British Journal of Anaesthesia **112** (3): 498–505 (2014)
Advance Access publication 15 November 2013 · doi:10.1093/bja/aet377

BJA

Evaluation of surgical conditions during laparoscopic surgery in patients with moderate *vs* deep neuromuscular block

C. H. Martini[1†], M. Boon[1†], R. F. Bevers[2], L. P. Aarts[1] and A. Dahan[1*]

[1] Department of Anesthesiology and [2] Department of Urology, Leiden University Medical Centre, P5-Q, Leiden 2300 RC, The Netherlands

* Corresponding author. E-mail: a.dahan@lumc.nl

Editor's key points

- Surgical conditions may be affected by the depth of neuromuscular block.
- This small study assessed conditions rated on a five-point scale by a single surgeon during retroperitoneal laparoscopic procedures.
- Surgical conditions were rated significantly better under deep neuromuscular block.
- The rating of surgical conditions on video analysis differed markedly between anaesthetists and the surgeon.

Background. The routine use of neuromuscular blocking agents reduces the occurrence of unacceptable surgical conditions. In some surgeries, such as retroperitoneal laparoscopies, deep neuromuscular block (NMB) may further improve surgical conditions compared with moderate NMB. In this study, the effect of deep NMB on surgical conditions was assessed.

Methods. Twenty-four patients undergoing elective laparoscopic surgery for prostatectomy or nephrectomy were randomized to receive moderate NMB (train-of-four 1–2) using the combination of atracurium/mivacurium, or deep NMB (post-tetanic count 1–2) using high-dose rocuronium. After surgery, NMB was antagonized with neostigmine (moderate NMB), or sugammadex (deep NMB). During all surgeries, one surgeon scored the quality of surgical conditions using a five-point surgical rating scale (SRS) ranging from 1 (extremely poor conditions) to 5 (optimal conditions). Video images were obtained and 12 anaesthetists rated a random selection of images.

Results. Mean (standard deviation) SRS was 4.0 (0.4) during moderate and 4.7 (0.4) during deep NMB ($P<0.001$). Moderate block resulted in 18% of scores at the low end of the scale (Scores 1–3); deep block resulted in 99% of scores at the high end of the scale (Scores 4 and 5). Cardiorespiratory conditions were similar during and after surgery in both groups. Between anaesthetists and surgeon, there was poor agreement between scores of individual images (average κ statistic 0.05).

Conclusions. Application of the five-point SRS showed that deep NMB results in an improved quality of surgical conditions compared with moderate block in retroperitoneal laparoscopies, without compromise to the patients' peri- and postoperative cardiorespiratory conditions.

Trial registration. The study was registered at clinicaltrials.gov under number NCT01361149.

Keywords: laparoscopy; nephrectomy; neuromuscular block; prostatectomy; rocuronium; sugammadex; urological surgical procedures

Accepted for publication: 22 August 2013

Administration of muscle relaxation is essential in a variety of procedures as it causes an improvement of surgical conditions. For example, King and colleagues[1] demonstrated that the routine use of neuromuscular blocking agents reduced the frequency of unacceptable surgical conditions in radical prostatectomies. Improvement of surgical conditions may be even more important when the surgeon has to work in a narrow space surrounded by muscles such as in the case of retroperitoneal laparoscopic surgery. It may be argued that in retroperitoneal laparoscopic surgery, a deep neuromuscular block (NMB), with train-of-four (TOF) values of 0 and a post-tetanic count (PTC) of 1–2, would further improve working conditions. However, the use of deep NMB may come with complications including long-reversal times, incomplete recovery of neuromuscular function compromising respiratory, and upper airway function, or the return of NMB after a period of seemingly normal neuromuscular function (recurarization).[1–3]

The development of sugammadex enables rapid reversal of deep NMB. Sugammadex is a modified γ-cyclodextrin, especially created to bind the free plasma molecules of the neuromuscular blocking agent rocuronium to which it has high affinity.[4] Recent studies demonstrate that sugammadex produces rapid reversal of deep NMB after administration of high-dose rocuronium.[5] Theoretically, the combination of rocuronium and sugammadex makes it possible to achieve deep NMB and consequently further improve surgical conditions in retroperitoneal laparoscopic surgery without the fear for prolonged reversal times or incomplete recovery of

† C.H.M. and M.B. contributed equally to this paper.

neuromuscular function. However, the association between the depth of NMB and surgical conditions has not been evaluated as yet.

In the current study, we investigated the effect of a deep NMB (TOF 0, PTC 1–2) against a moderate block (TOF 1–2) on surgical conditions in patients undergoing retroperitoneal laparoscopic surgery for a prostatectomy or (partial) resection of a kidney. Surgical conditions were rated using a five-point surgical rating scale (SRS) by one dedicated surgeon with ample experience in these surgeries (R.F.B.). We hypothesize that deep NMB is associated with improved ratings by the surgeon. Secondary end points of our study included the assessment of the level of agreement between anaesthetists (the providers of the NMB agents and consequently responsible for a large part of the surgical conditions) and surgeon in terms of their rating of the surgical conditions. To that end, 30 s video images of the surgical field, obtained at the time of scoring by the surgeon, were rated by the anaesthetists.

