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Sugammadex to reverse residual neuromuscular blockade and facilitate neurologic examination in an adolescent trauma patient in the Pediatric ICU setting

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Keypoints

1. Sugammadex, a modified gamma-cyclodextrin, is a novel pharmacologic agent that encapsulates free rocuronium or vecuronium, thereby reversing the clinical effect of these neuromuscular blocking agents.
2. Prospective trials in both adult and pediatric patients have demonstrated a more rapid and more complete reversal of rocuronium-induced neuromuscular blockade with a limited incidence of residual weakness when comparing sugammadex to the acetylcholinesterase inhibitor, neostigmine.
3. Given its clinical effects, there may be utility in the administration of sugammadex to reverse neuromuscular blockade in clinical scenarios in the ICU setting, especially when rapid and complete reversal of neuromuscular blockade may be indicated.

Abstract

Neuromuscular blocking agents (NMBAs) are frequently used in acute care scenarios to facilitate endotracheal intubation and permit effective mechanical ventilation. Despite their potential therapeutic efficacy, the immobility may prevent clinical evaluation of a patient's neurologic status. In specific clinical scenarios such as when immediate tracheal extubation is indicated or assessment of neurologic status is required, prompt reversal of neuromuscular blockade may be indicated. We present the novel use of sugammadex for reversal of NM blockade to allow for neurologic examination and tracheal extubation in an adolescent trauma patient. The pharmacology of sugammadex is reviewed, reports of its use in pediatric-aged patients discussed, and potential scenarios for use in the ICU setting presented.

Keywords

sugammadex; neuromuscular blockade; trauma; brain injury.

Introduction

Neuromuscular blocking agents (NMBAs) are frequently used in acute care and Pediatric ICU (PICU) settings for a variety of situations, including endotracheal intubation and maintenance of mechanical ventilation.[1] The administration of NMBAs during tracheal intubation improves conditions for laryngoscopy, decreases the incidence of airway trauma, and increases the success rate for tracheal intubation.[2,3] As an adjunct to the effective use of sedative and analgesic agents, NMBA may also be administered to provide immobility during transport, prevent shivering during therapeutic hypothermia, and to

improve outcomes during mechanical ventilation in patients with ARDS.[3-6] Despite their potential benefits, adverse effects related to the use of NMBAs may include patient awareness during paralysis, an increased risk of nosocomial infections, ICU-acquired myopathy and residual weakness, an increased incidence of thromboembolism, and prolonged duration of mechanical ventilation.[6-8]

In most clinical scenarios in the ICU setting, the effects of NMBAs are allowed to spontaneously dissipate when their use is no longer indicated. However, in specific clinical scenarios such as when immediate tracheal extubation is indicated, when assessment of neurologic status is required, or "in a cannot intubate-cannot ventilate scenario" prompt reversal of neuromuscular blockade may be indicated. We present the novel use of sugammadex for reversal of NM blockade to allow for neurologic examination and tracheal extubation in an adolescent trauma patient. The pharmacology of sugammadex is reviewed, reports of its use in pediatric-aged patients discussed, and potential scenarios for use in the ICU setting presented.

Case report

Review of this case and presentation in this format followed the guidelines of the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio). The patient was an 17-year old, 80 kilogram male who was a rear seat passenger involved in a motor vehicle accident that resulted in his car landing submerged in a pond. After self-extrication from the car, he made it to land at the edge of the pond, where according to bystanders he suffered a syncopal event or possible cardiopulmonary arrest. He was resuscitated by paramedics at the scene with a report of an initial rhythm of ventricular fibrillation that required defibrillation resulting in normal sinus rhythm. After resuscitation, he was transported to an outside hospital, where by report he had decorticate posturing. His trachea was intubated following the administration of vecuronium, fentanyl, and ketamine. He was transported to our emergency department where initial computed tomography scan of his head was within normal limits. Levetiracetam was administered for seizure prophylaxis. In the emergency department, his vital signs, oxygenation and cardiovascular examination were within normal limits. His pupils were equal (3 mm) and reactive. His GCS was 3 and there was no movement or response to pain. Following radiologic imaging, he was admitted to the PICU. Upon arrival, he had tremulous peripheral movements of his arms and legs that was concerning for possible seizure activity to the trauma team. On examination, he appeared to follow commands although motor examination demonstrated weakness (2/5 strength) throughout with generalized twitching and floppy movements of all four extremities. Qualitative train-of-four stimulation demonstrated 1 of 4 twitches. Sugammadex (200 mg) was administered with return of 4 twitches of the TOF within 2-3 minutes. Strength improved to 5/5 throughout and the patient was following commands. His trachea was extubated. He was transferred to the inpatient ward later that day and then discharged home. The remainder of his hospital course was unremarkable.

