Egyptian Journal of Anaesthesia (2016) 32, 175–180

HOSTED BY

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Assessment of the effect of dexmedetomidine in high risk cardiac patients undergoing laparoscopic cholecystectomy

Rabie Soliman [a,b,*], Gomaa Zohry [b,1]

[a] Department of Anesthesia, King Fahad Military Hospital, Khamis Mushait, Saudi Arabia
[b] Department of Anesthesia, Cairo University, Egypt

Received 28 January 2015; revised 2 December 2015; accepted 13 December 2015
Available online 14 January 2016

KEYWORDS

Laparoscopy;
Cardiac patients;
Heart rate;
Blood pressure;
Dexmedetomidine

Abstract *Background:* Laparoscopy results in pathophysiologic changes and potentiates a neurohormonal stress response which increases systemic vascular resistance, mean arterial blood pressure, and heart rate and the aim of present study was to evaluate the effect of dexmedetomidine in high risk cardiac patients undergoing laparoscopic cholycystectomy.
Methods: The study included 80 patients [cardiac patient with ASA physical status III–IV], and scheduled for elective laparoscopic cholycystectomy. The patients were classified randomly into two groups: Group D: The patients received a loading dose of 1 μg/kg dexmedetomidine over 15 min before induction and maintained with 0.3 μg/kg/h infusion during the procedure. Group C: The patients received an equal volume of normal saline.
Results: The heart rate increased greatly after induction in the control group compared to the group D ($P < 0.05$) and the heart rate remained elevated during the procedures and post-operatively. There was an attack of tachycardia affected 4 patients in group D and 10 patients in group C and the comparison was significant ($P = 0.044$). The mean arterial blood pressure increased greatly after induction in the control group compared to the group D ($P < 0.05$) and the mean arterial blood pressure remained elevated during the procedures and post-anesthesia care unit The total fentanyl dose was higher in the group C patients more than group D ($P < 0.001$). The end-tidal sevoflurane was lower in group D patients than group C patients ($P < 0.001$).
Conclusion: Dexmedetomidine is safe for cardiac patients undergoing laparoscopic cholycystectomy. It minimized the changes in heart rate and blood pressure and decreased the total dose of fentanyl and end-tidal sevoflurane and the requirement for medications in high risk cardiac patients.

* Corresponding author at: Department of Anesthesia, King Fahad Military Hospital, Khamis Mushait, Saudi Arabia. Tel.: +966 504852971.
E-mail addresses: rabiesoliman@hotmail.com (R. Soliman), gomaaneel@hotmail.com (G. Zohry).
[1] Tel.: +20 1140333553.

Peer review under responsibility of Egyptian Society of Anesthesiologists.

http://dx.doi.org/10.1016/j.egja.2015.12.005

1. Introduction

Laparoscopy has now become the standard technique for cholycystectomy. Pneumoperitoneum required for laparoscopy results in pathophysiologic changes and potentiates a neurohormonal stress response which increases the systemic vascular resistance, arterial blood pressure, and heart rate [1–3], and reduces the venous return, preload, stroke volume, and cardiac output [4,5]. These factors increase the afterload and decreases the preload which are tolerated in ASA I and II patients [6,7], and poorly tolerated by patients with cardiac dysfunction (ASA III–IV) [8,9].

Dexmedetomidine is a highly selective alpha-2 agonist that provides sedation and analgesia. It activates pro-survival kinases and attenuates ischemia and hypoxic injury, including cardioprotection [10]. Concurrent infusion during surgery reduces anesthetic consumption by 20–50% [11], and produces a decrease in heart rate and blood pressure that may be advantageous in ischemic heart disease by improving oxygen supply and demand balance [12].

The aim of the present study was to evaluate the effect of dexmedetomidine on the intraoperative hemodynamic stability in high risk cardiac patients undergoing laparoscopic cholycystectomy.

2. Methods and patients

After approval from the local ethics committee and obtaining written informed consent in the King Fahd hospital, Saudi Arabia, a study included 80 patients [cardiac patient with ASA physical status III–IV], undergoing elective laparoscopic cholycystectomy through 2012–2014. The inclusion criteria were patients with hypertension, coronary artery disease (ischemic heart disease or percutaneous transluminal coronary angioplasty, coronary artery bypass grafting), poor ventricular function, or valvular disease.

