MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2016; 22: 803-809
DOI: 10.12659/MSM.897608

Received: 2016.01.16
Accepted: 2016.02.10
Published: 2016.03.10

# Effects of Sugammadex and Neostigmine on Renal Biomarkers

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABEFG 1 Yasemin Isik
ABCD 2 Onur Palabiyik
DEF 3 Bilal Muhammed Cegin
EF 3 Ugur Goktas
FG 4 Ismail Kati

1 Department of Anesthesiology and Intensive Care, Izmir Katip Celebi University, Faculty of Medicine, Izmir, Turkey
2 Department of Anesthesiology and Intensive Care, Sakarya University Training and Research Hospital, Sakarya, Turkey
3 Department of Anesthesiology and Intensive Care, Yuzuncu Yil University, Faculty of Medicine, Van, Turkey
4 Department of Anesthesiology and Intensive Care, Gazi University, Faculty of Medicine, Ankara, Turkey

This report was previously orally presented, in part, at the 46th National Congress of the Turkish Anesthesiology and Reanimation Specialists Society, Girne, Turkish Republic of Northern Cyprus, 07–11 November 2012

**Corresponding Author:** Yasemin Isik, e-mail: yaseminmd@yahoo.com

**Source of support:** This study was supported by Yuzuncu Yil University, Department of Scientific Research Projects, Project Number 2010-TF-U123

**Background:** Neostigmine, the currently commonly used agent for reversal of neuromuscular blockade. Sugammadex is a novel and unique compound designed as an antagonist of steroidal neuromuscular blockers. In this study, we evaluated the effects of sugammadex or neostigmine on kidney functions in patients scheduled for elective surgery.

**Material/Methods:** Patients scheduled for a surgical procedure under desflurane/opioid anesthesia received an intubating dose rocuronium. Patients were divided into 2 groups receiving either sugammadex or neostigmine atropine to reverse neuromuscular blockade. Cystatin C, creatinine, urea, blood urea nitrogen, sodium, potassium, and calcium levels in the blood and $\alpha_1$microglobulin, $\beta_2$microglobulin, and microalbumin levels in the urine were measured.

**Results:** There was no significant difference between the groups with regard to the demographic data. In the Neostigmine Group, although $\beta_2$microglobulin and microalbumin were similar, a significant increase was found in the postoperative $\alpha_1$microglobulin and cystatin C values. In the Sugammadex Group, although $\beta_2$-microglobulin and cystatin C were similar, a significant increase was found in the postoperative $\alpha_1$-microglobulin and microalbumin values. The only significant difference was cystatin C value variation in the Neostigmine Group compared to the Sugammadex Group.

**Conclusions:** We believe that the use of more specific and sensitive new-generation markers like cystatin C to evaluate kidney function will provide a better understanding and interpretation of our results. Sugammadex has more tolerable effects on kidney function in patients than does neostigmine. However, when compared to preoperative values, there is a negative alteration of postoperative values. Neostigmine and sugammadex do not cause renal failure but they may affect kidney function.

**MeSH Keywords:** Anesthesia • Anesthesia, General • Neostigmine

**Full-text PDF:** http://www.medscimonit.com/abstract/index/idArt/897608

2536 2 2 31





Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

## Background

The reversal of the effects of muscle relaxant agents is an important issue in general anesthesia practice. The conventional cholinesterase-inhibiting agents, called anti-cholinesterase, exert their effect by indirectly inactivating cholinesterase in the neuromuscular junction. They are metabolized in the liver by acetyl cholinesterase and plasma esterase. Approximately 50% of these agents are excreted unchanged by the kidneys [1–3]. Neostigmine is the most potent and selective drug [4]. It is secreted from the tubular lumen, and its clearance is higher than the glomerular filtration rate (GFR). Additionally, its clearance is substantially decreased and its half-life is prolonged in patients with renal failure [5].

Cyclodextrins confine the muscle-relaxing agents via "molecular encapsulation" and render them water soluble. Sugammadex firmly binds one-to-one with steroid muscle relaxants and provides disposal through urine. The cavity of the sugammadex molecule encloses the 4 hydrophobic steroid rings through encapsulation [6–8]. The reason for the popularity of sugammadex is its reversal effect of blocking at any depth, both effectively and quickly, without waiting for a spontaneous reversal [9,10]. No metabolite of sugammadex has been found, and it has been determined to be excreted unchanged by the kidney. In healthy people, 48–86% of sugammadex is excreted unchanged in urine within 24 h [11].

