

CONTRACTION OF THE OCULOROTARY MUSCLES AND INTRAOCULAR PRESSURE*

A TONOGRAPHIC AND ELECTROMYOGRAPHIC STUDY OF THE EFFECT OF EDROPHONIUM
CHLORIDE (TENSILON) AND SUCCINYLSCHOLINE (ANECTINE) ON THE
INTRAOCULAR PRESSURE

WALTER KORNBLUETH,[†] M.D.

Jerusalem, Israel

AND

ARTHUR JAMPOLSKY, M.D., EDWARD TAMLER, M.D., AND ELWIN MARG,[‡] PH.D.

San Francisco, California

Numerous studies have shown that contraction of the oculorotary muscles increased the intraocular pressure.¹⁻⁵ The effect on the ocular tension was found to be similar if the muscles were stimulated mechanically, electrically or chemically.

The purpose of this paper is to show that an increase in the tonus of the oculorotary muscles is associated with and may be the cause of a rise in intraocular pressure and that the increase in intraocular pressure is proportional to the degree of contraction of the oculorotary muscles.

MATERIAL AND METHODS

Tonographic and electromyographic measurements were performed simultaneously in 10 patients. The patient was put on a table in an electrically shielded cage made of copper window screening. The electromyographic technique used here and the interpretation of electromyograms are described in detail elsewhere.^{6,7} In all the cases the electrodes were inserted into the horizontal or vertical recti of one eye, recording agonist and antagonist simultaneously. An electronic tonometer with a 5.5-gm. weight was used. This was attached to a recorder

outside the shielded cage; the wire connecting the electrically insulated tonometer hand-piece with the amplifier was led into the cage through a small hole in the screen. In two normal patients, and in three patients with limitation of eye movements due to myasthenia gravis, continuous electromyographic recordings were made for the duration of the experiment. The patients with myasthenia gravis discontinued drugs at least 24 hours before the test. The tonometer was placed on one eye, and after a tonography of one to two minutes' duration, 10 mg. of edrophonium chloride was injected intravenously and the tension recorded for a few minutes thereafter without removing the tonometer from the cornea. The same procedure with an additional injection of 10 mg. of edrophonium chloride was repeated five to 10 minutes later on the second eye.

In five normal subjects, succinylcholine in varying amounts (5.0 mg., 10 mg., 15 mg., 20 mg.) was injected intravenously while electromyography combined with tonography were performed as described above. All patients received a small amount of demerol as premedication, and two patients were given regulated Plane I general anesthesia with pentothal sodium.

OBSERVATIONS

Edrophonium chloride did not alter the electrical activity of the oculorotary muscles (in normal patients), nor the usual smoothly declining curve of tonography (fig. 1). Patients with myasthenia gravis showed a moderate increase of activity of the oculoro-

* From the Division of Ophthalmology, Department of Surgery, Stanford University School of Medicine. This study was supported by funds under O. N. R. Contract 225 (20) Nr 144 108, USPHS Grant B686 and by a Fight for Sight Research Fellowship of the National Council to Combat Blindness, Inc., New York.

[†] Department of Ophthalmology, Hadassah Rothschild University Hospital, Jerusalem, Israel.

[‡] School of Optometry, University of California, Berkeley.

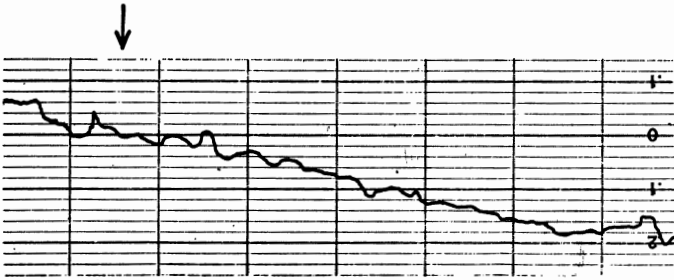


Fig. 1 (Kornblueth, et al.). Tonographic record of normal subject, showing no change in intraocular pressure following intravenous injection of 10 mg. of edrophonium chloride (Tensilon). Time is one-half minute between vertical lines.

tary muscles tested approximately 20 to 30 seconds following the injection of edrophonium chloride, and coinciding with this change of muscle activity there was a rise of 2.0 to 4.5 mm. Hg in the tonogram (figs. 2A and 3A). The intraocular pressure decreased after one-half minute in spite of continuous higher electrical activity of the oculorotary muscles (fig. 3B). The second injection of 10 mg. edrophonium chloride, repeated five to 10 minutes later for measurement of second eye, caused a much smaller increase of both the electrical activity of the muscles and of the intraocular pressure (fig. 2B).

