The Effects of Hexafluorenium in Preventing the Increase in Intraocular Pressure Produced by Succinylcholine

Ronald L. Katz, M.D., Kenneth E. Eakins, Ph.D.,† Clyde O. Lord, M.D.‡*

The interactions of succinylcholine and hexafluorenium on extraocular muscle, nictitating membrane and intraocular pressure were studied in the cat. Succinylcholine (1–400 μg./Kg.) increased extraocular muscle tension, nictitating membrane tension and intraocular pressure. These effects could be prevented by injecting 0.4 mg./Kg. hexafluorenium one to two minutes prior to succinylcholine. If the interval between hexafluorenium and succinylcholine was 10–30 minutes, the effects of succinylcholine were decreased in magnitude but the duration was prolonged. Hexafluorenium, if injected during the succinylcholine-induced increase in extraocular muscle tension, nictitating membrane tension and intraocular pressure, rapidly abolished these effects of succinylcholine. Hexafluorenium was also found to depress the twitch responses of the sciatic-tibialis and oculomotor-superior rectus nerve-muscle preparations. In man, 0.4 mg./Kg. hexafluorenium, injected two minutes prior to 0.3 mg./Kg. succinylcholine, prevented the increase in intraocular pressure produced by this dose of succinylcholine.

IN A RECENT STUDY of the effects of anticholinesterases on extraocular muscle, neostigmine (Prostigmine) and edrophonium (Tensilon) were found to increase the magnitude and duration of action of succinylcholine on: 1) the indirectly-evoked twitch response of the tibialis anterior muscle; 2) the indirectly-evoked twitch response of the superior rectus muscle (an extraocular muscle) and 3) the baseline tension of the superior rectus muscle.[1] In subsequent experiments, hexafluorenium (which inhibits plasma cholinesterase and is used clinically to increase the magnitude and duration of action of succinylcholine) was found to abolish rather than increase the action of succinylcholine on the superior rectus muscle tension. Since an increase in extraocular muscle tension is believed to be a factor in the increase in intraocular pressure produced by succinylcholine,[2-6] the present study was undertaken to determine individual effects and interaction of succinylcholine and hexafluorenium on extraocular muscle and intraocular pressure.

Methods

CAT

Cats weighing 2.5–4.5 Kg. were anesthetized with sodium pentobarbital (36 mg./Kg.) given by intraperitoneal injection. The trachea, femoral artery and femoral vein were cannulated.

Sciatic-tibialis preparation. The sciatic nerve was isolated and ligated at mid-thigh level, and a shielded Palmer bipolar electrode applied to its peripheral end. Supramaximal stimuli consisting of rectangular pulses of 1-msec. duration were delivered to the nerve from a Grass stimulator (Model SC4) at a frequency of 0.1 cps. The resulting twitch response (twitch height) of the ipsilateral anterior tibialis muscle was measured with a Grass force displacement transducer (FT-03).

Oculomotor-superior rectus preparation. The animal's head was immobilized in a stereotaxic apparatus. The superior rectus muscle of the left eye was separated from the globe and a

* Associate Professor of Anesthesiology.
† Assistant Professor of Ophthalmology Research.
‡ Postdoctoral Research Trainee, National Institutes of Health (Grant 5T1-GM-00056-09).

Received from the Departments of Anesthesiology and Ophthalmology Research, Columbia University, College of Physicians and Surgeons, and the Anesthesiology Service, Presbyterian Hospital in the City of New York, New York, N. Y. Accepted for publication July 31, 1967.
Presented at the fall meeting of the American Society of Anesthesiology, Oct. 3, 1967, in Los Vegas, Nevada.
Supported by NIH grants GM-09069 and NB-07079 and a grant-in-aid from the National Society for the Prevention of Blindness, Inc.

suture placed through the tendon, which was then attached to a Grass force displacement transducer (FT-03). A parietal craniotomy was performed and the dura mater was opened. The cerebral hemisphere was lifted gently to expose the third cranial nerve, which was then impaled with a needle electrode. Supramaximal stimuli consisting of rectangular pulses of 1-msec. duration were delivered to the nerve from a Grass stimulator (Model SC-4) at a frequency of 0.1 cps.

