Is Deep Neuromuscular Relaxation Beneficial in Laparoscopic, Abdominal Surgery?

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The core competence of anesthetists is to ensure perioperative patient safety and comfort and to provide the best possible surgical conditions (1). Muscle relaxants are important components of reaching these goals (1, 2). Neuromuscular blockade (NMB) facilitates intubation and may improve surgical conditions (3-6). Depending on the extent of NMB and the muscle relaxant used, spontaneous neuromuscular recovery may last significantly longer than the surgical intervention itself (7). This situation is not significantly altered by antagonizing with neostigmine. Thus, for many years, most anesthetists have avoided deep relaxation (train-of-four count [TOF count]=0, post tetanic count [PTC]=0) at the end of surgery (8, 9). In contrast, sugammadex allows fast and reliable recovery from any depth of NMB induced with rocuronium, vecuronium and pipecuronium after skin suture (9-13). This fact opens the opportunity of investigating possible indications for intraoperative deep NMB to improve surgical conditions. The need for and the clinical benefits of deep NMB are currently controversially discussed for several surgical procedures.

Adequate surgical conditions depend on several factors, for instance the physique and positioning of the patient, the skill of the surgeon, and the depth of anesthesia, but also on the depth of neuromuscular relaxation. The diaphragm is the muscle that is least sensitive to the effects of muscle relaxants (14-16); thus, complete paralysis of the diaphragm requires a TOF count of 0 and a PTC of 0 measured at the adductor pollicis muscle (6, 17). The number of minimally invasive, abdominal, surgical interventions has increased dramatically over the past decades. Laparoscopic intervention is not only less painful than laparotomy but is also associated with lower postoperative morbidity, faster recovery, higher patient satisfaction, and shorter hospitalization (18). In this context 'key hole surgery' represents the gold standard for cholecystectomy (18). The rationale behind using deep NMB in laparoscopic and robot-controlled surgery is the expectation to improve conditions during laparoscopic surgery and to possibly reduce intra-abdominal pressure during capnoperitoneum (4, 8, 19, 20). This way, low-pressure capnoperitoneum (≤11 mmHg) may contribute reducing postoperative pain and morbidity compared to routine-pressure capnoperitoneum (12-15 mmHg) (21-23).

Three interrelated aspects need to be assessed systematically in this respect:

1. Does deep NMB generally improve conditions during laparoscopic surgery?
2. Does deep NMB facilitate the use of low-pressure capnoperitoneum?
3. Does low-pressure capnoperitoneum improve treatment outcome compared to routine-pressure capnoperitoneum?

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Deep neuromuscular relaxation and conditions during laparoscopic surgery

The quality of or, in other words, the expansion of surgical space not only depends on unmodifiable factors, such as obesity, multiparity, and previous abdominal surgery, but also on modifiable factors, for instance the technique of anesthesia used, positioning of the patient, intra-abdominal pressure, and neuromuscular blockade (4). Compared to moderate NMB, deep NMB does not significantly increase abdominal compliance (0.31±0.15 L $mmHg^{-1}$ vs. 0.29±0.15 L $mmHg^{-1}$) in women with normal body mass index. An alternative measure for the expansion of the abdominal area is the distance between the sacral promontory and the skin. Three studies have shown that deep NMB may increase this distance by a mean of 5 to 15 mm during routine-pressure capnoperitoneum in comparison to moderate NMB (24-26). This increase by 3 to 4% was inter-individually highly variable and not observed in every patient (25). In gynecological laparoscopy, changing from low-pressure to routine-pressure capnoperitoneum without NMB significantly increased the distance between the sacral promontory and the skin by 7 mm (8.6 vs. 9.3 cm); use of deep NMB only resulted in an increase by 3 mm during both pressure levels. At the end of surgery during suturing, surgical conditions for patients were optimal (100%) with deep NMB during routine-pressure capnoperitoneum. Patients without NMB also showed highly clinical acceptable surgical conditions (29% optimal, 71% good) (26). Therefore, the authors of the current paper agree that the clinical relevance of the increase in surgical space achieved by deep NMB needs to be further investigated (25).

