Journal of Clinical Anesthesia 42 (2017) 26–30

Contents lists available at ScienceDirect

Journal of Clinical Anesthesia

Original Contribution

Influence of depth of neuromuscular blockade on surgical conditions during low-pressure pneumoperitoneum laparoscopic cholecystectomy: A randomized blinded study

Javier Barrio [a,*,1], Carlos L. Errando [b,1], Jaime García-Ramón [a,1], Rafael Sellés [a,2], Guillermo San Miguel [a,1], Juan Gallego [c,1]

[a] Hospital Arnau de Vilanova de Valencia, C/ San Clement 12, 46015 Valencia, Spain
[b] Consorcio Hospital General Universitario de Valencia, Av. Tres Cruces, 2, 46014 Valencia, Spain
[c] Department of Surgery, Faculty of Medicine and Odontology, University of Valencia, Avda. Blasco Ibáñez 15, 46010 Valencia, Spain

ARTICLE INFO

Article history:
Received 18 May 2017
Received in revised form 24 July 2017
Accepted 3 August 2017

Keywords:
Laparoscopy
Laparoscopic cholecystectomy
Neuromuscular blockade
Rocuronium
Sugammadex
Pneumoperitoneum

ABSTRACT

Study objective: To evaluate the influence of neuromuscular blockade (NMB) on surgical conditions during low-pressure pneumoperitoneum (8 mm Hg) laparoscopic cholecystectomy (LC), while comparing moderate and deep NMB. Secondary objective was to evaluate if surgical conditions during low-pressure pneumoperitoneum LC performed with deep NMB could be comparable to those provided during standard-pressure pneumoperitoneum (12 mm Hg) LC.
Design: Prospective, randomized, blinded clinical trial.
Setting: Operating room.
Patients: Ninety ASA 1–2 patients scheduled for elective LC.
Interventions: Patients were allocated into 3 groups: Group 1: low-pressure pneumoperitoneum with moderate-NMB (1–3 TOF), Group 2: low-pressure pneumoperitoneum with deep-NMB (1–5 PTC) and Group 3: standard pneumoperitoneum (12 mm Hg). Rocuronium was used to induce NMB and acceleromiography was used for NMB monitoring (TOF-Watch-SX).
Measurements: Three experienced surgeons evaluated surgical conditions using a four-step scale at three time-points: surgical field exposure, dissection of the gallbladder and extraction/closure.
Main results: Low-pressure pneumoperitoneum (Group 1 vs. 2): good conditions: 96.7 vs. 96.7%, 90 vs. 80% and 89.6 vs. 92.3%, respectively for the time-points, $p > 0.05$. No differences in optimal surgical conditions were observed between the groups. Surgery completion at 8 mm Hg pneumoperitoneum: 96.7 vs. 86.7%, $p = 0.353$. Standard-pressure pneumoperitoneum vs. low-pressure pneumoperitoneum with deep NMB (Group 3 vs. 2): good conditions: 100% in Group 3 for the three time-points ($p = 0.024$ vs. Group 2 at dissection of the gallbladder). Significantly greater percentage of optimal conditions during standard-pressure pneumoperitoneum LC at the three time points of evaluation.
Conclusions: The depth of NMB was found not to be decisive neither in the improvement of surgical conditions nor in the completion of low-pressure pneumoperitoneum LC performed by experienced surgeons. Surgical conditions were considered better with a standard-pressure pneumoperitoneum, regardless of the depth of NMB, than during low-pressure pneumoperitoneum with deep NMB.

1. Introduction

Benefits of working under low-pressure (intra-abdominal pressure (IAP) 8–10 mm Hg) instead of standard-pressure pneumoperitoneum (IAP 12–15 mm Hg) during laparoscopic surgery have been repeatedly pointed out. Low-pressure pneumoperitoneum may reduce the adverse effects associated to establishing pneumoperitoneum, including its impact on postoperative pain and recovery [1–8]. However, a low IAP could also limit surgical working space, modifying surgical conditions or surgeon's satisfaction, and it could negatively affect safety and efficiency of the procedure, when compared to routine standard-pressure pneumoperitoneum.

