

# Deep neuromuscular block to optimize surgical space conditions during laparoscopic surgery: a systematic review and meta-analysis

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## Abstract

Neuromuscular block (NMB) is frequently used in abdominal surgery to improve surgical conditions by relaxation of the abdominal wall and prevention of sudden muscle contractions. The evidence supporting routine use of deep NMB is still under debate. We aimed to provide evidence for the superiority of routine use of deep NMB during laparoscopic surgery. We performed a systematic review and meta-analysis of studies comparing the influence of deep vs moderate NMB during laparoscopic procedures on surgical space conditions and clinical outcomes. Trials were identified from Medline, Embase, and Central databases from inception to December 2016. We included randomized trials, crossover studies, and cohort studies. Our search yielded 12 studies on the effect of deep NMB on the surgical space conditions. Deep NMB during laparoscopic surgeries improves the surgical space conditions when compared with moderate NMB, with a mean difference of 0.65 (95% confidence interval (CI): 0.47–0.83) on a scale of 1–5, and it facilitates the use of low-pressure pneumoperitoneum. Furthermore, deep NMB reduces postoperative pain scores in the postanesthesia care unit, with a mean difference of –0.52 (95% CI: –0.71 to –0.32). Deep NMB improves surgical space conditions during laparoscopic surgery and reduces postoperative pain scores in the postanesthesia care unit. Whether this leads to fewer intraoperative complications, an improved quality of recovery, or both after laparoscopic surgery should be pursued in future studies. The review methodology was specified in advance and registered at Prospero on July 27, 2016, registration number CRD42016042144.

**Key words:** laparoscopy; neuromuscular blockade; pneumoperitoneum, artificial

In the last decades, the number of laparoscopic surgeries has increased tremendously. When compared with open surgery, laparoscopic procedures provide less postoperative pain, shorter duration of hospital admission, and improved patient satisfaction.<sup>1</sup> However, the elevated intra-abdominal pressure

(IAP) during pneumoperitoneum created during laparoscopic procedures can affect several homeostatic systems, causing alterations in cardiovascular, pulmonary, and renal physiology. It is also speculated that the pneumoperitoneum is an important factor in the cause of postoperative shoulder pain.<sup>2</sup>

Lowering the IAP might decrease postoperative pain and the risk of laparoscopy-related complications.<sup>3</sup> However, low-pressure pneumoperitoneum impairs the quality of the surgical field, which can increase the risk of intraoperative complications or conversion to open surgery.<sup>3</sup>

The quality of the working space is determined by non-modifiable factors (i.e. patients' obesity, previous pregnancies, or previous abdominal surgery) and by modifiable factors, such as anaesthesia-related factors, IAP, and body position.<sup>4</sup> Several trials have been performed showing that deep neuromuscular block (NMB) improves surgical conditions in different types of laparoscopic procedures.<sup>1 5 6</sup> The depth of NMB is assessed mostly by acceleromyography, also known as train-of-four (TOF) monitoring. During the use of non-depolarizing neuromuscular blocking agents, such as rocuronium, a TOF of 4 means there are four twitches after stimulation, meaning 0–75% of the acetylcholine receptors at the neuromuscular junction receptors are blocked and there is no or shallow NMB. In moderate NMB, there are one to three responses to TOF, meaning that 75–90% of the receptors are blocked. During deep NMB, there are no responses to TOF and two or fewer responses to post-tetanic count (PTC).<sup>7</sup>

