Anesthesiology
67:50–53, 1987

"Defasciculation" with Metocurine Prevents Succinylcholine-induced Increases in Intracranial Pressure

Joseph A. Stirt, M.D., Kenneth R. Grosslight, M.D.,† Robert F. Bedford, M.D.,‡ Dennis Vollmer, M.D.§*

In order to determine whether a small, "defasciculating" dose of metocurine could prevent increases in intracranial pressure (ICP) induced by succinylcholine (Sch), the authors studied 12 patients (ages 25–79 yr) undergoing craniotomy for excision of malignant supratentorial gliomas. After insertion of a subarachnoid bolt for ICP monitoring and a radial arterial cannula for determination of blood pressure and blood gas tensions, six patients (group I) were randomly allocated to receive MTC 0.03 mg/kg 3 min before induction of general anesthesia with thiopental 4 mg/kg and nitrous oxide 70% in O_2. Six other patients (group II) received saline 0.015 ml/kg instead of MTC, followed by the same induction sequence. After induction of anesthesia, ventilation was controlled by mask (Pa_{CO_2} = 40 mmHg ± 2 SE), and arterial and intracranial pressures were allowed to stabilize. Four minutes after thiopental administration (7 min after MTC), after a 1-min period of relatively stable arterial pressure and ICP, Sch 1 mg/kg was administered as a bolus. ICP and blood pressure were recorded continuously until normal twitch tension was restored. In group I (MTC pretreatment), ICP did not change significantly from the mean value observed before Sch, 14 mmHg ± 2 SE. In group II (saline pretreatment), ICP increased from 11 mmHg ± 2 SE to 23 mmHg ± 4 SE ($P < .05$). This study not only confirms previous work showing that Sch may induce marked ICP increases in lightly anesthetized patients with intracranial mass lesions, but also indicates that pretreatment with a "defasciculating" dose of MTC can prevent these potentially deleterious ICP increases in patients known to be at risk. (Key words: Brain: intracranial pressure. Muscle, skeletal: fasciculation. Neuromuscular relaxants: metocurine; succinylcholine.)

SUCCINYLCHOLINE (SCH) has been suspected of causing an increase in ICP in patients with compromised intracranial compliance.[1–8]¶ A recently published study has demonstrated that Sch-induced ICP changes can be prevented by complete paralysis with a nondepolarizing neuromuscular blocking agent.[8]

A clinical question unresolved by that report[8] was the issue of whether or not Sch-induced ICP increases could be prevented by a small "defasciculating" dose of a nondepolarizing agent. Therefore, we undertook a prospective, placebo-controlled study to determine whether a "defasciculating" dose of metocurine (MTC) would be effective in preventing increases in ICP from Sch in patients known to be at risk.

Methods and Materials

The subjects of this study were 12 consecutive patients with malignant supratentorial gliomas, ages 25–79 yr, scheduled for elective craniotomy. All patients were receiving dexamethasone, 20 mg PO daily. Preoperative computed tomographic (CT) scans of their heads indicated that all tumors were at least 3 cm in diameter, all patients had significant cerebral edema, and most had a shift of midline intracranial structures. The protocol for this study was reviewed and approved by the institution's Human Investigation Committee, and written consent was obtained from each patient or the nearest relative.

No premedication other than dexamethasone was administered. Using local anesthesia, peripheral venous and radial arterial catheters and a subarachnoid bolt were inserted. Arterial and intracranial pressures were continually transduced (Bentley® Model 800 transducers) and recorded (Brush® Model 440 recorder) with the zero reference point at the external auditory meatus. Neuromuscular blockade was monitored with a force transducer (Grass® Model FT-10) measuring adductor pollicis twitch tension in response to supramaximal ulnar nerve stimulation at 0.15 Hz delivered for a duration of 0.15 ms *via* subcutaneously placed 25-gauge needles.

In random sequence and in a double-blind fashion, six of the patients (group I) received MTC, 0.03 mg/kg iv, 3 min before induction of general anesthesia, whereas the other six patients (group II) received normal saline, 0.015 ml/kg. With patients in the supine 15° head-up position, anesthesia was induced with thiopental 4 mg/kg iv, and maintained with 70% nitrous oxide in oxygen. Ventilation was controlled by mask to maintain a relatively stable end-tidal CO_2 concentration (Hewlett-Packard® Model 47310-A capnometer), and verified by repeated arterial blood gas determinations 1 min before and 3 min after Sch administration.