The depth of neuromuscular blockade (NMB) is a potentially modifiable factor that can influence the working space during laparoscopy. Deep NMB (defined as train-of-four (TOF) count 0, 1–5 post-tetanic

* Corresponding author at: C/ Reina Dª Germana N° 1, Pta 12, 46005 Valencia, Spain.
E-mail address: jbarrio.ma@gmail.com (J. Barrio).
[1] Staff anesthesiologist.
[2] Staff surgeon.

http://dx.doi.org/10.1016/j.jclinane.2017.08.005
0952-8180/

count (PTC) stimuli responses) allows an increase of intra-abdominal volume upon establishing pneumoperitoneum when compared with other NMB depth level [9–12]. However, whether this variation on the working space induced by deep NMB is decisive to improve surgical conditions is yet to be proven at a clinical setting. The impact of deep NMB on the surgical procedure will be crucial if it can provide better surgical conditions, especially in those cases in which the working space could be limited, as during low-pressure pneumoperitoneum laparoscopy. Results of two previous publications evaluating the impact of NMB on surgical conditions for low-pressure pneumoperitoneum laparoscopic cholecystectomy (LC) differ, with only one of them showing deep NMB as determinant in the improvement of surgical conditions and in the success of the surgical procedure when compared with moderate NMB (TOF 1–3) [13,14].

The main goal of the study was to evaluate the influence of depth of NMB on surgical conditions during low-pressure pneumoperitoneum LC, while comparing moderate and deep NMB. The secondary objective was to evaluate if surgical conditions during low-pressure pneumoperitoneum LC performed with deep NMB could be comparable to those provided during standard-pressure pneumoperitoneum LC.

2. Material and methods

This prospective, randomized, blinded clinical trial was approved by the Institutional Clinical Research and Ethics Committee of Hospital Arnau de Vilanova, Valencia, Spain and written informed consent was obtained from all the participants.

Ninety adult patients (18–65 year-old), American Society of Anesthesiologists (ASA) physical status class I-II, scheduled for elective LC between February 2014 and January 2015, were included in the study. A computer-generated random sequence (Excel, Microsoft, San Francisco, CA, USA), conducted by a person who was not involved in the study, was used to allocate the patients in three groups:

- Group 1: LC performed under low-pressure pneumoperitoneum (IAP 8 mm Hg) with moderate NMB throughout the procedure.
- Group 2: LC performed under low-pressure pneumoperitoneum (IAP 8 mm Hg) with deep NMB throughout the procedure.
- Group 3: LC performed under standard-pressure pneumoperitoneum (IAP 12 mm Hg).

Exclusion criteria were: ASA physical status >II, age <18 or >65 year-old, body mass index (BMI) <18.5–>30 kg/m^2, renal insufficiency (glomerular filtration rate < 40 ml/min), impaired liver function (hepatic cirrhosis, cholestatic jaundice), neuromuscular disease, pregnancy, breastfeeding, predicted difficult airway, patients receiving medications known to interact with neuromuscular blocking agents, or allergy to any drug included in the anesthetic protocol.

Anesthetic protocol for patients allocated to low-pressure pneumoperitoneum LC consisted of induction with propofol (2 mg/kg) and maintenance with a propofol infusion titrated for a bispectral index (BIS) between 40 and 60. Acceleromiography was used for NMB monitoring (TOF-Watch-SX, Organon-Teknika, Oss, The Netherlands) as recommended [15]. Moderate NMB was defined as a TOF count of 1–3 and deep NMB was defined as a TOF count of 0 and PTC < 5. Rocuronium 0.3 mg/kg was used to facilitate tracheal intubation. Patients in Group 1 received an infusion of rocuronium (concentration 1 mg/ml) titrated to maintain 1–3 TOF responses (starting rate 0.4 mg/kg/h). Patients in Group 2 received an additional bolus dose of 0.6 mg/kg rocuronium after intubation and rocuronium infusion was titrated to maintain 1–5 PTC responses. Sugammadex was used as a reversal agent (dose ranging between 2 mg/kg for moderate NMB and 4 mg/kg for deep NMB). NMB was monitored until a TOF ratio > 90% was obtained.

