Failure of Nondepolarizing Neuromuscular Blockers to Inhibit Succinylcholine-induced Increased Intraocular Pressure, A Controlled Study

Elsie F. Meyers, M.D.,[*] Theodore Krupin, M.D.,[†] Mark Johnson, M.D.,[†] Harry Zink, M.D.[†]

Ordinary skeletal muscles differ from extraocular muscles both histologically and morphologically.[1,2] Depolarizing drugs, such as succinylcholine (SCh) cause fasciculations of white muscles, followed by paralysis. The effect of SCh on extraocular muscles is a slow and prolonged tonic contraction.[3,4] Contraction of extraocular muscles may result in an elevation of intraocular pressure (IOP), which can be detrimental in the presence of certain ocular disorders.

A portion of the increase of IOP may be secondary to choroidal vascular dilatation and possibly due to relaxation of orbital smooth muscle, although in man this structure is poorly developed.[4–7]

Pretreatment with small doses of nondepolarizing neuromuscular blockers has been reported to prevent increased IOP associated with the use of SCh.[8] This previous study did not include a control group receiving saline pretreatment for comparison, the age of the patient population was not reported, and premedication was not standardized. Data from cats were included, although cat eyes differ anatomically from human eyes. We have investigated the effects of pretreatment with two nondepolarizing muscle relaxants, d-tubocurarine (dTc) and gallamine, on SCh-induced elevation of intraocular pressure in adults and children.

METHOD

Seventy patients 3 years old or older were anesthetized for a variety of intraocular and extraocular surgical procedures. Premedication consisted of droperidol 0.1 mg/kg, im, with a maximum dose of 6 mg, and atropine 0.02 mg/kg, im or iv, with a maximum dose of 0.6 mg. Inhalation induction with halothane–N_2O–

* Assistant Professor of Anesthesiology.

† Assistant Professor of Ophthalmology.

‡ Fellow in Ophthalmology.

O_2 was used in patients less than 9 years old. Older patients received thiopental, 2–7 mg/kg, iv, for induction.

The 60 patients who received SCh were given halothane, 1.5 per cent with N_2O–O_2 1:1 during tonometry preceding intubation. Ten children who received no muscle relaxant (saline pretreatment and saline control) were given halothane, 3–4 per cent, with N_2O–O_2 1:1 during tonometry just before endotracheal intubation. All endotracheal intubations were orotracheal and were accomplished in less than 40 seconds, utilizing standard straight or curved laryngoscope blades. Ventilation was controlled 2 minutes prior to endotracheal intubation. A semiclosed circle system with a CO_2 absorber was employed for patients weighing more than 25 kg. A nonrebreathing system with a gas flow equal to 2.5 times minute volume was used for patients weighing less than 25 kg. All patients were given halothane, 1.5 per cent, and N_2O–O_2 3:2 immediately following endotracheal intubation.

Baseline IOP measurements were made on one eye when the eyelid reflex was absent and the pupils were centrally fixed. No patient studied had glaucoma or corneal disease. The eye not operated on was studied in unilateral operations. All patients were in the supine position. IOP measurements were performed by one of three ophthalmologists using a portable Perkins applanation tonometer and topical fluorescein with tetracaine, 0.5 per cent 1–3 drops. Pretreatment with d-tubocurarine (dTc), 0.09 mg/kg, gallamine, 0.3 mg/kg, or saline solution 1 ml, was given. IOP was remeasured 3 minutes after pretreatment. SCh, 1–1.5 mg/kg, iv, or saline solution, 1 ml, was then administered and IOP remeasured a minute later, just prior to intubation. IOP was also measured in 30 patients just after intubation.

Statistical analyses were performed utilizing the t test for paired data for comparisons within treatment groups and Student's t test for comparisons between groups.

RESULTS

d-Tubocurarine was given as pretreatment before SCh to ten children (mean age 6 years) and ten adult patients (mean age 33.9 years) and saline solution pretreatment was given before SCh to ten children (mean age 6.7 years) and ten adult patients (mean age 33.6

TABLE 1. Effects of Succinylcholine (SCh) on Intraocular Pressure: Pretreatment with d-Tubocurarine (dTc)

Number of Patients	Pretreatment*	Mean Age (Years)	Intraocular Pressure (Torr, Mean ± SEM)		
			Baseline	3 Min after Pre-treatment	1 Min after SCh†
Children 10	dTc	6.0	12.9 ± 1.1	11.7 ± 0.8	25.1‡ ± 1.8
10	Saline control	6.7	12.8 ± 1.3	12.1 ± 1.3	23.3‡ ± 2.1
Adults 10	dTc	33.9	11.4 ± 1.3	9.5 ± 0.7	21.1‡ ± 1.7
10	Saline control	33.6	12.6 ± 0.7	12.1 ± 1.0	20.2‡ ± 1.6

* d-Tubocurarine, 0.09 mg/kg, im, or saline solution, 1 ml, im. Ten patients per group.
† 1 to 1.5 mg/kg, iv.
‡ Significant difference between baseline and after pretreatment, t test for paired data, P < 0.005.

years). dTc and saline pretreatment did not alter baseline IOP's which were similar in all four groups. After iv administration of SCh there were elevations of IOP in all four groups (P < 0.001) (table 1). The responses were also similar: the numbers of patients showing increases in IOP of more than 6 torr were: 5 saline control and 5 dTc-pretreatment adults; 9 saline control and 8 dTc-pretreatment children.

