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Temperature Change and Neuromuscular Blockade by *d*-Tubocurarine or Pancuronium in Man

WOO YOUNG PARK, M.D.,* AND THOMAS E. MACNAMARA, M.B., CH.B.†

It has been held that the neuromuscular blocking action of nondepolarizing muscle relaxants is diminished by low temperatures.¹⁻⁴ However, recent investigations in animals rendered hypothermic revealed augmentation of the neuromuscular blocking effects of both *d*-tubocurarine and pancuronium.^{5,6} Because of these contradictory findings, an investigation was undertaken to determine the effects of temperature changes on the neuromuscular blocking actions of *d*-tubocurarine and pancuronium in man.

METHODS

Sixteen informed patients undergoing elective open-heart surgery and extracorporeal circulation were studied. Premedication consisted of diazepam, 5-10 mg, and morphine sulfate, 5-15 mg, im, approximately an hour prior to operation. Anesthesia was induced with incremental administration of morphine and diazepam, iv, while 100 per cent oxygen was administered by mask. Six patients needed additional small doses of thiopental for induction of anesthesia.

When anesthesia was deemed adequate, the ulnar nerve was stimulated at the wrist or elbow through percutaneous needles, using a Grass S48 Nerve Stimulator with supramaximal impulses of 0.2-msec duration at a rate of 0.2 Hz. The response of the adductor pollicis was measured via a force displacement transducer (Grass FT-10).

Patients were divided into four groups of four patients each: Group I received *d*-tubocurarine and hypothermia; Group II, *d*-tubocurarine and normothermia; Group III, pancuronium and hypothermia; Group IV, pancuronium and normothermia. After attainment of a control twitch height, *d*-tubocurarine

or pancuronium was administered iv in increments until the twitch height was depressed to less than 25 per cent of control. At this point the trachea was intubated. Anesthesia was maintained with nitrous oxide (50-70 per cent)-oxygen, morphine, and either *d*-tubocurarine or pancuronium. Supplemental doses of *d*-tubocurarine or pancuronium were administered to maintain twitch height between 5 and 25 per cent of control until 30 minutes before cardiopulmonary bypass, after which no further *d*-tubocurarine or pancuronium was given during the period of investigation.

As soon as the patients in Group I and Group III were on bypass, they were cooled to rectal temperatures of 28-30 C, a process that took approximately 15-25 min. These temperatures were maintained throughout bypass during the cardiac surgical procedure. At the completion of operation, patients were rewarmed to normal temperatures (36-37 C).

In patients in Group II and Group IV, on the other hand, temperatures were kept near normal (35-36.5 C) during bypass. Changes in twitch height obtained from normothermic patients in each muscle relaxant group were compared with those obtained from the corresponding hypothermic group.

Temperatures were monitored by nasopharyngeal and rectal temperature probes. Two patients in Group I had thenar muscle temperatures monitored as well, by use of a needle thermistor. Other variables monitored during the study included direct radial arterial pressure, by use of a Statham pressure transducer, and arterial blood gases, by use of a Corning pH and gas analyzer. The pump was primed with blood, 500-1,000 ml, lactated Ringer's solution, 2,000 ml, CaCl₂ (10 per cent), 5-10 ml, sodium bicarbonate (7.5 per cent), 5-10 ml, heparin, 9,000-12,000 units.

RESULTS

Comparison of the hypothermic and normothermic groups for each muscle relaxant showed that ages of the patients, body weights, and total doses of morphine, diazepam and muscle relaxant needed before bypass were very similar. Values of arterial blood gases and electrolytes, particularly potassium (K⁺), during bypass were also similar in all groups. Mean plasma K⁺ levels during bypass were about 3.8 mEq,

* Chief of Anesthesiology, Veterans Administration Hospital; Associate Professor in Anesthesiology, Georgetown University Medical School Washington, D. C.

† Professor and Chairman, Department of Anesthesiology, Georgetown University Medical School, Washington, D. C.

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Address reprint requests to Dr. Park: Department of Anesthesiology, Veterans Administration Hospital, 50 Irving Street, NW, Washington, D. C. 20422.