It is well known that Cr is an indicator of renal function. However, as long as the GFR decreases it to less than 50 ml/min/1.73 $m^2$, the serum Cr concentration does not change. Furthermore, its value is affected by age, sex, muscle mass, and dietary proteins. Unlike Cr, cystatin C (Cys C), a novel renal biomarker (cysteine protease inhibitor), is not affected by these factors. Moreover, it is freely filtered by the glomerulus, completely reabsorbed by the proximal tubule, and not secreted [12,13]. In evaluating renal function, the sensitivity of Cys C is 70%, and its specificity is 100%. It has been demonstrated that Cys C is a better parameter than serum Cr for detecting the smallest changes in GFR [15,16].

With regard to the other sensitive biomarkers, although alpha1 microglobulin (α1μg) and beta2 microglobulin (β2μg) are important indicators of renal tubular dysfunction, microalbumin (μA) is an indicator that is associated with glomerular barrier damage [12,17]. New serum and urinary biomarkers are now available, including serum and urinary cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), urinary kidney injury molecule 1 (KIM-1), interleukin 18 (IL-18), liver-type fatty acid binding protein (L-FABP), and N-acetyl-β-glucosaminidase (NAG). However, these biomarkers are still under investigation [14].

There are studies in the literature comparing the effects of sugammadex and neostigmine [8,13,18,19]. However, few of these studies were primarily designed to evaluate the effects of sugammadex and neostigmine on renal function. Therefore, we aimed to compare the short-term effects of sugammadex and neostigmine on renal glomerular filtration and tubular functions using new more sensitive biomarkers in patients with normal renal function.

## Material and Methods

### Study design and patient selection

This study, which was supported by Yuzuncu Yil University, Department of Scientific Research Projects, with the Project Number 2010-TF-U123, was carried out with the approval of the Yuzuncu Yil University Local Ethics Committee (no. 07/11.04.2011), and it was conducted in an operating room at Yuzuncu Yil University, Dursun Odabas Medical Center. This study was conducted with written informed consent from the study subjects.

This study involved a total of 50 patients between the ages of 18 and 65 years who were scheduled for elective surgery under general anesthesia. For inclusion, the patients had normal renal function (serum Cr <1.5 mg/dL) and were classified as American Society of Anesthesiologists (ASA) Class I-II. Exclusion criteria were: liver failure, kidney failure, neuromuscular disorders, pregnant or breastfeeding, being treating with corticosteroids or oral contraceptives, a contraindication to the study drugs, an allergy to the drugs, a body mass index over 30 kg/$m^2$, receiving medication known to interfere with the action of rocuronium (e.g., amino glycoside antibiotics and anticonvulsants), or did not wish to participate.

### Anesthesia protocol

Premedication was not given to the patients. The patients were taken into the operating room and were monitored for heart rate (HR), mean arterial blood pressure (MAP), and peripheral oxygen saturation ($SpO_2$). The neuromuscular blockade was monitored by acceleromyography at the adductor pollicis muscle in response to ulnar nerve stimulation using the TOF-Watch SX device (Schering-Plough, Dublin, Ireland). The forearm was immobilized and surface skin electrodes were placed over the ulnar nerve proximal to the wrist. A train-of-four (TOF) stimulation was initiated. Following the initiation of 0.9% sodium chloride (NaCl) infusion, routine anesthesia induction was performed with 2 μg/kg fentanyl (fentanyl, Janssen-Cilag, Beerse, Belgium), 2 mg/kg propofol (propofol 1%, Fresenius Kabi, Austria), and 0.6 mg/kg rocuronium (Esmeron, N.V. Organon, Oss, Holland). When there was no response to TOF stimulation, orotracheal





Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

**Table 1.** Baseline characteristics and total rocuronium dose.

| | Group Sugammadex | Group Neostigmine | p |
|---|---|---|---|
| Age (year) | 39.25±6.6 | 39.92±10.0 | 0.785 |
| Gender F/M (n) | 22/3 | 21/4 | 0.424 |
| Weight (kg) | 68.46±6.7 | 68.64±7.4 | 0.929 |
| Height (cm) | 159.92±5.6 | 160.44±6.8 | 0.770 |
| BMI | 27.24±6.1 | 26.79±7 | 0.798 |
| ASA I/II (n) | 10/14 | 9/16 | 0.692 |
| Duration of operation (min) | 77.08±36.1 | 82.00±44.8 | 0.675 |
| Total rocuronium dose (mg) | 47.92±6.6 | 48.40±6.9 | 0.803 |

