## CASE SERIES

# Sugammadex use in liver transplantation: a case series and literature review

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## ABSTRACT

Postoperative residual neuromuscular blockade is associated with significant morbidity in liver transplantation. We report postoperative outcomes of sugammadex in a case series of 6 adult patients underwent liver transplantation at our institution in 2013. Sugammadex administration did not lead to any differences in the patients' heart rates, mean arterial pressures and electrocardiograms. In this case series, we observed that administration of rocuronium and sugammadex was effective and safe in liver transplant recipients. Postoperative residual neuromuscular blockade reversal with sugammadex may reduce the risk of pulmonary complications in liver transplant recipients.

**Key words:** Liver transplantation; Sugammadex; Neuromuscular blockade; Endotracheal extubation; Rocuronium; Neuromuscular Nondepolarizing Agents

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## INTRODUCTİON

Due to developments in surgical techniques, expansion of indications for transplantation, better understanding of pathophysiology and perioperative care, today more and more liver transplants are performed in many centers.[1,2]

Liver transplantation necessitates anesthesia management that requires invasive hemodynamic monitoring, rapid and excessive transfusions, frequent and close follow-up of coagulation parameters with thromboelastography, values of blood gases and blood biochemistry.[3] Liver transplantation is a surgical procedure performed in high-risk patients, and the length of the surgery is usually not short and varies from one center to another. Therefore, if anesthesiologists plan to extubate the patient, they should consider postoperative residual curarization developing due to prolonged effects of muscle relaxant agents.

Residual curarization is still a common and an important problem in modern anesthesia, posing a serious threat to patient safety.[4] Therefore, it is of more importance in liver transplant anesthesia in which the length of surgery is significantly longer. Nowadays, for traditional decurarization, cholinesterase inhibitors are widely used in combination with muscarinic antagonists. In recent years, use of sugammadex, a modified γ-cyclodextrin, in the steroidal neuromuscular agents has been a new alternative to traditional decurarization process performed with cholinesterase inhibitors.[5-7]

Sugammadex is used for the selective and rapid reversal of neuromuscular block. In several human and animal studies, it has been demonstrated that sugammadex can reverse rocuronium-induced deep neuromuscular blockade without leading to muscle weakness.[8] Therefore, in recent years, it has gained popularity in the practice of anesthesia. Since sugammadex provides quick and unproblematic recovery, now it is preferred by anesthesiologists more and used in anesthesia management more widely.

## CASE SERIES

Following the institutional Noninvasive Clinical

Research Ethics Committee approval, the data about 6 adult patients who were extubated in the operating room right after the liver transplantation procedure and received at least one dose of sugammadex during 2013 were analyzed. Prior to the procedure, vascular access was established in all cases, and electrocardiogram (ECG), arterial blood pressure, peripheral oxygen saturation (SpO2) and body temperature were monitored (Hewlett Packard, M1094B-Saronno, Italy). All the patients were given oxygen with a face mask at a rate of 4-6 L / min. To prevent aspiration, a $H_2$ receptor antagonist was administered intravenously 15-20 minutes before the process. All the patients underwent standard general anesthesia. Anesthesia was induced with inj. remifentanil 0.1-0.2 μg/kg, thiopental sodium 3-5 mg/kg and rocuronium 1 mg/kg administered intravenously (IV). After orotracheal intubation, further monitoring of the patients was performed through invasive arterial catheterization and pulmonary artery catheterization. Anesthesia was maintained with desflurane (end-tidal 4-5%), inj. remifentanil 0.05-0.2 μg/kg/min and inj. rocuronium 0.4 mg/kg/hr. While coagulation parameters were monitored with thromboelastography, for the monitoring of ventilation parameters, arterial blood gases and $EtCO_2$ were used. During the surgery, neuromuscular monitoring (TOF Guard İNMT, Biomet International Odense, Denmark) was performed. Immediately after the operation, sugammadex 4 mg/kg IV was administered to hemodynamically and metabolically stable patients and these suitable patients were extubated without problem when the TOF ratio of 0.9 was reached in the operating room. All the patients were transferred to the intensive care unit.

Characteristics of the patients are shown in Table 1. Standard monitoring including neuromuscular monitoring (TOF) was applied to all patients. Only in two cases, TOF could not be used for neuromuscular monitoring due to some technical problem. In the patients who were not monitored with TOF, rocuronium infusion was discontinued 30 min before the operation ended. The patients were extubated without problem after sugammadex 4 mg/kg IV was administered. Sugammadex administration did not lead to any differences in

