Effect of dexmedetomidine on opioid consumption and pain control after laparoscopic cholecystectomy: a meta-analysis of randomized controlled trials

Yang Liu, Guomin Zhao, Xuefeng Zang, Feiping Lu, Ping Liu, Wei Chen

Department of Intensive Care Unit, Beijing Shijitan Hospital, Capital Medical University, Beijing, China

Abstract

Introduction: The clinical evidence on dexmedetomidine (DEX) for postoperative pain scores and opioid consumption remains unclear in laparoscopic cholecystectomy (LC).

Aim: To evaluate whether DEX could reduce opioid consumption and pain control after LC.

Material and methods: A meta-analysis search of EMBASE, PubMed and Cochrane CENTRAL databases was performed and randomized controlled trials (RCTs) comparing DEX with control for adult patients undergoing LC were searched. The primary outcome was opioid consumption in the first 24 h after the operation. The secondary outcomes were the time of first request of analgesia, visual analogue scale (VAS) scores 24 h after the operation, the incidence of patients' need for rescue analgesics, opioid-related adverse effects, DEX-related adverse effects and other complications.

Results: There were fourteen aspects of twelve trials and 967 patients included in the analysis. DEX use significantly reduced the opioid consumption in the first 24 h after the operation (weighted mean difference (WMD), −19.17; 95% confidence interval (CI), −30.29 to −8.04; p = 0.0007), lengthened the time of first request of analgesia (WMD = 38.90; 95% CI: 0.88–76.93; p = 0.04) and lowered post-operative nausea or vomiting (PONV) (odds ratio (OR) = 0.49; 95% CI: 0.27–0.89; p = 0.02).

Conclusions: Intravenous DEX infusion significantly improved the duration of the analgesic effect and reduced post-operative opioid consumption. Moreover, lower incidence of post-operative nausea or vomiting was found in the DEX group.

Key words: dexmedetomidine, pain, opioid consumption, visual analogue scale, meta-analysis.

Introduction

Although pain after laparoscopic cholecystectomy (LC) is less intense than that after open cholecystectomy, some patients still experience considerable discomfort during the first 24 h. Pain after LC is still the main complaint which prolongs hospital stay [1]. Opioids are one of the choices for perioperative analgesia [2]. However, the use of opioids may cause excessive sedation and induce respiratory depression. Many patients may experience nausea and vomiting [3]. All of these may lower the benefits of analgesia. Non-opioid drugs were recommended to be used first to decrease the number of opioids after abdominal surgery [4]. Therefore, we need to study and evaluate newer non-opioid pain medications for an opioid-reduction strategy.

Address for correspondence
Dr Wei Chen, Department of Intensive Care Unit, Beijing Shijitan Hospital, Capital Medical University, Beijing, China,
e-mail: heart2008whu@163.com
Dexmedetomidine (DEX) is widely used to provide sedation, analgesia, and sympatholysis [5, 6]. Previous studies show that DEX may be a potential non-opioid pain medication in the perioperative period and decrease the opioid consumption and opioid-associated adverse events [7, 8]. Some randomized controlled trials have investigated DEX use in patients undergoing LC, but evidence on DEX for postoperative pain scores and opioid consumption remains unclear due to the small sample sizes.

Aim

We performed this meta-analysis to evaluate the DEX use for the opioid consumption and pain control after LC.

Material and methods

Search strategy and study criteria

We carried out this meta-analysis following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines [9] and no ethical approval was required. A systematic literature search of RCTs was conducted from 1999 to March 2019 in PubMed, EMBASE, and Cochrane Library. The search strategy included the combination of the keywords: “dexmedetomidine”, and “cholecystectomy”, or “laparoscopic cholecystectomy”, or “LC”, and “gallbladder”, or “cholecyst”, or “cholecystitis”.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) randomized controlled trials only, and as an original article, (2) studies published in English, (3) trials compared the clinical indicators between DEX and placebo or other drugs.

We excluded studies that (1) were expert consensuses, reviews, case reports, letters to the editor or retrospective studies, (2) articles without the full text, (3) were performed by open operations, and (4) lacked clinical outcome data and it was not possible to contact the authors.