Intraocular pressure preparation. The technique used was similar to that described by Eakins.[9] A 21- or 23-gauge needle attached to plastic tubing was connected to a Statham pressure transducer (P23Db) by a series of stopcocks, and the pressure transducer connected to a saline reservoir by a series of stopcocks. The reservoir could be raised or lowered to change the hydrostatic pressure. With the stopcocks arranged so that the saline reservoir was open to the pressure transducer and the pressure transducer open to the needle, the anterior chamber of the right eye was cannulated. The reservoir pressure was 25 mm. Hg and saline was dripping freely through the end of the needle at the time of cannulation. The anterior chamber was entered by grasping the conjunctiva firmly with tooth forceps and pushing the needle obliquely through the cornea from the limbal region until the tip lay in front of the pupil. After permitting equilibration of the anterior chamber with the saline reservoir, the stopcocks were turned so as to cut off the reservoir and to leave the eye connected directly to the pressure transducer. The pressure in the anterior chamber was allowed to decay until the normal steady state of intraocular pressure was reached. A minimum of 10 minutes of a stable interocular pressure was obtained before injecting any drugs.

Femoral arterial pressure was measured with a Statham pressure transducer (P23Db). The left nictitating membrane was pulled laterally and attached to a Grass force displacement transducer (FT-03). All recordings were made on a Grass polygraph (Model 5). Animals were artificially ventilated with a Frumin-Lee respirator. Hexafluorenium bromide and succinylcholine chloride were injected into the femoral vein.

Man

In five patients intraocular pressure was measured with a Schiötz's tonometer. The patients received thiopental (2–3 mg./Kg.), and succinylcholine (1 mg./Kg.), and the trachea was then intubated. After 30 minutes' inhalation of nitrous oxide (8 l.), oxygen (4 l.) and trichloroethylene (0.3 per cent), intraocular pressure was measured three times at five-minute intervals. Succinylcholine (0.3 mg./Kg.) was injected intravenously two or three times at 15-minute intervals and the increase in intraocular pressure measured. Hexafluorenium (0.4 mg./Kg.) was then injected, intraocular pressure measured one minute later, and succinylcholine injected one minute later. Intraocular pressure was measured for the next ten minutes.

Results

Cat

The injection of 0.1–0.8 mg./Kg. of hexafluorenium had no effect on the baseline tension of the superior rectus muscle in four of five cats. In one cat baseline tension increased 0.5 Gm. In two animals, 25 μg./Kg. of succinylcholine given previously had increased superior rectus muscle tension 5 Gm. and 9 Gm. However, the injection of succinylcholine after hexafluorenium no longer increased superior rectus muscle tension. Since the increase in intraocular pressure produced by succinylcholine is believed to be due, at least in part, to contraction of extraocular muscles, the effect of hexafluorenium on the action of succinylcholine on intraocular pressure and extraocular muscle was determined. First the effect of increasing doses of succinylcholine (1–400 μg./Kg.) was determined. A representative example of the increase in superior rectus muscle tension and intraocular pressure produced by succinylcholine is shown in fig. 1. A suitable submaximal test dose of succinylcholine was then chosen, usually 25 or 50 μg./Kg. Following three consecutive consistent responses to the test dose of succinylcholine, hexafluorenium (0.4 mg./Kg.) was injected. Little or no effect was seen on supe-

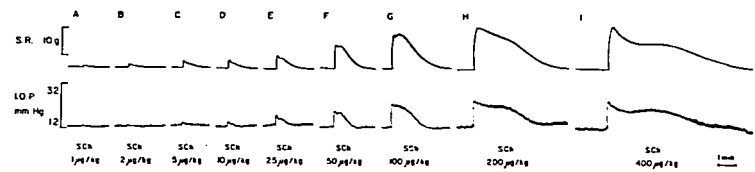

FIG. 1. The effects of succinylcholine (SCh) on the superior rectus muscle (S.R.) of the left eye and the intraocular pressure (I.O.P.) of the right eye.

