International Journal of Obstetric Anesthesia (2018) **xxx**, xxx–xxx
0959-289X/$ - see front matter
https://doi.org/10.1016/j.ijoa.2018.01.005

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ORIGINAL ARTICLE

Comparison of rocuronium-induced neuromuscular blockade in second trimester pregnant women and non-pregnant women

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ABSTRACT

Background: This study set out to compare the onset and duration of rocuronium-induced neuromuscular blockade in second trimester pregnant women and non-pregnant women receiving general anesthesia.

Methods: Forty-seven pregnant (Group P) and forty-seven non-pregnant (Group C) women were enrolled. Anesthesia was induced with propofol 2.0 mg/kg and rocuronium 0.6 mg/kg, and neuromuscular blockade was assessed with an accelerometric sensor using train-of-four stimulation (TOF-Watch® SX). Tracheal intubation was performed at maximum depression of the first twitch (T1) and anesthesia was maintained with sevoflurane 1.5–2.5% and 50% oxygen in air. We recorded the times to maximum T1 depression and 5% and 25% T1 recovery, as well as the mean arterial pressure and heart rate at baseline, injection of rocuronium, intubation, and 5% and 25% T1 recovery.

Results: The onset of rocuronium-induced neuromuscular blockade (time to maximum T1 depression) did not differ significantly between the groups. The duration (time to 25% T1 recovery) was significantly longer in Group P than in Group C (45.7 ± 12.9 min vs 40.6 ± 10.4 min, $P < 0.037$). During the recovery period from the blockade, the mean arterial pressure was significantly lower in Group P than in Group C.

Conclusion: Our data showed that the rocuronium-induced neuromuscular blockade did not significantly differ in onset but lasted significantly longer in second trimester pregnant women compared with non-pregnant women.

Keywords: Anesthesia; Obstetric; Neuromuscular blockade; Onset; Duration; Rocuronium

Introduction

Pregnancy induces physiologic changes in various organs, including an altered plasma volume, blood volume, cardiac output, systemic vascular resistance (SVR), hepatic blood flow, and protein binding; and altered sensitivity to drugs.[1–4] These changes manifest from the first to the third trimester of pregnancy, and they have an impact on the rate of onset and the duration of action of muscle relaxants.[1–4] Rocuronium is a neuromuscular blocking drug used for general anesthesia that is generally metabolized by the liver and excreted in bile.[5] It belongs to the Food and Drug Administration pregnancy category B, and is a common neuromuscular blocker used for general anesthesia in pregnant women. In a previous study that used rocuronium or vecuronium to induce neuromuscular blockade in peripartum patients, the peripartum patient group had a longer duration of action than the non-pregnant patient group.[6,7] Studies to date have mainly focused on peripartum patients. There has been little research on the onset and duration of action of rocuronium in pregnant women, in their second trimester, receiving general anesthesia for non-obstetric or obstetric surgery (for example transabdominal cerclage (TAC) or the McDonald procedure in women with cervical insufficiency). This study planned to evaluate and compare the onset and duration of rocuronium-induced neuromuscular blockade in second trimester pregnant women and in non-pregnant women, undergoing general anesthesia.

Accepted January 2018
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Please cite this article in press as: Jun IJ et al. Comparison of rocuronium-induced neuromuscular blockade in second trimester pregnant women and non-pregnant women. *Int J Obstet Anesth* (2018), https://doi.org/10.1016/j.ijoa.2018.01.005

Methods

The study was approved by the Ethics Committee of our hospital, and registered at ClinicalTrials.gov: NCT02797860. Written informed consent was obtained from all subjects and the data collection was carried out between January and October 2016. We enrolled 50 second trimester pregnant women (Group P) scheduled for elective TAC or the McDonald operation; and 50 non-pregnant women (Group C) scheduled for elective open gynecologic surgery with general anesthesia, as controls. All the patients were between 20 and 45 years of age and of American Society of Anesthesiologists (ASA) physical status I or II. Women with a history of sensitivity to neuromuscular blockade, impaired renal or hepatic function, an allergic reaction to rocuronium, medication intake affecting neuromuscular blocking drugs or of body weight <50 kg or >100 kg, were excluded.