Data extraction

The data of eligible studies were extracted independently by two investigators (GMZ and PL). The following contents were collected: age, gender, weight, the time of surgery and anaesthesia, and the method of DEX application. We solved disagreements through discussion for consensus and considered the PubMed database in preference. The authors used the Cochrane risk of bias tool and Jadad scale to assess the quality of the eligible studies.

Outcomes

Opioid consumption in the first 24 h after the operation, the time of first request of analgesia, visual analogue scale (VAS) scores in the 24 h after the operation, the incidence of patients’ need for rescue analgesics, opioid-related adverse effects, DEX-related adverse effects and other complications

Statistical analysis

We used odds ratios (OR) with 95% confidence intervals (95% CI) in all analyses for dichotomous variable (reported with incidence). The statistical method of Hozo et al. [10] and weighted mean difference (WMD) with 95% CI were used for continuous variable (reported as mean ± standard deviation, median and interquartile range, or median and range). The inconsistency statistic ($I^2$) was calculated to assess the heterogeneity. A random effect model was suitable for high heterogeneity ($I^2 \geq 50\%$), and a fixed effects model for low heterogeneity ($I^2 < 50\%$). Begg’s and Egger’s funnel plot analysis were conducted to evaluate publication bias. Sensitivity analysis, meta-regression and subgroup analysis were performed to explore possible heterogeneity when necessary with significance defined as $p < 0.1$. All statistical analysis was performed in REVMan (version 5.0; Cochrane Collaboration, Oxford, UK), SAS (version 9.4; SAS Institute Inc) and Stata (version 9.0; StataCorp LP), and the significance was defined as $p < 0.05$, except where specially mentioned.

Results

Study characteristics

Selection of the randomized controlled trials for this meta-analysis is shown in Figure 1. Fourteen aspects of twelve trials enrolling 967 patients were subjected to analysis (Figure 1) [11–22]. Eight trials used placebo as a control [11–13, 15–18, 20], whereas three used paracetamol [14, 21, 22], one used dexamethasone [19], and one used clonidine or tramadol [16]. DEX infusion commenced at a rate
of 0.05 to 0.6 μg/kg/h in 9 studies [11, 12, 14, 15, 17, 18, 20–22]. Among these, patients received DEX with a loading dose of 0.5 or 1 μg/kg in 6 studies [11, 14, 17, 20–22]. DEX was infused at a loading dose of 0.5 or 1 μg/kg in another 3 studies [13, 16, 19].

For outcomes, opioid consumption in the first 24 h after the operation was reported in eight trials [11–15, 19–21], the time of first request of analgesia was reported in seven aspects of five trials [12–14, 16, 19], VAS scores 24 h after the operation was reported in six trial [12, 13, 17, 18, 21, 22], and the incidence of patients’ need for rescue analgesics was reported in six aspects of four trials [15, 16, 18, 20].

Tables I and II show the general characteristics of the included studies. Table III and Figure 2 summarize the quality scores.

Effect of DEX on opioid consumption in first 24 h after operation

The opioid consumption in the first 24 h after the operation was investigated in 577 enrolled participants and was significantly reduced by DEX (eight studies; WMD = –19.17; 95% CI: –30.29 to –8.04; p = 0.0007; I² = 97%; Figure 3). No significant publication bias existed (Begg’s test, p = 0.27; Egger’s test, p = 0.43; Figure 4).

A subgroup analysis was conducted to explore heterogeneity for the primary outcome, and there were eight groups according to different characteristics as shown in Table IV. Significant heterogeneity was found in the subgroups of patients grouped by age, male proportion, administration timing (before induction versus after induction), and Jadad score. No heterogeneity was detected for opioid consumption in the first 24 h after the operation in other subgroups (Table IV).

Table V presents the results of a meta-regression analysis. No significant differences for opioid consumption in the first 24 h after the operation were found.

A sensitivity analysis was conducted and showed that all studies had the same opioid reduction effect (p < 0.05) except Sharma R [14].

Effect of DEX on the time of the first request of analgesia

The time of the first request of analgesia was reported in 476 study participants, and DEX infusion significantly prolonged the time of the first request of analgesia (five studies; WMD = 38.90; 95% CI: 0.88–76.93; p = 0.04; I² = 99%; Figure 5).