Methods

The study (acronym BLISS trial) was carried out between November 2012 and February 2013 at the Leiden University Medical Centre (Leiden, The Netherlands) and was performed according to guidelines of Good Clinical Practice and Good Research Practice. Approval of the protocol was obtained from the institutional review board (Commissie Medische Ethiek, Leiden, The Netherlands). Patients scheduled to undergo an elective laparoscopic prostatectomy or nephrectomy (partial or total) were approached 2 weeks before surgery and received oral and written information about the study. All patients who were willing to participate gave written informed consent before enrolment. The study was registered at clinicaltrials.gov (NCT01361149); the protocol was published earlier online.[6] The design of the study was randomized (deep NMB against standard or moderate block) and blinded (the surgical team, the research team and the anaesthetists who scored the video were all blinded to the treatment); the attending anaesthetist was not blinded. Randomization was performed using a computer-generated randomization code. The code was presented to the attending anaesthetist who prepared the medication and took care of patient dosing during anaesthesia.

Patients enrolled in the study had prostate or renal disease and were all eligible for surgical resection by laparoscopic approach. All procedures were performed by one surgeon (R.F.B.). Excluded from participation were patients with ASA class $>$III, age $<$18 yr, inability to give informed consent, known or suspected neuromuscular disease, allergy to medication to be used during anaesthesia, a (family) history of malignant hyperthermia, renal insufficiency (serum creatinine $>$2 times normal, urine output <0.5 ml kg^{-1} h^{-1}, glomerular filtration rate <60 ml h^{-1}, or proteinuria), previous retroperitoneal surgery, and a body mass index of ≥ 35 kg m^{-2}.

Perioperative protocol

All patients received total i.v. anaesthesia with propofol and sufentanil. During the procedure, routine monitoring was applied [electrocardiography, arterial blood pressure, heart rate, electroencephalographic monitoring using the Philips bispectral index (BIS) module system (Philips, Eindhoven, The Netherlands)]. Propofol dosing was such that BIS values remained within the range of 40–50. Additionally, the cardiac output was measured non-invasively using an inflatable finger cuff attached to the Nexfin haemodynamic monitor (*bmeye*, Amsterdam, The Netherlands).

With respect to NMB the patients were randomly assigned to one of the two treatment groups:

Group 1: moderate NMB, in which the goal was to realize a moderate NMB (TOF 1–2 twitches). NMB was induced with a bolus dose of atracurium of 0.5 mg kg^{-1}, followed by a continuous infusion of mivacurium of 0.5 mg kg^{-1} h^{-1}. In the case of deviations from the target TOF values, the pump speed could be increased or decreased or a bolus dose could be given. This was left to the discretion of the attending anaesthetist. We used atracurium/mivacurium in Group 1 rather than low-dose rocuronium, as this combination is the current standard of care in our hospital. This approach enables us to qualify our current local practice against a new paradigm, which is deep NMB for the chosen surgical procedures.

Group 2: deep NMB, in which the goal was to realize a block of zero twitches in the TOF, but 1–2 twitches in the PTC. To that end, patients received a loading dose of rocuronium of 1.0 mg kg^{-1} followed by a continuous infusion of 0.6 mg kg^{-1} h^{-1}. In the case of deviations from the target TOF and PTC, the pump speed could be increased or decreased or a bolus dose could be given. This was left to the discretion of the attending anaesthetist.

In the case of poor or extremely poor surgical conditions (as scored by the surgeon, see below), mivacurium or rocuronium infusion rates were increased by 20% after the administration of a bolus dose of 15 mg.

At the end of surgery, all patients received a reversal agent: neostigmine after a moderate NMB (1–2 mg combined with 0.5–1 mg atropine) and sugammadex (4 mg kg^{-1}) after a deep NMB. Extubation occurred when the TOF ratio was >0.9.

Administration of all drugs was performed by the attending anaesthetists and not corresponded to the surgical team or the anaesthesia research team.

Monitoring

Neuromuscular function using an acceleromyograph was measured at the wrist (TOF-watch-SX, MSD BV, Oss, The Netherlands). The TOF-watch generates an electrical stimulus to the ulnar nerve and measures contractions of the adductor pollicis muscle (causing adduction of the thumb) through a sensor attached to the tip of the thumb. The thumb was placed in a flexible adaptor that applied a constant preload to the thumb. Before administration of any NMB agent, the device was calibrated according the specifications of the manufacturer. To that end, before administration of any neuromuscular blocking agent, but after induction of general anaesthesia, the following procedures were conducted to