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CASE REPORT

Sugammadex administration in pregnant patients undergoing non-obstetric surgery: a case series

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KEYWORDS

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Abstract The use of sugammadex for reversal of rocuronium-induced neuromuscular blockade after caesarean section is nowadays common practice, but concerns exist about its use in pregnant women undergoing non-obstetric surgery. We report six cases of pregnant women submitted to general anesthesia for non-obstetric surgery in which neuromuscular blockade was reversed with sugammadex. We followed the outcome of both mother and baby during and after delivery. Sugammadex seemed to be a safe option for both mother and baby but more reports are necessary to fill the evidence gap and increase the global knowledge about its safety in this special group of patients.

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Introduction

Sugammadex (Bridion®), a modified cyclodextrin molecule, encapsulates rocuronium and other aminosteroid neuromuscular blocking agents to provide rapid and reliable reversal of neuromuscular blockade (NMB). Its use was approved in

2008 in Europe and in 2010 at our hospital. Although sugammadex has been well studied in pregnant patients at conclusion of cesarean deliveries, clinical evidence guiding its use in pregnant women undergoing non-obstetric surgery is sparse, with only three cases described so far,¹⁻³ and the possible effects on the fetus unknown. We report a series of six pregnant women submitted to general anesthesia for non-obstetric surgery in which NMB was reversed with sugammadex.

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Table 1 Demographic and clinical data about non-obstetric surgery.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	37	22	39	32	36	21
BMI (kg.m ⁻²)	22.8	27.9	25.3	22.7	20.1	27.5
ASA-PS	II	II	II	II	II	II
Comorbidities			Crohn disease		Hypothyroidism	
Gestational age (weeks) at the time of surgery	8	22	24	10	18	15
Diagnosis Surgery	Appendicitis Laparoscopy	Appendicitis Laparoscopy	Breast Abscess Surgical Drainage	Ovarian torsion Laparoscopy	Appendicitis Laparoscopy	Appendicitis Laparoscopy
Duration of surgery (minutes)	65	50	25	50	40	83
Dose of Rocuronium (mg.kg ⁻¹)	0.6	0.7	0.9	0.9	1.0	1.1
Dose of Sugammadex (mg.kg ⁻¹) ^a	3.2	0.7	3.7	3.4	3.4	2.0
Adverse event during surgery	None	None	None	None	None	None

ASA-PS, The American Society of Anesthesiologists Physical Status.

^a Dose of sugammadex: 3-4 mg.kg⁻¹ if TOF = 0 and PTC ≥ 1; 1-2 mg.kg⁻¹ if TOF > 2; 0-1 mg.kg⁻¹ if T4/T1 ≥ 0,9 (prevention of residual neuromuscular blockade) based on Groudine SB, Soto R, Lien C, Drover D, Roberts K. A randomized, dose-finding, phase II study of the selective relaxant binding drug, Sugammadex, capable of safely reversing profound rocuronium-induced neuromuscular block. *Anesth Analg.* 2007;104:555-62.

Methods

This is a case series with a retrospective single-center design, reporting all consecutive cases of pregnant patients submitted to non-obstetric surgery to whom sugammadex was administered to reverse NMB.

Ethical approval for this study (Ethical Committee N° CA-0428/19-0t.MP/CC) was provided by the Ethical Committee of Centro Hospitalar de Entre o Douro e Vouga EPE, Santa Maria da Feira, Portugal (Chairperson Nurse José David).

Data collection took place between January and November 2019. A database including pregnant patients submitted to non-obstetric surgery, from January 2010 to November 2019, was obtained by cross-checking data on deliveries or abortions with surgery in the previous 9 months in the hospital database. All anesthesia records were retrospectively reviewed and the six cases in which sugammadex was used to reverse NMB were selected. Data concerning age, parity, duration of gestation, type of surgery, and adverse events during general anesthesia or at the postanesthesia care unit were collected. The type of delivery and birth outcomes were also analyzed based on both mothers and babies records, with the most updated health status obtained by telephone interview with the mothers. All patients have been contacted and gave consent to be included in this report.