A current meta-analysis of Bruintjes et al. (4), evaluating the surgical conditions on a 5point- Leiden-Surgical-Rating-Scale, showed significantly improved laparoscopic surgery conditions of 0.65 points (95%-CI: 0.47-0.83) during cholecystectomy, hysterectomy, robot-assisted prostatectomy, colon surgery, and nephrectomy with deep NMB compared to reduced or even totally absent NMB. Another recently published study on laparoscopic nephrectomy showed by means of the Leiden-Surgical-Rating-Scale that deep NMB overall improved surgical conditions during low-pressure capnoperitoneum (4.5 vs. 4.0) compared to moderate NMB. However, looking at single time points during surgery, overall improvement was only significant once, i.e. 15 min after the initiation of capnoperitoneum (4.5 vs. 4.1) (21). Also Rosenberg et al. (27) described statistically significant improved surgical conditions by 1.1 points on a 11point Likert Scale by using deep NMB; yet, an improvement by 3.0 points was achieved by increasing intra-abdominal pressure by 4 mmHg. Bariatric surgical conditions were also statistically significant improved with deep NMB compared to moderate NMB as shown by means of the Leiden-Surgical-Rating-Scale (4.2 vs. 4.8) (28).

Yet, many authors question the clinical relevance of the above-mentioned statistically significant differences of 0.5 to 0.7 points on the Leiden-Surgical-Rating-Scale or, in other words, the significant difference between good and optimal surgical conditions on the basis of these scientific studies. A further subsequent question is if deep NMB is preferable to moderate NMB (26). Furthermore, no gold standard for assessing surgical conditions exists, although the most commonly used Leiden-Surgical-Rating-Scale seems to come close in this respect (28). Interestingly, when assessing the quality of surgical conditions by means of the abovementioned scale, Martini found inter-individual differences between different surgeons as well as between surgeons and anesthetists (29).

Deep neuromuscular blockade and low-pressure capnoperitoneum

Generally, the use of low-pressure capnoperitoneum seems to impair significantly visibility of the surgical field in gynecological interventions because of particular surgical-technical constraints (risk ratio of 10.3). In turn, such impairment may increase the risk of intraoperative complications and subsequently the rate of conversion to open surgery (30). For laparoscopic cholecystectomy, Staehr-Rye et al. (31) could show that surgical interventions during low-pressure capnoperitoneum (8 mmHg) and deep NMB could be completed in 60% of cases compared to 35% with moderate NMB. Deep NMB resulted in optimal surgical conditions in 28% compared to 4% with moderate NMB. Additionally, surgical conditions during low-pressure capnoperitoneum were inacceptable in 40% of cases despite deep NMB compared to 65% with moderate NMB. The authors concluded that surgical conditions are only marginally better with deep NMB than with moderate NMB.

In a further study, surgical interventions during low-pressure capnoperitoneum could be successfully completed with deep NMB in 83% and with moderate NMB in 73% of cases. All surgical interventions during routine-pressure capnoperitoneum could be completed without any intervention. Optimal surgical conditions were significantly more often achieved during routine-pressure capnoperitoneum than during low-pressure capnoperitoneum (20-26.7%), both with deep NMB (53.3%) as well as with moderate NMB (56.7%) (27). In laparoscopic donor nephrectomy with deep NMB and insufflational pressure of 6 mmHg, only 30% of surgical interventions could be conducted without any increase in intraabdominal pressure. To achieve acceptable surgical conditions, insufflational pressure had to be increased to 8 mmHg in 6% of surgical interventions, to 10 mmHg in another 6%, and to 12 mmHg in 18%. In contrast, optimal conditions were achieved in nearly 90% of surgical interventions during routine-pressure capnoperitoneum (vs. 40% of surgical interventions during low-pressure capnoperitoneum (6 mmHg) (32). Further studies have confirmed that deep NMB facilitates surgery during low-pressure capnoperitoneum, but also that surgical conditions are significantly improved during routine-pressure capnoperitoneum, independent of the level of relaxation (21, 33-36).