Succinylcholine produced some enophthalmus in all patients appearing 20 to 30 seconds following the injection. None of the subjects became apnoeic and there was no need for artificial respiration. There was a rise in intraocular pressure coinciding with the appearance of the enophthalmus, which was less in the patients under general anesthesia, 2.0 to 4.0 mm. Hg (fig. 4), than in the fully conscious patients, 5.0 to 14 mm.

Hg (fig. 5). It seemed that the duration of increase in intraocular pressure, rather than the amount of increase, was related to the dosage of the drug administered. The rise in ocular tension occurred at the moment the electrical activity of the oculorotary muscles became extremely small. There was no sudden burst of electrical activity of the oculorotary muscles immediately before the onset of electrical silence of these muscles (fig. 6).

DISCUSSION

EDROPHONIUM CHLORIDE (TENSILON)

This product, an analogue of neostigmine, is a rapidly acting cholinergic drug and is characterized by prompt, brief action in patients with myasthenia gravis.^{8,9} The response consists of a temporary increase of muscle strength within one-half to five minutes following an intravenous injection. It causes fasciculations in normal patients without increase in muscle strength.

The increase in electrical activity of oculorotary muscles in patients with myas-

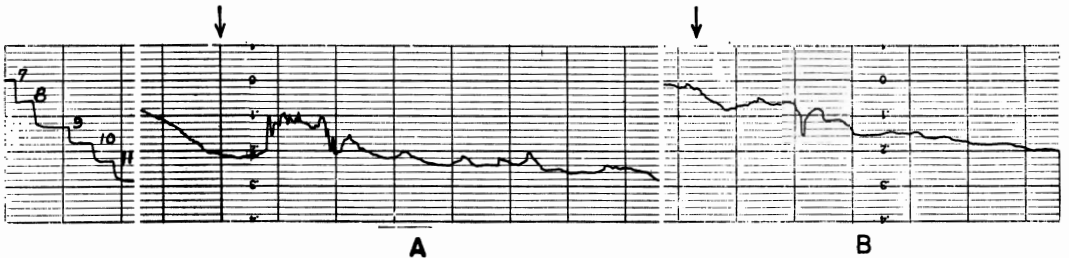


Fig. 2 (Kornblueth, et al.). (A) Tonographic record of a subject with myasthenia gravis, showing increase in intraocular pressure following intravenous injection of 10 mg. of edrophonium chloride (arrow). (B) Tonographic record of other eye of same subject as in Figure 2A, showing smaller rise in tension following a second injection of 10 mg. of edrophonium chloride approximately five minutes after the first injection.