**Table 1: Characteristics of the cases**

| Cases | Anthropo-metric Measurements | Donor type | Diagnosis | Anesth time (min) | Dose of roc. (mg) | Dose of sug. (mg) | Re-intubation | Transfusion (unit) |
|---|---|---|---|---|---|---|---|---|
| **Case 1** | Age: 48<br>Weight: 94 kg<br>Height: 1,65 m<br>BMI: 34,81 kg/m$^2$ | Cadaver | HBV-related liver cirrhosis | 600 | 460 | 400 | No | No RBC<br>FFP 6 |
| **Case 2** | Age: 40<br>Weight: 55 kg<br>Height: 1,55 m<br>BMI: 22,91 kg/m$^2$ | Cadaver | HBV- related liver cirrhosis | 500 | 264 | 200 | No | No RBC<br>FFP 4 |
| **Case 3** | Age: 60<br>Weight: 63 kg<br>Height 1,55 m<br>BMI: 26,25 kg/m$^2$ | Donor | Unknown cause | 650 | 340 | 240 | No | RBC 2<br>FFP 2<br>Thrombocyte 2 |
| **Case 4** | Age: 48<br>Weight: 78 kg<br>Height: 1,72 m<br>BMI: 26,82 kg/m$^2$ | Donor | Cryptogenic liver cirrhosis | 510 | 850 | 400 | Yes | RBC 3<br>FFP 5<br>Thrombocyte 4 |
| **Case 5** | Age: 54<br>Weight:65 kg<br>Height: 1,63 m<br>BMI: 24,52 kg/m$^2$ | Donor | HCV-HCC | 640 | 340 | 260 | No | RBC 4<br>FFP 5<br>Thrombocyte 1 |
| **Case 6** | Age: 33<br>Weight: 80 kg<br>Height: 1,90 m<br>BMI: 22,22 kg/m$^2$ | Cadaver | Wilson cirrhosis | 680 | | 320 | No | RBC 2<br>FFP 10<br>Thrombocyte 1 |

RBC = Red Blood Cell; FFP = Fresh Frozen Plasma; Roc. = Rocuronium; Sug. = sugammadex

the patients' heart rates, mean arterial pressures and electrocardiograms.

When the patients were transferred to the intensive care unit, they were conscious and cooperative, and breathing spontaneously with 4-6 L/min of oxygen support from a face mask. Adequate pain palliation could not be achieved in one of the patients because she could not use the patient-controlled analgesia (PCA) pump effectively in the intensive care unit and she was re-intubated due to severe agitation one hour after extubation.

In other patients, neither signs of residual curarization nor other side effects of sugammadex were observed.

## DISCUSSION

It takes longer to perform major surgery interventions such as liver transplantation, and in such operations, more neuromuscular blockers are required in order to achieve adequate muscle relaxation. Hence, in such operations there is a risk of residual curarization.[6,9] Among the well-known factors affecting postoperative residual block are type and dose of muscle relaxants used, administration of additional intraoperative doses, patient's clinical characteristics, and type and length of surgery.[10]

Prolongation of neuromuscular block and mechanical ventilation requirement resulting from the residual neuromuscular block during the postoperative period lead to increases in postoperative morbidity.[4] Atelectasis is a complication related with prolonged mechanical ventilation and it is associated with postoperative pulmonary complications such as pneumonia.[11] Therefore, in cases requiring muscle relaxation, continuous, objective neuromuscular monitoring should be performed and residual block should be avoided.

It is known that organ failure alone is a risk factor for residual block.[11] Thus, it is essential that respiratory and upper airway muscles of liver transplant patients should not be damaged, and that the patients should get rid of secretions by coughing. Residual block also destroys the respiratory response to hypoxia.[12] Therefore, recovery should be quickened by administering an agent for the reversal of neuromuscular blockade. Concomitant use of cholinesterase inhibitors and muscarinic antagonists is a safe and effective method to reverse residual block; however, their effects are limited in such cases as the complete reversal of deep residual blockade and they lead to tachycardia, bradycardia, dry mouth, and emesis.[5,13] In liver transplant patients , these undesirable side effects might adversely affect their healing process during the postoperative period; thus, we administered sugammadex and also sugammadex is an ideal agent that can be used for the reversal of deep and shallow neuromuscular blockade.[5,14] Sugammadex is a modified gamma-cyclodextrin molecule introduced to the market recently. Sugammadex acts as a synthetic receptor by encapsulating steroidal neuromuscular blocking agents (NMBA) and promoting NMBA's disassociation from the nicotinic acetylcholine receptor.[14-16] No metabolites of sugammadex have been observed; it is excreted in the urine. For liver transplant patients, the absence of drug metabolites is important. Another important advantage of sugammadex is that it can reverse any level of a block. Sacan et al.[17] confirmed that sugammadex could rapidly reverse moderate rocuronium-induced neuromuscular blockade without any undesirable side effects. Most importantly, sugammadex promotes rapid and complete reversal and does not cause dry mouth which is common after surgeries in which cholinesterase inhibitors are used. Ledowski et al[18] reported postoperative residual neuromuscular blockade reversal with sugammadex was associated with the lowest rate of postoperative nausea and vomiting and may reduce the risk of pulmonary complications in elderly ASA 3/4 patients.

After liver transplantation, early extubation can be safely achieved. For the successful extubation of a liver transplant patient, the patient should be comprehensively evaluated by an experienced anesthesiologist.[19] Skurzak et al[20] performed early extubation in 594 liver transplant patients in the operating room based on a SORELT scoring prepared by them and none of the patients were re-intubated in the first 48 hours post-operation. We decided to achieve extubation in patients who did not receive much blood or blood product transfusion, had stable hemodynamics/metabolic profile and developed no complications during the surgery. Sugammadex administration did not lead to any differences in the patients' heart rates, mean arterial pressures and electrocardiograms. Although the respiratory signs and arterial blood gases were normal, one patient was re-intubated in the intensive care unit because of severe agitation related with inadequate pain palliation.

In this case series, we observed that administration of rocuronium and sugammadex was quite effective

and safe in liver transplant recipients. Postoperative residual neuromuscular blockade reversal with sugammadex may reduce the risk of pulmonary complications in liver transplant recipients. But before suggesting its routine use in liver transplant patients, the results of large clinical randomised controlled trials should be awaited.

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**Author Contribution:** All the authors contributed in concept, manuscript preparation and review.

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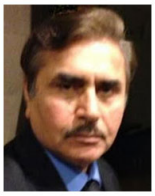


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