The patients were assessed using New York Heart Association (NYHA) [13], and American Society of Anesthesiologists Physical Status Score (ASA) [14]. Exclusion criteria included patients with congestive heart failure, obese patients or emergency. All patients were evaluated preoperatively by cardiologists and anesthesiologists. Investigations such as ECG and transthoracic echocardiography were done for all patients for evaluating the function of the myocardium and cardiac valves, diagnosis and treatment of ischemic heart diseases and patients on anticoagulants were managed by cardiologist preoperatively. All patients received their medications for hypertension, ischemic heart disease, or arrhythmia approximately two hours prior to anesthesia induction. The patients were classified randomly by simple randomization through a process of coin-tossing into two groups:

Group D: The patients received dexmedetomidine as a loading dose of 1 μg/kg over 15 min before induction and maintained with 0.3 μg/kg/h infusion during the procedure.

Group B (control group): The patients received equal amount of normal saline.

2.1. Anesthetic technique

For all patients and under local anesthesia, a radial arterial cannula and peripheral venous cannula G 18 or 16 were inserted and central venous line was inserted after induction for administration of inotropic drugs and vasodilators if needed. Anesthesia induction was started by preoxygenation with 100% oxygen, intravenous fentanyl (1–2 μg/kg), etomidate (0.3 mg/kg), and cisatracurium (0.2 mg/kg). After tracheal intubation, the anesthesia was maintained with sevoflurane (1–3%), fentanyl infusion (1–3 μg/kg/h), cisatracurium (1–2 μg/kg/min) and oxygen:air (50:50%).

For all patients, carbon dioxide insufflation was initiated and maintained at 5 L/min and the highest limit of intra-abdominal pressure was kept at 10 mmHg and the surgery was done in the supine position. Intraoperative fluids were given cautiously. Intraoperative increased heart rate and systemic hypertension were managed by bolus doses of fentanyl (1–2 μg/kg) and increasing of sevoflurane concentration 1–2%, and if hypertension persists, nitroglycerine infusion 0.5–1 μg/kg/min was started. Intraoperative hypotension was managed by bolus doses of ephedrine 5–10 mg and if persisted, dopamine infusion was started. At the end of the intervention and deflation of peritoneum, dopamine infusion was weaned gradually and discontinued in the operative room. The patients were transferred to post-anesthesia care unit with closed monitoring and observation for 2–4 h. Most of the patients were shifted to the ward, while few patients were transferred to the intensive care unit according to preoperative plan.

2.2. Monitoring of patients

The monitors included the heart rate, mean arterial blood pressure (MAP), a continuous electrocardiograph with automatic ST-segment analysis (leads II and V), arterial oxygen saturation, end-tidal carbon dioxide, end tidal sevoflurane, total dose of fentanyl, arterial blood gases. The heart rate and mean blood pressure were serially collected at the baseline; after induction of anesthesia; every 5 min during the procedure; at the end of surgery; and every 5 min in the post-anesthetic care unit. Also the incidence of hypotension, hypertension, tachycardia or bradycardia, and any adverse effects were recorded.

2.3. Outcomes

The primary outcome was stability of the hemodynamic status of the patients assessed by changes in the heart rate and blood pressure.

Secondary outcomes were total dose of fentanyl and end-tidal sevoflurane %. The safety of the procedure was assessed by the occurrence of any adverse events and the requirements to pharmacological support.

