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Rocuronium-Cisatracurium Combinations

To the Editor:—In a recent study, Naguib et al. reported dose-response data of rocuronium and cisatracurium administered alone or in combination. We would like to ask the authors to clarify an inconsistency between (1) the degree of potentiation as described in the Results section, table 1, and figure 2, and (2) the dose-response curves shown in figure 1 and maximum depression data presented in table 3. The authors state that "The experimentally determined ED₅₀ (and 95% confidence interval) for the combinations was 7.1 (5.4-8.7) μ g/kg for rocuronium and 1.7 (1.3-2) μg/kg for cisatracurium. The theoretical additive ED₅₀ was calculated to be 55.5 (53.3-57.7) µg/kg for rocuronium and 13.1 (12.6-13.6) μg/kg for cisatracurium." Figure 2 in their article is entirely consistent with this statement, which implies that when administered together, rocuronium and cisatracurium would be eight times more potent than expected from pure additivity! However, the dose-response curves in figure 1 of their article indicate that the ED_{50} of the combination is approximately $0.65 \times ED_{50}$ equivalents. Thus, one would expect the ED₅₀ of the combination to be 36 μ g/kg rocuronium plus 8.5 μg/kg cisatracurium, that is, 0.65 times the expected values of 55.5 µg/kg and 13.1 µg/kg, respectively. Table 3 is consistent with the calculations made from figure 1, because the ED, of each drug (rocuronium 28 μ g/kg and cisatracurium 6.5 μ g/kg) yielded 32.3% block, whereas the ED₅₀ (56 μ g/kg and 13 μ g/kg, respectively) yielded 77% block. From these data it can be estimated that 50% blockade would be produced by intermediate doses between the ED_{25} and the ED_{50} of both drugs as previously mentioned, which represents approximately 36 μ g/kg rocuronium plus 8.5 μ g/kg cisatracurium. This estimate is several times greater than the doses of 7.1 (5.4-8.7) μ g/kg for rocuronium and 1.7 (1.3-2) μ g/kg for cisatracurium reported in the Results section. We believe that this is a rather important discrepancy that the authors must clarify.

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Reference

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