholine in Clinical Practice

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Classic teaching divides the neuromuscular blocking characteristics of paralytic drugs into 2 categories: "depolarizing" (such as produced by succinylcholine) and "nondepolarizing" (such as produced by curare, pancuronium, and rocuronium). The actions of depolarizing agents such as succinylcholine are traditionally divided into "Phase I" and "Phase II," first described in 1954.[1] In 1966, Churchill-Davidson examined this issue.[2] A Phase I block (also called "depolarization block") was originally described as a block that was not associated with either fade to tetanic stimulation or post-tetanic facilitation (PTF). With the introduction of the train-of-four (TOF) in 1970,[3] the definition was expanded to a block that, while associated with decreasing twitch amplitudes, did not exhibit fade to TOF during either onset oroffset of the blockade. By contrast, a Phase II block (also called "dual lock" or "desensitization block") is similar to that produced by nondepolarizing relaxants, characterized by fade to TOF, fade to tetanus, as well as PTF.[2] This description can now be found in many textbooks and online locations.[4]

However, personal observation as well as literature dating back to the 1960s calls all this into question. While there is no question that the Phase I block exists, it is unclear whether it is ever seen in routine clinical practice. The author hence conducted a small study to determine whether this contention is, in fact, correct. The study was approved by the University of Minnesota Institutional Review Board (IRB), on the condition that no protected health information would be collected. Written informed consent was waived.

In all, 20 elective surgical patients were studied. All were scheduled for procedures in which the attending anesthesiologist determined that the anesthetic induction would include a single dose of succinylcholine, and where subsequent paralysis with a nondepolarizing relaxant was not planned or would be delayed—and hence full recovery from succinylcholine could be recorded. There were no other inclusion or exclusion criteria. Monitoring of the ulnar nerve and adductor policis was performed with a TwitchView EMG system (Blink Device Co) with an attached datalogger (provided by the manufacturer). Since it was inappropriate to delay the induction (a number of patients were undergoing rapid sequence inductions), the startup mode of the device was bypassed, and the stimulus current was set at 60 mAmps, with a 15-second cycle time. The device's automatic change to post-tetanic count (PTC) was turned off since the 5-minute PTC cycle (which is triggered when the TOF shows no responses) would obscure the TOF during rapid recovery from succinylcholine. No effort was made to influence the conduct of the anesthetic or the dose of succinylcholine. Other than the information from the dataloggers, only the patient's total body weight and the dose of succinylcholine were collected.

The patients' mean (± standard deviation [SD]) total body weight was 90 (± 32) kg and the dose of succinylcholine was 115 (± 29 mg) or 1.38 (± 0.42) mg/kg (range 0.54 to 2.55 mg/kg TBW). The baseline TOF ratio was 1.01 (± 0.02). In all 20 patients, one or 2 TOF cycles during drug onset showed fade. The lowest ratio (before the disappearance of twitches) averaged (± SD) 0.77 (± 0.01 [range 0.51–0.88]). In no patient were <4 twitches observed before the disappearance of all twitches.

The mean (± SD) duration of succinylcholine action (defined as the duration of zero twitches) was 9.02 (± 4.22) minutes (with a dose relationship). Fade was observed in all 20 patients, with an initial mean TOF ratio of 0.68 (± 0.13 [range 0.44–0.89]). The mean duration of such fade (time from first observed TOF ratio to a TOF ratio ≥0.9) was 2.88 (± 1.78) minutes. There were 11 patients in whom at a single cycle twitch count of 1 was observed before the first count of 4. Detailed examples from 6 patients are shown in the Figure.

