The Dose-effect Relationship of Metocurine: EMG Versus MMG

To the Editor—I read with great interest the recent Clinical Report by Kopman,1 who described how both the method used to quantify neuromuscular blockade and the data handling technique may affect the ED₉₀ values calculated for metocurine. I would suggest that his report also illustrates the importance of identifying the muscle whose activity is being monitored (by either EMG or MMO). Thus, his ED₉₀ values (pooled data) were 0.209 mg/kg by integrated EMG alone in group 1 (no preload), and 0.252 and 0.271 mg/kg by simultaneously evoked EMG (group 2, with preload) and MMO, respectively. Each of these three ED₉₀ values was reported as being statistically significantly different (P < 0.05) from the other two. Similar differences were found among the three mean ED₉₀ values derived by averaging the calculated individual ED₉₀ values for each patient. Based on our current understanding of neuromuscular transmission, it seems unlikely that electrical stimulation of the ulnar nerve at the wrist could evoke a mechanical (MMG) response in the absence of an electrical (EMG) response in the same muscle. Harper et al.4 recorded simultaneous EMG and MMO responses in the same muscle (adductor pollicis) during onset of neuromuscular blockade with atracurium and alcuronium. In no case did they observe an MMO response in the absence of an EMG response; indeed, when the MMO T₁/ΤC was zero, the EMG T₁/ΤC ratio was 0.2–0.3.5 One must, therefore, also conclude from Dr. Kopman’s study1 that the first dorsal interosseous muscle whose EMG was being recorded is more sensitive to the effects of metocurine than is the adductor pollicis, whose MMO was being simultaneously recorded.

Another possible explanation for the observation that the ED₉₀ by EMG was less than that by MMO is based upon the method described whereby the cumulative dose-MMG effect curves were constructed.1 Thus, incremental doses of metocurine were given when the evoked T₁/ΤC ratio by EMG was stable for three consecutive trains-of-four delivered at 20-s intervals (i.e., EMG T₁/ΤC was stable for 1 min), and the simultaneous MMO T₁/ΤC ratio was recorded at this time. If the MMO T₁/ΤC ratio had not yet reached a plateau and was still decreasing at this time, then this ratio would have been artificially increased, indicating relative resistance to metocurine at the cumulative dose-level given and in the ED₉₀ values ultimately calculated.

The effect of preload on the sensitivity to metocurine as measured by EMG is also an interesting phenomenon. Dr. Kopman offers as one possible explanation that, in group 2, because the thumb was abducted under tension, the distance between recording electrode and muscle may have been reduced, resulting in a larger EMG signal. Since, during calibration, the Datex® 221 monitor prints the gain setting used, one wonders whether there were any differences in gain between the two groups. Such a difference, if present, might lend support to the explanation offered.

Finally, it is interesting to note that no significant differences were reported among the six ED₉₀ values derived for metocurine.1 The statistical description of the dose-effect curve is most powerful in its designation of the midpoint, i.e., the ED₉₀.2 This raises the question of the possibility of the introduction of artifact during the calculation of the ED₉₀ values. In generating dose-effect curves, various data transformations, such as log-probit,1 logit, or arc-sine, are often employed for the effect axis, while other studies1 used no such data transformation. Differences among studies in their use of such transformations may also contribute to variations in the ED₉₀ and ED₉₀ values ultimately reported for the same relaxant. Differences in estimated potency arising from use of pooled data versus the mean values from individual patients have been demonstrated by Dr. Kopman.1 Perhaps it is time to standardize the derivation of these indices of potency for neuromuscular blockers and thereby avoid the Humpty Dumpty practice of, “When I use a word, ‘‘ . . . . ’’ it means just what I choose it to mean—neither more nor less.”

* Lewis Carroll. Through the Looking-Glass, 1872.

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In Reply—Dr. Eisenkraft raises several important issues in his well-thought-out letter. Assuming that EMG and MMO instrumentation are equally sensitive, it is indeed difficult to see how evoked mechanical activity can exist in the absence of an electromyoographic response. Although the small (7%) difference in the ED₉₀ of metocurine that we calculated using these two methods was statistically significant (P < 0.03,

Student's paired t test), I would not place too much importance on this disparity. If the series had been stopped at 19 patients, the respective EMG and MMO values for the ED₉₀ would have been 0.237 and 0.250 mg/kg with a P value of >0.05. However, as Dr. Eisenkraft suggests, it may well be that the first dorsal interosseous (DI) muscle is slightly more sensitive to the action of nondepolarizing blockers than the ad-
Spinal Administration of Somatostatin in Animals and Humans

To the Editor—In a recent article by Gaumann and Yaksh,1 the authors suggest that we have administered spinal somatostatin without proper prior studies in animals to rule out toxicity. We wish to point out some inaccuracies on spinal (epidural, intrathecal) use of somatostatin. Our clinical studies were preceded by investigations in dogs which showed that the peptide in a dosage proposed to be used later in humans did not result in any histopathological spinal cord changes.2,3

It has to be stated that the intrathecal bolus somatostatin doses used in rats (40–400 μg/kg) and cats (200 μg/kg),1 as well as the concentrations of the somatostatin solutions employed (0.1–1.0% in rats, 1.0% in cats) tremendously exceeded any that have ever been repeatedly employed in humans4 (4 μg/kg of an 0.025% somatostatin solution intrathecally; 10–15 μg/kg of an 0.1% somatostatin solution epidurally (only small amounts of somatostatin reach the intrathecal space4)). Moreover, a species dependent effect might be assumed. A naloxone-reversible respiratory depression in rats2 and the occurrence of urinary retention in cats1 suggest that spinal opiate receptors are involved in the somatostatin effect mechanism. In contrast, somatostatin analgesia could not be reversed by naloxone in humans5 and investigations using Reed’s rebreathing method revealed that in humans the risk of respiratory depression was negligible following epidural injection of 1 mg somatostatin.2 Similar to local anesthetics, a segmental dermatome limit of analgesia could be demonstrated that was independent of the injection volume employed and could be maintained during epidural low-dose somatostatin infusion.7

Emphasizing a general rule concerning the animal model and the factor by which the clinically effective per body weight dose and the concentration of the solution have to be multiplied and spinaly employed without deleterious side effects, we have no doubt that somatostatin will pass, but we do doubt that local anesthetics, for example, would pass those restrictions.6,9

Although the number of patients who have received spinal somatostatin is not large and somatostatin nonresponsiveness6 is an unresolved problem, we and others who have recently administered somatostatin into the intrathecal or epidural space of some patients7,8 have not observed any adverse effects due to the peptide. Careful observation has to be exercised to recognize presently unknown side effects in patients as early as possible.

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