The patients were administered 0.2 mg of intramuscular glycopyrrolate preoperatively. Upon arrival in the operating room, standard monitoring devices (the patient monitor M1205A, Philips, USA or the Micro O2, Siemens, Germany), including an electrocardiogram, a pulse oximeter, and a noninvasive blood pressure cuff, were applied. The patients were connected to a bispectral index (BIS) monitor (Model A 3000, Aspect Medical Systems, Inc., Natick, MA, USA), and their baseline mean arterial pressure (MAP), heart rate (HR), and BIS were recorded. Ulnar nerve stimulation at the wrist was established to assess neuromuscular function by acceleromyography of the adductor pollicis muscle (TOF-Watch SX®; Organon Ltd., Dublin, Ireland). The electrodes were applied to an appropriate location, in accordance with the manufacturer's guidelines. The transducer was placed on the volar side of the thumb, and the contraction of the muscle was measured. Throughout the study period, the results of the train-of-four (TOF) stimulation were displayed on a laptop computer using the TOF-Watch SX with TOF-Link® (Organon Ltd., Dublin, Ireland).

Anesthesia was induced with propofol 2.0 mg/kg and loss of consciousness confirmed by checking the eyelash reflex and noting a BIS value under 60. After calibration of the acceleromyograph for supramaximal TOF stimulation, 0.6 mg/kg of rocuronium was administered over 5 seconds. Immediately thereafter, TOF stimulation was initiated with four pulses lasting 0.2 ms at a 2-Hz frequency and a 15 s interval. The patient's lungs were ventilated using a facemask with oxygen. The time to 25%, 50%, 75%, and maximum T1 (the first twitch of the TOF) depression were recorded. Tracheal intubation was performed when the maximum T1 depression (a T1 value of zero) was reached. The anesthesia was maintained with sevoflurane 1.5–2.5%, targeting a BIS value of 40–60. Ventilation with 50% oxygen in air was controlled to maintain an end-tidal carbon dioxide value between 30 and 40 mmHg. The patient temperature was maintained between 36°C and 37.5°C. The neuromuscular monitoring was continued until the T1 of the TOF recovered to 25%.

The onset time was defined as the time from administration of the rocuronium to the occurrence of maximum T1 depression. The duration was defined as the time from initiation of the rocuronium administration until T1 recovery to 25%. We recorded the time to 25%, 50%, 75%, and maximum T1 depression; and the time to 5% and 25% T1 recovery. We also recorded the MAP and HR at baseline, injection of the rocuronium, intubation, and at 5% and 25% T1 recovery.

The statistical analysis was performed with SAS (version 9.2, SAS Inc., Cary, NC, USA). The data were expressed as the mean ± SD, the median (range), or the number of patients. The sample sizes were calculated by assuming that the difference in the 25% T1 recovery time would be more than 5 min, with an alpha error of 0.05 and a power of 80%. A total of 42 patients per group were needed to demonstrate statistical significance. We assigned 50 patients to each group to allow for possible protocol violations over the study period.

To compare the variables between the two groups, the Kolmogorov–Smirnov test was used to identify the variables with a normal distribution. These variables were compared with independent t-tests, while those without a normal distribution were compared with the Mann–Whitney *U*-test. A *P*-value <0.05 was considered statistically significant.

Results

One hundred patients were initially enrolled. Six patients were excluded on account of changes in the surgical plan and patient refusal. Forty-seven second trimester pregnant women (Group P) and forty-seven non-pregnant women (Group C) were eventually studied.

The demographic data of the patients are presented in Table 1. The mean gestational age in Group P was 14.3 ± 0.6 weeks. The patients' other characteristics did not differ significantly between the two groups.

The comparisons of the onset time and of the time of recovery from rocuronium between Groups P and C are presented in Table 2. The mean time to 25%, 50%, and 75% T1 depression did not differ significantly between the two groups. The onset time of rocuronium was not significantly different either. However, the mean time to 5% T1 recovery was significantly longer in Group P than in Group C; and the duration was also significantly longer in Group P than in Group C (45.7 ± 12.9 min vs 40.6 ± 10.4 min, *P* <0.037).

Table 3 shows the MAP and HR over the study period. The MAP at baseline and at induction of anesthesia showed inconsistent differences between the two groups. However, during the recovery period from the

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