where \( n \) is the sample size and \( p \) is the level of credibility, *i.e.*, if 95% confidence is required, then \( p = 0.05 \). If \( n = 8 \) and \( p = 0.05 \) as used by Sears, the maximum risk for significant bradycardia or asystole in a very large group of similar patients is actually 31%. Since bradycardia or asystole is undesirable and the true incidence could be as high as 31% based on Sears’ study, we believe their conclusion would be more correctly stated that the incidence of bradycardia or asystole with a second dose of succinylcholine after ketamine induction is (with 95% confidence) no higher than 31%.

When \( n \) is greater than 30, the computation is considerably simplified, and is referred to as the rule of 3.\(^3\) When \( p = 0.05 \), “if none of \( n \) patients shows the event about which we are concerned, we can be 95% confident that the chance of this event is at most 3 in \( n \), (i.e., 3/\( n \)).\(^4\) Thus, if Sears et al. had observed zero incidence in 50 subjects, they could have predicted the maximum incidence to be no higher than 6% (3/50) in a similar but large group.

When negative results are reported, the author should be careful about extrapolating results to the universe of patients as a whole.

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_in Reply:_ We agree with Benefiel et al. that our statement “the administration of a second dose of succinylcholine to healthy adult patients after induction with ketamine is safe with respect to cardiac rate and rhythm” may be too strong if only statistical analysis is considered. However, in clinical situations, other factors, such as patient’s physical status, the pharmacological properties of the drug, or combination of drugs, must also be considered in the clinical conclusion of a particular study. In our study,\(^5\) although the number is small (\( n = 8 \)), we believe that our conclusion may not be too strong. This conclusion is not only based on the statistical analysis but also on the physical status of the patients (healthy adults) and the pharmacodynamic property of ketamine as a drug with a sympathomimetic effect.\(^6\)

The practical problem is the number of patients one should study before concluding that a technique is safe or dangerous. Based on our study, we feel it is appropriate to continue to use a second dose of succinylcholine after ketamine where required and continue to observe the patient response. If any serious side effects are encountered, we will of course report them. Thus far we still have not seen any problems with a second dose of succinylcholine in patients who received ketamine.

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**References**


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**References**


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**Succinylcholine and Trismus**

_to the Editor:_ The recent publication of various articles and letters to the editor about succinylcholine and trismus has resulted in a reevaluation of the use of succinylcholine and a reassessment of our clinical practice when trismus occurs after the administration of succinylcholine.\(^1\)\(^4\)\(^5\)\(^6\) The major problem in this whole issue centers around the clinical judgment issue of what constitutes trismus. Unfortunately, Dorland’s Medical Dictionary does not clarify the issue, nor is it clarified in any of the papers that have been written. The reason is that it is a clinical judgment call with a broad spectrum of possibilities. At one end of the spectrum, the masseter muscle tone may be so increased that there is a complete inability to open the mouth. At the other end of the spectrum, there may be a mild increase in muscle tone that can be easily overcome. Van Der Spek has certainly thrown an entirely different light on the issue of succinylcholine and “trismus,” with the finding
that there is a routine increase of masseter muscle tone in normal patients anesthetized with halothane or enflurane and given succiny-
choline at the same time there was complete relaxation of limb muscle
clinically, as well as loss of thener muscle twitch.12 There is certainly
good evidence from in vitro studies to suggest that partial depolarization
(produced by succinylcholine) combined with prior exposure to halo-
thane will result in tension development in normal muscle. This is due
to a halothane-induced shift in the voltage dependence of calcium re-
lease in the muscle.13 It now becomes evident why the clinical deter-
mination of trismus is so difficult. It is very difficult to determine the
difference between an exaggerated normal response to succinylcholine
and a pathological response in which the increase in masseter tone may
herald malignant hyperthermia susceptibility. Ideally, the use of the
word “trismus,” or “masseter spasm,” should be reserved for the ab-
normal response of the masseter muscle to succinylcholine, but, prac-
tically, this may be very difficult. Fortunately, the incidence of malignant
hyperthermia is very rare, occurring anywhere from 1 in 15,000 chil-
dren up to 1 in 50,000 adults. The incidence of abnormal masseter
muscle response (masseter spasm) with a combination of halothane and
succinylcholine occurs in 1% of the patients in Boston (1 in 100) and
0.01% of the patients in Charlottesville (1 in 10,000).6 The reason for
the great differences in occurrence is not apparent, although it may
represent subtle differences in clinical practice.