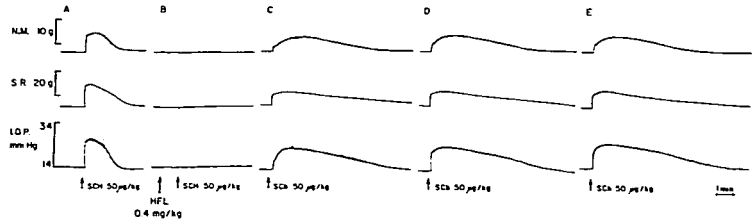

FIG. 2. Modification of actions of succinylcholine (SCh) by hexafluorenium (HFL). Panel A. Increase in nictitating membrane (N.M.) tension of left eye, superior rectus muscle (S.R.) tension of left eye and intraocular pressure (I.O.P.) of the right eye produced by 50 μg./Kg. of succinylcholine. Panel B. Note that hexafluorenium (0.4 mg./Kg.) injected approximately one minute prior to succinylcholine prevented the effects of succinylcholine seen in Panel A. Panel C. The injection of succinylcholine 10 minutes after hexafluorenium now produced a smaller increase but a greater duration of action than seen in Panel A. Similar responses are seen in Panels D and E when succinylcholine was injected 20 and 30 minutes after hexafluorenium.

rior rectus muscle tension and intraocular pressure. Injection of the test dose of succinylcholine one to two minutes after hexafluorenium did not produce an increase in superior rectus muscle tension or intraocular pressure, but 10–30 minutes after hexafluorenium the test dose of succinylcholine did produce an increase in superior rectus muscle tension and intraocular pressure (fig. 2). Although the magnitude of increase produced by succinylcholine was less than that seen prior to hexafluorenium, the duration of action was prolonged (fig. 2). These results were observed in seven cats. In three additional cats the experiment was modified slightly. Following injection of hexafluorenium, succinylcholine was injected after 10 minutes rather than after one to two minutes. Succinylcholine increased superior rectus tension and intraocular pressure. The magnitude of increase was less than prior to hexafluorenium, but the duration of action was prolonged.

In another set of experiments it was observed that succinylcholine produced a contraction of the nictitating membrane. Since the orbital smooth muscle responds in a fashion similar to the nictitating membrane [10] and may contribute to the increase in intraocular pressure produced by succinylcholine, the effect of hexafluorenium on the nictitating membrane response to succinylcholine was determined in four of the ten cats described above. In all four cats the nictitating membrane responded in a fashion similar to that of the superior rectus muscle and intraocular pressure (fig. 2).

In five animals, succinylcholine (50 μg./Kg.) was given, and after the maximum increase in superior rectus muscle tension, nictitating membrane tension and intraocular pressure had been obtained, hexafluorenium (0.4 mg./Kg.) was injected. A rapid decrease in superior rectus muscle tension, nictitating

membrane tension and intraocular pressure to control levels was seen (fig. 3).

It has been reported that *d*-tubocurarine blocks the action of succinylcholine on extraocular muscle and intraocular pressure.[3, 8, 11] Hexafluorenium is known to produce a neuromuscular block which, although nondepolarizing in nature, is thought to differ from that of *d*-tubocurarine.[12] Since the nondepolarizing neuromuscular blocking action of hexafluorenium might account for its modification of the action of succinylcholine on intraocular pressure and extraocular muscle, the effect of hexafluorenium on the oculomotor-superior rectus neuromuscular preparation was determined in five cats. The action of hexafluorenium on the sciatic-tibialis neuromuscular preparation was also simultaneously determined. Doses of 0.1, 0.2 and 0.4 mg./Kg. were injected 30 minutes apart. Twitch responses were unaffected by 0.1 mg./Kg., decreased 20–60 per cent by 0.2 mg./Kg. and decreased 80–100 per cent by 0.4 mg./Kg. (fig. 4). Tibialis anterior block was slightly greater in magnitude and duration than superior rectus block (fig. 4).

Since inhibition of the effect of succinylcholine on superior rectus muscle tension was seen one to two minutes after the injection of hexafluorenium (when the neuromuscular block would be greatest) but not 10–30 minutes later (when the neuromuscular block of hexafluorenium would be minimal), it seemed reasonable to assume that the neuromuscular blocking action of hexafluorenium could account for its action in blocking the increase in superior rectus tension and intraocular pressure produced by succinylcholine. Therefore, an attempt was made in five animals to correlate the superior rectus neuromuscular block produced by hexafluorenium with its action in blocking the superior rectus tension rise produced by succinylcholine. This was unsuccessful. It was possible to block the re-