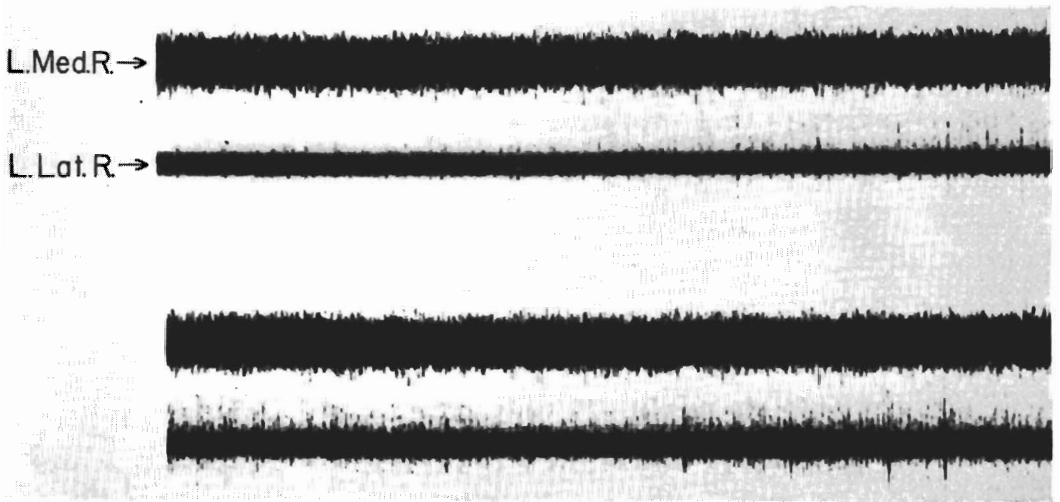


Fig. 3A (Kornblueth, et al.). Same subject as in Figure 2A, showing increasing activity of the left lateral rectus and no significant change in the antagonist left medial rectus which indicates no eye movement following intravenous injection of 10 mg. of edrophonium chloride. [This is a continuous record.] The increased activity coincided with the rise in intraocular pressure seen in Figure 2A.

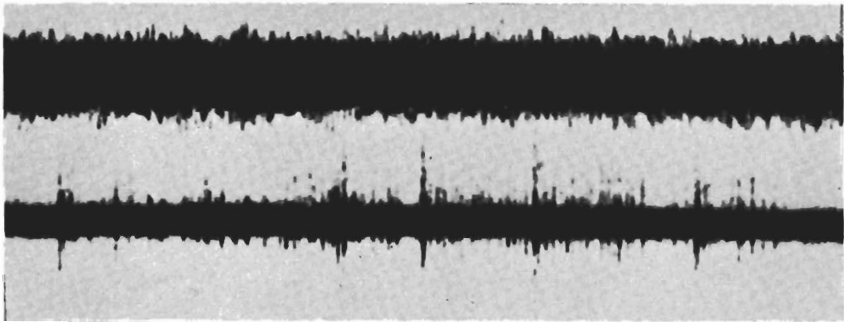


Fig. 3B (Kornblueth, et al.). Two and one-half minutes after intravenous injection of edrophonium chloride in same subject showing maintained increased activity of left lateral rectus, during which time the intraocular pressure was decreasing.

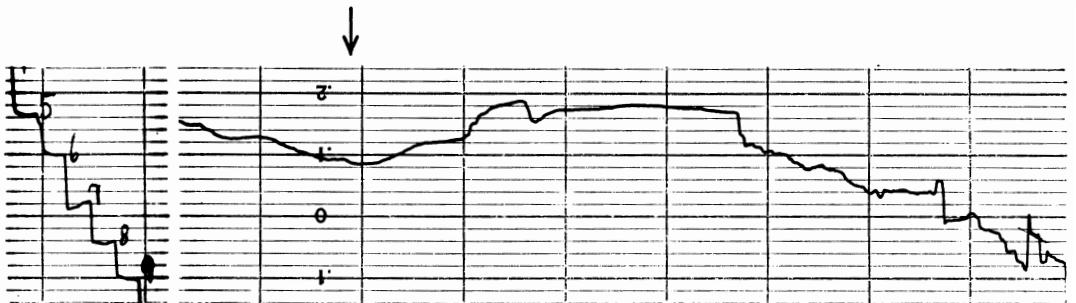


Fig. 4 (Kornblueth, et al.). Tonographic record of a seven-year-old subject under general anesthesia, showing small increase in intraocular pressure following intravenous injection of 5.0 mg. succinylcholine (arrow).