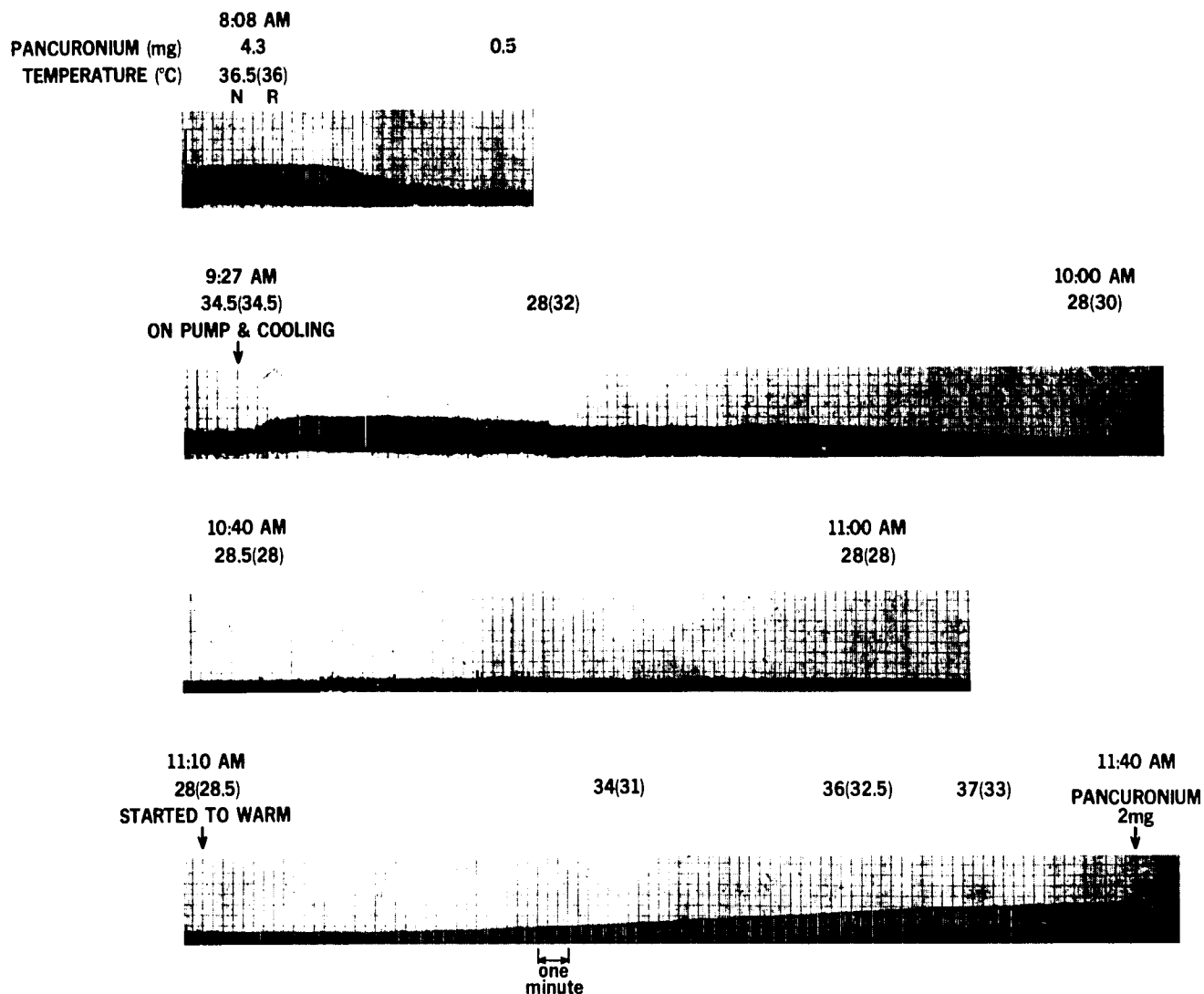


FIG. 1. Changes in twitch height following administration of pancuronium, at the start of extracorporeal circulation, and during hypothermia and rewarming. N = nasopharyngeal temperature (R = rectal temperature).

significantly lower than preoperative values of approximately 4.3 mEq in all groups. One patient in Group I needed iv administration of KCl to increase plasma K^+ from 2.6 to 4.6 mEq during bypass.