A major advantage of NMB is the improvement of intubation conditions for the anaesthetist. Nevertheless, NMB (and especially deep NMB) can lead to postoperative residual curarization, which exposes the patient to additional risks of a delayed recovery of respiratory function, including aspiration. Since the discovery of sugammadex, it is possible to antagonize a deep NMB, which minimizes the risk of occurrence of adverse events of residual NMB.<sup>8</sup> Nowadays, NMB is frequently used in abdominal surgery to improve surgical conditions, by relaxation of the abdominal wall and prevention of sudden muscle contractions.<sup>9</sup> However, the (routine) use of deep NMB is still under debate. Last year, Madsen and colleagues<sup>10</sup> and Kopman and Naguib<sup>11</sup> wrote, respectively, a 'pro-' and 'con-' position paper concerning the available evidence supporting (or not) the clinical practice of deep NMB during laparoscopic procedures. Madsen and colleagues<sup>10</sup> stated that there are a few low-risk-of-bias studies to indicate that the use of deep NMB improves surgical conditions and patient outcomes, such as postoperative pain. In contrast, Kopman and Naguib<sup>12</sup> concluded that there is not enough good evidence available to justify the routine use of deep NMB in laparoscopic procedures. They stated that evidence for the superiority of deep NMB vs moderate block is non-existent.

We performed the first systematic review including a meta-analysis to obtain data regarding the influence of moderate and deep NMB during laparoscopic surgeries on surgical space conditions and clinical outcomes.

## Methods

This review was performed in accordance with the PRISMA guidelines; see Supplementary material supplement 1 (S1). The review methodology was specified in advance and registered at Prospero on July 27, 2016, registration number CRD42016042144, provided as Supplementary material supplement 2 (S2).

### Amendments to the review protocol

In order to optimize the meta-analysis of the surgical space conditions, we converted the scales to 1–5 instead of 0–100. Furthermore, we specified the item 'other risks of bias' of the Cochrane risk-of-bias tool. We took into account whether studies reported on calibration of the TOF watch, defined deep NMB

as  $PTC \leq 2$ , and if they mentioned use of rocuronium as an escape in the moderate NMB group in the event of insufficient surgical field. To invest the robustness of our findings on post-operative pain, we added a sensitivity analysis to evaluate the influence of different levels of IAP.

### Literature search strategy

We conducted a systematic, computerized search on PubMed, EMBASE, and Cochrane library. We used the search components 'laparoscopic surgery' and 'deep neuromuscular blockade'. The search strategy is provided as Supplementary material supplement 3 (S3). We also conducted a search on ClinicalTrials.gov and World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) on December 1, 2016 (see Supplementary material S3). Search results from each database were combined, with removal of duplicates. In addition, we checked the reference lists of all included studies and relevant reviews identified by our search for additional eligible references. No language or publication date restrictions were applied. The search was performed on August 3, 2016 and updated on December 1, 2016. The search update yielded one additional included reference.

### Study selection

Two authors (M.H.B., E.V.v.H.) independently screened the studies for eligibility based on title and abstract. In a second phase, the same authors performed a full-text assessment for final inclusion. Studies were included if they met all of the following criteria: (i) the study was an original full paper that presented unique data; (ii) the study was performed in human adults; (iii) the study compared deep or intense NMB with no, shallow, or moderate NMB; (iv) the study was performed in patients undergoing a laparoscopic (intra-abdominal) procedure; and (v) the study reported on the outcome measure surgical space conditions.

### Type of outcome measures

The primary outcome measure was the quality of the surgical space conditions. Studies measuring the distance between the skin and sacral promontory were included in the systematic review but not in the meta-analysis. Secondary outcome measures were post-operative pain, conversion to higher pneumoperitoneum pressure or open surgery, duration of surgery, intraoperative complications, and length of hospital stay.

### Study characteristics and data extraction

The following characteristics were extracted: author, journal and year of publication, sex, age, weight, BMI, and ASA class, body positioning during surgery, type of procedure, type of NMB, level of NMB in experimental and control groups, scale used to score the surgical space conditions, pain scores, conversion rates, complications, and timing of scoring the outcome measurements. Two review authors (M.H.B., E.V.v.H.) extracted the data independently; discrepancies were identified and resolved through discussion. Data were extracted if the mean, SD, and number of patients (*n*) were reported, or could be calculated, for the experimental and control groups. If the SEM, the range, or the 95% confidence interval (CI) was reported, it was converted to SD for meta-analysis. In the event of incomplete data, we contacted authors via e-mail with a request for additional data.

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