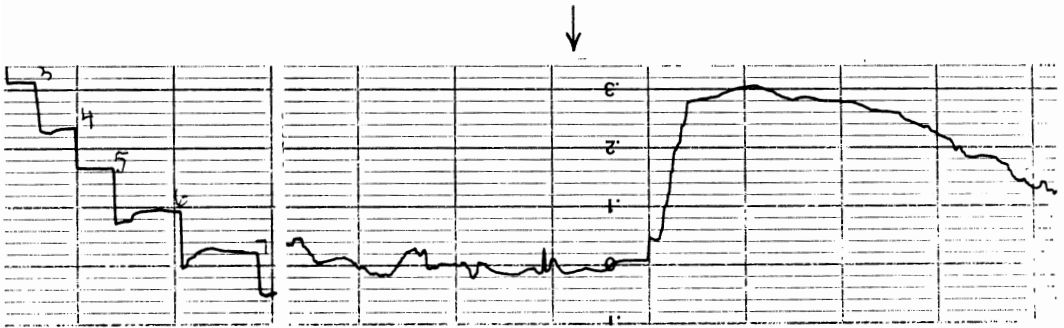


Fig. 5 (Kornblueth, et al.). Tonographic record of a fully conscious patient, showing a marked increase in intraocular pressure following intravenous injection of 5.0 mg. of succinylcholine (arrow).



Fig. 6A (Kornblueth, et al.). Decreased activity in horizontal recti 30 seconds after intravenous injection of 10 mg. succinylcholine.

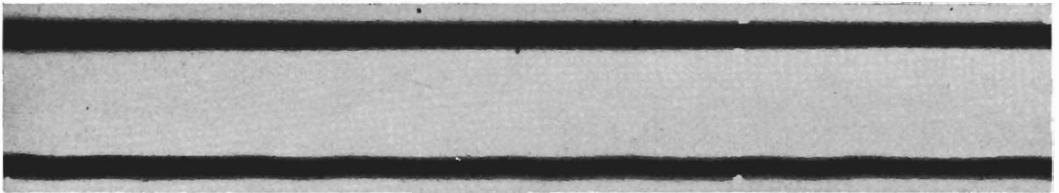


Fig. 6B (Kornblueth, et al.). Electrical silence in horizontal recti of same subject approximately 60 seconds after intravenous injection of 10 mg. of succinylcholine.

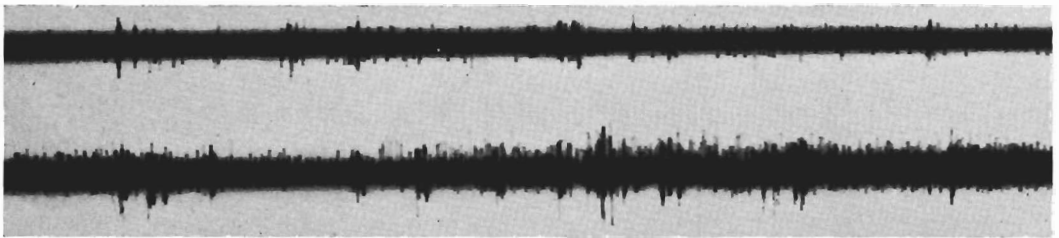


Fig. 6C (Kornblueth, et al.). Shows return of activity in horizontal recti muscles of same subject approximately two minutes after intravenous injection of 10 mg. of succinylcholine.

themia gravis following an injection of edrophonium chloride was described previously.^{10,11} It was stated that increased activity was not necessarily accompanied by much or any improvement of ocular motility.

Our study confirmed the demonstration

of a moderate increase in the electrical activity of only those oculorotary muscles which showed a lowered activity before the injection of edrophonium chloride. Increase of electrical activity of the oculorotary muscles was accompanied by a moderate rise of

intraocular pressure which subsided after one-half minute in spite of continued higher electrical activity, of the oculorotary muscles. The rise in intraocular pressure might be explained by the sudden increase of the oculorotary muscle tonus. Consequently, more aqueous humor is expelled from the eye through the normal outflow channels, and the eye apparently adjusted readily to the changed muscle tonus. There was only a slight increase of electrical activity of the oculorotary muscles, and of the ocular tension, following the second injection which was given five to 10 minutes after the first injection and before the effect of the first injection had completely subsided. In normal subjects, there was no rise in intraocular pressure, and following the edrophonium chloride injection, there was no demonstrable change in the recorded electrical activity of the oculorotary muscles.

SUCCINYLCOLINE

This agent, a competitor of acetylcholine, blocks the myoneural junction by depolarizing the motor endplate of the muscle and is not destroyed as rapidly as acetylcholine. It causes a temporary flaccid paralysis of the skeletal musculature, and because of this action it is widely used in general anesthesia and general surgery.