Effect of DEX on VAS scores 24 h after operation

VAS scores 24 h after the operation were reported in 452 study participants and were lower with DEX use, but the difference was not statistically significant (six studies; WMD = –1.16; 95% CI: –2.46 to 0.14; p = 0.08; I² = 98%; Figure 6).

Effect of DEX on incidence of patients’ need for rescue analgesics

The occurrence of patients’ need for rescue analgesics was reported in 312 study participants and was lower with DEX use, but the difference was not statistically significant (four studies; OR = 0.63; 95% CI: 0.38–1.04; p = 0.07; I² = 42%; Figure 7).

Effect of DEX on opioid related-adverse events

Opioid related-adverse events were reported in five studies [12, 13, 16, 18, 19]. Among these, post-operative nausea or vomiting (PONV) was reported in seven aspects of five trials enrolling 406 study participants and was significantly reduced by DEX (five studies; OR = 0.49; 95% CI: 0.27–0.89; p = 0.02; I² = 0%; Figure 8). Pruritus was only reported in one study [12], and there was no statistically significant difference between groups (p = 0.28).
Table I. General design of studies included in this meta-analysis

| Study          | Country | Surgery   | Dexmedetomidine dose                  | Control     | Time and duration of intervention or control                       | No. of patients | Clinical end point                                                                 | Follow-up |
|----------------|---------|-----------|---------------------------------------|-------------|---------------------------------------------------------------------|-----------------|-------------------------------------------------------------------------------------|-----------|
| Park JK 2012   | Korea   | LC        | 1 μg/kg, 0.05 μg/kg/h                 | Placebo     | Before induction, until removal of the gall bladder                 | 21 vs. 21       | Opioid consumptions in first 24 h after operation, incidence of patients’ requirement of rescue analgesics, DEX-related adverse effects (bradycardia) | In hospital |
| Kang SH 2013   | Korea   | LC        | 1 μg/kg, 0.05 μg/kg/h                 | Placebo     | After induction, until the end of surgery                          | 24 vs. 23       | Opioid consumptions in first 24 h after operation                                      | In hospital |
| Swaike S 2013  | India   | LC        | 1 μg/kg over 10 min, 0.2–0.4 μg/kg/h for 24 h | Paracetamol | Pre-operatively and thereafter for 24 h                           | 40 vs. 40       | VAS scores                                                                          | In hospital |
| Khanduja S 2014| India   | LC        | 0.5–0.6 μg/kg/h                       | Placebo     | Before induction, until the end of surgery                          | 30 vs. 30       | Opioid consumptions in first 24 h after operation, incidence of patients’ requirement of rescue analgesics | In hospital |
| Bakri MH 2015  | Egypt   | LC        | 1 μg/kg                                | Dexamethasone| After induction                                                     | 43 vs. 43       | Opioid consumptions in first 24 h after operation, the time of first request of analgesia, opioid-related adverse effects (PONV) | In hospital |
| Park HY 2016   | Korea   | LC        | 0.3 μg/kg/h                           | Placebo     | From 5 min before induction to the end of pneumoperitoneum         | 15 vs. 15       | Opioid consumptions in first 24 h after operation, VAS scores, PONV, mean extubation time | In hospital |
| Sahi S 2016    | India   | LC        | 1 μg/kg                                | Clonidine/tramadol/placebo | At the beginning of wound closure, over a period of 5 min | 30 vs. 30 | The time of first request of analgesia, incidence of patients’ requirement of rescue analgesics, PONV | In hospital |
| Sharma R 2017  | India   | LC        | 1 μg/kg, 0.5 μg/kg/h                  | Paracetamol | After induction, until the removal of the gall bladder             | 50 vs. 50       | Opioid consumptions in first 24 h after operation, the time of first request of analgesia, VAS scores | In hospital |
| Sharma P 2017  | India   | LC        | 0.5 μg/kg, 0.5 μg/kg/h                | Placebo     | Before induction, until the end of surgery                          | 50 vs. 50       | VAS scores, PACU length of stay                                                      | In hospital |
| Bielka K 2018  | Ukraine | LC        | 0.5 μg/kg/h                           | Placebo     | From induction to extubation                                       | 30 vs. 30       | Opioid consumptions in first 24 h, the time of first request of analgesia, VAS scores | In hospital |
| Kamali A 2018  | Iran    | LC        | 1 μg/kg, 0.5 μg/kg/h                  | Paracetamol | Start after anesthesia induction up to 6 h after surgery           | 66 vs. 66       | Opioid consumptions in first 24 h after operation, the time of first request of analgesia, VAS scores | In hospital |
| Chilkoti GT 2019| India   | LC        | 0.5 μg/kg                             | Placebo     | After removal of gall bladder                                       | 25 vs. 25       | Opioid consumptions in first 24 h after operation, the time of first request of analgesia, VAS scores | In hospital |

