Journal of Clinical Anesthesia (2016) **32**, 208–213

ELSEVIER

Journal of Clinical Anesthesia

Original contribution

Reversal of neuromuscular blockade with sugammadex or neostigmine/atropine: Effect on postoperative gastrointestinal motility

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Received 13 January 2015; revised 9 March 2015; accepted 5 March 2016

Keywords:
Neuromuscular agents;
Sugammadex;
Neostigmine;
Postoperative period;
Constipation

Abstract
Study objective: To compare sugammadex with conventional reversal of neuromuscular block in terms of postoperative gastrointestinal motility.
Design: Double blinded, randomized, controlled clinical trial.
Setting: Operating room, postoperative recovery area.
Patients: Seventy-two patients with ASA physical status I or II, scheduled for total thyroid surgery were studied.
Interventions: When 4 twitches were observed on train-of-four stimulation, neuromuscular block was reversed conversatively in the control group, and with sugammadex in the study group.
Measurements: Time to first flatus and feces, incidence of postoperative nausea, vomiting, diarrhea and constipation were collected.
Main results: Median time of first flatus was 24 hours (18-32 [10-36]) in the neostigmine group, and 24 (18-28 [12-48]) in the sugammadex group ($P > .05$). Median (IQR) time of first feces was 24 hours (18-36 [10-48]) in neostigmine group, 32 hours (28-36 [12-72]) in sugammadex group ($P > .05$). There were no occurrences of nausea, vomiting, diarrhea, or constipation.
Conclusions: Sugammadex may be safely used in cases where postoperative ileus is expected.

1. Introduction

Sugammadex is a γ-cyclodextrine, rapidly reversing rocuronium-induced neuromuscular block [1]. Sugammadex is mainly used to decrease the incidence of postoperative residual block in elderly and asthmatic patients [2]. Nowadays, sugammadex found new uses in laparoscopic surgery, where it is combined with deep neuromuscular block to provide better surgical conditions and still early extubation [3]. It is known that the conventional drug neostigmine stimulates intestinal motility [4]. We investigated whether reversing the neuromuscular block with sugammadex or neostigmine differs in terms of gastrointestinal motility by comparing time-to-first-flatus and feces, and incidence of postoperative nausea, vomiting, diarrhea, and constipation in patients undergoing thyroidectomy with general anesthesia.

Disclosures: No external funding and no competing interests declared.
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http://dx.doi.org/10.1016/j.jclinane.2016.03.010
0952-8180/

2. Materials and methods

The flow diagram of the study is presented in Fig. 1. After obtaining approval of the local ethics committee (Number: 2014/93), and patient consent forms, patients scheduled for total thyroidectomy surgery with general anesthesia in December 2013 and January 2014 were enrolled in the study. Patients younger than 30 years, older than 70 years, patients with an American Society of Anesthesiologists (ASA) score higher than 2, history of diabetes mellitus, peripheral arterial disease, gastrointestinal diseases (diarrhea, chronic constipation, gastritis, ulcers, irritable bowel disease, ulcerative colitis, Crohn's disease), laxative use, history of ileus or stroke, abnormal levels of serum electrolyte or thyroid hormones were excluded.

Using closed envelope technique, patients were randomized into two groups to receive intravenously either: neostigmine 0.04 $mg.kg_{-1}$ (Neostigmin; Organon, Istanbul, Turkey) plus atropine 0.015 $mg.kg_{-1}$ (Atropin; Osel, Istanbul, Turkey); sugammadex 2 $mg.kg_{-1}$ (Bridion: Schering-Plow Corporation, Oss, Netherlands) as reversal agent at the end of the operation.

All patients were ordered to fast after midnight. To obtain a standard duration of fasting, patients operated later than 12 AM were excluded. Following routine monitorization of the vital signs, anesthesia was induced with 2 $mg.kg_{-1}$ of IV fentanyl and 2 $mg.kg_{-1}$ of IV propofol, and patients received a total of 10 $mL.kg_{-1}$ of IV isotonic saline (0.9%) during the operation. Anesthesia was maintained with sevoflurane 2% to 3% and 40/60% oxygen/air mixture to achieve a minimum alveolar concentration of 1.5. Neuromuscular block was induced with a bolus dose of 1 $mg.kg_{-1}$ IV rocuronium, and monitored by measuring response of adductor pollicis muscle to stimulation of the ulnar nerve with a TOF-Watch SX (Organon, Dublin, Ireland).

At the end of the operation, sevoflurane was turned off, and pressure support mode was initiated (trigger threshold 0.5 $mL.min^{-1}$, frequency 10 min^{-1}, pressure support 8 cmH_2O, positive end expiratory pressure 5 cmH_2O, Draeger Primus anesthesia machine, Draegerwerk AG, Lübeck, Germany). Reversal agents were administered after observing 4 twitches on the train-of-four stimulation. Postoperative analgesia was provided with tenoxicam 20 mg IV 2 times a day (first dose at the beginning of the operation).

In addition to routine postanaesthetic evaluations, exact times of first passage of a flatus and feces were recorded in the surgical ward. Patients were asked by a nurse hourly, if they are aware of the passage of a flatus or feces. Postoperative meal type and time (postoperative 8th hour) were standardized for all patients. Postoperative level of serum calcium was monitored and replaced on a daily basis starting at the first postoperative day.

Based on our previous records in the general surgery ward, first flatus occurred within a median of 24 hours (standard deviation 6 hours) in patients receiving general anesthesia for non-abdominal surgery. Power analysis with an alpha error of 5% and β error of 10% showed that a sample size of 72 for both groups is sufficient. Results were analyzed using the SPSS software (SPSS 12 for Windows; IBM, Chicago, IL). To minimize the bias due to personal differences in bowel movements, patients in each group were matched by their stool frequency (according to the information obtained from the patients during pre-anesthetic visit). Gender and ASA status were expressed as number (proportion). Differences between categorical variables (ASA status, presence of hypocalcemia or passage of flatus within the first 24 hours) were analyzed with χ^2 test. Numerical data were tested for normal distribution using Shapiro-Wilk test. Age and postoperative levels of serum calcium showed normal distribution. These results were expressed as mean (SD) and were analyzed with Student *t* test.

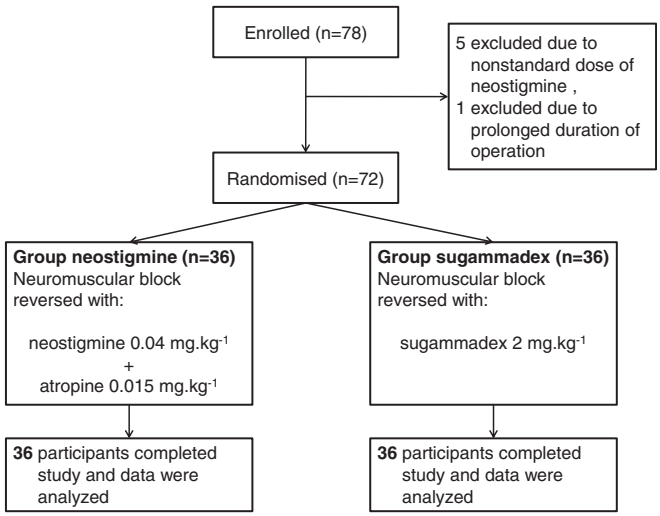

Fig. 1 The flow diagram depicting the recruitment, randomization, dropout, and analysis phases of the study.