Case description

In all cases, general anesthesia was induced with propofol, fentanyl and rocuronium, and maintained with a mixture of oxygen, air and a volatile anesthetic (sevoflurane or desflurane). Neuromuscular function was monitored

using acceleromyograph (TOF-Watch® Device, Organon). Two skin electrodes were placed over the ulnar nerve and an accelerometer sensor was placed on the tip of the thumb. Stabilization and calibration were performed before administration of the muscle relaxant and TOF stimulation was initiated and reiterated every 15 seconds. Following stabilization, rocuronium was administered, and tracheal intubation was performed after obtaining the adequate neuromuscular block (TOF_c = 0). Repetitive TOF stimulations were applied every 15 minutes during surgery. At the end of surgery, sugammadex was given, and patients extubated once full recovery (TOF ≥ 0.9) occurred.

In the immediate postoperative period, the patients were admitted to the recovery room for surveillance. A cardiocography was performed before and after the procedure.

Demographic and clinical data about the non-obstetric surgery are summarized in [Table 1](#). Delivery data and baby outcome are summarized in [Table 2](#).

Patient 1

A 37-year-old primigravida, ASA 2, was submitted to a laparoscopic appendectomy at 8 weeks of gestation, under general anesthesia with NMB, reversed with 200 mg of sugammadex, without immediate complications. Her remaining pregnancy was uneventful. At 40 weeks of gestation, she was admitted in spontaneous labor, but due to prolonged labor caused by cephalopelvic disproportion, a c-section was performed under epidural anesthesia. A healthy male baby was born, with an Apgar score of 9/10/10 and 3710 g weight. The baby is now 3 years old and healthy.

Table 2 Delivery data.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Gestational age (weeks) at delivery	40 + 0	35 + 6	39 + 0	41 + 1	39 + 5	39 + 0
Type of delivery	c-section	c-section	c-section	assisted vaginal delivery	c-section	spontaneous vaginal delivery
Type of anaesthesia	Epidural	Spinal	Combined spinal-epidural	Epidural	Epidural	Epidural
Apgar score (1/5/10 min)	9/10/10	9/10/10	9/9/10	9/10/10	9/10/10	10/10/10
Birth weight (g)	3710	2150	2840	3360	3130	3845
Pregnancy or intrapartum complications	-	pre-eclampsia	-	postpartum haemorrhage	-	-
Congenital abnormalities	No	No	No	No	No	No

Patient 2

A 22-year-old primigravida, ASA 2, was submitted to laparoscopic appendectomy at 22 weeks of gestation, under general anesthesia with NMB, reversed with 50 mg of sugammadex, without immediate complications. Her pregnancy was uneventful until 35 + 6 weeks of gestation, when she was admitted due to severe pre-eclampsia. Labor was induced with misoprostol and magnesium sulphate protocol initiated, but after 36 hours, due to prolonged labor, a c-section was performed under spinal anesthesia, and a healthy male baby was born, with an Apgar score of 9/10/10 and 2150 g weight. The baby is now 13 months old and healthy.

Patient 3

A 39-year-old primigravida, ASA 2, was submitted to a surgical drainage of a breast abscess at 24 weeks of gestation, under general anesthesia with NMB, reversed with 200 mg of sugammadex, without immediate complications. Her remaining pregnancy was uneventful. At 39 weeks of gestation, she was admitted for a planned c-section due to maternal disease (Crohn disease). The surgery was performed under combined spinal-epidural anesthesia, and a healthy female baby was born, with an Apgar score of 9/9/10 and 2840 g weight. The baby is now 12 months old and healthy.

Patient 4

A 32-year-old primigravida, ASA 2, was submitted to an exploratory laparoscopy at 10 weeks of gestation due to ovarian torsion, under general anesthesia with NMB, reversed with 200 mg of sugammadex, without immediate complications. Her remaining pregnancy was uneventful. At 41 weeks of gestation, she was admitted to induction of labor. A vacuum assisted vaginal delivery was performed under epidural analgesia and a healthy female baby was born, with an Apgar score of 9/10/10 and 3360 g weight. A postpartum hemorrhage occurred due to uterine atony

that was successfully resolved with conservative management, without need of blood transfusion. The baby is now 4 months old and healthy.