Low-pressure capnoperitoneum vs. routine-pressure capnoperitoneum and outcome-relevant benefits

According to a current Cochrane review comparing the safety and efficacy of low-pressure capnoperitoneum with that of routine-pres-

sure capnoperitoneum during laparoscopic cholecystectomy, no differences exist with regard to the duration of surgery, surgical morbidity, the rate of conversion to open surgery, hemodynamics, the duration of hospital stay, renal function and patient satisfaction (4, 32, 37). Moreover, decreasing insufflational pressure does not reduce the rate of accidental gas embolization (38). In steep Trendelenburg positioning during robot-assisted radical prostatectomy, however, deep NMB significantly reduced intra-ocular pressure by up to 4 mmHg, at least in some patients (36).

Low-pressure capnoperitoneum compared to routine-pressure capnoperitoneum and postoperative pain

33 to 55% of patients who undergo laparoscopic cholecystectomy typically develop shoulder pain (39). There is only very little scientific evidence that low-pressure capnoperitoneum may reduce the intensity of postoperative pain (8, 23).

Postoperative pain due to laparoscopy is caused by several components and has a multi-factorial etiology. Reasons for visceral pain are capnoperitoneal acidosis, residual intra-abdominal accumulation of carbon dioxide, insufficient gas conditioning (heat and moisture), and the algetic effects of abdominal drainage. Distension-induced neuropraxia of the phrenic nerves and the volume of the insufflated gas are also important factors in the development of shoulder pain (40). In their controversial Cochrane review, Gurusamy et al. (22) described significant pain reduction four to eight hours after surgery with low-pressure capnoperitoneum compared to routine-pressure capnoperitoneum. Pain reduction by 1.0 to 1.5 points on the 11-point-numerical pain-rating-scale (0-10) was considered clinically relevant (41, 42). The updated version of the meta-analysis could only show pain reduction below the measurement accuracy of the instrument that may have been clinically relevant from the second or third day onwards. The same result was found with regard to shoulder pain. The meta-analysis only included four blinded studies, of which only one had investigated the level of pain for more than 24 hours after surgery (4, 23, 43).

Three subsequently published articles did not show any advantages of low-pressure capnoperitoneum with regard to the level of pain and the use of pain medication (27, 32, 44, 45). In conclusion, there is hardly any evidence that morbidity rates are improved by low-pressure capnoperitoneum (23, 30, 32, 37). Thus, pain relief, particularly of shoulder pain, may be much more efficacious by individual multimodal pain therapy and active gas aspiration (46).

Indications for deep relaxation

For both pragmatic clinical as well as evidence-based reasons, it may be more reasonable to administer deep relaxation individually and situationally in the sense of goal-directed relaxation instead of routinely administrating deep relaxation at any cost.

Because of the lack of evidence that pain is reduced during low intra-abdominal pressure and the lasting improvement of surgical conditions, an increase in insufflation pressure to 15 mmHg is preferable to increasing the depth of NMB (26, 27). Clinically acceptable surgical conditions also necessitate optimal positioning of the patient to enlarge the intracavitary space (47).

Deep relaxation is without any doubt a suitable method for avoiding extremely poor surgical conditions and involuntary movements of the patients (29, 48, 49). However, no outcome-relevant data exist in this context because of the low incidence of complications caused by patient movement during surgery (4).

Summary

Deep NMB significantly streamlines surgical conditions in laparoscopic surgery, similar to those in non-laparoscopic surgery. The clinical relevance is yet unclear. Deep neuromuscular relaxation just marginally improves space conditions in laparoscopic surgery using low-pressure capnoperitoneum (≤11 mmHg). In laparoscopic surgery, lower intra-abdominal pressure has no outcome-relevant advantage to higher intra-abdominal pressure. However, surgical conditions are impaired during low-pressure capnoperitoneum in comparison to routine-pressure capnoperitoneum (12-15 mmHg). Reduced postoperative pain scores have been observed during low-pressure capnoperitoneum, but the quality of evidence is rather poor.

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