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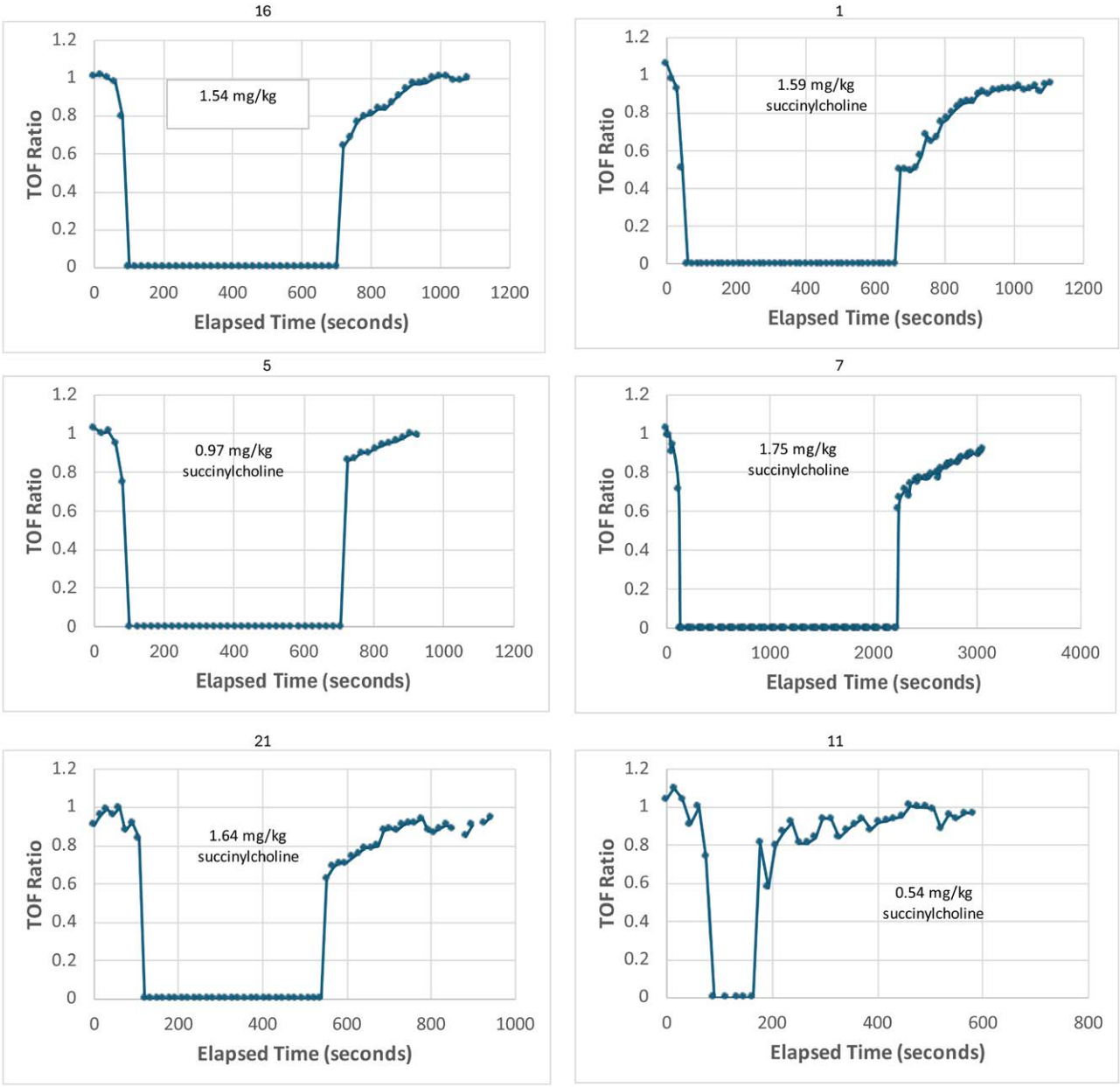

Figure. Showing data from 6 subjects. The *x*-axis represents the elapsed time after the initial TOF stimulus (with a cycle time of 15 s), and the *y*-axis represents the recorded TOF ratios. The administered dose of succinylcholine is also given in each panel. A TOF ratio of 0 indicates the loss of at least the 4th twitch (although in nearly all cases, represents the loss of all twitches). All data were extracted from the dataloggers attached to the TwitchView monitors. This device records all aspects of the delivered stimulus, as well as the amplitudes of each of the 4 resultant responses, as well as the calculated TOF Ratio and the elapsed time. To avoid the use of protected health information both the initially recorded date and clock times for all records were deleted. TOF indicates train-of-four.

