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Original Contribution

Comparison of sugammadex and conventional reversal on postoperative nausea and vomiting: a randomized, blinded trial☆,☆☆,★

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Abstract

Study Objective: To determine whether the new selective binding agent sugammadex causes less postoperative nausea and vomiting (PONV) than the cholinesterase inhibitor neostigmine.

Design: Prospective, randomized, double-blinded study.

Setting: University-affiliated hospital.

Patients: One hundred American Society of Anesthesiologists physical status 1 and 2 patients scheduled for extremity surgery.

Interventions: Patients were randomly assigned to neostigmine (70 μg/kg) and atropine (0.4 mg per mg neostigmine) or sugammadex 2 mg/kg for neuromuscular antagonism at the end of anesthesia, when 4 twitches in response to train-of-four stimulation were visible with fade.

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Measurements: We recorded PONV, recovery parameters, antiemetic consumption, and side effects.
Main Results: Nausea and vomiting scores were lower in the sugammadex patients upon arrival in the postanesthesia care unit (med: 0 [min-max, 0-3] vs med: 0 [min-max, 0-3]; $P < .05$), but thereafter low and comparable. Postoperative antiemetic and analgesic consumption were similar in each group. Extubation (median [interquartile range], 3 [1-3.25] vs 4 [1-3.25]; $P < .001$) first eye opening (4 [3-7.25] vs 7 [5-11]; $P < .001$), and head lift (4 [2-7.25] vs 8 [11-25]; $P < .001$) in minutes were shorter in patients given sugammadex. Postoperative heart rates were significantly lower in all measured times patients given neostigmine.
Conclusions: Nondepolarizing neuromuscular blocking antagonism with sugammadex speeds recovery of neuromuscular strength but only slightly and transiently reduces PONV compared with neostigmine and atropine.

1. Introduction

The cholinesterase inhibitor neostigmine remains the most commonly used neuromuscular blocking agent antagonist. Neostigmine causes bradycardia, gastrointestinal motility, and gastric secretions. Furthermore, neostigmine is thought to increase the risk of postoperative nausea and vomiting (PONV) [1,2], possibly by provoking gastric spasms, which lower barrier pressure and increasing afferent input to central vomiting centers. The combination of neostigmine and atropine may be emetogenic [3]. Neostigmine in doses ≥2.5 mg increases the incidence of PONV [4]. Neostigmine does not increase the risk of postoperative vomiting, and there is insufficient evidence to conclude that neostigmine leads to a clinically important increase in the risk of PONV [5].

Sugammadex is a new selective relaxant binding agent, which has a different mechanism of action from anticholinesterase neuromuscular antagonists. Specifically, sugammadex encapsulates steroidal neuromuscular blocking agents, leading to rapid movement of free neuromuscular agent from the tissues into plasma.

Sugammadex has various side effects, including mild headache, nausea, the injection site irritation, dry mouth, fatigue, a cold sensation at the injection site, and oral discomfort [6-9]. Furthermore, the most common adverse effect of sugammadex is nausea [10]. McDonagh et al [11] also reported that 30% of patients given 2 mg/kg sugammadex for antagonism experienced nausea, whereas others report that the drug is well tolerated [12,13]. However, none of these studies was primarily designed to evaluate the effect of sugammadex on PONV. Therefore, the primary hypothesis that there is less PONV when neuromuscular block is antagonized with sugammadex than neostigmine was tested.

2. Materials and methods

This single-center, randomized, double-blind study was conducted at Mustafa Kemal University Hospital. Ethics committee approval (April 2012, approval number 154) was obtained, and written consent was obtained from all patients.

One hundred American Society of Anesthesiologists (ASA) physical status 1 and 2 patients scheduled for extremity surgery (tendon repair and skin graft surgery) during general anesthesia over the course of a year, starting April 2012, were enrolled. Patients were excluded if they had any contraindication to sugammadex or neostigmine administration; were having emergency or urgent procedures; and had a body mass index ≥27 kg/m^2, hepatic impairment (alanine aminotransferase or aspartate aminotransferase >2 times normal), or renal impairment (serum creatinine >2 mg/dL).

2.1. Protocol

Patients were premedicated with 1-3 mg intravenous midazolam. Qualifying patients were randomly assigned 1:1 without stratification to neuromuscular antagonism with (1) sugammadex 2 mg/kg or (2) neostigmine 70 μg/kg and atropine 0.4 mg atropine per mg neostigmine. Randomization was Web based.

Anesthesia was induced with propofol 2-2.5 mg/kg and fentanyl 1 μg/kg and maintained with 5%-6% desflurane in 66% nitrous oxide in oxygen. Rocuronium 0.6 mg/kg was given intravenously to facilitate tracheal intubation; additional boluses of rocuronium, 0.15 mg/kg, were given to maintain 2 twitches in response to supramaximal electrical stimulation of the ulnar nerve as determined by a TOF-Watch-SX (Schering-Plough Ireland, Dublin, Ireland). Meperidine 0.5 mg/kg was given intravenously when skin closure began. At the end of anesthesia, when 4 twitches of TOF were visible with fade, participants were given the designated neuromuscular antagonist. All patients were extubated when the TOF ratio is ≥90%. Antiemetic medications were not given intraoperatively.

When postoperative visual analog scale exceeded 5 cm, diclofenac sodium 75 mg was given intravenously; tramadol (1 mg/kg) intramuscularly was used as rescue analgesic. PONV was treated with ondansetron 4 mg intravenously and, if persistent, with metoclopramide 10 mg intravenously.

2.2. Measurements

Baseline risk of PONV was assessed using the Apfel score. According to this preoperative risk assessment tool, there are 4