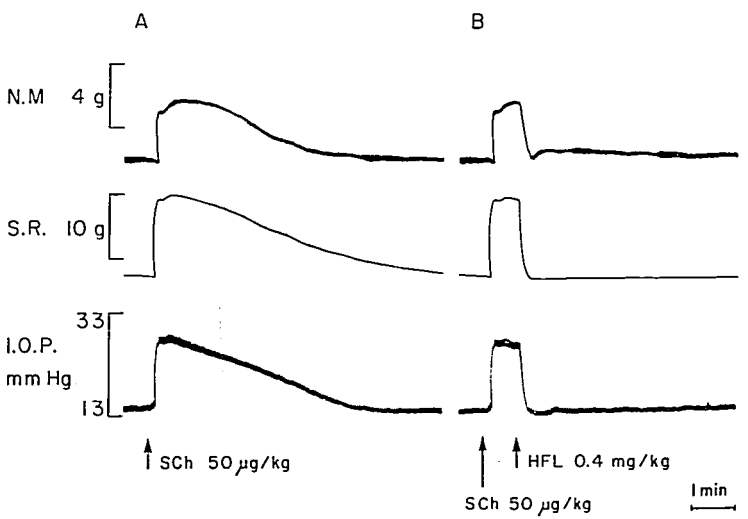

FIG. 3. Effect of hexafluorenium (HFL) on action of succinylcholine (SCh). Panel A. Increase in nictitating membrane (N.M.) tension of left eye, superior rectus muscle (S.R.) tension of the left eye and intraocular pressure (I.O.P.) of right eye produced by 50 µg./Kg. of succinylcholine. Panel B. Note that injection of hexafluorenium (0.4 mg./Kg.) during peak of response to succinylcholine rapidly abolished the effects of succinylcholine.

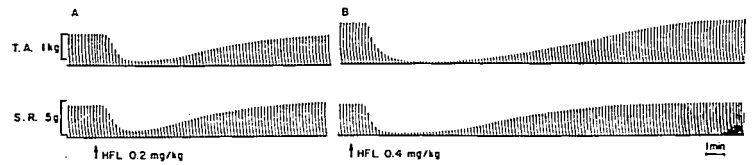

FIG. 4. Effects of hexafluorenium (HFL) on tibialis anterior muscle (T.A.) and superior rectus muscle (S.R.). Panels A and B. Note decrease in twitch responses produced by 0.2 mg./Kg. and 0.4 mg./Kg. of hexafluorenium. Note slightly greater action on tibialis anterior muscle.

sponse to succinylcholine with a dose of hexafluorenium (0.1 mg./Kg.) which produced no decrease in twitch height. It was also possible for succinylcholine to increase superior rectus muscle tension markedly at a time when the twitch height of the superior rectus muscle had been abolished by 1 mg./Kg. of hexafluorenium. The failure to correlate twitch depression produced by hexafluorenium with suppression of superior rectus muscle tension increase produced by succinylcholine may be attributed to the fact that we were monitoring the effect of hexafluorenium on the twitch neuromuscular system, whereas succinylcholine increases superior rectus baseline tension by its action on the tonic neuromuscular system.[11]

MAN

In five anesthetized patients, the effects of succinylcholine and hexafluorenium on intraocular pressure were determined. The intravenous injection of 0.3 mg./Kg. of succinylcholine increased intraocular pressure 7–12 mm. Hg for two to four minutes. Repeating this dose of succinylcholine once or twice at 15-minute intervals produced similar increases in intraocular pressure. Hexafluorenium, 0.4 mg./Kg., was then injected intravenously. One minute later, the intraocular pressure was found to be unchanged. Injection of succinylcholine two minutes after hexafluorenium did not produce an increase in intraocular pressure, which was measured over the following ten minutes. Originally it had been planned to study a minimum of 25 patients. However, for technical reasons, it was impossible to complete this clinical portion of the study.

