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Title : COMPARATIVE NEUROMUSCULAR EFFECTS OF NORCURON AND PANCURONIUM AND THEIR REVERSAL WITH NEOSTIGMINE

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Introduction. Norcuron (Organon NC 45), a new non-depolarizing muscle relaxant similar in structure to pancuronium was recently introduced to the United States for clinical trials. The results of extensive investigations of Norcuron in animals[1] suggest that it has a short duration of action and no cardiovascular effects. We compared the potency, duration of action, and reversibility of Norcuron in man with those of pancuronium.

Methods. We obtained informed consent and approval from the Committee on Human Research to study 21 ASA I or II patients scheduled for surgery. Anesthesia was induced with thiopental, 100 to 150 mg iv, and the trachea was intubated without the use of muscle relaxants. Ventilation was controlled and anesthesia maintained with halothane, 0.4 to 1.0% end-tidal concentration, as measured continuously by mass spectrometry. Neuromuscular function was monitored by quantitating force-of-thumb adduction with a Grass FT-10 force transducer in response to supramaximal stimulation of the ulnar nerve at the wrist. After at least 30 min of halothane anesthesia, patients were divided into three groups and received 0.01, 0.014, or 0.02 mg/kg of Norcuron as an intravenous bolus. Data were obtained for the following: onset (time from injection to maximal effect); duration (time from injection to return of muscle twitch tension to 90% of control); recovery time (time necessary for the muscle twitch tension to recover from 25 to 75% of control); and the maximal depression of the control muscle twitch tension occurring with each dose. From these data, a dose-response relationship was defined by analysis of linear regression. Further doses of Norcuron were given to maintain surgical relaxation. At the end of the surgical procedure, when the muscle twitch tension had spontaneously recovered to 5% of control, an intravenous bolus of neostigmine, 3.5 µg/kg, was given with atropine, 0.1 mg, every 3 min until sustained tetanus to a 50-Hz stimulus occurred. Data were then used to extrapolate the dose of neostigmine needed to achieve 20, 50, and 80% recovery of control muscle twitch tension. Nine additional patients were studied in the same manner to obtain a dose-response relationship for pancuronium, the only exception being that dose-response data were generated by a cumulative method[2] in which pancuronium was given in 5 µg/kg doses repeatedly until total paralysis was achieved. This differs from the dose-response method used for Norcuron, in which patients received a single dose of the drug. A dose-response relationship for pancuronium was obtained again by analysis of linear regression and was compared with that for Norcuron by calculating the ED_{50} (dose of muscle relaxant causing a 50% depression of twitch tension) for each relaxant.

Results. The time course of action of Norcuron is summarized in Table 1. A comparison of our data on Norcuron's time course of action with existing data on pancuronium[3] shows that the two drugs have a similar time of onset but that Norcuron has a shorter duration, particularly when the dose is 0.02 mg/kg or higher. The dose-response linear regression lines were parallel, and the ED_{50}'s were 0.015 mg/kg for Norcuron ($r = 0.830$) and 0.022 mg/kg for pancuronium ($r = 0.913$). Less neostigmine was required to reverse the effects of Norcuron (fig. 1). Data for pancuronium reversal were previously published by Miller et al.[4]

Conclusions. Comparing the ED_{50}'s of Norcuron and pancuronium shows that Norcuron is 1.5 times more potent. Also, Norcuron has a significantly shorter duration of action than does pancuronium.[3] Less neostigmine is required to antagonize a neuromuscular block produced by Norcuron. However, this may reflect a faster rate of spontaneous recovery of muscle twitch tension in those patients receiving Norcuron rather than a specific ability of neostigmine to antagonize Norcuron more effectively than pancuronium. These results and the fact that no cardiovascular side effects have yet been reported in animals or man indicate that Norcuron has clinical advantages over pancuronium and merits further clinical trials.

References

1. Booij LHDJ, Edwards R, Sohn YJ, et al: Cardiovascular and neuromuscular effects of Org NC 45, pancuronium, metocurine, and d-tubocurarine in dogs. Anesth Analg 59:26-30, 1980

2. Donlon JV Jr, Ali HH, Savarese JJ: A new approach to the study of four non-depolarizing relaxants in man. Anesth Analg 53:934-939, 1974

3. Katz RL: Clinical neuromuscular pharmacology of pancuronium. Anesthesiology 34:550-556, 1971

4. Miller RD, Larson CP Jr, Way WL: Comparative antagonism of d-tubocurarine, gallamine, and pancuronium induced neuromuscular blockade by neostigmine. Anesthesiology 37:503-509, 1972

Table 1. Time Course of Norcuron (Mean ± SEM)

Norcuron (mg/kg)	Onset (min)	Duration (min)	Recovery Time (min)
0.01 (n = 7)	6.0 ± 1.0	13.8 ± 5.0	N/A
0.014 (n = 9)	6.1 ± 0.6	21.4 ± 6.0	N/A
0.02 (n = 5)	5.9 ± 0.5	34.4 ± 6.8	14.1 ± 2.9

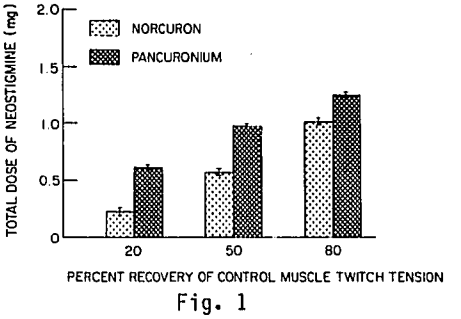

Fig. 1