LC – laparoscopic cholecystectomy, DEX – dexmedetomidine, VAS – visual analog scale, PONV – post-operative nausea or vomiting, PACU – post anesthesia care unit.
Effect of dexmedetomidine on opioid consumption and pain control after laparoscopic cholecystectomy: a meta-analysis of randomized controlled trials

Table II. General characteristics of patients included in each study

| Study          | Age [years] | Weight [kg] | Male (%) | Duration of anesthesia [min] | Duration of surgery [min] | ASA I (%) |
|----------------|-------------|-------------|----------|------------------------------|----------------------------|------------|
| Park JK 2012   | 42.9        | 66          | 45.24    | 58.9                         | 29.25                     | 69.05      |
| Kang SH 2013   | 45.55       | 65.4        | NA       | 56                           | 39.45                     | NA         |
| Swaika S 2013  | 37.52       | 51.905      | NA       | NA                           | NA                        | NA         |
| Khanduja S 2014| 48.2        | 56.8        | 20       | NA                           | NA                        | NA         |
| Bakri MH 2015  | 31.7        | 70.45       | 17.44    | 94.7                         | 74.25                     | 77.91      |
| Park HY 2016   | 42.5        | 67.5        | 46.67    | 84                           | 56                        | NA         |
| Sahi S 2016    | NA          | NA          | NA       | NA                           | 72.95                     | NA         |
| Sharma R 2017  | NA          | NA          | NA       | NA                           | NA                        | NA         |
| Sharma P 2017  | 43.9        | 63.95       | 21       | NA                           | 40.45                     | 72         |
| Bielka K 2018  | 54          | NA          | 11.5     | NA                           | NA                        | NA         |
| Kamali A 2018  | 52.35       | NA          | 55.35    | NA                           | NA                        | NA         |
| Chilkoti GT 2019| 38.6        | 54.58       | NA       | NA                           | 113.7                     | 94         |

Values are given as means unless otherwise specified. ASA – American Society of Anesthesiologists, NA – not available.

Table III. Quality scores of studies included in this meta-analysis

| Study          | Random sequence generation | Allocation Concealment | Blinding of participants and personnel | Blinding of outcome assessment | Attrition bias | Selective reporting | JADAD |
|----------------|-----------------------------|------------------------|---------------------------------------|-------------------------------|----------------|---------------------|-------|
| Park JK 2012   | Unclear                     | Unclear                | Unclear                               | Low risk                      | Unclear        | Unclear             | 4     |
| Kang SH 2013   | Low risk                    | Low risk               | Low risk                              | Low risk                      | Low risk       | Low risk            | 7     |
| Swaika S 2013  | Low risk                    | Low risk               | Unclear                               | Unclear                       | Unclear        | Unclear             | 6     |
| Khanduja S 2014| Unclear                     | Unclear                | Unclear                               | Unclear                       | Unclear        | Unclear             | 4     |
| Bakri MH 2015  | Low risk                    | Low risk               | Low risk                              | Low risk                      | Unclear        | Low risk            | 6     |
| Park HY 2016   | Low risk                    | Low risk               | Low risk                              | Low risk                      | Low risk       | Low risk            | 7     |
| Sahi S 2016    | Low risk                    | Low risk               | Low risk                              | Low risk                      | Low risk       | Low risk            | 7     |
| Sharma R 2017  | Low risk                    | Low risk               | Low risk                              | Low risk                      | Low risk       | Low risk            | 7     |
| Sharma P 2017  | Low risk                    | Low risk               | Low risk                              | Low risk                      | Low risk       | Low risk            | 7     |
| Bielka K 2018  | Low risk                    | Low risk               | Low risk                              | Low risk                      | Low risk       | Low risk            | 7     |
| Kamali A 2018  | Unclear                     | Unclear                | Unclear                               | Unclear                       | Unclear        | Unclear             | 4     |
| Chilkoti GT 2019| Low risk                  | Low risk               | Low risk                              | Low risk                      | Low risk       | Low risk            | 7     |

DEX related adverse events

Only one trial reported DEX related adverse events [12]. No differences were found in the incidences of hypotension and bradycardia.