Discussion

In 1953, shortly after succinylcholine was introduced into clinical practice, Hofmann and Holzer[2] reported that succinylcholine increased intraocular pressure in unanesthetized man. Although an increase of as much as 18 mm. Hg was observed in these unanesthetized patients, under general anesthesia the magnitude of increase in intraocular pressure was less. It was also observed that, associated with the increase in intraocular pressure, the eyes became divergent and remained fixed. Movement of the eyes returned at the same time that the intraocular pressure decreased. It was therefore suggested that the increase in intraocular pressure might be associated with or produced by contraction of the extraocular muscles. The ability of succinylcholine to contract extraocular muscle had been demonstrated by Hofmann and Lembeck in 1952.[3] Subsequent studies supported and extended the work of Hofmann and Holzer. Lincoff *et al.*, in 1955,[4] simultaneously measuring intraocular pressure and extraocular muscle tension, found that succinylcholine produced a contraction of extraocular muscle as well as an increase in intraocular pressure of the cat. Cutting all six extraocular muscles (superior rectus, inferior rectus, lateral rectus, medial rectus, superior oblique, inferior oblique) virtually abolished the increase in intraocular pressure. They therefore felt that the increased intraocular pressure produced by succinylcholine was attributable to the contraction of the extraocular muscles. Extending their study to patients who received 2.5 mg./Kg of thiopental, they observed that 0.3 mg./Kg. of succinylcholine increased intraocular pressure by as much as 38 mm. Hg. The average increase seen in their study was 7.9 mm. Hg. Lincoff *et al.* in 1957[5] reported vitreous expulsion in patients who received succinylcholine during ocular surgery. This

was attributed to the increase in intraocular pressure produced by succinylcholine. Dillon *et al.*[6] and Macri and Grimes [8] supported the role of extraocular muscles in increasing intraocular pressure. Dillon *et al.*[6] found that succinylcholine contracted the extraocular muscles of cats and man *in vitro*, an effect which was blocked by *d*-tubocurarine. These workers later reported [7] *in vivo* studies in which succinylcholine increased extraocular muscle tension and intraocular pressure of the cat, thus confirming the work of Lincoff *et al.*[5] discussed above. Macri and Grimes [8] also found that succinylcholine increased extraocular muscle tension and intraocular pressure in the cat. They were able to prevent this effect by injecting *d*-tubocurarine prior to succinylcholine. In addition, sectioning the six extraocular muscles of the eye markedly reduced the increase in intraocular pressure produced by succinylcholine.

Although the laboratory studies reported above have not been challenged (with the exception of Wretlind and Wåhlin,[13] discussed below), some of the clinical effects of succinylcholine on intraocular pressure have been questioned. Wynands and Crowell [14] found only a small increase in intraocular pressure produced by succinylcholine. They also found that a succinylcholine infusion (0.1 per cent) did not increase intraocular pressure significantly. Lewallan and Hicks [15] found that succinylcholine did not increase intraocular pressure. They also reported that succinylcholine did not rotate the eye. In the present study, in both cats and man, succinylcholine was found to produce a divergence and fixation of the eye as well as an increase in intraocular pressure. Unlike Wynands and Crowell,[14] Craythorne *et al.*[16] found that a succinylcholine infusion (0.1–0.2 per cent) increased intraocular pressure. Wretlind and Wåhlin [13] reported that in the cat *d*-tubocurarine did not prevent succinylcholine from increasing intraocular pressure. They therefore concluded that extraocular muscle contraction was not the cause of the increased intraocular pressure produced by succinylcholine. However, in studies of succinylcholine we found, as had others,[6, 8] that *d*-tubocurarine markedly suppressed or abolished the increase in intraocular pressure produced by succinylcholine as well as decreasing or abolishing the extraocular muscle contraction. It seems reasonable to conclude from the weight of evidence of the published studies that the extraocular muscles do have a role in the increase in intraocular pressure produced by succinylcholine.

Since the extraocular muscles play a role in succinylcholine-induced intraocular pressure rise, a discussion of their anatomy, physiology and pharmacology is in order. The extraocular muscles of the rabbit and cat, which have recently been the object of a number of studies,[1, 17–21] are rather unusual, in that they contain two separate neuromuscular systems, a twitch system and a tonic system. The twitch system is characterized by muscle fibers with small, regular, well-defined fibrils (*Fibrillenstruktur*). The nerve endings to these fibers have single large plaque-like (*en plaque*) nerve endings derived from efferent fibers of large diameter. Stimulation of these nerves produces twitches accompanied by fast propagated muscle potentials. This system is similar to the usual neuromuscular system found in mammals. The tonic system is characterized by muscle fibers with large, irregular, poorly-defined fibrils (*Felderstruktur*). The nerve endings to these fibers have multiple small grape-like (*en grappe*) endings, which are derived from efferent fibers of small diameter. Stimulation of these fibers results in slow, graded muscle contractions, which are accompanied by nonpropagated muscle potentials of small amplitude and long duration. These small nerve fibers are not mechanically excited by single shocks but require tetanic rates of stimulation. This system is commonly found in amphibian and avian muscles. In mammals, including the cat and man,[22] this system is found in the extraocular muscles. Although this system has been termed tonic, Bach-y-Rita and Ito [20] recently reported that these multiply-innervated fibers of cat extraocular muscles have some characteristics of twitch fibers and also differ somewhat from the classical tonic fibers found in amphibians. They refer to these fibers as "slow multi-innervated twitch fibers."