Data are presented as mean ±SD or n. ASA – American Society of Anesthesiologists; F – Female; M – Male; n – number of patient; p – significant level; SD – standard deviation.

intubation was performed, and the patients were ventilated with anesthesia equipment with 4–6 L/min fresh gas flow, with the tidal volume maintained at 8 mL/kg and a frequency of 12/min. For the continuation of anesthesia, 60% $N_2O$-$O_2$ and 4–6% desflurane (Suprane, Baxter Healthcare, Puerto Rico, USA) were administered. For the continuation of muscle relaxation, an additional dose of rocuronium 0.15 mg/kg was administered at the reappearance of a second twitch of TOF, as needed. The HR, MAP, and $SpO_2$ levels of the patients were recorded preoperatively, at every 10 min during anesthesia, and at 5 and 10 min after the drugs were administered. Patients were randomized preoperatively into 2 groups: the Neostigmine group (Group N, n: 25) and the Sugammadex group (Group S, n: 25). Randomization was performed by one of the authors (OP) using previously prepared, sealed, opaque envelopes. Randomization sequence was generated by using computer-generated random numbers. At the end of the surgical procedure, Group S was given 4 mg/kg sugammadex (Bridion, N.V. Organon, Oss, Holland) intravenously upon the reappearance of a post-tetanic count 1–2 or a second twitch of TOF after the last dose of rocuronium, because sugammadex had sufficient efficiency to reverse a deep and moderate neuromuscular blockade. Group N was administered a combination of 0.04 mg/kg neostigmine (neostigmine, Adeka, Samsun, Turkey) with 0.01 mg/kg atropine (Atropinsulfat, Drogsan, Ankara, Turkey) intravenously at the reappearance of a second twitch of TOF after the last dose of rocuronium, because neostigmine does not have adequate efficiency to reverse a deep neuromuscular blockade.

### Sample collection and analysis

Preoperative blood and urine samples were collected from the patients before they were taken into the operating room. At 12 h following decurarization, blood and urine samples were collected postoperatively. The serum Cys C, Cr, urea, blood urea nitrogen (BUN), sodium (Na), potassium (K), and calcium (Ca) levels and the urine α1μg, β2μg, and μA levels were preoperatively and postoperatively determined. Routine biochemical parameters were measured by the colorimetric method and serum Cys C, urine α1μg, β2μg, and μA were measured using a nephelometric method. The primary endpoint was the acute effects of sugammadex or neostigmine on renal function as determined with more specific and sensitive tests.

To avoid affecting renal functions, we tried to keep the type of surgery, fluid resuscitation, and duration of anesthesia similar in both groups. Central body temperature was measured continuously during anesthesia and normothermia was maintained.

### Sample size calculation and statistical analysis

According to the power analysis, sample size was calculated as a minimum 23 patients, based on our results to detect a minimum difference of 10% in the values of cystatin C between the 2 groups with a power of 80%, an α of 0.05, and a β of 0.2. Taking into account that approximately 10% of the enrolled patients might be excluded from the intent-to-treat evaluation, we decided to enroll 25 patients in each group [20].

Data are expressed as the means ± standard deviation (SD) or n, as appropriate. The Shapiro-Wilk test were used for a normality test of the data. The *t* test was used for comparisons of parameters that showed normal distribution, and the Mann-Whitney U test was used for comparisons of parameters that did not show a normal distribution. A one-way variance analysis with repeated measures was used to determine the differences in continuous variables between the groups. A P value of less than 0.05 was accepted as statistically significant. All analyses were performed using the Statistical Package for Social Sciences for Windows (SPSS 20.0.1; SPSS Inc.; Chicago, IL).





Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

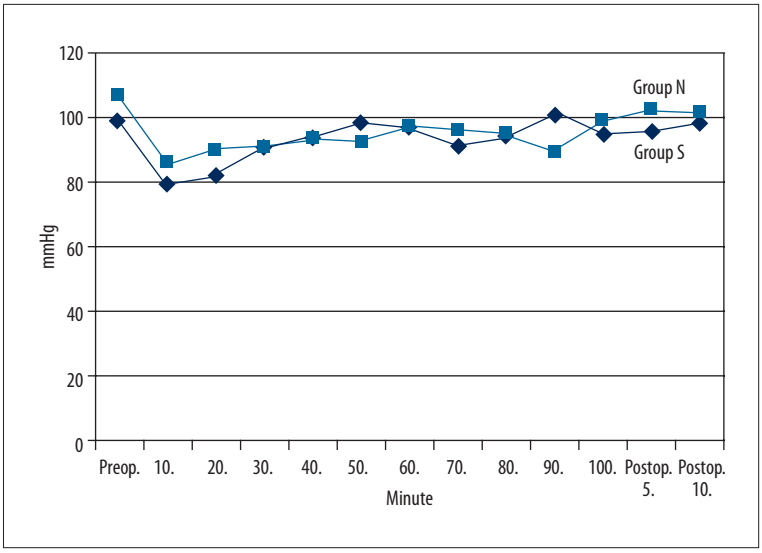


**Figure 1.** Mean arterial blood pressure of groups.

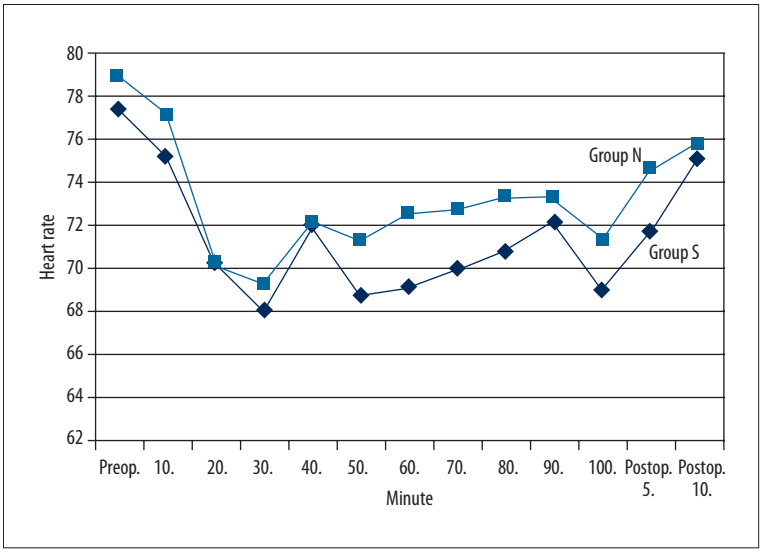


**Figure 2.** Mean heart rate of groups.

## Results

The baseline characteristics data and total rocuronium doses were comparable in both groups and are presented in Table 1. There was no statistically difference between the 2 groups with regard to the MAP or HR (Figures 1, 2).

There was no significant difference between the 2 groups with regard to Cr, urea, Na, or K values (p>0.05). When Group N was compared with Group S, both the preoperative and postoperative BUN values were increased (p=0.026 and p=0.012, respectively), but their value variation was similar (p>0.05). These values were not clinically significant. In both groups, the postoperative Ca values were decreased compared with the preoperative values when they were analyzed within the groups (p=0.015 and p=0.032, respectively; Table 2).

In both groups, the β2μg values and their value variations were similar (p>0.05), and the postoperative α1μg values were increased compared with preoperative values (p=0.008 and p=0.022, respectively; Table 2). For intra-group comparisons, the postoperative μA value was increased in Group S (p=0.001) but it was similar in Group N (p>0.05; Table 2). Additionally, their value variation was similar when Group N was compared with Group S (p>0.05). Although there was no difference between the preoperative and postoperative Cys C values in Group S, the postoperative Cys C value was increased relative to the preoperative value in Group N (p=0.008; Table 2). Additionally, the value variation was increased when Group N was compared with Group S (p=0.033).





Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

**Table 2.** The levels of renal biomarkers.

| | Group Sugammadex (n=25) | | Group Neostigmine (n=25) | |
|---|---|---|---|---|
| | Preoperative | Postoperative | Preoperative | Postoperative |
| Cr (mg/dL) | 0.65±0.2 | 0.65±0.1 | 0.72±0.2 | 0.74±0.3 |
| Urea (mg/dL) | 26.56±8.2 | 26.64±9.0 | 28.89±10.8 | 30.26±10.8 |
| BUN (mg/dL) | 12.27±4.1 | 12.42±5.2 | 15.20±4.8# | 16.82±6.5# |
| Na (mmol) | 139.38±2.6 | 138.96±2.9 | 140.00±3.2 | 139.64±3.6 |
| K (mmol) | 4.06±0.4 | 4.15±0.4 | 4.08±0.4 | 4.12±0.3 |
| Ca (mg/dL) | 8.95±0.7 | 8.49±0.8* | 8.96±0.9 | 8.65±0.8* |
| β2μg (mg/L) | 0.31±0.3 | 0.94±1.7 | 0.51±0.8 | 0.76±1.4 |
| α1μg (mg/L) | 9.32±9.2 | 15.99±18.9* | 7.95±6.1 | 16.20±18.8* |
| μA (mg/dL) | 0.02±0.02 | 0.05±0.05* | 0.08±0.28 | 0.13±0.27 |
| CysC(mg/dL) | 0.57±0.16 | 0.59±0.13 | 0.56±0.28 | 0.67±0.24*& |

Data are presented as mean ±SD; * p<0.05 *vs.* preoperative values; # p<0.05 *vs.* Group S; & p<0.05 *vs.* Group S when compared with the variations of parameters. $\alpha_1$μg – $\alpha_1$microglobulin;$\beta_2$μg – $\beta_2$microglobulin; BUN – blood urea nitrogen; Ca – Calcium; Cr – Creatinine; Cys C – Cystatin C; K – Potassium, μA – microalbumin; Na – sodium; n – number of patients.

## Discussion

This study revealed that sugammadex and neostigmine affected renal glomerular filtration and tubular functions minimally, which was unexpected, because they are excreted unchanged. However, this effect was greater with neostigmine than sugammadex.

There were contradictions between the obtained results and the hemodynamic changes reported in the literature when sugammadex and neostigmine were compared. Two studies reported no differences in the MAP of patients administered neostigmine and sugammadex; however, this was only in the neostigmine group, whereas the HR was lower at first and subsequently became higher [18,21]. Other studies determined that there were no significant differences in the HR and MAP for both agents [11,19,22].

In this study, the hemodynamic changes were similar in both groups. There was no hemodynamic instability that could have affected renal function.

β2μg has a molecular weight of 11.000 Daltons and is found in all nucleated cells. α1μg is completely reabsorbed in the tubules. Both β2μg and α1μg are important indicators of renal tubular dysfunction. However, μA is a medium-sized protein. An increase in its level in the urine is an indicator of damage in the glomerular barrier [12,17].

Sugammadex is biologically inactive and has no effect on animal tissues *in vitro* [8]. Although urinary excretion times of rocuronium and sugammadex are less than 2 h, the rocuronium sugammadex complex is excreted in urine within 24 h [5,23]. With respect to the renal biomarkers, because most of the studies were primarily designed to compare the reversal effects of sugammadex and neostigmine, the literature presents limited data. The routine biochemistry and urine analyses were similar in the reported studies [24,25]. In patients with mild or moderate renal failure, a change in dosage is not recommended. In patients with severe renal failure, the excretion of sugammadex or the sugammadex-rocuronium complex is somewhat delayed; however, no sign of recurrence of neuromuscular block has been observed [26]. Therefore, in the present study, to evaluate the glomerular function, in addition to microalbumin and Cr, we used Cys C, which is a more specific marker of glomerular function.

Bostan et al. reported that application of 1 mg/kg rocuronium +96 mg/kg sugammadex caused a histopathological degeneration in the kidneys. They determined glomerular vacuolation, tubular dilatation, vascular vacuolation and hypertrophy, lymphocyte infiltration, and tubular cell sloughing. However, they suggested that these histopathological changes did not cause any deterioration in renal function [27].

Sparr et al. [11] administered a placebo and different doses of sugammadex to 99 patients; 4 patients displayed an abnormality in μA, 2 patients were determined to have an abnormality of NAG, and 3 patients were determined to have an abnormality in $\beta_2$μg values. Furthermore, they reported that in 1 patient, the Cr level was increased on the first postoperative day but returned to normal on the 20th postoperative day.





Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Sorgenfrei et al. [28] determined that 5 of the 27 patients receiving sugammadex had increased NAG levels, which is another renal tubular damage marker, and observed an increase in urinary albumin levels in 1 patient.

Ghoneim and El Beltagy [29] reported that the levels of serum Na, K, and kidney enzymes were similar in their study that compared the reversal effects of sugammadex and neostigmine in neurosurgical pediatric patients.