Other outcomes

The effect of DEX on the duration of stay in the post-anaesthesia care unit (PACU) was explored in one study [17], which showed that DEX shortened the PACU stay in the control group than in the DEX group (61.4 ± 5.7 min vs. 69.7 ± 14.1 min, respectively, p = 0.001). The effect of DEX on the mean extubation time was reported in two studies [12, 18]. Our meta-analysis showed that there was no statistically significant difference in the mean extubation time owing to the DEX use (two studies; WMD = -5.69; 95% CI: -14.22 to 2.83; p = 0.19; I² = 98%).
Discussion

Our meta-analysis suggested that compared with the control intervention, DEX use significantly reduced postoperative opioid consumption, improved the duration of the analgesic effect, and lowered the incidence of PONV during LC.

DEX has been demonstrated to be effective for improved analgesia and may be an optimal drug for pain relief effects [23]. A meta-analysis performed by Schnabel reported that DEX infusion relieved postoperative pain and reduced opioid consumption in various elective surgeries [24]. Another meta-analysis by Le Bot showed a similar reducing effect of DEX for opioid, postoperative pain and PONV in multiple types of elective surgery [25]. There were studies focused on the efficacy of DEX in LC, but the conclusions are conflicting. Our study was the first meta-analysis to evaluate the efficiency of DEX for opioid consumption and pain control and indicated that intravenous DEX significantly decreased postoperative opioid consumption for adult patients undergoing LC.

Age-related reduction in renal and hepatic function may decrease the systemic clearance of opioids. Among older adults, we should start with the lower available dose of opioids compared with their younger counterparts [26]. A recent article reported that opioid metabolism differed according to gender due to the difference of the inhibitory circuit modulated by gonadal steroids [27]. Opioid use is more effective in males, so these sex differences must be considered in pain management [28]. In this meta-analysis, opioid consumption in the first 24 h after the operation was reduced in the subgroup of younger age (< 45 years) or lower male proportion (< 30%).

Opioid consumption was regularly used for pain relief after surgery. However, opioid associated adverse effects must be taken into account. In our study, the incidence of PONV was reduced in the DEX group, which was consistent with previous studies [29, 30].

There are several limitations to our study: (1) There were only twelve RCTs with 976 patients in our study. More RCTs with higher quality will be helpful for future study; (2) There was a tremendous amount of clinical heterogeneity between studies. Some important data were not reported, so these may influence the outcomes; (3) Although subgroup analysis, meta-regression analysis and sensitivity analysis were performed, heterogeneity still existed due to design differences of included RCTs. (4) The enormous heterogeneity of included studies with

---

**Table 1.** Quality scores of studies included in this meta-analysis

| Study or subgroup | Risk of bias | (A) Random sequence generation (selection bias) | (B) Allocation concealment (selection bias) | (C) Blinding of participants and personnel (performance bias) | (D) Blinding of outcome assessment (detection bias) | (E) Incomplete outcome data (attrition bias) | (F) Selective reporting (reporting bias) | (G) Other bias |
|-------------------|-------------|----------------------------------|----------------------------------|---------------------------------|---------------------------------|--------------------------------|--------------------------------|-------------|
| Park JK 2012      | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Swaiika S 2013    | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Kang SH 2013      | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Khanduja S 2014   | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Bakri MH 2015     | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Sahi S 2016       | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Park HY 2016      | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Sharma P 2017     | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Sharma R 2017     | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Bieik K 2018      | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Kamali A 2018     | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |
| Chilkoti GT 2019  | ++          | ++                               | ++                               | +                               | +                               | +                               | +                               |             |

