

## CORRESPONDENCE

Anesthesiology  
1999; 91:1554  
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### The Onset/Offset Profiles of Rapacuronium and Succinylcholine Are Not Identical

*To the Editor:*—In their article on the pharmacodynamics of rapacuronium, Wright *et al.*<sup>1</sup> stated that after a 1.5-mg/kg dose, the drug's time course of action (at the adductor pollicis) is similar to what they observed in a previous study after 1.0 mg/kg of succinylcholine.<sup>2</sup> I think this statement is somewhat misleading. Although the onset profiles of both drugs do indeed seem equivalent, the same is not true of offset.

In their study, they reported a bolus to 25% recovery interval of  $13.4 \pm 3.2$  min after rapacuronium. This is not clinically comparable to their data for succinylcholine ( $8.0 \pm 2$  min). Certainly, the recovery index noted for rapacuronium ( $8.8 \pm 1.6$  min) is far longer than the value usually cited for succinylcholine, which is at most 2-3 min. It should also be noted that 1.5 mg/kg rapacuronium represents not more than 2 times the ED<sub>95</sub>, whereas 1.0 mg/kg succinylcholine represents 3-4 times the ED<sub>95</sub>.

Based on currently available information, rapacuronium should be viewed as a rapid-onset blocking agent of short rather than ultrashort duration.

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### Rapid Onset/Offset of Rapacuronium Bromide Explained?

*To the Editor:*—The recent article by Wright *et al.*<sup>1</sup> provided interesting and important information on the pharmacokinetic/pharmacodynamics of rapacuronium at the laryngeal adductors and the adductor pollicis. However, we have a number of comments and concerns.

In the Discussion section, the authors mention the observed inverse correlation between the potency (ED<sub>95</sub>) of nondepolarizing muscle relaxants and their speed of onset, and present their explanation, referencing Hull.<sup>2</sup> We would like to call the readers' attention to other work in the field, in particular that of Donati and Meistelman,<sup>3</sup> who explained these observations on the basis of "buffering" and presented a plausible pharmacokinetic/pharmacodynamic model quantifying the influence of the acetylcholine receptor concentration and affinity on the time course of action.

The aforementioned explanation is based on the buffering phenomenon by the acetylcholine receptors in the neuromuscular junction (page 20 of Wright *et al.*'s article). Although there is evidence for the buffering effect in iontophoretic studies *in vitro*, there is no convincing evidence that buffering plays a role under clinically relevant conditions; therefore, the explanation is still a hypothesis. In addition, the authors do not give an explanation for the rapid offset of rapacuronium.

In the Discussion section, the authors state, "Despite the lack of comparative data, Schiere *et al.* concluded that Org 9488 is more potent than Org 9487 (rapacuronium)," suggesting that there was no solid base for this statement. At that time, however, Schiere *et al.* already had the data from

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### References

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(Accepted for publication June 23, 1999.)

a similar study on rapacuronium<sup>4</sup> and therefore could make this statement on a sound scientific base. In addition, Wright *et al.* disputed the study design used by Schiere *et al.*, in which the same patients did not receive both rapacuronium and Org 9488 on separate occasions. It should be clear that such a crossover design cannot be performed in a study in surgical patients. The cited study of Caldwell *et al.*<sup>5</sup> was conducted in volunteers. Of course, if the main goal of a study is the assessment of the relative potency of two compounds, a crossover design is preferable. However, if the primary aim of the study is to delineate the pharmacokinetics and clarify the pharmacokinetic/pharmacodynamic relationships in surgical patients, the study design of Schiere *et al.* might be preferable.

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