In the hypothermic groups, cooling the patient at 28 to 30 C during bypass, and maintaining this temperature, resulted in an initial rapid increase in twitch height. Then, twitch height began to decline steadily, before it again began to recover very slowly (fig. 1).

Warming the patients of both hypothermic groups (Group I and Group III) to normal temperatures resulted in faster recovery of twitch height (table 1, fig. 1). There was time-lag of approximately 15 to 20 min in rectal temperature change behind nasopharyngeal temperature change during either cooling or rewarming. Muscle temperatures monitored in two

patients showed changes comparable to the changes in rectal temperatures. In the normothermic group (temperatures 35–36.5 C), twitch heights showed continued slow recoveries after initial rapid recoveries at the start of bypass. Twitch heights in *d*-tubocurarine- and pancuronium-treated groups changed similarly during normothermia, hypothermia, and rewarming.

DISCUSSION

When cardiopulmonary bypass was begun, twitch height showed a sudden rapid recovery, within 30 sec. A plausible explanation for this phenomenon could be a rapid dilution with prime solution, which would suggest that the changes in twitch height cor-

related well with changes in plasma concentrations of the muscle relaxants.⁷

Average plasma K⁺ levels in all groups decreased from 4.3 mEq preoperatively to 3.8 mEq during bypass. Low plasma K⁺ is known to decrease twitch height.⁸ With either agent, twitch heights in the normothermic group showed a continuous steady recovery during bypass. This suggests that the effects of changes in plasma K⁺ were not significant in our study.

The enhancement of the neuromuscular blockade produced by *d*-tubocurarine or pancuronium during hypothermia might have been due either to a direct effect of hypothermia on the myoneural junction or to a direct effect on the action of muscle relaxant, or to a combination of the two. When the myoneural junction is exposed to hypothermia, quantal release of acetylcholine is increased and the motor end-plate becomes more sensitive to acetylcholine.^{9,10} These two factors can produce significantly increased isometric twitch tension of both directly and indirectly stimulated muscle. In spite of this increase in twitch tension, the neuromuscular blockade induced by either neuromuscular blocking agent was increased by hypothermia, implying that hypothermia probably affected the action of the neuromuscular blocking agent. The mechanisms involved in this phenomenon, however, are not yet clear. Further study will be needed to delineate the exact cause.

In summary, our study indicates that lowering the temperature enhances, while rewarming antagonizes, the neuromuscular blocking actions of *d*-tubocurarine and pancuronium. It is, therefore, recommended that usual doses of *d*-tubocurarine or pancuronium be reduced during hypothermia, and that muscle temperature of the patient be kept normal to insure adequate recovery from the muscle relaxant.

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Postpartum Uterine Pressures with Different Doses of Ketamine

GERTIE F. MARX, M.D.,* HUAN S. HWANG, M.D.,† PRASANTA CHANDRA, M.B., B.S.‡

The effects of ketamine on uterine tone and activity in term-pregnant women have been controversial, as

TABLE I. Twitch Height Changes at the Start of the Pump and during Hypothermia and Rewarming

Time	Twitch Height (Percentage of Control)	
	<i>d</i> -Tubocurarine	Pancuronium
At the start of the pump	18.5 ± 4.9	24.8 ± 11.9
During hypothermia (lowest)	7.3 ± 1.9	13.5 ± 6.7
30 minutes before start of warming	10.6 ± 4.7	16.7 ± 7.9
At start of warming	12.1 ± 4.1	22.8 ± 11.8
30 minutes after start of warming	59.8 ± 14.7*	63.8 ± 24.4*

Mean ± SEM.

* Recoveries in twitch height during the 30 minutes after the start of warming were significantly greater than those during the corresponding 30-minute period before warming for both *d*-tubocurarine and pancuronium.

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both increases^{1,2} and decreases^{3,4} have been observed. Recently, results obtained in late-first-trimester and

ogy-Obstetrics, Albert Einstein College of Medicine, Bronx, New York. Accepted for publication June 9, 1978.

Address reprint requests to Dr. Marx: Department of Anesthesiology, Albert Einstein College of Medicine—J-1224, 1300 Morris Park Avenue, Bronx, New York 10461.

* Professor of Anesthesiology.

† Senior Resident in Anesthesiology (present address: Moline, Ill.).

‡ Assistant Professor of Gynecology and Obstetrics.

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