**Figure 2.** Quality scores of studies included in this meta-analysis

---

**Table 2.** DEX reduced opioid consumption in the first 24 h after the operation

| Study or subgroup | Mean difference IV, random, 95% CI |
|-------------------|-----------------------------------|
| Park JK 2012      | -22.50 (-41.10, -3.90)            |
| Kang SH 2013      | 0.00 (-10.97, 10.97)               |
| Khanduja S 2014   | -11.50 (-13.63, -9.37)            |
| Bakri MH 2013     | -25.00 (-28.89, -21.11)           |
| Sharma R 2017     | 0.00 (-10.00, -10.00)              |
| Bieik K 2018      | -61.16 (-99.05, -23.27)           |
| Kamali A 2018     | -61.16 (-99.05, -23.27)           |
| Chilkoti GT 2019  | -61.16 (-99.05, -23.27)           |

**Figure 3.** DEX reduced opioid consumption in the first 24 h after the operation

---

Heterogeneity: $t^2 = 199.91, \chi^2 = 252.32, df = 7 (p < 0.00001), I^2 = 97$

Test for overall effect: $Z = 3.38 (p = 0.0007)$
Effect of dexmedetomidine on opioid consumption and pain control after laparoscopic cholecystectomy:
a meta-analysis of randomized controlled trials

In conclusion, our study indicates that DEX use significantly improves the duration of the analgesic effect and reduces postoperative opioid consumption after LC. Moreover, there is less opioid-related PONV as a result of DEX use.

Conflict of interest
The authors declare no conflict of interest.

Figure 4. Funnel plot assessment of potential publication bias

Table IV. Subgroup analysis for heterogeneity of primary outcome

| Subgroup           | Endpoint                              | No. of comparisons | WMD   | 95% CI        | P-value | $I^2$ | P_heterogeneity value |
|--------------------|---------------------------------------|--------------------|-------|---------------|---------|------|-----------------------|
| Age [years]:       | Opioid consumptions in first 24 h     | 7                  | -9.63 | -19.07–0.44  | 0.06    | 90.4%| 0.001                 |
| ≥45                |                                       | 4                  | 0.38  | -11.24–12.01 | 0.95    | 97%  |                       |
| ≤45                |                                       | 3                  | -27.69| -40.08–15.27| 0.0001  | 44%  |                       |
| Gender (male%):    | Opioid consumptions in first 24 h     | 5                  | -8.14 | -19.33–3.05  | 0.15    | 98%  | 0.02                  |
| ≥30                |                                       | 2                  | 1.83  | -44.15–47.81 | 0.94    | 95%  |                       |
| ≤30                |                                       | 3                  | -15.32| -22.73–7.91 | 0.0001  | 95%  |                       |
| Weight [kg]:       | Opioid consumptions in first 24 h     | 5                  | -17.39| -27.80–6.98  | 0.001   | 92%  | 0.52                  |
| ≥60                |                                       | 3                  | -15.79| -33.46–1.88  | 0.08    | 89%  |                       |
| ≤60                |                                       | 2                  | -32.58| -80.69–15.53 | 0.18    | 85%  |                       |
| Surgery duration [min]: | Opioid consumptions in first 24 h | 4                  | -21.64| -38.99–11.96 | 0.01    | 86%  | 0.17                  |
| ≥50                |                                       | 2                  | -37.97| -71.96–3.98  | 0.41    | 47%  |                       |
| ≤50                |                                       | 2                  | -9.94 | -31.84–11.96 | 0.04    | 76%  |                       |
| Infusion method:   | Opioid consumptions in first 24 h     | 8                  | -19.17| -30.29–8.04  | 0.007   | 97%  | 0.43                  |
| Load + continuous infusion |              | 4                  | -33.97| -85.40–7.47  | 0.11    | 98%  |                       |
| Others             |                                       | 4                  | -17.02| -24.69–9.34  | 0.0001  | 94%  |                       |
| Control drugs:     | Opioid consumptions in first 24 h     | 8                  | -19.17| -30.29–8.04  | 0.0007  | 97%  | 0.14                  |
| Placebo            |                                       | 5                  | -10.74| -15.22–6.26  | 0.00001 | 69%  |                       |
| Others             |                                       | 3                  | -46.18| -92.89–0.52  | 0.05    | 99%  |                       |
| Dex administration:| Opioid consumptions in first 24 h     | 8                  | -19.17| -30.29–8.04  | 0.0007  | 97%  | 0.10                  |
| After induction    |                                       | 5                  | -37.86| -37.86–5.41  | 0.02    | 98%  |                       |
| Before induction   |                                       | 3                  | -10.96| -12.80–9.13  | 0.00001 | 12%  |                       |
| Jadad:             | Opioid consumptions in first 24 h     | 8                  | -19.17| -30.29–8.04  | 0.0007  | 97%  | 0.05                  |
| ≥4                 |                                       | 5                  | -34.84| -51.37–18.30 | 0.0001  | 97%  |                       |
| ≤4                 |                                       | 3                  | -2.43 | -30.29–25.62 | 0.86    | 98%  |                       |