Discussion

The two general classes of NMBA's (depolarizing and non-depolarizing agents) differ in their basic mechanism of action.[9] The depolarizing agent, succinylcholine, mimics the cellular actions of acetylcholine, binding to the acetylcholine receptor at the neuromuscular junction, and activating it. Outside of its use for emergent tracheal intubation, succinylcholine's pharmacologic properties do not lend itself to continuous infusion in the ICU for ongoing neuromuscular blockade.

The non-depolarizing NMBA's act as competitive antagonists at the neuromuscular junction, blocking the effects of acetylcholine at the receptor. These agents can be separated into aminosteroid and benzylisoquinolinium compounds, based on their primary chemical structure. Non-depolarizing NMBA's such as rocuronium may be used to facilitate endotracheal intubation or administered by

continuous infusion to provide ongoing neuromuscular blockade. As the non-depolarizing NMBAs act as competitive antagonists of acetylcholine at the nicotinic receptor on the sarcolemma, when their concentration is low enough, reversal is feasible by the administration of medications that inhibit acetylcholinesterase (neostigmine).[10] However, a significant degree of residual neuromuscular function is necessary to allow for effective reversal of neuromuscular blockade with acetylcholinesterase inhibitors. In general clinical practice, this means that there should be 1-2 twitches in the TOF or recovery of the first twitch of the TOF (T1).[11] Therefore, reversal with a drug that inhibits acetylcholinesterase is not feasible immediately after the administration of an NMBA or during continuous infusions when profound neuromuscular blockade is present. Rather, depending on the dose and depth of blockade, there may be a significant period of time after discontinuation of drug administration where neuromuscular blockade remains.

Sugammadex, a modified gamma-cyclodextrin, received approval for clinical use by the US Food and Drug Administration in 2015 for adults and subsequently in 2021 for pediatric patients.[12] This novel pharmacologic agent is an alternative to acetylcholinesterase inhibitors for the reversal of neuromuscular blockade. Sugammadex encapsulates free rocuronium or vecuronium in the plasma, creating an inactive rocuronium-sugammadex or vecuronium-sugammadex complex. This lowers the plasma concentration of rocuronium or vecuronium, creating a concentration gradient between the neuromuscular junction and the plasma. As a result, free rocuronium or vecuronium shifts away from the neuromuscular junction into the plasma and is continuously encapsulated by sugammadex, leading to a rapid decrease in rocuronium or vecuronium at the neuromuscular junction, and allowing for the rapid return of neuromuscular function even with a profound depth of blockade.

Prospective trials in both adult and pediatric patients have demonstrated a more rapid and more complete reversal of rocuronium-induced neuromuscular blockade with a limited incidence of residual weakness when comparing sugammadex to the acetylcholinesterase inhibitor, neostigmine.[13-17] Unlike the acetylcholinesterase inhibitors, sugammadex can reverse intense or complete neuromuscular blockade. It may also be effective in situations where reversal of neuromuscular blockade is problematic including patients with neuromyopathic conditions or when acetylcholinesterase inhibitors are contraindicated.[18]

Given its clinical effects, there may be utility in the administration of sugammadex to reverse neuromuscular blockade in clinical scenarios in the ICU setting, especially when rapid and complete reversal of neuromuscular blockade may be indicated. We present one of these unique ICU scenarios, as rapid reversal of neuromuscular blockade was indicated in our patient to allow for neurologic examination, rule out ongoing seizure activity, and permit rapid tracheal extubation. The beside examination of our patient revealed what appeared to be residual paralysis from the use of rocuronium for endotracheal intubation. This was interpreted as possible seizure activity when in fact, residual neuromuscular blockade, resulted in weakness and abnormal motor movements. Residual paralysis was confirmed by qualitative TOF monitor. Following the administration of sugammadex, motor function returned to normal within 2-3 minutes with normal strength. This allowed for a thorough neurologic examination and tracheal extubation.

Recommendations for sugammadex dosing include 2 mg/kg when there is a moderate degree of neuromuscular blockade present (≥ 2 twitches of the TOF) and 4 mg/kg if there are only 1-2 post-tetanic twitches present. The largest dose (16 mg/kg) is recommended when there is no residual neuromuscular function present. Given the depth of blockade present in our patient, we chose to use a dose of approximately 2 mg/kg. The two most worrisome of the reported adverse effects related to sugammadex include bradycardia and rare reports of anaphylaxis. Although no mechanism has been proposed, anecdotal reports have supported the temporal association of

bradycardia or cardiac conduction disturbances following its administration. Reported clinical symptoms of allergic reactions have spanned the entire spectrum including a mild skin rash, urticaria, bronchospasm, and anaphylactic shock requiring resuscitation.

In summary, we present anecdotal experience with the use of sugammadex to reverse residual neuromuscular blockade in a 17-year-old ICU patient to allow for a thorough neurological examination to rule out seizure activity. When compared to acetylcholinesterase inhibitors, sugammadex offers the potential to reverse deep neuromuscular blockade, more rapidly and effectively. These properties have led to its increased use in the perioperative setting. Additionally, as illustrated by our case, there may be specific clinical scenarios in the ICU setting where sugammadex may be indicated.

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