* Assistant Professor of Anesthesiology
† Research Fellow in Anesthesiology
‡ Professor of Anesthesiology and Neurological Surgery
§ Assistant Professor of Neurological Surgery

Received from the Departments of Anesthesiology and Neurological Surgery, University of Virginia Medical Center, Charlottesville, Virginia. Accepted for publication February 17, 1987. Presented in part at the Annual Meeting of the American Society of Anesthesiologists, 1986, Las Vegas, Nevada.

Address reprint requests to Dr. Stirt: Department of Anesthesiology, Box 238, University of Virginia Medical Center, Charlottesville, Virginia 22908.

¶ Marsh ML, Dunlop BJ, Shapiro HM, Gagnon RL, Rockoff MA: Succinylcholine-intracranial pressure effects in neurosurgical patients (Abstract). Anesth Analg 59:550–551, 1980

Four minutes after thiopental administration (7 min after MTC), after a 1-min period of stable arterial pressure and ICP, Sch, 1 mg/kg iv, was administered as a bolus. Blood pressure, heart rate, and ICP were continuously recorded until muscle twitch returned to baseline height. Presence or absence of gross muscle fasciculations after Sch was noted by three independent observers.

Changes in ICP and mean arterial pressure (MAP) for both groups were tabulated at each min after Sch administration. Student's *t* test for paired data was used to make intragroup comparisons. For intergroup comparisons, multiple analysis of variance (MANOVA) was employed. If MANOVA showed significant differences between groups, Bonferroni's method of correction for multiple comparisons was employed. The incidence of Sch-induced fasciculations occurring with or without MTC pretreatment was compared using Fisher's exact test. $P \leqq 0.05$ was considered significant.

Results

Mean ages and weights were not significantly different between the two groups. Table 1 summarizes our observations before and after Sch administration in both groups of patients. The values reported after Sch represent the maximal changes which occurred. "Defasciculation" with MTC prevented the increase in ICP observed after Sch in the patients who received only placebo. In both groups, after Sch, Pa_{CO_2} was unchanged from values prior to Sch. Mean arterial pressure prior to Sch was not significantly different between groups, and changes in MAP following Sch were not significant.

Figure 1 graphically demonstrates the effect of MTC pretreatment on Sch-induced ICP changes over time. Baseline values for ICP were similar between the two groups. In group II (no pretreatment), mean ICP had increased significantly by 1 min after Sch and remained elevated for 7 min, after which recovery from Sch-induced neuromuscular blockade began to occur and ICP decreased toward baseline values. The maximum increase in ICP in group II occurred 4 min following Sch administration.

In all patients in both groups, 100% neuromuscular blockade followed Sch administration. No fasciculations were observed following Sch when MTC pretreatment was employed; visible fasciculations occurred in two patients who received Sch without prior MTC. The incidence of Sch-induced fasciculations when no MTC pretreatment was employed was not statistically significant when compared to the group which received MTC pretreatment.

TABLE 1. Intracranial Pressure (ICP), Mean Arterial Pressure (MAP), Cerebral Perfusion Pressure (CPP), and Arterial Co_2 (Pa_{CO_2}) Tension Before and After Succinylcholine (Sch) 1 mg/kg With and Without Metocurine (MTC) 0.03 mg/kg Pretreatment

	Group I (MTC Pretreatment)		Group II (Saline Pretreatment)	
	Before Sch	After Sch	Before Sch	After Sch
ICP (mmHg)	14 ± 2	13 ± 1	11 ± 2	23 ± 4*†
MAP (mmHg)	80 ± 7	73 ± 5	80 ± 8	85 ± 5
CPP (mmHg)	66 ± 6	60 ± 5	69 ± 7	62 ± 4
Pa_{CO_2} (mmHg)	40 ± 2	39 ± 2	40 ± 2	40 ± 1

All values are mean ± SEM. Values after Sch represent maximal changes which occurred.
* $P < 0.05$ *vs.* group II value before Sch.
† $P < 0.05$ *vs.* group I value after Sch.

Discussion

Succinylcholine can induce clinically significant increases in ICP in patients with malignant supratentorial tumors, and, presumably, with other disorders of intracranial compliance as well. This phenomenon has been described by Lanier *et al.*,[9] who noted EEG activation and a marked increase in cerebral blood flow (CBF) and ICP in lightly anesthetized dogs that received Sch.