2.4. Sample size calculation

Power analysis was performed using Chi square test for independent samples on frequency of patients complaining of perioperative hemodynamic instability, because it was the main outcome variable in the present study. A pilot study was done before starting this study because there are no available data in the literature for the role of dexmedetomidine in high risk cardiac patients undergoing laparoscopic cholycystectomy. The results of the pilot study showed incidence of hemodynamic instability was of 20% in dexmedetomidine group, and 50%

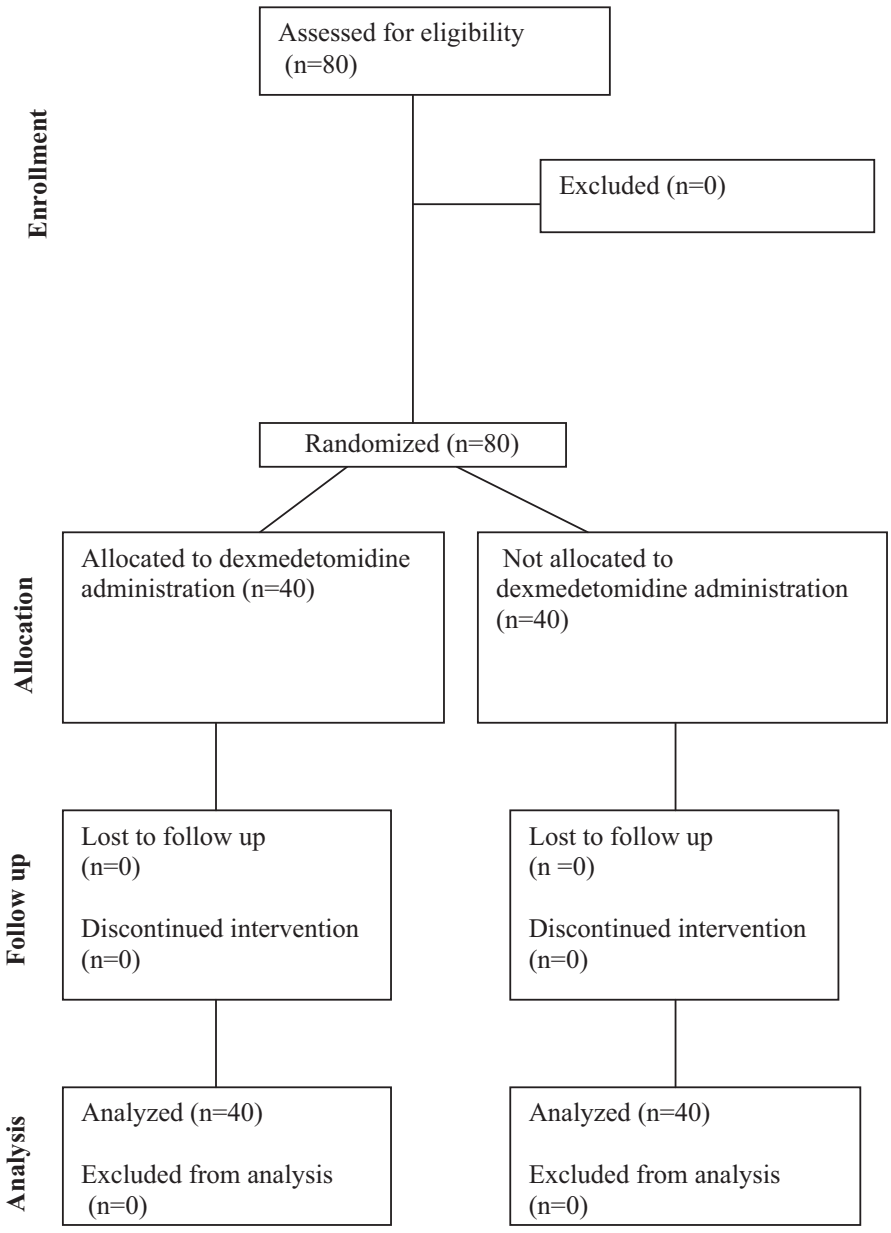

Figure 1 CONSORT diagram for the flow of participants through each stage of the present study.

in control group. Taking power 0.8 and alpha error 0.05, a minimum sample size of 38 patients was calculated for each group. The total number of patients in each group was 40 to compensate for possible dropouts.

2.5. The statistical paragraph in material and methods

Data were statistically described in terms of mean ± standard deviation (±SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student *t* test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. *P* values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

3. Results

Fig. 1 shows the CONSORT diagram for the flow of participants through each stage of the present study.