The first problem faced by the clinician is what to do if a patient
does develop masseter spasm after succinylcholine. The recom-
endations cover a broad spectrum. Gronert recommends that the anes-
thesiologists continue the anesthetic with nontriggering agents, while
monitoring end-expired CO2, venous and/or arterial blood gases, blood
pressure, pulse, temperature, and muscle tone.5 If there is any aberra-
tion, then the case is cancelled and treatment begun with dantrolene.
On the other hand, if the situation is stable, the anesthetic can proceed
with nontriggering agents. We agree with this management. At the
other end of the spectrum is the opinion as expressed by Rosenberg
with whom we strongly disagree.4 He would cancel all surgery where
there is “trismus” following succinylcholine. We disagree because of
the aforementioned variability in the definition of trismus, and because
we have monitoring techniques which permit us to detect developing
malignant hyperthermia and dantrolene to treat a malignant hyper-
thermic episode.

A second problem that must be addressed when masseter spasm
occurs is whether or not to obtain a muscle biopsy for an MH-suscep-
tibility contracture study. Rosenberg and Gronert recommend it in all
patients who develop trismus with succinylcholine.4,6 If truly 1% of
pediatric patients develop trismus with succinylcholine and halothane,
then muscle biopsy would be the most frequently performed operation
in the United States. Another problem with muscle biopsy is that there
are a limited number of centers doing it,5,13 and it would require great
time and expense for families to travel to these centers.

There is an ongoing debate about the role of succinylcholine in the
armamentarium of the anesthesiologist. There is no question that every
drug has a risk/benefit ratio. There is also no question that there are
certain risks from succinylcholine that are infrequent, recognizable,
and treatable. On the other hand, there are certain benefits from succi-
nycholine that no other muscle relaxant possesses. These benefits are
1) rapid onset, 2) rapid offset, and 3) effectiveness following intra-
muscular injection. It is evident that the “ideal” muscle relaxant is not
yet available for clinical practice. Until such time, the anesthesiologist
must weigh the risk/benefits of all of the muscle relaxants, just as is
done with every other drug that is used. This is the basis for the “art”
of anesthesia.

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REFERENCES

1. Van Der Spek AF, Fang WB, Ashton-Miller JA, Stohler CS,
Carlson DS, Schork MA: The effects of succinylcholine on mouth opening.

2. Van Der Spek AF, Fang WB, Ashton-Miller JA, Stohler CS,
Carlson DS, Schork MA: Increased masticatory muscle stiffness
during limb muscle fasciculility associated with succinylcholine
administration. ANESTHESIOLOGY 69:11-16, 1988

3. Gronert GA: Management of patients in whom trismus occurs

4. Rosenberg H: Management of patients in whom trismus occurs
following succinylcholine (reply to letter). ANESTHESIOLOGY 68:654-655, 1988

5. Gallant EM, Gronert GA, Taylor SR: Cellular membrane potentials
and contractile threshold in mammalian skeletal muscle susceptible

6. Schwartz L, Rockoff MA, Koka BV: Masseter spasm with succi-
nycholine. ANESTHESIOLOGY 61:772-775, 1984

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In Reply: The letter from Drs. Barry and Lynch succinctly raises
many questions plaguing clinicians concerning the management of
trismus following succinylcholine. Based on the findings that approx-
imately 50% of patients with masseter spasm are truly MH susceptible
on contracture testing,2 and also Van Der Spek's work2 showing that
succinylcholine may increase muscle tone of the masseter muscle in
normal patients, it is certainly clear that increased muscle tone after
succinylcholine may or may not be related to MH. Whether MH can
be differentiated from this hypertonic response found in normals by
quantitatively measuring the extent of muscle tone increase has not
yet been explored. Clearly, therefore, there is a subjective element to
diagnosing trismus.

Again, because of the subjective nature of trismus, the incidence of
trismus has been difficult to establish with accuracy. Unfortunately,
studies of the incidence of trismus are retrospective. The published
studies indicate a range of incidence of 1% in children following halo-
thane and succinylcholine8 to 1 in 12,000 in the Danish population.4
I suspect that the much lower incidence of trismus in Charlottesville
is in part related to the mode of administration of succinylcholine. I
understand the im route of administration of succinylcholine is more

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