The oculorotary muscles react differently to succinylcholine than the general skeletal musculature. The oculorotary muscles show either a contraction or a sustained contracture. Excellent studies on man and experimental animals¹²⁻¹⁹ showed that a steep rise in intraocular pressure (amounting to as much as 38 mm. Hg) was due to a contraction or contracture of the oculorotary muscles. This finding is evidenced by the appearance of enophthalmus and immobility of the globe following an injection of succinylcholine. Small doses of this drug in experimental animals produced a tetanic contraction while higher doses caused a contracture of the oculorotary muscles.¹⁸ (A contraction of the oculorotary muscles is evidenced by

an increased muscle tension and an increased electrical activity. In contracture the development of marked muscle tension is attended by complete absence of electrical activity of the muscle.) The steep instant rise (fig. 5) in intraocular pressure was most probably due to strong mechanical pressure on the globe produced by the marked contracture of the oculorotary muscles tested. In deep anesthesia, which customarily produced electrical silence of all oculorotary muscles, succinylcholine did not induce any electrical activity in this state.

Our study confirmed previous findings that the rise in intraocular pressure was less marked in patients under superficial general anesthesia (who had little electrical tonus as a result of the anesthesia) than in conscious subjects (who had normal electrical tonus). The amount of the drug did not necessarily determine the amount of rise of the intraocular pressure. Previous electromyographic studies by others, of the effect of succinylcholine were performed in man and experimental animals during general anesthesia only.^{17, 18, 20}

In the present study electromyography was done on conscious patients following an injection of succinylcholine and the electrical activity of the oculorotary muscles was correlated with the rise in intraocular pressure by simultaneous tonography. Our electromyographic findings are not in complete agreement with those described previously. In all our cases tested the rise in intraocular pressure coincided with the occurrence of electrical silence of the oculorotary muscles. The initial burst of increased electrical activity (before electrical silence) found by others was not seen in any of our cases.

One possible explanation for this discrepancy lies in the different technique employed. Whereas we use simultaneous, multichannel recordings of agonist-antagonist pairs of muscles, other investigators have often used single channel recordings. With simultaneous multichannel recordings one can easily distinguish a co-activity of muscle groups as

compared to a rotation of the eye which is evidenced by an increased electrical activity of the agonist and a reciprocal reduction of activity of the antagonist. An increased electrical activity in the one recorded muscle when one channel only is used, could therefore be a part of co-activity or simply an eye rotation often found shortly after an injection of succinylcholine before the eye is fixed in position by the contracture of the oculorotary muscles.

The different effect of edrophonium chloride and succinylcholine on the duration and amount of rise in intraocular pressure might have the following explanation. Edrophonium chloride caused a moderate increase in the tonus of the oculorotary muscles, and the eye adjusted easily to the new situation in spite of continued increased activity of the oculorotary muscles. Succinylcholine caused the whole globe to be squeezed by the mechanical force of marked muscle contractures, and aqueous humor could only be pushed out through the outflow channels when the muscles started to relax and to release the squeeze. Thus two different drugs with similar action on the oculorotary muscles caused changes in the intraocular pressure according to the degree of contraction of the oculorotary muscles produced by these drugs.

SUMMARY

The effect of edrophonium chloride (Ten-

silon) and succinylcholine (Anectine) on the state of contraction of the oculorotary muscles and its influence on the intraocular pressure were studied with the aid of electromyography and tonography. It was found that edrophonium chloride, which increased the activity of the oculorotary muscles only in patients with myasthenia gravis, produced a moderate rise in intraocular pressure coinciding with the increased tonus of the oculorotary muscles. In normal subjects no demonstrable change in electrical activity of the oculorotary muscles, and consequently no change in the intraocular pressure, was seen. Succinylcholine which produced a marked contracture of the oculorotary muscles, as evidenced by electrical silence at the height of the effect of the drug, caused an appreciably greater increase in intraocular pressure in conscious normal subjects.

It was shown that the two different drugs, one producing a contraction, and the other a contracture of the oculorotary muscles caused a change in intraocular pressure corresponding to the degree of shortening of the oculorotary muscles produced by each of these drugs.

