these doses were roughly equipotent. This is not the case. While vecuronium, atracurium, and rocuronium were given in doses equivalent to $0.2 \times$ the ED_{95} , the dose of d-tubocurarine administered represents only $0.1 \times ED_{95}$, and $0.20 \text{ mg} \cdot \text{kg}^{-1}$ mivacurium equals almost $0.3 \times ED_{95}$.

- The authors cite McCoy *et al.* in hypothesizing that the variations in effects observed among the drugs tested might be secondary to differences in prejunctional activity. A more recent paper² by these authors suggests otherwise. They examined differences in pre-junctional effects of different relaxants by measuring the TOF fade during the onset and recovery of neuromuscular block. The relaxants studied were atracurium, mivacurium, rocuronium and vecuronium. Differences among the relaxants were insignificant.
- Since rocuronium pre-treatment delayed the onset of succinylcholine-induced block to the greatest extent, perhaps the manuscript should be retitled "Rocuronium is the worst nondepolarizing relaxant...".

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- McCoy EP, Connolly FM, Mirakhur RK, Loan PB, Paxton LD. Nondepolarizing neuromuscular blocking drugs and train-of-four fade. *Can J Anaesth* 1995; 42: 213–6.

To the Editor:

We read with much interest the article by Martin *et al.*¹ regarding the use of non-depolarizing muscle relaxants to prevent succinylcholine-induced fasciculations and myalgias. Convincing evidence was presented indicating that rocuronium is the most effective agent in preventing fasciculations. However, it was unclear how long before succinylcholine one should administer rocuronium. The methods section of the paper indicated that rocuronium was given seven minutes before the succinylcholine, whereas the discussion and abstract stated that it was administered 5.5 and 4 minutes before succinylcholine, respectively. From a clinician's perspective, it is important to know exactly when rocuronium should be given.

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REPLY

We would like to thank Drs. Kopman, Daley, Norman and Mensink for their interesting and constructive remarks concerning our paper.¹

As stated in our paper, the doses employed were taken from a table of Miller's textbook, *Anesthesia*. They represent 10% of the suggested doses providing good intubating conditions under light anaesthesia.²

Concerning the pre-junctional activity, we apologize for not having quoted McCoy *et al.*³ As established in their study, fade is greater during recovery of block than during onset. Rocuronium showed a slightly greater fade at that time and it is possible that its rapid onset allows little time for development of fade.

Pre-treatment, especially with rocuronium, effectively delay the time for maximal twitch depression following succinylcholine.

Concerning the timing of the pre-treatment in regard to the succinylcholine injection, in our study, pre-treatment was given at time 0 and succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ was given four minutes later. Tracheal intubation was achieved 1.5 min after succinylcholine, that is 5.5 min after pretreatment.

We apologize for the title which should have been: "Rocuronium is the best non-depolarizing relaxant to prevent fasciculations". Rocuronium and all the other pre-treatment drugs studied did not prevent myalgia.

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Density of cerebrospinal fluid and intrathecal spread

To the Editor:

We read with interest the report by Lui *et al.*¹ and would like to make a few comments. In spinal anaesthesia, regardless of the density/baricity of the drug solution, the volume of the solution is always the most immediate factor affecting the extent of spread due to simple "bulk replacement" or area contact, the greater the volume, the more extensive is the spread. In clinical doses, dilution into much larger volumes will not produce the lower levels of block that smaller volumes may.^{2,3} However, when a non-isobaric solution is used, the baricity/position interaction becomes the main determinant of the direction and speed of intrathecal spread. Since non-isobaric solutions in small volumes are commonly used, that may explain why volume of injectate is not a determinant of block height in most clinical settings. Density is the weight in grams of 1 mL of a solution at a specified temperature while baricity is the density of the solution relative to that of CSF. Thus, baricity, not the density, of the solution affects the spread. Since the density of CSF varies, the baricity of any given solution will vary. However, except for tetracaine, which is available in lyophilised powder (niphanoïd) form, spinal anaesthetics are aqueous solutions. They are generally formulated with sodium chloride to be isotonic and thus nearly isobaric. In practice, adding glucose produces hyperbaric solutions, diluting with water makes hypobaric solutions, and using only CSF to dissolve lyophilised tetracaine achieves the best possible isobaric solution.

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REPLY:

Baricity is an important determinant of the distribution of spinal anaesthetic solutions as demonstrated in an in vitro study.¹ Hence, knowledge of the densities of the local anaesthetic solutions relative to the densities of the cerebrospinal fluid (CSF) in the surgical population is a necessary first step. Although saline is isotonic, it is not isobaric, but is by definition, hypobaric. Likewise, tetracaine in saline solution is also hypobaric.²

*Many other factors contribute to the final distribution which also depends on its dilution with CSF. Carpenter *et al.*⁴ demonstrated the correlation between lumbosacral CSF volume and sensory block height, concluding that the common diluent, namely CSF, is a major variable in determining local anaesthetic spread. In short, it is the dose of local anaesthetic, mixed with CSF (which has high interindividual variability in volume) that accounts for the variable block height observed in practice. There is little evidence to support volume of the solution as playing a major role in its distribution except for the situation where hypobaric solution is used to "float" the solution cephalad. In this instance, perhaps the phenomenon of "bulk replacement" that Drs. King and Wood alluded to might apply.*

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