While the mechanism by which Sch affects the CNS remains somewhat conjectural, it is thought to be due to

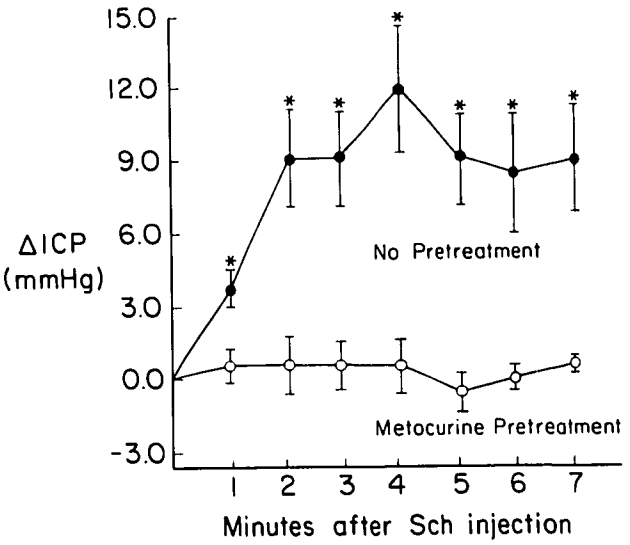

FIG. 1. Changes (mean ± SEM) in intracranial pressure (ICP) after administration of succinylcholine (Sch) 1 mg/kg to anesthetized patients with malignant brain tumors. Open circles indicate values following metocurine 0.03 mg/kg and Sch (group I); solid circles indicate values following saline and Sch (group II). Baseline values prior to Sch were similar; following Sch, ICP increased significantly in group II and remained elevated. *$P \leqq 0.05$ compared to baseline value prior to Sch injection.

afferent input from muscle spindle receptors.[10,11] Such input can be blocked by complete nondepolarizing neuromuscular blockade,[10,11] and this, in turn, prevents increases in ICP after Sch.[8,9] The similarity in time course for ICP increases after Sch alone in both animals[9] and humans (fig. 1) to the duration of human cortical EEG arousal after Sch[10] indicates that, at least temporally, the two phenomena are related.

There is some disagreement as to how effective a "defasciculating" dose of nondepolarizing agent might be in preventing cortical EEG activation and subsequent increases in CBF and ICP. The only previous study in humans[1] described the use of d-tubocurarine 3 mg prior to Sch 1.5 mg/kg in four patients. For comparison, the authors used a group of eight patients given pancuronium 0.1 mg/kg. All had evidence of elevated ICP secondary to either tumor or aneurysm. All patients received thiopental, with total doses ranging from 450–800 mg, and were hyperventilated. Laryngoscopy and intubation were performed 2 min following either pancuronium or Sch, and hyperventilation with 1% enflurane employed in all patients following intubation. Intracranial pressure was measured just prior to, during, and 2 min after intubation, and the d-tubocurarine/Sch group was noted to have a statistically significant increase in ICP during laryngoscopy and intubation compared to the pancuronium group. The authors concluded that pancuronium was superior to d-tubocurarine/Sch for control of ICP.

Two animal studies allowed complete nondepolarizing blockade with pancuronium[4] or gallamine[11] to dissipate, and found that Sch induced increased ICP[4] or EEG arousal,[11] although neither study actually measured residual neuromuscular blockade. These studies indicated that "defasciculating" doses of nondepolarizing agents might not be effective in preventing increases in ICP.

The term "defasciculation" may be less than accurate to describe the phenomenon under consideration in this paper. In both animals[4] and humans,[8¶] no correlation between the presence of visible fasciculations and the magnitude of ICP increases after Sch has been demonstrated. In fact, the greatest increases in ICP appear to occur in patients without fasciculations; visible fasciculations seem to correlate with little, if any, ICP increase.[8] Abundant experimental evidence exists to implicate increases in afferent muscle spindle activity with resultant increased cerebral blood flow as the cause of Sch-induced ICP increases and EEG arousal.[9–11] Thus, the term "partial spindle blockade" to describe the inhibiting effect of small doses of nondepolarizing relaxants on subsequent Sch-induced muscle spindle activity, while speculative, might be more descriptive and appropriate.

