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CORRESPONDENCE

Failure of sugammadex to reverse rocuronium-induced neuromuscular blockade

Simply an outlier or are we missing something?

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Editor,

We read, with great interest, the recently published case report by Ortiz-Gomez *et al.*,[1] which describes a failure of sugammadex to reverse a rocuronium-induced neuromuscular block. However, we have some questions about this report. Reversal delays after sugammadex have been previously described and were caused by the lack of neuromuscular monitoring, underestimation of the level of the neuromuscular block, underdosing of sugammadex, or a combination thereof.[2,3] The maximum reversal time of these outliers was 12 min. In the case described, the time from the first dose of sugammadex to extubation was 208.5 min. The total dose of sugammadex was 1120 mg (9.74 mg kg^{-1}), which should have been sufficient to reverse the relatively low dose of 153 mg rocuronium (a bolus of 0.6 mg kg^{-1} and 0.12 mg kg^{-1} h^{-1}) given over 6 h. Therefore, it is unlikely that this was an outlier. Are we missing something that explains this failure?

How was sugammadex administered? Did all vials contain sugammadex? An infusion problem such as retrograde flow into the infusion bag or a paravenous infusion could have occurred. Even if less sugammadex was administered, one vial would have been sufficient to provide some reversal of the relatively low dose of rocuronium received by the patient. Sugammadex could have lost its capacity to encapsulate rocuronium. Although sugammadex might have changed in colour because of oxidation under light, it would still remain active in encapsulating rocuronium, even when outdated. Thus, this possibility cannot explain the total lack of effects.

Was neuromuscular block monitoring inaccurate? Neuromuscular block monitoring can be affected by many factors and may lead to the misinterpretation of the actual extent of neuromuscular block. Exact results of neuromuscular monitoring after the spontaneous recovery of succinylcholine were lacking. Thus, it is possible that this patient had a pseudocholinesterase deficiency that caused a prolonged neuromuscular block that sugammadex could not reverse. Neostigmine was used and may have caused a phase II neuromuscular block. More information, such as the results of laboratory tests, should be obtained to ensure the appropriate use of neuromuscular blocking drugs in any future treatment of this patient.

Was a nonsteroidal neuromuscular blocking agent used instead of rocuronium? At train-of-four (TOF) count 1, the 4 mg kg^{-1} total body weight dose of sugammadex should have been sufficient.[4] Additional sugammadex treatment up to a total dose of 10 mg kg^{-1} resulted in no significant change and the TOF count remained at 1 without the onset of spontaneous breathing. A low dose of neostigmine (1 mg followed by 1.5 mg, 8.5 μg kg^{-1} up to 22 μg kg^{-1}, respectively) was given whereas the recommended dose was 50–70 μg kg^{-1} at a TOF count of 3 or 4. Thereafter, the patient started to breath spontaneously, and the TOF count changed from 1 to 4 responses with a TOF ratio of 9%. Information about circulating rocuronium was not available, and plasma levels of other neuromuscular blocking drugs were not checked, thus human error cannot be excluded.

Was interindividual variability potentiated by other factors? Although the possibility of an abnormally low free calcium or high free magnesium should have been checked as a possible reason for a prolonged neuromuscular block, this would not have prevent reversal by sugammadex.[5–7] As the administered dose of rocuronium was low this may indicate an abnormally sensitive type of acetylcholine receptor that could be blocked at less than the normal 70% occupancy[8]; this is theoretically possible but has never been clinically described.

Was there undiagnosed myasthenia gravis?[9] This could explain the low requirement for rocuronium as even the smallest dose may lead to a profound neuromuscular block. Since sugammadex is always able to reverse the neuromuscular block in such cases, myasthenia gravis can probably be excluded.

Was sugammadex encapsulating other molecules such as steroids? One in-vitro study reports that dexamethasone, given in an equimolar concentration with rocuronium and sugammadex at 10 μM, can reduce the reversal effect of sugammadex.[10] However, these in-vitro concentrations

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would require a supratherapeutic dose of dexamethasone and in normal clinical use such a concentration would occur for only a very short time after an intravenous bolus above 0.15 mg kg^{-1}. In this case, there was no information reported on either the dose or the timing of dexamethasone treatment.

This case report, including the difficulties encountered, is informative for clinicians. However, from the information provided it is impossible to state definitively that sugammadex failed to reverse the rocuronium block. An outlier seems unlikely. More likely is the unintentional administration of a nonsteroidal neuromuscular blocking agent, not reversible with sugammadex. Human error might possibly be a better explanation than a pharmacological extreme outlier. Before concluding that this patient was an extreme pharmacological outlier or a sugammadex failure, more information is required.

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