Pediatric Anesthesia and Critical Care Journal 2015; 3(1):49-52
doi:10.14587/paccj.2015.9

PACCJ

Sugammadex for the reversal of prolonged neuromuscular blockade in a preterm neonate. Case report

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Key points

1. Long term infusions of neuromuscular blocking agents can lead to prolonged neuromuscular blockade in susceptible infants.
2. Sugammadex is an effective treatment for the reversal of prolonged blockade secondary to vecuronium even at relatively low doses.
3. Whilst further research is required our experience suggests that Sugammadex can be safely administered to preterm neonates.

Abstract

We report a case of a pre-term neonate, with intestinal and pulmonary lymphangiectasia who was, admitted to our neonatal intensive care unit (NICU) for supportive management of cardiovascular, respiratory and renal failure. By day 23 of life she was making good progress and the decision was made to stop her sedation and muscle relaxant infusion. Over the subsequent ten days the neonate showed no signs of respiratory effort or consciousness. After brain injury was ruled out as a cause of her symptoms it was thought that she may be suffering from prolonged neuromuscular blockade. A test dose of neostigmine showed no demonstrable effect, however following a dose of sugammadex the neonate showed a nearly instantaneous motor and respiratory response. Multiple doses were required over the next few days in order to maintain the response.We discuss the potential causes of her prolonged paralysis, the neonate's electromyogram (EMG) responses to sugammadex, and the safety and efficacy of using the drug in neonates.

Keywords: Neonatal intensive care, sugammadex, neuromuscular blockade, vecuronium bromide, neural conduction, respiratory insufficiency

Introduction

Sugammadex is a modified γ-cyclodextrin, a family of chemicals whose basic chemical structure is comprised of sugar molecules in a ring formation[1], which acts as a selective relaxant binding agent. It forms a complex with the aminosteroid muscle relaxants rocuronium[2] and vecuronium[3] reducing the amount available to bind at the neuromuscular junction. There is limited data for its use in children less than two years of age[4].

We report a case where sugammadex was used to reverse neuromuscular blockade in a preterm neonate with evidence of persistent paralysis ten days after stopping a

vecuronium infusion.

Case report

The neonate was born in good condition by spontaneous vaginal delivery, after prolonged rupture of membranes, at 30+5 weeks gestation, weighing 1535 grams. The only problem of note during the pregnancy had been oligohydramnios. Neonatal sepsis was suspected on day 1, requiring ventilator support for respiratory failure.

She deteriorated, continuing to require ventilator and inotropic support and on day 19 developed acute renal failure. At this point she was transferred to our NICU for renal support. Abdominal compartment syndrome was diagnosed and an intra-abdominal peritoneal catheter was inserted. A large volume of chyle was drained which allowed a partial resolution of her renal function. A provisional diagnosis of intestinal and pulmonary lymphangiectasia was made, and was supported by findings of a CT scan.

To facilitate difficulties in ventilation over her first 23 days of life she received a vecuronium infusion for a total of 17 days at an average rate of 2 mcg/kg/min. On day 23 due to her clinical improvement, the muscle relaxant and morphine infusions were stopped to facilitate ventilator weaning. By day 33 despite 10 days free of vecuronium she remained hypotonic, without movement or respiratory effort.

Due to the lack of any motor or respiratory response the main differential diagnosis included intracerebral haemorrhage, diffuse brain injury secondary to hypoxia and/or ischaemia from prolonged hypotension. Between days 24 and 32 cranial ultrasounds and magnetic resonance imaging of her brain were performed which were normal with no evidence of brain injury. An electroencephalogram showed no signs of seizure activity.

After ruling out an intracranial cause it was thought that there may be a pharmacological reason for her symptoms. Weight appropriate doses of naloxone and then neostigmine were administered without any discernible effect.

On day 33 a 4 mg/kg dose of sugammadex was administered with an almost immediate response. The neonate opened her eyes, was able to squeeze a finger and there was some respiratory response noted by triggering of the ventilator.

Unfortunately the response was transient and over the next 12 hours the neonate returned to her previous state. A further 4mg/kg dose was administered at this point which elicited the same effect. Subsequent to these findings EMG and nerve conduction studies were performed demonstrating evidence of residual neuromuscular blockade (abnormal repetitive nerve stimulation) and improvement following an 8 mg/kg dose of sugammadex (Figures 1 and 2). No other side effects of sugammadex were noted. Following discussion with the relevant medical teams she commenced treatment with 3 mg/kg/day of pyridostigmine in 4 daily divided doses. She was treated for a number of weeks whilst waiting for her EMG to normalise. During this time she was tested to rule out myasthenia gravis but was found not to have acetyl choline receptor antibodies. Unfortunately despite an improvement in her motor function the baby died on day 70 of life from complications relating to her pulmonary lymphangectasia.

