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Case report

Sugammadex in the neonatal patient☆

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ABSTRACT

Introduction: The inclusion of drugs that effectively reverse the neuromuscular junction blockade enhances the profile of drugs used for relaxation of the neuromuscular junction; better yet if these agents are free from any clinically important adverse effects and amenable to use in neonates.
Objectives: This article describes a case of two pediatric patients who received Sugammadex to reverse neuromuscular relaxation.
Methodology: Retrospective, descriptive, observational study designed as a case report.
Results: This is a description of a Sugammadex successful reversal of Rocuronium-induced neuromuscular blockade in two neonates with no adverse events.
Discussion: The literature on the use of Sugammadex in newborn patients is scarce and controversial which does not contribute to a broad prescription of the drug in neonatology settings due to the shortage of studies attesting to its effectiveness and absence of adverse effects. There are no recommended doses per age group and a list of expected adverse effects to contraindicate its administration. However, the idea is to have available drugs that reverse the relaxation resulting from the use of neuromuscular blockers at any age, including neonates.
Conclusions: Following the administration of a dose of Sugammadex the reversal of neuromuscular blockade in neonate patients is described with effective functional recovery of the neuromuscular junction. Further experimental controlled trials are needed to recommend the use of Sugammadex in newborn babies.

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Sugammadex en paciente neonatal

Palabras clave:
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RESUMEN

Introducción: La inclusión de drogas que revierten efectivamente el bloqueo de la placa neuromuscular mejora el perfil de uso de los medicamentos que la relajan, y más aún si estos carecen de efectos adversos de importancia clínica y se pueden emplear en neonatos.
Objetivos: Este artículo describe el caso de 2 pacientes pediátricos en quienes se aplicó sugammadex para la reversión de la relajación neuromuscular.
Metodología: Estudio observacional descriptivo retrospectivo con un diseño de reporte de casos.
Resultados: Se describe el uso exitoso de sugammadex para la reversión del bloqueo neuromuscular inducido por rocuronio en 2 pacientes neonatos y la ausencia de eventos adversos.
Discusión: La literatura para el uso de sugammadex en pacientes recién nacidos es poca y controvertida, lo cual no apoya su amplia prescripción en neonatología debido a la falta de estudios que aseguren su efectividad y la ausencia de efectos adversos. No existen dosis recomendadas por grupo etario y una lista de efectos adversos esperables que contraindiquen su administración. Aun así, es ideal poder disponer de medicamentos que reviertan la relajación derivada del uso de bloqueadores neuromusculares en cualquier edad, lo cual incluye a los pacientes neonatos.
Conclusiones: Tras una dosis de sugammadex se describe la reversión del bloqueo neuromuscular en 2 pacientes neonatos, siendo esta efectiva para la restauración funcional de la placa neuromuscular. Para poder recomendar su amplio uso en recién nacidos es ideal la realización de estudios experimentales controlados.

Introduction

Historically, poor predictability and significant adverse effects have characterized drugs used to revert residual relaxation. Sugammadex was introduced in the medical-surgical setting as an option with superior reversal effectiveness and a broad safety margin as compared to conventional management (Neostigmine) in the adult patient.

Cases

Case 1

Eutocic male, weight 2650 g, height 48 cm, undergoing Pyloroplasty because of congenital pyloric hypertrophy in July 2011 (age: 20 days).

Induction anesthesia with Propofol and Rocuronium (3 mg), balanced with Sevofluorane and Remifentanil. Maintenance with Remifentanil and Sevoflurane. Pressure-controlled mechanical ventilation, thermal and eye protection; analgesia with Dipyrone and Tramadol; length of surgery: 35 min.

Train of Four (*TOF*) response for peripheral nerve neurostimulation at the end of the procedure was four; 12 mg of Sugammadex administered; due to 100% recovery of T4/T1 ratio after 2 min the patient was extubated, maintaining oxygen saturations >98%, with no signs of respiratory distress and hemodynamic stability. The patient is then transferred to the pediatric ICU for monitoring and is discharged after three days.