Group 3 was used as a control group reflecting the standard clinical practice in the hospital. In this group, the anesthesiologist in charge decided the anesthetic induction and maintenance protocol and the NMB agent and reversal drug used. Utilization of NMB or BIS monitors was also under the discretion of staff anesthesiologist. The rest of the anesthetic protocol, equal for the three groups, is shown in Table 1.

Surgery was performed by one of three surgeons with >15 years' experience in laparoscopic surgery. Surgical technique included standard 4-hole incision in the French position and 25° anti-Trendelemburg. Pneumoperitoneum (Storz Thermoinflator 264320 20, Tuttlingen, Germany) and port access were established always with an IAP of 12 mm Hg. Afterwards IAP was decreased to 8 mm Hg or maintained at 12 mm Hg depending on the group of allocation. The surgeon was blinded to the degree of NMB and to IAP of pneumoperitoneum (monitors were out of his field of view); the attending anesthesiologist was not blinded. Surgical conditions were assessed at three time-points during the procedure: 1 - surgical field exposure (access to the gallbladder), 2 - dissection of the gallbladder and 3 - hemostasis, extraction of the gallbladder and surgical closure.

Surgical conditions were evaluated by the surgeons using a four-step scale that was based in scales previously used [16,17]:

Level 1 - Optimal conditions.

Level 2 - Good conditions: adequate surgical conditions to perform the surgery, but not optimal.

Level 3 - Acceptable conditions: an intervention is considered to improve surgical conditions.

Level 4 - Poor conditions: surgery cannot be performed. An intervention is necessary.

For statistical analysis, cases were grouped into two categories: good surgical conditions (levels 1 and 2) and bad surgical conditions (levels 3 and 4). The intervention protocol in the scenario of poor conditions (level 4) consisted of:

- Group 1: to increase the depth of NMB and if still inadequate to increase the preset IAP to 12 mm Hg.
- Group 2: to increase the preset IAP to 12 mm Hg.
- If still inadequate at IAP of 12 mm Hg, the surgeon could proceed under his own criteria.

Cases classified as level 4 (intervention needed) were excluded for evaluation of the surgical conditions in the next time-point of the procedure. Bleeding or bile duct injury was considered major surgical complications.

2.1. Statistical analysis

According to previous data, sample size was calculated in order to detect a difference in proportion of good surgical conditions of 20%. Sample size was calculated with a power of 80% and a type 1 error risk of 5%. A minimum of 30 patients were required in each group. A

Table 1
Anaesthesthic protocol.

1 - Standard hemodynamic and respiratory monitoring (electrocardiography, noninvasive arterial blood pressure, pulse oximetry).
2 - Premedication: midazolam 1 mg iv.
3 - Intraoperative analgesia: fentanyl 1.5 μg/kg iv. before induction, remifentanil (0.1–0.5 μg/kg/min as demand) and fentanyl 1.5 μg/kg iv. after dissection of the gallblader. Paracetamol 1 g iv. and dexketoprofen 50 mg iv. 15 min before the end of surgery.
4 - Antiemetic prophylaxis: dexametasone 4 mg iv. before induction and ondansetron 4 mg iv. 15 min before the end of surgery.
5 - Wound infiltration with levobupivacaine 0,25% 20 ml.
7 - Antibiotic prophylaxis: cefuroxime 1.5 g iv.
8 - Airway management: tracheal intubation.
9 - Ventilation (volume-controlled) adjusted to maintain normocapnia (Et CO_2 35–40 mm Hg).
10 - Fluid therapy: ringer-lactate 7–8 ml/kg/h.
11 - Skin temperature over the adductor pollicis brevis muscle maintained at >32 °C.