There was no statistical difference regarding the age, weight, gender, preoperative co-morbidities, ejection fraction and ASA physical status of patients ($P > 0.05$) (Table 1). Table 2 shows the comparison of heart rate between the two groups. The heart rate increased greatly after induction in the group C compared with the group D ($P < 0.05$) and the heart rate remained elevated during the procedures and

Table 1 Preoperative data of patients. Data are presented as mean ± SD, number,%.

Variables	Group A (n = 40)	Group B (n = 40)	P-value
Age (year)	59.70 ± 9.17	60.17 ± 9.09	0.816
Weight (kg)	77.45 ± 12.92	76.92 ± 12.01	0.662
Gender			
Male	15	18	0.495
Female	25	22	0.357
Diabetes mellitus	32	36	0.210
Ejection fraction (%)	38.54 ± 4.94	38.75 ± 5.21	0.965
Atrial fibrillation	4	2	0.323
Ischemic heart disease	17	14	0.491
PCTA	7	5	0.754
CABG	3	2	0.213
Valvular disease	2	1	1.000
ASA III	24	27	0.485
ASA IV	16	13	0.437

PCTA: Percutaneous transluminal coronary angioplasty, CABG: Coronary artery bypass grafting, ASA: American Society of Anesthesiologists Physical Status Score.

Table 2 Heart rate of patients. Data are presented as mean ± SD.

Timepoints	T0	T1	T2	T3	T4
Group A (n = 40)	72.02 ± 9.56	74.72 ± 8.84	70.25 ± 8.43	69.22 ± 10.17	70.42 ± 8.58
Group B (n = 40)	70.15 ± 10.36	90.02 ± 9.43	91.00 ± 8.0	81.00 ± 10.62	83.11 ± 9.04
P-value	0.990	0.024	0.001	0.032	0.047

T0: Baseline reading, T1: reading after induction, T2: reading 30 after induction, T3: reading at the end of surgery, T4: reading in the post-anesthesia care unit.

Table 3 Mean arterial blood pressure of patients. Data are presented as mean ± SD.

Timepoints	T0	T1	T2	T3	T4
Group A (n = 40)	97.28 ± 5.59	93.17 ± 4.54	95.57 ± 3.92	92.02 ± 3.45	93.10 ± 4.46
Group B (n = 40)	97.25 ± 5.62	114.00 ± 4.20	115.12 ± 3.33	106.05 ± 3.39	104.90 ± 4.22
P-value	0.984	0.002	0.004	0.001	0.001

T0: Baseline reading, T1: reading after induction, T2: reading 30 after induction, T3: reading at the end of surgery, T4: reading in the post-anesthesia care unit.

post-anesthesia care unit. There was an attack of tachycardia affected 4 patients in group D and 10 patients in group C and the comparison was significant (P = 0.044) (Table 4). Table 3 shows the comparison of mean arterial blood pressure of patients between the two groups. The mean arterial blood pressure increased greatly after induction in the group C compared with the group D (P < 0.05) and the mean arterial blood pressure remained elevated during the procedures and post-anesthesia care unit. There was attack of hypertension included 5 patients in group D and 14 patients in group C (P = 0.035). There were 6 patients in group D and 4 patients in group C suffered from hypotension and the comparison was statistically insignificant (P = 0.735) (Table 4). Table 4 shows the intraoperative data of patients. There was no statistical difference regarding the duration of anesthesia (P = 0.846) and end-tidal carbon dioxide (P = 0.530). Ephedrine was need to manage hypotension in 6 patients in group D and 4 patients in group C and the comparison was insignificant (P = 0.735). Dopamine was needed to manage hypotension in 3 patients in group D and 2 patients in group C and the comparison was statistically insignificant (P = 0.213). The total fentanyl dose was higher in the group C more than group D (P < 0.001). The end-tidal sevoflurane was lower in group D patients than group C patients (P < 0.001). There was only one patient in group C suffered from acute myocardial infarction and the patient died through a few hours after infarction.

4. Discussion

The previous studies evaluated the effect of dexmedetomidine on ASA physical status I–II and there is not any study on cardiac patients ASA III–IV during laparoscopic cholycystectomy; therefore, the present study was done to assess the effect of dexmedetomidine in high risk cardiac patients during laparoscopic cholycystectomy.