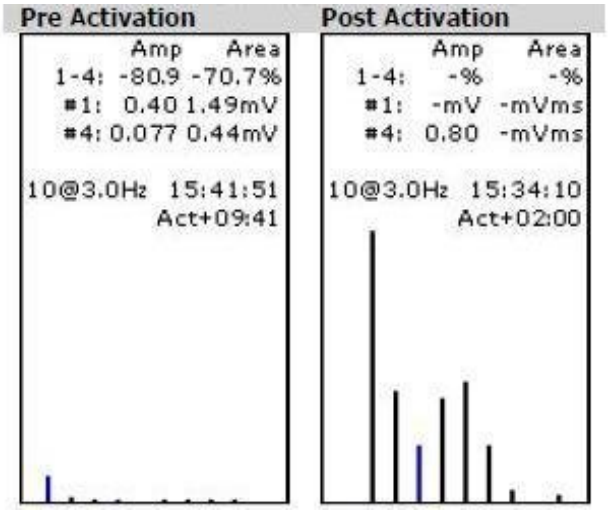

Figure 1. Before administration of Sugammadex. Motor nerve conduction study showing an 80.9% reduction in the amplitude of compound muscle action potential (pre-activation), with a marked decrement of amplitude during repetitive nerve stimulation with 3 Hz stimulation (post-activation), suggesting residual effects of muscle relaxants causing weakness and paralysis .

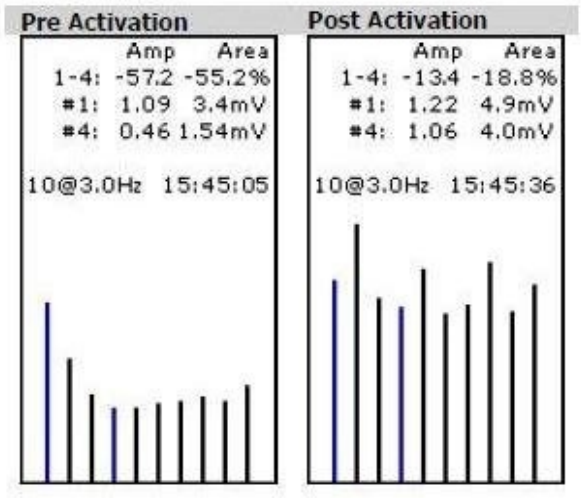

Figure 2. Administration of Sugammadex produced a marked improvement in the response to repetitive stimulation with a 13.4% decrement in amplitude.

Discussion

Many neonatal intensive care units (NICUs) in the United Kingdom use repeated doses of a long acting muscle relaxant or infusions of intermediate acting muscle relaxants to assist ventilation in critically unwell babies[5]. One of the most commonly used for infusions is vecuronium. The clinical response to sugammadex and the results of the nerve conduction studies suggest prolonged paralysis secondary to vecuronium. There is no pharmacological data on the use of vecuronium in preterm neonates. However in studies of neonates it has been shown to have an increased potency and prolonged duration of action[6]. It is theorised that this response is likely due to the increased proportion of extracellular fluid, lower serum protein, and a greater dependence on renal clearance. This patient was preterm, had renal failure, and an underlying condition that resulted in a significant increase in extracellular fluid and extensive loss of protein. We believe that this combination of factors resulted in severe prolonged neuromuscular blockade. In general a single dose of sugammadex is sufficient to reverse the neuromuscular blockade. It is unclear why this neonate required subsequent doses of the drug but her altered physiology may have contributed to this.

Due to limited data sugammadex is not recommended in preterm neonates or any children under the age of two. It is also only currently indicated for the routine reversal of neuromuscular blockade in children undergoing anaesthesia and surgery[7]. This case report however suggests that it is an effective and safe treatment in this patient group and that it should be considered for any neonate showing signs of prolonged neuromuscular blockade.

Acknowledgements

The authors would like to thank the department of neurophysiology at Great Ormond Street Hospital for their assistance.

Source of funding

The study has not been funded

Conflict of interest

The authors declare no conflict of interests

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