Our results indicate that "defasciculating" doses of MTC are effective in preventing intracranial hypertension associated with Sch in patients with intracranial tumors undergoing elective surgery, and we now incorporate this routinely in our clinical practice. Whether use of this technique prevents Sch-induced ICP changes in patients with acute head injuries, intracranial bleeding, or cerebrovascular disease remains to be determined.

As an alternative to Sch, use of the intermediate-duration nondepolarizing relaxants atracurium[12,13] or vecuronium[14] in neurosurgical patients has been shown not to result in adverse effects on ICP. These agents do have the disadvantage, however, of a recovery time substantially longer than that of Sch, even when pharmacologically aided reversal is employed. This may not be a substantive objection to their use in the operative setting, but, in other circumstances, may present problems.

For tracheal intubation in the emergency room or ICU setting without subsequent planned operative intervention, and where immediate reassessment of neurological status is critically important, use of Sch in selected patients with intracranial masses, for example, those at risk for aspiration, may still have a place in the therapeutic armamentarium. However, we would emphasize that laryngoscopy and intubation, tracheal suctioning, or surgical incision will result in marked ICP increases in patients who are not otherwise protected by the imposition of additional measures to stabilize ICP.[1,7] Use of Sch and controlled ventilation alone, even when preceded by a small dose of a nondepolarizing relaxant, will not protect against the ICP elevating effects of such potent stimuli.

In summary, in patients with brain tumors, a small dose of MTC (0.03 mg/kg) was used prior to induction with thiopental and Sch 1 mg/kg. No ICP increase occurred following this induction sequence. Use of a small dose of MTC prior to Sch prevents Sch-induced ICP increases in this patient population.

References

1. McLeskey CH, Cullen BF, Kennedy RD, Galindo A: Control of cerebral perfusion pressure during induction of anesthesia in high risk neurosurgical patients. Anesth Analg 53:985–992, 1974
2. Lewelt W, Moszynski K, Kozniewska H: Effect of depolarizing and non-depolarizing muscle relaxants and intubation on ventricular fluid pressure, Intracranial Pressure III. Edited by Beks JWF, Bosch DA, Brock M. New York, Springer-Verlag, 1976, pp 214–218

3. Moszynski K: Dynamic changes in cerebrospinal fluid pressure during neurosurgical operations. Acta Neurochir (Wien) 34:285–286, 1976
4. Cottrell JE, Hartung J, Giffin JP, Shwirey B: Intracranial and hemodynamic changes after succinylcholine administration in cats. Anesth Analg 62:1006–1009, 1983
5. Halldin M, Wahlin A: Effect of succinylcholine on the intraspinal fluid pressure. Acta Anaesthesiol Scand 38:155–161, 1959
6. Marx GF, Andrews IC, Orkin LR: Cerebrospinal fluid pressures during halothane anesthesia. Can Anaesth Soc J 9:239–245, 1962
7. Burney R, Winn R: Increased cerebrospinal fluid pressure during laryngoscopy and intubation for induction of anesthesia. Anesth Analg 54:687–690, 1975
8. Minton MD, Grosslight K, Stirt JA, Bedford RF: Increases in intracranial pressure from succinylcholine: Prevention by prior non-depolarizing blockade. ANESTHESIOLOGY 65:165–169, 1986
9. Lanier WL, Milde JH, Michenfelder JD: Cerebral stimulation following succinylcholine in dogs. ANESTHESIOLOGY 64:551–559, 1986
10. Mori K, Iwabuchi K, Fujita M: The effects of depolarizing muscle relaxants on the electroencephalogram and the circulation during halothane anesthesia in man. Br J Anaesth 45:605–610, 1973
11. Motokizawa F, Fujimori B: Arousal effect of afferent discharges from muscle spindles upon electroencephalograms in cats. Jpn J Physiol 14:344–353, 1964
12. Minton MD, Stirt JA, Bedford RF, Haworth C: Intracranial pressure after atracurium in neurosurgical patients. Anesth Analg 64:1113–1116, 1985
13. Rosa G, Orfei P, Sanfilippo M, Vilardi V, Gasparetto A: The effect of atracurium besylate (Tracrium®) on intracranial pressure and cerebral perfusion pressure. Anesth Analg 65:381–384, 1986
14. Stirt JA, Maggio W, Haworth C, Minton MD, Bedford RF: Vecuronium: Effect on intracranial pressure and hemodynamics in neurosurgical patients. ANESTHESIOLOGY 1987 (in press)