The present study showed that dexmedetomidine is safe for cardiac patients who underwent laparoscopic cholycystec-

Table 4 Intraoperative data and outcome of patients. Data are presented as mean ± SD, number.

Variables	Group A (n = 40)	Group B (n = 40)	P-value
Duration	93.50 ± 15.19	92.87 ± 13.62	0.846
Hypertension (SAP ⩾ 20% above Baseline)	5	14	0.035
Hypotension (SAP ⩽ 20% below Baseline)	6	4	0.735
Tachycardia (HR > 100 bpm)	4	10	0.044
Bradycardia (HR < 60 bpm)	2	1	1.000
Total dose of fentanyl (μg)	124.00 ± 31.62	215.30 ± 42.12	0.001
End-tidal carbon dioxide (mmHg)	30.24 ± 3.15	31.51 ± 3.73	0.530
End tidal sevoflurane (%)	1.59 ± 0.71	1.98 ± 0.76	0.003
Ephedrine	6	4	0.735
Acute MI	–	1	1.000
Mortality	–	1	1.000

SAP: Systolic arterial pressure; HR: Heart rate; Acute MI: Acute myocardial infarction.

tomy. The patients were hemodynamically stable and there were minimal changes in heart rate and arterial blood pressure with dexmedetomidine compared to the control group. There were no changes in the ST-segment during the procedure. There were fewer patients suffering from hypertension with dexmedetomidine than the control group. The total dose of fentanyl and end-tidal sevoflurane decreased greatly with dexmedetomidine than the control group. There was only one mortality case in the control group. The patient was hypertensive preoperatively and hemodynamically stable during the surgery and recovery. After 6 h from transferring to the ward, the patient complained of epigastric pain (not chest pain), and ECG showed massive myocardial infarction. The patient deteriorated rapidly in spite of the inotropic support; therefore, the coronary catheterization could not be done and the patient expired within 4 h later.

Li-rong et al. [15] evaluated the myocardial protective effect of dexmedetomidine during non-cardiac surgery in patients ASA II–III with coronary heart disease undergoing elective upper abdominal surgery. They found that patients were hemodynamic stable and the incidence of tachycardia and myocardial ischemia was significantly lower with dexmedetomidine. A large cohort study included 15,656 non-cardiac surgical cases, of whom 2688 received dexmedetomidine preoperatively or intraoperatively and 12,968 did not receive dexmedetomidine. There was no significant intraoperative hypotension or bradycardia with dexmedetomidine [16].

Xu et al. [17] studied the effects of dexmedetomidine on perioperative myocardial injury by observing peripheral circulatory changes in myocardial enzyme levels and hemodynamic changes in patients with coronary heart disease undergoing elective hip replacement surgery. Dexmedetomidine reduced myocardial injury and the patients were hemodynamically stable. Sadhu et al. [18] studied 28 patients NYHA II–III with a significant cardiac dysfunction (ejection fraction 20–40%, cardiomyopathy, valvular disease, heart block, prior cardiac interventions) and scheduled for laparoscopic cholycystectomy. The anesthesia was maintained with either sevoflurane or isoflurane without dexmedetomidine. The commonest and significant events were hypertension, hypotension, tachyarrhythmia and bradycardia and the patients required nitroglycerine, epinephrine, norepinephrine, and amiodarone infusion according to the complication and there was one mortality case as a result of acute myocardial infarction (third postoperative day), and other studies showed the same results [19,20].

Sidorowicz et al. [21] found that patients ASA II–III who received dexmedetomidine during carotid endarterectomy were hemodynamically stable and there were no fluctuation in the blood pressure compared to patients who did not receive dexmedetomidine.

The present study and other studies showed that dexmedetomidine is protective for the cardiovascular system in cardiac patients undergoing non-cardiac surgery. Dexmedetomidine decreases stress hormones (epinephrine, norepinephrine, vasopressin) during pneumoperitoneum [3,22–24], and these hormones cause tachycardia, hypertension and perioperative myocardial infarction [25–29]. Also the dexmedetomidine has an antiarrhythmic effect [29–33], and decreases the dose of anesthetics and narcotics that may affect the hemodynamic stability in cardiac patients during laparoscopic cholycystectomy [34–36].