The effects of neuromuscular blocking agents on these two neuromuscular systems of cat

extraocular muscle have been studied and compared with the tibialis anterior muscle, which contains only twitch fibers.[1, 19] The depolarizing agents, succinylcholine, decamethonium and imbretil, all in small doses, increase the baseline tension of extraocular muscle, without affecting the twitch system of the extraocular muscle or tibialis anterior muscle. Larger doses of the depolarizing agents produce greater increases in extraocular muscle tension and also a decrease in the twitch response of the tibialis anterior muscle. With succinylcholine, it is possible to abolish the twitch response of the tibialis anterior muscle without producing any depression of the twitch response of the superior rectus muscle. However, if sufficiently large doses of succinylcholine are given, the twitch response of the superior rectus muscle can be abolished. The dose required to do this produces a profound, long-lasting neuromuscular block of the tibialis anterior muscle and markedly increases superior rectus muscle tension. The results observed with decamethonium and imbretil were qualitatively similar.

The effects of nondepolarizing neuromuscular blocking agents on the two neuromuscular systems differed from that seen with depolarizing agents.[1, 19] Gallamine (Flaxedil) and dimethyl tubocurarine produced no effect on the baseline tension of the extraocular muscle. Although there were some differences in sensitivity of the extraocular and tibialis anterior muscle to these neuromuscular blocking agents, the magnitude and duration of twitch suppression were fairly similar. A different result was obtained with *d*-tubocurarine. In 50 per cent of the animals, *d*-tubocurarine increased superior rectus muscle tension, while in the other 50 per cent of the animals studied, no change in baseline tension occurred. In addition, the twitch response of the superior rectus muscle was less sensitive to the action of *d*-tubocurarine than was the tibialis anterior twitch system. Similar results have been observed in man. Drucker *et al.*[23] found that the extraocular muscles were less affected by *d*-tubocurarine than was grip strength, while with dimethyl tubocurarine (Metubine) approximately equal depression of grip strength and extraocular muscle movement was observed.

In a previous study of hexafluorenium,[12] it was pointed out that this agent has a number of actions. These include a nondepolarizing neuromuscular blocking action, a plasma cholinesterase inhibiting effect ,and a junctional membrane effect. Although neostigmine and edrophonium, inhibitors of red cell cholinesterase, will themselves increase the extraocular muscle tension as well as increase the effect of succinylcholine on extraocular muscle tension, hexafluorenium produced different effects. Hexafluorenium, if given less than two minutes before succinylcholine, prevented the succinylcholine-induced increase in extraocular muscle tension and intraocular pressure. However, if succinylcholine was given 10–30 minutes after hexafluorenium, the magnitude of increase in extraocular muscle tension and intraocular pressure was decreased, but the duration of action was increased. Although the nondepolarizing neuromuscular blocking action of hexafluorenium seemed a reasonable explanation for its blocking the action of succinylcholine, this could not be demonstrated in the present study. In addition, this action of hexafluorenium could not explain the prolongation of the duration of action of succinylcholine on extraocular muscle tension and intraocular pressure. The plasma cholinesterase-inhibiting action of hexafluorenium cannot account for its modification of the action of succinylcholine. It is not possible at present to state whether the effect of hexafluorenium on the junctional membrane can explain the actions of hexafluorenium observed in the present study. It is clear, however, that hexafluorenium, if given just before succinylcholine, will prevent succinylcholine from increasing extraocular muscle tension and intraocular pressure. Whether the increase in intraocular pressure is prevented solely by inhibition of the increase in extraocular muscle tension is not known. It is possible that part of the increase in intraocular pressure produced by succinycholine is the result of contraction of orbital smooth muscle, which is also blocked by hexafluorenium.

Our results with succinylcholine and hexafluorenium in man differ from those of Sobel.[24] We found that hexafluorenium could prevent the increase in intraocular pressure produced by succinylcholine, while Sobel found that hexafluorenium did not block this response.