*Hadassah Rothschild University Hospital.
Stanford University Hospitals (15).*

We are indebted to Mr. William Houweling and to Niles Roth, B.A., M.O., for technical assistance, to Mr. Wilmer Renner for photographic assistance, and Parsons Optical Laboratory for loan of equipment.

REFERENCES

1. v. Hippel, A., and Gruenhagen, A.: Ueber den Einfluss der Nerven auf die Hoehe des intraocularen Druckes. Arch. f. Ophth., 14:219, 1868.
2. Wessely, K.: Ueber den Einfluss der Augenbewegungen auf den intraocularen Druck. Arch. f. Augenh., 81:102, 1916.
3. Hine, M. L.: Some observations on the normal eye. Ophthalmoscope, 14:360, 1916.
4. Duke-Elder, S.: Textbook of Ophthalmology. St. Louis, Mosby, 1838, v. 1, p. 508.
5. Greaves, D. P., and Perkins, E. S.: Influence of the third cranial nerve on intraocular pressure. Brit. J. Ophth., 37:54, 1953.
6. Marg, E., Jampolsky, A., and Tamler, E.: Elements of human extraocular electromyography. A.M.A. Arch. Ophth., 61:258-269, 1959.
7. Jampolsky, A., Tamler, E., and Marg, E.: Artifacts and normal variations in human ocular electromyography. A.M.A. Arch. Ophth., 61:402, 1959.
8. Osserman, K. E., and Kaplan, L. I.: Rapid diagnostic test for myasthenia gravis. J.A.M.A., 150:265, 1952.

9. Osserman, K. E., and Teng, P.: Studies in myasthenia gravis: A rapid diagnostic test. Further progress with edrophonium (Tensilon) chloride. *J.A.M.A.*, **160**:153, 1956.
10. Breinin, G. M.: Quantitation of extraocular muscle innervation. *A.M.A. Arch. Ophth.*, **57**:644, 1957.
11. ———: New aspects of ophthalmoneurologic diagnosis. *A.M.A. Arch. Ophth.*, **58**:375, 1957.
12. Hoffmann, H., and Lembeck, F.: Das Verhalten der ausseren Augenmuskeln gegenueber Curare, Decamethonium (clo) und Succinylcholin. *Arch. f. exp. Path. & Pharmakel*, **216**:552, 1952.
13. Hoffmann, H., and Holzer, H.: Wirkung von Muskelrelaxantien auf den Intraocularen Druck. *Klin. Monatsbl. f. Augenh.*, **123**:1, 1953.
14. Hoffmann, H.: Ueber die Wirkung von Muskelrelaxantien am Auge. *Klin. Monatsbl. f. Augenh.*, **130**:32, 1957.
15. Hoffmann, H., and Lembeck, F.: Pharmakologische Untersuchungen am isolierten ausseren Augenmuskel. *Arch. f. Ophth.*, **158**:277, 1957.
16. Lincoff, H. A., Ellis, C. H., DeVoe, A. G., de Beer, E. J., Impastato, D. J., Berg, S., Orkin, L., and Magda, H.: The effect of succinylcholine on intraocular pressure. *Am. J. Ophth.*, **40**:501, 1955.
17. Lincoff, H. A., Breinin, G. M., and DeVoe, A. G.: The effect of succinylcholine on the extraocular muscles. *Am. J. Ophth.*, **43**:440, 1957.
18. Macri, F. J., and Grimes, P. A.: The effect of succinylcholine on the extraocular striate muscles and on the intraocular pressure. *Am. J. Ophth.*, **44**:221 (Oct. Pt. II) 1957.
19. Dillon, B., Sabawala, P., Taylor, D. B., and Gunter, R.: Action of succinylcholine on extraocular muscles and intraocular pressure. *Anesthesiology*, **18**:44, 1957.
20. Björk, A.: Enophthalmus elicited by succinylcholine, *Acta Anaesthesiology. Scand.*, **1**:41, 1957.

Reprinted from
AMERICAN JOURNAL OF OPHTHALMOLOGY
Vol. 49, No. 6, June, 1960