A study that compared the effects of sugammadex and neostigmine on vecuronium-induced neuromuscular blockade reported that the routine biochemistry and urine analyses, including the μA, $\beta_2$μg, and NAG levels, were similar in both groups [30].

Another study compared the effects of sugammadex and neostigmine on rocuronium-induced neuromuscular blockade under sevoflurane anesthesia and reported that in the neostigmine group, albumin was presented in the urine and the urine $\beta_2$μg values were increased [31]. Flocton et al. [22] detected increased NAG levels in 7 of the 34 patients in the sugammadex group and 1 of the 39 patients in the neostigmine group.

In a study that evaluated the effectiveness and safety of sugammadex in patients with normal renal function and terminal-stage renal failure, the researchers reported that the postoperative serum BUN and Cr, as well as urinary NAG, $\beta_2$μg, and μA levels, of terminal-stage renal failure patients were higher than the preoperative values.

In the present study, in terms of sensitive biomarkers, because the postoperative values were higher than preoperative values, both agents also affected the kidneys. Additionally, the Cys C values were higher with neostigmine than with sugammadex. Although all the values in both groups were within the reference values, in the neostigmine group, a significant increase was found in the postoperative α1μg levels and the μA and Cys C levels. In the sugammadex group, there was a significant increase in the β2μg and μA levels. In the sugammadex group, the Cys C level was not changed. Therefore, we decided that sugammadex has more tolerable effects on the glomerular and tubular systems in patients than neostigmine does.

## Conclusions

We found that when neostigmine and sugammadex were compared, neither affected hemodynamic parameters. Although neither neostigmine nor sugammadex affected the tubular and glomerular functions in the kidney, it must be remembered that both medications changed the renal parameters in patients who have normal kidney function.

Accordingly, we do not suggest that these medications should be used seamlessly, even in patients with mild renal dysfunctions. There is a need to study greater numbers of patients in evaluating long-term renal functions. A study limitation is that although patients with impaired or borderline renal function may be good choice as subjects in this type of study, we did not include these patients due to recommendations for use of sugammadex. Unfortunately, there was no control group of patients who reversed NMB spontaneously.

### Conflict of interest

None.

## References:

1. Williams NE, Calvey TN, Chan K: Clearance of neostigmine from circulation during the antagonism of neuromuscular block. Br J Anaesth, 1978; 50: 1065–67
2. Husain MA, Roberts JB, Thomas BH, Wilson A. Metabolism and excretion of 3 hydroxyphenyltrimethylammonium and neostigmine. Br J Pharmacol, 1969; 35: 344–50
3. Bevan DR, Donati F, Kopman AF. Reversal of neuromuscular blockade. Anesthesiology, 1992; 77: 785–805
4. Morgan GE, Mikhail MS, Murray MJ. Clinical Pharmacology. Ed. Clinical Anesthesiology. 4th ed. Lange Medical boks/McGraw-Hill, Medical pub. Division, 2006; 205–42
5. Staals LM, Snoeck MMJ, Driessen JJ et al: Multicentre, parallel-group, comparative trial evaluating the efficacy and safety of sugammadex in patients with end-stage renal failure or normal renal function. Br J Anaesth, 2008; 101: 492–97
6. Zhang MQ: Drug specific cyclodextrins: The future of rapid neuromuscular block reversal. Drugs Fut, 2003; 28: 347
7. Gijsenbergh F, Ramael S, Houwing N, Van Iersel T: First human exposure of Org 25969, a novel agent to reverse the action of rocuronium bromide. Anesthesiology, 2005; 103: 695–703
8. Geldner G, Niskanen M, Laurila P et al: A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. Anaesthesiology, 2012; 67: 991–98
9. Naguib M. Sugammadex: Another milestone in clinical neuromuscular pharmacology. Anesth Analg, 2007; 104: 575–81
10. Welliver M, McDonough J, Kalynych N, Redfern R: Discovery, development, and clinical application of sugammadex sodium, a selec-tive relaxant binding agent. Drug Des Devel Ther, 2008; 2: 49–59
11. Sparr HJ, Vermeyen KM, Beaufort AM et al: Early reversal of profound rocuronium-induced neuromuscular blockade by sugammadex in a randomized multicenter study efficacy, safety and pharmacokinetics. Anesthesiology, 2007; 106: 935–43
12. Van Meer L, Moerland M, Cohen AF, Burggraaf J: Urinary kidney biomarkers for early detection of nephrotoxicity in clinical drug development. Br J Clin Pharmacol, 2014; 77: 947–57
13. Ozgun C, Cakan T, Baltacı B, Başar H. Comparison of reversal and adverse effects of sugammadex and combination of Anticholinergic-Anticholinesterase agents in pediatric patients. J Res Med Sci, 2014; 19: 762–68
14. Parikh CR, Devarajan P: New biomarkers of acute kidney injury. Crit Care Med, 2008; 36: 159–65
15. Newman DJ: Cystatin C. Ann Clin Biochem, 2002; 39: 89–104





Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

16. Herget-Rosenthal S, Marggraf G, Hüsing J et al: Early detection of acute renal failure by serum cystatin C. Kidney Int, 2004; 66: 1115–22
17. Kang J, Liu J, Ding H et al: Urine alpha1-microglobulin is a better marker for early tubular dysfunction than beta2-microglobulin among tenofovir-exposed human immunodeficiency virus-infected men who have sex with men. Braz J Infect Dis, 2015; 19: 410–16
18. Gaszynski T, Szewczyk T, Gaszynski W: Randomized comparison of sugammadex and neostigmine for reversal of rocuronium-induced muscle relaxation in morbidly obese undergoing general anaesthesia. Br J Anaesth, 2012; 108: 236–39
19. Tas N, Korkmaz H, Yagan O, Korkmaz M: Effect of Sugammadex on postoperative bleeding and coagulation parameters after septoplasty: A randomised prospective study. Med Sci Monit, 2015; 21: 2382–86
20. Whitley E, Ball J: Statistics review 4: Sample size calculations. Crit Care, 2002; 6: 335–41
21. Sacan O, White PF, Tufanogullari B, Klein K: Sugammadex reversal of rocuronium-induced neuromuscular blockade: A comparison with neostigmine-glycopyrrolate and edrophonium-atropine. Anesth Analg, 2007; 104: 569–74
22. Flockton EA, Mastronardi P, Hunter JM et al: Reversal of rocuronium-induced neuromuscular block with sugammadex is faster than reversal of cisatracurium-induced block with neostigmine. Br J Anaesth, 2008; 100: 622–30
23. Szenohradszky J, Fisher DM, Segredo V et al: Pharmacokinetics of rocuronium bromide (ORG 9426) in patients with normal renal function or patients undergoing cadaver renal transplantation. Anesthesiology, 1992; 77: 899–904
24. Lemmens HJ, El-Orbany MI, Berry J et al: Reversal of profound vecuronium-induced neuromuscular block under sevoflurane anesthesia: Sugammadex versus neostigmine. BMC Anesthesiol, 2010; 10: 5
25. Rahe-Meyer N, Fennema H, Schulman S et al: Effect of reversal of neuromuscular blockade with sugammadex versus usual care on bleeding risk in a randomized study of surgical patients. Anesthesiology, 2014; 121: 969–77
26. Adam JM, Bennett DJ, Bom A et al: Cyclodextrin-derived host molecules as reversal agents for the neuromuscular blocker rocuronium bromide: Synthesis and structure-activity relationships. J Med Chem, 2002; 45: 1806–16
27. Bostan H, Kalkan Y, Tomak Y et al: Reversal of rocuronium-induced neuromuscular block with sugammadex and resulting histopathological effects in rat kidneys. Renal Failure, 2011; 33: 1019–24
28. Sorgenfrei IF, Norrild K, Larsen PB et al: Reversal of rocuronium-induced neuromuscular block by the selective relaxant binding agent sugammadex: A dose-finding and safety study. Anesthesiology, 2006; 104: 667–74
29. Ghoneim AA, El Beltagy MA: Comparative study between sugammadex and neostigmine in neurosurgical anesthesia in pediatric patients. Saudi J Anaesth, 2015; 9: 247–52
30. Khuenl-Brady KS, Wattwil M, Vanacker BF et al: Sugammadex provides faster reversal of vecuronium-induced neuromuscular blockade compared with neostigmine: A multicenter, randomized, controlled trial. Anesth Analg, 2010; 110: 64–73
31. Blobner M, Eriksson LI, Scholz J et al: Reversal of rocuronium-induced neuromuscular blockade with sugammadex compared with neostigmine during sevoflurane anaesthesia: Results of a randomised, controlled trial. Eur J Anaesthesiol, 2010; 27: 874–81





Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]