WMD – weighted mean difference, CI – confidence interval, Dex – dexmedetomidine.
### Table V. Meta-regression analysis for heterogeneity of primary outcome

| Parameter     | Regression coefficient | 95% CI          | P-value |
|---------------|------------------------|-----------------|---------|
| Age [years]   | 0.068                  | -0.088 – 0.224  | 0.39    |
| Gender (male%)| 0.082                  | 0.042 – 0.123   | 0.21    |
| Weight [kg]   | -0.004                 | -0.212 – 0.204  | 0.97    |
| Surgery duration [min] | -0.010             | -0.049 – 0.029  | 0.60    |
| Infusion method | 0.790               | 0.249 – 3.331   | 0.23    |
| Control drugs | -0.237                 | -2.388 – 1.914  | 0.83    |
| Dex administration | -0.010           | -3.023 – 1.004  | 0.33    |
| Jadad score   | -0.186                 | -0.922 – 0.550  | 0.62    |

CI = confidence interval, Dex – dexmedetomidine.

---

### Figure 5. DEX lengthened the time of first request of analgesia

Figure 6. Meta-analysis of DEX on VAS scores

### Figure 7. Meta-analysis of DEX on the incidence of patients’ need for rescue analgesics
Effect of dexmedetomidine on opioid consumption and pain control after laparoscopic cholecystectomy: a meta-analysis of randomized controlled trials