However, if the experimental protocols are carefully examined, it is clear that these differences are more apparent than real. The injection of succinylcholine within two minutes after hexafluorenium prevented the increase in intraocular pressure, in both clinical and laboratory studies. In the study of Sobel, succinylcholine was injected more than five minutes after hexafluorenium and an increase in intraocular pressure was seen. In our animal studies, hexafluorenium, under similar circumstances, failed to block the increase in intraocular pressure. Thus, in our studies as well as those of Sobel, unless the interval between hexafluorenium and succinylcholine was brief, hexafluorenium did not prevent succinylcholine from increasing intraocular pressure.

Although we were able to demonstrate that hexafluorenium could block the increase in intraocular pressure produced by succinylcholine, we are somewhat hesitant to recommend this technique for routine use in man. First, although the laboratory data about the blocking action are complete, it was not possible to carry out a large-scale clinical investigation of the action of hexafluorenium on the succinylcholine-induced increase in intraocular pressure. In addition, the use of hexafluorenium and succinylcholine is potentially dangerous, since the increase in intraocular pressure produced by succinylcholine may be only slightly decreased, yet markedly prolonged, if the interval between succinylcholine and hexafluorenium is more than just a few minutes. Further clinical studies of the interaction of hexafluorenium and succinylcholine on intraocular pressure clearly are indicated.

Summary

Succinylcholine increased extraocular muscle tension, nictitating membrane tension and intraocular pressure in the cat. These effects could be abolished by the injection of hexafluorenium during the response to succinylcholine. These effects could also be prevented by injecting hexafluorenium one to two minutes before succinylcholine. When the interval between hexafluorenium and succinylcholine was 10–30 minutes, hexafluorenium decreased the magnitude of response to succinylcholine but the duration was prolonged. Hexafluorenium also decreased the twitch responses of the sciatic-tibialis and oculomotor-superior rectus nerve-muscle preparations. In man, hexafluorenium injected two minutes prior to succinylcholine prevented succinylcholine from increasing intraocular pressure.

We wish to thank Dr. Max Forbes of the Department of Ophthalmology, Columbia-Presbyterian Medical Center, for his invaluable assistance in the studies carried out on anesthetized patients.

References

1. Katz, R. L., and Eakins, K. E.: A comparison of the effects of neuromuscular blocking agents and cholinesterase inhibitors on the tibialis anterior and superior rectus muscles of the cat, J. Pharmacol. Exp. Therap. 152: 304, 1966.
2. Hofmann, H., and Holzer, H.: Die Wirkung von Muskelrelaxantien auf den intraokularen Druck, Klin. Monatsbl. Augenh. 123: 1, 1953.
3. Hofmann, H., and Lembeck, F.: Das Verhalten der äusseren Augenmuskelen gegenüber Curare, Dekamethonium (C-10) und Succinylcholin (M 115), Arch. Exper. Path. U. Pharmakol. 216: 552, 1952.
4. Lincoff, H. A., Ellis, C. H., DeVoe, A. G., DeBeer, E. J., Impastato, D. J., Berg, S., Orkin, L., and Magda, H.: The effect of succinylcholine on intraocular pressure, Amer. J. Ophthal. 40: 501, 1955.
5. Lincoff, H. A., Breinin, G. M., and DeVoe, A. G.: The effect of succinylcholine on the extraocular muscles, Amer. J. Ophthal. 43: 440, 1957.
6. Dillon, J. B., Sabawala, P., Taylor, D. B., and Gunter, R.: Action of succinylcholine on extraocular muscles and intraocular pressure, ANESTHESIOLOGY 18: 44, 1957.
7. Dillon, J. B., Sabawala, P., Taylor, D. B., and Gunter, R.: Depolarizing neuromuscular blocking agents and intraocular pressure in vivo, ANESTHESIOLOGY 18: 439, 1957.
8. Macri, F. J., and Grimes, P. A.: The effects of succinylcholine on the extraocular striate muscles and on the intraocular pressure, Amer. J. Ophthal. 44: 221, 1957.
9. Eakins, K. E.: The effect of intravitreous injections of norepinephrine, epinephrine and isoproterenol on the intraocular pressure and aqueous humor dynamics of rabbit eyes, J. Pharmacol. Exp. Therap. 140: 79, 1963.
10. Eakins, K. E., and Katz, R. L.: The effects of sympathetic stimulation and epinephrine on the superior rectus muscle of the cat, J. Pharmacol. Exp. Therap. 157: 524, 1967.
11. Eakins, K. E., and Katz, R. L.: The action of succinylcholine on the tension of extraocular muscles, Brit. J. Pharmacol. 206: 205, 1966.