Against the results of the present study, a meta-analysis study included 840 patients and evaluated the cardiac outcomes of dexmedetomidine following non-cardiac surgery and showed that dexmedetomidine is associated with significant perioperative hypotension, myocardial ischemia and bradycardia and anticholinergic did not reduce the incidence of bradycardia associated with dexmedetomidine [12].

The present study recognizes some limitations such as a being single center study as well the small number of patients.

5. Conclusion

Dexmedetomidine is safe for cardiac patients undergoing laparoscopic cholycystectomy. It minimized the changes in heart rate and blood pressure and decreased the total dose of fentanyl, end-tidal sevoflurane and the requirement for medications in high risk cardiac patients without complications related to dexmedetomidine.

6. Disclosures

The authors declare that they have no competing interests or fund for the present study.

Acknowledgments

The authors thank all staff-nurses in the operative rooms and post anesthesia care unit for their efforts and performance during the study.

References

[1] Dexter SP, Vucevic M, Gibson J, McMahon MJ. Hemodynamic consequences of high and low-pressure capnoperitoneum during laparoscopic technique. Surg Endosc 1999;13:376–81.
[2] Odeberg S, Ljunggvist O, Sevenberg T, Gannedahl P, Bäckdahl M, von Rosen A, et al. Hemodynamic effects of pneumoperitoneum and the influence of posture during anesthesia for laparoscopic surgery. Acta Anaesthesiol Scand 1994;38:276–83.
[3] Joris JL, Noriot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholycystectomy. Anesth Analg 1993;76:1067–71.
[4] Dorsay DA, Greene FL, Baysinger CL. Hemodynamic changes during laparoscopic cholecystectomy monitored with transesophageal echocardiography. Surg Endosc 1995;9:128–34.
[5] Willams MD, Murr PC. Laparoscopic insufflations of abdomen depress cardiopulmonary function. Surg Endosc 1993;7:12–6.
[6] Wahba RWM, Beique F, Kleiman SJ. Cardiopulmonary function and laparoscopic cholecystectomy. Can J Anaesth 1995;42:51–63.
[7] Sharma KC, Brandstetter RD, Brensilver JM, Jung LD. Cardiopulmonary physiology and pathophysiology as a consequence of laparoscopic surgery. Chest 1996;110:810–5.
[8] Westerband A, Van de Water JM, Amzallag M, Lebowitz PW, Nwasokwa ON, Chardavoyne R, et al. Cardiovascular changes during laparoscopic cholecystectomy. Surg Gynecol Obstet 1992;175:535–8.
[9] Safran D, Sgambati S, Orlando III R. Laparoscopy in high-risk cardiac patients. Surg Gynecol Obstet 1993;176:548–54.
[10] Ibacache M, Sanchez G, Pedrozo Z, Galvez F, Humeres C, Echevarria G, et al. Dexmedetomidine preconditioning activates pro-survival kinases and attenuates regional ischemia/reperfusion injury in rat heart. Biochim Biophys Acta 2012;1822:537–45.
[11] Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. Anesthesiology 1997;86:1055–60.
[12] Biccard BM, Goga S, De Beurs J. Dexmedetomidine and cardiac protection for non-cardiac surgery: a meta-analysis of randomised controlled trials. Anesthesia 2008;63:4–14.
[13] The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and blood vessels. 9th ed. Boston, Mass: Little, Brown & Co; 1994. p. 253–6.
[14] Wolters U, Wolf T, Stützer H, Schröder T. ASA classification and perioperative variables as predictors of postoperative outcome. Br J Anaesth 1996;77:217–22.
[15] Li-rong G, Jian-bo, Yuan Z, McQuillan PM. Myocardial protective effect of dexmedetomidine during non-cardiac surgery in patients with coronary heart disease. Chin J Anesthesiol 2011;31:160–2.