References

1. Barazanchi AWH, MacFater WS, Rahiri JL, et al. Evidence-based pain management after laparoscopic cholecystectomy: a PROSPECT review update. Br J Anaesth 2018; 121: 787-803.
2. Mark J, Argentieri DM, Gutierrez CA, et al. Ultrarestrictive opioid prescription protocol for pain management after gynecologic and abdominal surgery. JAMA Network Open 2018; 1: e185452.
3. Lavand’homme P, Steyaert A. Opioid-free anesthesia opioid side effects: tolerance and hyperalgesia. Best Pract Res Clin Anaesthesiol 2017; 31: 487-98.
4. Hill MV, Stucke RS, McMahon ML, et al. An educational intervention decreases opioid prescribing after general surgical operations. Ann Surg 2018; 267: 468-72.
5. Nguyen V, Tiemann D, Park E, et al. Alpha-2 agonists. Anesthesiol Clin 2017; 35: 233-45.
6. Keating GM. Dexmedetomidine: a review of its use for sedation in the intensive care setting. Drugs 2015; 75: 1119-30.
7. Liu Y, Liang F, Liu X, et al. Dexmedetomidine reduces perioperative opioid consumption and postoperative pain intensity in neurosurgery: a meta-analysis. J Neurol Surg Anesthesiol 2018; 30: 146-55.
8. Naik BI, Nemergut EC, Kazemi A, et al. The effect of dexmedetomidine on postoperative opioid consumption and pain after major spine surgery. Anesth Analgesia 2016; 122: 1646-53.
9. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015; 4: 1.
10. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 2005; 5: 13.
11. Kang SH, Kim YS, Hong TH, et al. Effects of dexmedetomidine on inflammatory responses in patients undergoing laparoscopic cholecystectomy. Acta Anaesthesiol Scand 2013; 57: 480-7.
12. Bielka K, Kuchyn I, Babych V, et al. Dexmedetomidine infusion as an analgesic adjuvant during laparoscopic cholecystectomy: a randomized controlled study. BMC Anesthesiol 2018; 18: 44.
13. Chilkoti GT, Kumar M, Mohta M, et al. Comparison of postoperative analgesic efficacy of low-dose bolus intravenous dexmedetomidine and intraperitoneal dexmedetomidine with bupivacaine in patients undergoing laparoscopic cholecystectomy: a randomised, controlled trial. Indian J Anaesth 2019; 63: 106-13.
14. Sharma R, Gupta R, Choudhary R, et al. Postoperative analgesia with intravenous paracetamol and dexmedetomidine in laparoscopic cholecystectomy surgery: a prospective randomized comparative study. Int J Appl Basic Med Res 2017; 7: 218-22.
15. Khaduja S, Ohri A, Panwar M. Dexmedetomidine decreases requirement of thiopentone sodium and pentazocine followed with improved recovery in patients undergoing laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol 2014; 30: 208-12.
16. Sahi S, Singh MR, Katyal S. Comparative efficacy of intravenous dexmedetomidine, clonidine, and tramadol in postanesthesia shivering. J Anaesthesiol Clin Pharmacol 2016; 32: 240-4.
17. Sharma P, Gombar S, Ahuja V, et al. Sevoflurane sparing effect of dexmedetomidine in patients undergoing laparoscopic cholecystectomy: a randomized controlled trial. J Anaesthesiol Clin Pharmacol 2017; 33: 496-502.
18. Park HY, Kim JY, Cho SH, et al. The effect of low-dose dexmedetomidine on hemodynamics and anesthetic requirement during bis-spectral index-guided total intravenous anesthesia. J Clin Monitoring Computing 2016; 30: 429-35.
19. Bakri MH, Ismail EA, Ibrahim A. Comparison of dexmedetomidine and dexmethasone for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Korean J Anesthesiol 2015; 68: 254-60.
20. Park JK, Cheong SH, Lee KM, et al. Does dexmedetomidine reduce postoperative pain after laparoscopic cholecystectomy with multimodal analgesia? Korean J Anesthesiol 2012; 63: 436-40.
21. Kamali A, Ashrafi TH, Rakel S, et al. A comparative study on the prophylactic effects of paracetamol and dexmedetomidine for controlling hemodynamics during surgery and postoperative pain in patients with laparoscopic cholecystectomy. Medicine 2018; 97: e13330.
22. Swaika S, Parta N, Chattopadhyay S, et al. A comparative study of the efficacy of intravenous Paracetamol and Dexmedetomidine on peri-operative hemodynamics and post-operative analgesia for patients undergoing laparoscopic cholecystectomy. Anesth Essays Res 2013; 7: 331-5.
23. Giovannitti JA, Thoms SM, Crawford JJ. Alpha-2 adrenergic receptor agonists: a review of current clinical applications. Anesth Progress 2015; 62: 31-9.
24. Schnabel A, Meyer-Friessem CH, Reichl SU, et al. Is intraoperative dexmedetomidine a new option for postoperative pain...
500

Videosurgery and Other Minimally Invasive Techniques 3, September/2021

25. Le Bot A, Michelet D, Hilly J, et al. Efficacy of intraoperative dexmedetomidine compared with placebo for surgery in adults: a meta-analysis of published studies. Minerva Anestesiologica 2015; 81: 1105-7.

26. Naples JG, Gellad WF, Hanlon JT. The role of opioid analgesics in geriatric pain management. Clin Geriatr Med 2016; 32: 725-35.

27. Averitt DL, Eidson LN, Doyle HH, et al. Neuronal and glial factors contributing to sex differences in opioid modulation of pain. Neuropsychopharmacology 2019; 44: 155-65.

28. Campbell CI, Weisner C, Leresche L, et al. Age and gender trends in long-term opioid analgesic use for noncancer pain. Am J Public Health 2010; 100: 2541-7.

29. Jin S, Liang DD, Chen C, et al. Dexmedetomidine prevent postoperative nausea and vomiting on patients during general anesthesia: a PRISMA-compliant meta analysis of randomized controlled trials. Medicine 2017; 96: e5770.

30. Sridharan K, Sivaramakrishnan G. Drugs for preventing postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: network meta-analysis of randomized clinical trials and trial sequential analysis. Int J Surg 2019; 69: 1-12.

Received: 28.09.2020, accepted: 13.12.2020.