12. Katz, R. L., Gissen, A. J., and Karis, J. H.: Effects of hexafluorenium and edrophonium on the neuromuscular blocking action of succinylcholine, decamethonium, imbretil and d-tubocurarine, ANESTHESIOLOGY 26: 154, 1965.
13. Wretlind, A., and Wåhlin, Å.: The effect of succinylcholine on the orbital musculature of the cat, Acta Anaesth. Scandinav. 3: 101, 1959.
14. Wynands, J. E., and Crowell, D. E.: Intraocular tension in association with succinylcholine and endotracheal intubation: A preliminary report, Can. Anaes. Soc. J. 7: 39, 1960.
15. Lewallen, W. M., Jr., and Hicks, B. L.: The use of succinylcholine in ocular surgery. Amer. J. Ophthal. 49: 773, 1963.
16. Craythorne, N. W. B., Rottenstein, H. S., and Dripps, R. D.: The effects of succinylcholine on introcular pressure in adults, infants and children during general anesthesia, ANESTHESIOLOGY 21: 59, 1960.
17. Matyushkin, D. P.: Phasic and tonic neuromotor units in the oculomotor apparatus of the rabbit, Sechenov Physiol. J. USSR 47: 65, 1961.
18. Hess, A., and Pilar, G.: Slow fibers in the extraocular muscles of the cat, J. Physiol. 169: 780, 1963.
19. Katz, R. L., and Eakins, K. E.: The effects of succinylcholine, decamethonium, hexacarbacholine, gallamine and dimethyl tubocurarine on the twitch and tonic neuromuscular systems of the cat, J. Pharmacol. Exp. Therap. 154: 303, 1966.
20. Bach-y-Rita, P., and Ito, F.: In vivo studies on fast and slow muscle fibers in cat extraocular muscle, J. Gen. Physiol. 49: 1177, 1966.
21. Sanghvi, I. S.: Stimulation of mammalian extraocular muscle by cholinomimetics, Ph.D. Thesis. University of Illinois, 1966.
22. Dietert, S. E.: The demonstration of different types of muscle fibers in human extraocular muscle by electron microscopy and cholinesterase staining, Invest. Ophthal. 4: 51, 1965.
23. Drucker, A. P., Sadove, M. S., and Unna, K. R.: Ophthalmic studies of curare and curare-like drugs in man, Amer. J. Ophthal. 34: 543, 1951.
24. Sobel, A. M.: Hexafluorenium, succinylcholine, and intraocular tension, Anesth. and Analg. Curr. Res. 41: 399, 1962.

Surgery

SURGICAL RISK IN LUNG DISEASE Preoperative assessment of pulmonary disease is essential to estimate properly the patient's chances of survival from major surgery. Almost all patients will tolerate operative intervention if adequate ventilatory assistance is provided. Postoperatively, in both obstructive and restrictive lung disease, adequate spontaneous ventilation may be difficult to achieve if the supine position must be used. Therapy postoperatively may include mechanical ventilation and measures to liquify secretions. Steroids may be extremely helpful in the severe asthmatic, both to liquify secretions and relieve bronchospasm. (*Olsen, A. M.: Evaluation of Surgical Risk in Patients with Chronic Obstructive Lung Disease and other Respiratory Handicaps, Med. Clin. N. Amer. 51: 341 (March) 1967.*)

CAROTID SURGERY Patients with transient cerebral ischemia or asymptomatic carotid stenosis are the best candidates for carotid surgery. Operative mortality has been reduced to 1 per cent with use of internal shunts and modification of anesthetic technique. At the start of anesthesia, the patient is given 10 mg. of dexamethasone to protect against cerebral edema. Before arteriotomy, 5,000 units of heparin are given. The CO_2 absorber is turned off to increase cerebral blood flow and elevate jugular venous blood P_{CO_2} and P_{O_2}. Frequent extrasystoles, attributed to excessive elevation of CO_2, are an indication to turn in the soda lime again. The blood pressure is not permitted to fall below normal at any time, phenylephrine being used if necessary. (*Movius, H. J., Zuber, W. F., and Gaspar, M. R.: Carotid Thromboendarterectomy, Arch. Surg. 94: 585 (May) 1967.*)