[16] Klinger RY, White WD, Hale B, Habib AS, Bennett-Guerrero E. Hemodynamic impact of dexmedetomidine administration in 15,656 noncardiac surgical cases. J Clin Anesth 2012;24:212–20.
[17] Xu L, Hu Z, Shen J, McQuillan PM. Does dexmedetomidine have a cardiac protective effect during non-cardiac surgery? A randomised controlled trial. Clin Exp Pharmacol Physiol 2014;12:879–83.
[18] Sadhu S, Sarkar S, Jahangir TA, Verma R, Shaikh F, Dubey SK, et al. Laparoscopic cholecystectomy in patients with cardiac dysfunction. Indian J Surg 2011;73:90–5.
[19] Popken F, Küchle R, Heintz A, Junginger T. Laparoscopic cholecystectomy in high risk patients. Chirurg 1997;68:801–5.
[20] Hein HA, Joshi GP, Ramsay MA, Fox LG, Gawey BJ, Hellman CL, et al. Hemodynamic changes during laparoscopic cholecystectomy in patients with severe cardiac disease. J Clin Anesth 1997;9:261–5.
[21] Sidorowicz M, Owczuk R, Kwiecińska B, Wujtewicz MA, Wojciechowski J, Wujtewicz M. Dexmedetomidine sedation for carotid endarterectomy. Anesthesiol Intens Ther 2009;2:65–70.
[22] O'Leary E, Hubbard K, Tormey W, Cunningham AJ. Laparoscopic cholecystectomy: hemodynamic and neuroendocrine responses after pneumoperitoneum and changes in position. Br J Anaesth 1996;76:640–4.
[23] Sari R, Sevinc A. The effects of laparascopic cholecystectomy operation on C-reactive protein, hormones, and cytokines. J Endocrinol Invest 2004;27:106–10.
[24] Yu L, Yongfu Z, Guozhong L. Effect of dexmedetomidine on the level of catecholamines and hemodynamics in patients undergoing laparoscopy. Chin J Minim Invas Surg 2011;2:119–22.
[25] Scheinin B, Lindgren L, Randall T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and perioperative fentanyl. Br J Anaesth 1992;68:126–31.
[26] Lawrence CJ, De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative hemodynamic stability. Anesthesia 1997;52:736–44.
[27] Karapandzic VM, Vujisic-Tesic BD, Pesko PM, Rankovic VI, Milicic BR. Perioperative myocardial ischemia in coronary artery disease patients undergoing abdominal nonvascular surgery. Exp Clin Cardiol 2009;14:9–13.
[28] Myre K, Rostrup M, Buanes T, Stokland O. Plasma catecholamines and hemodynamic changes during pneumoperitoneum. Acta Anaesthesiol Scand 1998;42:343–7.
[29] Walder AD, Aitkenhed AR. Role of vasopressin in the haemodynamic response to laparoscopic cholecystectomy. Br J Anaesth 1997;78:264–6.
[30] Ruesch S, Levy JH. Treatment of persistent tachycardia with dexmedetomidine during off-pump cardiac surgery. Anesth Analg 2002;95:316–8.
[31] Parent BA, Munoz R, Shiderly D, Chrysostomou C. Use of dexmedetomidine in sustained ventricular tachycardia. Anaesth Intensive Care 2010;38:781.
[32] Chrysostomou C, Sanchez-de-Toledo J, Wearden P, Jooste EH, Lichtenstein SE, Callahan PM, et al. Perioperative use of dexmedetomidine is associated with decreased incidence of ventricular and supraventricular tachyarrhythmias after congenital cardiac operations. Ann Thorac Surg 2011;92:964–72.
[33] Ohsugi E, Nagamine Y, Ohtsuka M. The effect of dexmedetomidine in a child with intractable supraventricular tachyarrhythmias after total cavopulmonary connection. Masui 2011;60:493–5.
[34] Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. Anesth Analg 2008;106:1741–8.
[35] Nakagawa I, Omote K, Kitahata LM, Collins JG, Murata K. Serotonergic mediation of spinal analgesia and its interaction with nonadrenergic systems. Anesthesiology 1990;73:474–8.
[36] El-Tahan MR, Mowafia HA, Al Sheikhb IH, Khidr AM, Al-Juhaiman RA. Efficacy of dexmedetomidine in suppressing cardiovascular and hormonal responses to general anesthesia for caesarean delivery: a dose-response study. Int J Obstet Anesth 2012;21:222–9.