Patient 5

A 36-year-old primigravida, ASA 2, was submitted to laparoscopic appendectomy at 18 weeks of gestation, under general anesthesia with NMB, reversed with 200 mg of sugammadex, without immediate complications. At 39 + 5 weeks of gestation, she was admitted in spontaneous labor, but due to prolonged labor a c-section was performed under epidural anesthesia. A healthy male baby was born, with an Apgar score of 9/10/10 and 3130 g weight. The baby is now 12 weeks old and healthy.

Patient 6

A 21-year-old primigravida, ASA 2, was submitted to laparoscopic appendectomy at 15 weeks of gestation, under general anesthesia with NMB, reversed with 150 mg of sugammadex, without immediate complications. Her remaining pregnancy was uneventful. At 39 weeks of gestation a spontaneous vaginal labor was performed under epidural analgesia. A healthy male baby was born, with an Apgar score of 10/10/10 and 3845 g weight. The baby is now 6 weeks old and healthy.

Discussion

To the best of our knowledge, this is the first case series regarding the use of sugammadex in pregnant women undergoing non-obstetric surgery. Only three cases have been earlier reported: two cases of pregnant women with severe pathology (pheochromocytoma and persistent atrial fibrillation) reporting good fetal outcome^{1,3}; and a third case reporting a rescue situation after unintentional maternal neuromuscular blockade during intrauterine transfusion but omitting the baby outcome.³

In our series, the decision to use sugammadex was based on our large experience with its use and the undoubtedly superiority over neostigmine, believing that this would be in the best interest of both mother and baby. According to the Cochrane review about efficacy and safety of sugammadex versus neostigmine, sugammadex can more rapidly reverse rocuronium-induced NMB regardless of the depth of the block and appears to have a better safety profile than neostigmine, with 40% fewer adverse events.⁴

In our study, no adverse events during general anesthesia or in the immediate postoperative period were reported; all fetuses showed good vitality in the cardiotocogram performed after the procedure; and all babies are healthy, without congenital abnormalities. The late pregnancy complications described in patient 2 (severe preeclampsia) and patient 4 (uterine atony) do not seem to be related to the administration of sugammadex several months before.

The current Bridion® package insert states that there are no data to inform drug-associated risks in pregnancy. In addition, a statement published by the Society for Obstetric Anesthesia and Perinatology in April 2019 advise against the use of sugammadex in patients in early pregnancy until the clinical implications of in vitro studies indicating that sugammadex binds to and encapsulates progesterone are clarified.⁵

In fact, the current evidence comes from limited preclinical studies in primary cell cultures and rats. Potential effects of sugammadex on the developing human fetus are completely unknown, as is evidence regarding maternal–fetal placental transfer, which is a prerequisite to cause fetal exposure. Theoretically, its very large molecular size and polarization in aqueous solution, predict limited, if any, placental transfer. Additionally, there is no evidence about the potential effect of sugammadex administration on maintenance of early pregnancy. A single study that exposed 1st trimester pregnant rats to high dose sugammadex (30 mg.kg⁻¹) failed to demonstrate any changes in either endogenous progesterone levels, live birth, or stillbirth rates.

The major limitation of our investigation is its retrospective design with inclusion of only six patients. Nevertheless, it is the first case series to follow the outcome of both mother and baby during and after delivery. We believe there might be many more cases of sugammadex use in similar circumstances, that have not been reported. Thus, we appeal to our colleagues to share their experience by writing and publishing those cases in order to fill the evidence gap and increase the global knowledge about its safety in this special group of patients.

Conclusion

In these six cases of urgent non-obstetric surgery during pregnancy, sugammadex seemed to be a safe option for reversal of rocuronium-induced NMB for both mother and baby.

Conflicts of interest

The authors declare no conflicts of interest.

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