In the double-blind gallamine- or dTc-pretreatment study (table 2), IOP's were similarly increased (P < 0.001) in both groups following SCh administration. Showing increases of more than 6 torr in IOP were nine gallamine-pretreatment patients and ten dTc-pretreatment patients.

Ten children received saline solution instead of muscle relaxants and had their tracheas intubated with only halothane anesthesia (table 3). IOP's measured when the children were just asleep and later just prior to endotracheal intubation were similar. Immediately following endotracheal intubation IOP was significantly elevated (P < 0.001). However, IOP following endotracheal intubation after only halothane was significantly lower (P < 0.001) than IOP with gallamine or dTc pretreatment before SCh. One of 10 children whose tracheas were intubated using only halothane had an increase of IOP of more than 6 torr.

Of 40 patients pretreated with nondepolarizing muscle relaxants before SCh, observable muscle fasciculations developed in only two (5 per cent). Of 20 patients pretreated with saline solution before SCh, all of the adults and seven of ten children (85 per cent of the combined group) had fasciculations.

DISCUSSION

The present study confirms that IOP may increase following administration of iv SCh. This elevation oc-

curs in children and adults and is unrelated to the presence or absence of muscle fasciculations. However, this IOP response does not occur in all patients. Only 14 (70 per cent) of 20 control adults and children had increases of more than 6 torr in IOP after SCh (table 1). Animal studies indicate that dTc may cause some increase in baseline tension of extraocular muscles, while gallamine does not.[9] According to our results, neither pretreatment with dTc nor pretreatment with gallamine prevents elevated IOP after SCh. Of 40 patients receiving gallamine or dTc pretreatment, 33 (82.5 per cent) had increases of more than 6 torr.

These findings disagree with those in the previous report,[8] which concluded that similar doses of nondepolarizing neuromuscular blockers prevented SCh-induced increases of IOP. There are two possible reasons for this discrepancy. First, our study was double-blind, since the ophthalmologist was unaware of the drugs administered. Second, applanation tonometry was used in our study. The end point utilizes corneal patterns that must be properly centered to obtain an accurate reading. Applanation methods read directly the grams needed to produce flattening of a given corneal area, and are directly convertible to torr. The weight applied to the eye (0.5 g) is very small, with minimal artificial elevation of intraocular pressure. The result is not affected by the rigidity of the ocular coats.[10,11]

Other factors may affect IOP,[12] making meaningful controlled studies difficult to obtain. Factors that may

TABLE 2. Effects of Succinylcholine (SCh) on Intraocular Pressure: Double-blind d-Tubocurarine (dTc) or Gallamine Pretreatment

Number of Patients	Pretreatment*	Mean Age (Years)	Intraocular Pressure (Torr, Mean ± SEM)			
			Baseline	3 Min after Pre-treatment	1 Min after SCh†	1 Min after Intubation
10	dTc	13.4	13.0 ± 1.0	12.3 ± 1.2	24.0 ± 1.3	25.0 ± 1.4
10	Gallamine	8.7	10.9 ± 1.1	10.6 ± 1.0	23.4 ± 2.3	25.5 ± 1.8

* dTc, 0.09 mg/kg, or gallamine, 0.3 mg/kg.
† 1 to 1.5 mg/kg, iv.

TABLE 3. Intraocular Pressure in Children Using Halothane for Endotracheal Intubation without Muscle Relaxants

Number of Patients	Mean Age (Years)	Intraocular Pressure (Torr, Mean ± SEM)		
		Just Asleep	Prior to Endotracheal Intubation	1 Min after Endotracheal Intubation
10	4.8	9.5 ± 1.2	9.8 ± 0.9	13.7* ± 1.2

* Significant between just asleep and prior to endotracheal intubation, t test for paired data, P < 0.01.

increase IOP, in addition to SCh, are: squeezing eyelid muscles, external pressure, hypoxia, hypercarbia,[13] increased venous pressure, retrobulbar pressure from hemorrhage or injection of a local anesthetic, and endotracheal intubation. Factors that may lower IOP include: hypocarbia, decreased venous pressure, osmotic agents, and central nervous system depressants including hypnotics, tranquilizers, neuroleptic agents, narcotics, and potent inhalation agents.[14-17] The role of ketamine in IOP seems unclear, as reports are conflicting.[18-21] Factors that affect IOP only slightly are: diurnal variation, age, fluctuations in arterial pressure, atropine premedication, and nondepolarizing neuromuscular blockers in the presence of adequately assisted ventilation.[22,23] Among other factors that may influence IOP are body temperature and metabolic acidosis or alkalosis.[24]

In this study, three patients in whom there were clinical difficulties were excluded. All premedicant drugs, anesthetic agents, and muscle relaxant drugs were standardized. Local laryngotracheal anesthesia was avoided to decrease the number of drugs utilized.

Droperidol was chosen as a premedicant because of its desirable tranquilizing and antiemetic effects. We considered alpha-adrenergic blocking effects to be minimal or absent with the small doses given. Although Ausinsch et al.[17] found no correlation between depth of anesthesia and IOP, others[15,25,26] found decreased pressures during halothane anesthesia similar to that administered to the patients in our control group (table 3), who received no SCh.

We believe that iv administration of SCh is contraindicated by: penetrating eye injury, weakened cornea or sclera in danger of perforation, intraocular surgery, extraocular surgery in which the sclera is incised or weakened (scleral buckling), and following intraocular surgery before complete wound healing. Common sense dictates that in a life-threatening situation, SCh may need to be administered even though the eye may be jeopardized. We believe it prudent to avoid SCh whenever possible when integrity of the eye is lost or threatened.

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