DISCUSSION

These results show that following a typical induction dose of succinylcholine, the characteristics of a Phase I block were never seen, either during block onset or recovery. This does not mean that there is no such thing as a Phase I block—but rather than it does not occur in routine practice. There are clearly limitations to the observations.

No effort was made to control the dose of succinylcholine; perhaps, if lower doses were studied, something different might have been seen. However, the doses given were chosen by the providers and hence presumably reflect ordinary practice. In addition, no effort was made to control the administration of other medications—and nearly all of these patients' received sevoflurane which (like other inhaled agents) is well known to interact with neuromuscular blockers.

The terms "Phase I and Phase II block" were introduced by Jenden et al in 1954, working in animals with the depolarizing relaxant decamethonium.[1] He did not examine either fade to repetitive stimulation (eg, tetanus) or post-tetanic changes. He did, however,

demonstrate that a Phase II block could be reversed with neostigmine. Katz et al[5] examined the actions of succinylcholine in humans—and noted that with small doses of the drug (<0.4 mg/kg) tetanus resulted in sustained contractions without post-tetanic facilitation (PTF) —while larger doses were associated with fade to tetanus and PTF—characteristic of a Phase II block. Crul et al made similar observations in 1966.[6] Phase I block was seen only with lower doses of succinylcholine with Phase II block appearing with larger doses. de Jong et al showed a similar pattern with 20 mg of succinylcholine– but the presence of fade to tetanus after 100 mg.[7] In 1970, in the seminal publication that first introduced the concept of the TOF, Ali et al gave 20 to 65 mg of succinylcholine to anesthetized patients.[3] Figure 5 from that publication shows that after "a small dose" of succinylcholine (actual dose not mentioned), 4 equal twitches of slightly reduced amplitude were seen.

More recently, several authors described fade to TOF with clinical doses of succinylcholine. This can be seen in Figure 2 from Lee following 1.5mg/kg of succinylcholine.[8] In 2001, Naguib demonstrated fade in the TOF during block onset and recovery after 0.3-0.5mg/kg of drug.[9] In a more extensive study in 2004, Naguib et al showed consistent TOF fade during both recovery with doses as low as 0.1 mg/kg.[10]

Based on the above, the observations here are not new but rather appear to have been largely forgotten. Based on our educational literature, there appears to be a widespread misconception about the actions of succinylcholine. Nevertheless, the classic textbook description of a Phase I block appears to be largely a myth, at least in the face of normal clinical induction doses of succinylcholine.

Why has this myth persisted? This author believes that the data gathered here may shed some light on this. In none of the subjects in this study was a TOF ratio of <0.44 ever observed. As noted initially by Viby-Mogensen et al, this is above the threshold at which fade can reliably be detected, either visually or by manual assessment.[11] It is hence probable that a clinician using only a peripheral nerve stimulator (rather than a quantitative monitor) and looking at the hand would see only "four equal twitches" of changing amplitude during both onset and offset and hence conclude the presence of a "Phase I block." Much of the aforementioned work showing evidence of a Phase II block with succinylcholine was done under research conditions, using equipment that is not available to the practicing clinician (eg, mechanomyography). User-friendly, automated, quantitative monitors (based on EMG, accelerometry, or kinemyography) have only been introduced relatively recently. When such careful—and routine—quantitative monitoring is used, we see something quite different from what would be observed with only a peripheral nerve stimulator.

Are there any clinical ramifications of these observations? Probably not. It's unlikely that providers will change their use of succinylcholine based on this material. However, it is hoped that they may be a bit more skeptical about what they've been taught and what they teach their trainees. And perhaps it may encourage some to consider using quantitative monitoring when giving succinylcholine (interestingly a recommendation arising from the 5th National Audit Project on accidental awareness during general anesthesia in the United Kingdon; NAP5).[12] While the availability of rocuronium and sugammadex has certainly reduced the use of succinylcholine, the drug still has a useful place in our practice and, at least in our institution, is still commonly used.

In conclusion, historical evidence and the results of this study strongly suggest that a Phase I block does not occur after routine use of succinylcholine.

DISCLOSURES

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