Case 2

Preterm 34-weeks female (43 weeks after conception at the time of surgery), weight 3200 grams; multiple admissions due to bronco-obstructive syndromes and apneas; managed with Salbutamol and home oxygen; in the current hospitalization she presented with bronchiolitis, multilobar pneumonia and mixed shock (septic and cardiogenic) that required ten days of mechanical ventilation and multiple support (including cardiac arrest with early and favorable response). The child is diagnosed with grade IV gastroesophageal reflux and hence was programmed for anti reflux surgery and pyloroplasty (August, 2011).

Monitoring with Pulse Oxymetry, DII cardioelectric visoscope, and Thermometer, in addition to invasive right radial artery blood pressure monitoring. Intravenous induction with Fentanyl, Ketamine and Rocuronium (1.8 mg); thermal and eye protection was provided. Combined anesthetic technique (caudal and general). Additional doses of Rocuronium were required during surgery (0.4 mg at 20 min for T4/T1 > 25% and at 70 min for T4/T1 > 25%). At the end of the procedure (90 min) the last *TOF* measurement indicated a T4/T1 ratio <25%.

Since there were no oxygenation, ventilation or perfusion disorders the patient was extubated; however, a T4/T1 ratio <25% was observed, leading to the decision to prescribe 6 mg of Sugammadex, achieving 100% of the T4/T1 ratio after 2 min. Adequate respiratory pattern at

extubation and the patient was transferred to the ICU for monitoring and control for four days and then was discharged.

Discussion

The use of neuromuscular relaxants (NMR) under general anesthesia (part of the balanced technique)[1] facilitates mechanical ventilation and the surgical procedure.[2,3]

One of the key issues when using neuromuscular blockers is residual relaxation,[4] reflecting insufficient recovery of the neuromuscular junction and higher morbidity.[5] Routine relaxation monitoring has proven to reduce the occurrence of adverse events[6]; in fact, reversal of neuromuscular relaxation according to protocol was correlated with lower morbidity and mortality (OR = 0.1).[7]

Initially Sugammadex was tested for reversing aminosteroid relaxants and this explains why its use was endorsed to reverse Rocuronium.[8]

Several studies in adult population have described the doses used (2 and 4 mg/kg) for deep blockade reversal; in this case, its administration to a former premature baby at high risk and in a healthy baby sowed similar effectiveness.

The doses were standardized according to the depth of the blockade measured with the *TOF* and protocols have been developed for several formulae to recover the neuromuscular activity within a range of 1.3 min to 2.9 min (versus 50.4 min with Neostigmine)[9] using Rocuronium at doses ranging between 0.6 mg/kg and 1.2 mg/kg[10,11] and with T4/T1 ratios >0.9,[12] regardless of the cardiac, pulmonary or other conditions.[13–15] Higher doses of this product have even been used (up to 96 mg/kg) in adults, with no evidence of adverse events attributable to the drug.[16]

The above results should not encourage the clinician to replace good clinical practices and, above all, the clinician shall accept the responsibility for proper titration of relaxants, in accordance with the anesthetic and surgical requirements supervised with monitoring in the OR.[17]

In our reported cases, the doses used could be controversial because of the lack of hard epidemiological studies on the doses administered to this age group; moreover, some authors do not recommend Sugammadex for this population because of the absence of data.[18]

Most trials include individuals over 18 years of age and a small percentage of patients over 28 days old such as in Plaud's study[15]; nevertheless, few publications recommend the agent as effective in children and teenagers.[19]

Sugammadex has been studied under low creatinine clearance conditions (<30 ml/min) demonstrating the non-recurrence of relaxation and no changes in latency times; despite these results, Sugammadex is not yet recommended for end-stage kidney disease.[20]

The pharmacological profile of Sugammadex guarantees the reversal of relaxation, regardless of the patient's pH[21]; additionally, latency, duration and quality of relaxation remain unchanged with renal function.[22] In contrast, Neostigmine has shown a slow or inefficient reversal in several trials with deep neuromuscular blockade[21–24] and a higher incidence of hypotension and bradycardia.[23,25]

Conclusions

The use of Sugammadex in the neonatal population lacks a strong clinical support and for this reason the experience is rather limited; however, this report highlights its effectiveness in neonate patients and suggests a dynamic profile similar to that described for healthy adults. Consideration should be given to the development of experimental clinical trials in Neonates to properly support the prescription of Sugammadex.

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Conflict of interest

The authors claim no conflict of interest.

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