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Full Length Research Paper

Effect of dexmedetomidine on myocardial oxygen consumption during extubation for old patients: A bispectral index-guided observation study

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The aim of this study was to investigate the effect of dexmedetomidine (DEX) maintenance on myocardial oxygen consumption during extubation for generally-anesthetized old patients under bispectral index (BIS) monitoring. A total of 40 patients who were subjected to thyroid operation and laparoscopic cholecystectomy under general anesthesia (ASA I or II) were randomized into the experimental (n = 20) and control (n = 20) groups. General anesthesia was induced using midazolam, etomidate, sufentanil, and vecuronium bromide and was maintained using propofol, remifentanil, and atracurium besilate. The experimental group received micropump infusion of DEX at 0.2 ug kg^{-1} h^{-1} from 30 min before the end of operation to the end of extubation. The control group was given physiological saline with the same volume during the same period. BIS monitors were connected. Hemodynamic indexes [systolic blood pressure (SBP), diastolic arterial blood pressure (DBP), and heart rate (HR)] were recorded, and myocardial oxygen consumption index and the recovery time of consciousness were determined. HR of the experimental group decreased from 65 ± 8 to 60 ± 5 times/min at 10 min after micropump infusion, whereas that of the control group increased from 73 ± 10 to 85 ± 12 times/min, showing a significant difference (*P* < 0.01). Both groups did not show significant changes in HR during the following maintenance period. The two groups showed significant differences in SBP, DBP, HR, and BIS at 1, 5, and 10 min during extubation period (*P* < 0.05). They did not show any significant difference in extubation score, the recovery time of consciousness, or extubation time (*P* > 0.05). BIS-guided DEX has a stable effect on myocardial oxygen consumption in generally-anesthetized old patients during extubation period. It has no obvious influences on extubation score and the recovery time of consciousness. Thus, 0.2 ug kg^{-1} h^{-1} is a proper DEX micropump infusion rate.

Key words: Bispectral index, dexmedetomidine, myocardial oxygen consumption.

INTRODUCTION

Post-operative endotracheal catheter extraction can easily cause restlessness, bucking, hypertension, and increased heart rate (HR) to patients; to the elderly undergoing generally anesthesia, it easily causes a change in myocardial oxygen consumption during the recovery time of consciousness (Basali et al., 2000; Tanskanen et al., 2006). Particularly, due to vascular elastic change, the extubation is more likely to cause hemodynamic changes in old patients or even an increase in myocardial oxygen consumption in them which leads to myocardial ischemia and arrhythmia, and increases their post-operative risks. Rate-pressure product (RPP) is an

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index which is primarily used for myocardial oxygen consumption observance. RPP increases when myocardial oxygen requirement or consumption exceeds myocardial oxygen supply. As an increase in RPP can ultimately lead to pathological changes in myocardial cells and tissues, which can further induce risk factors of angina pectoris and myocardial infarction, reducing myocardial oxygen consumption during operation plays an important role in decreasing the risk of coronary artery blood-supply insufficiency.

Dexmedetomidine (DEX) is a highly selective adrenoceptor α2 agonist. DEX has sedative and analgesic effects which can inhibit sympathetic tone; it can decrease blood pressure (BP) and slow HR down in a dose-dependent manner to enhance hemodynamic stability; in addition, it has little influence on respiration (Souter et al., 2007). The application of DEX in anesthesia induction can relieve patients' reactions to tracheal cannula (Nenmann et al., 2009). DEX in total intravenous anesthesia for medium and minor operations can ease hemodynamic reactions and effectively reduce myocardial oxygen consumption during extubation (Han et al., 2011). Yet, to the best of our knowledge, there is no study on the effect of DEX on myocardial oxygen consumption during extubation under bispectral index (BIS) monitoring reported in literature.

In the current study, old patients undergoing general operations were selected and divided into two groups. They were respectively given DEX and physiological saline from the time close to the end of the operations. The effect of DEX on myocardial oxygen consumption index was then BIS-monitored.

MATERIALS AND METHODS

General data

A total of 40 patients, including 12 undergoing thyroid operation and 28 undergoing laparoscopic cholecystectomy under general anesthesia (ASA I or II) in Dongyang Peoples' Hospital between January and November, 2011 were involved in this study. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Dongyang People's Hospital. Written informed consent was obtained from all participants. Their ages ranged from 60 to 75 years. Among them, 18 were males and 22 were females. Patients with uncontrolled endocrine diseases, hyperthyroidism, and serious cardiovascular diseases were excluded from the current study. The enrolled patients were randomized into the experimental and control groups with 20 in each. The experimental group was given DEX micropump infusion from 30 min before the end of operation, whereas the control group was given physiological saline with the same volume from the same time point. The double-blind method was adopted.

Anesthesia

Electrocardiogram (ECG), pulse blood oxygen saturation (SpO_2), invasive blood pressure (ABP), and BIS index were monitored in the operating room. Peripherally intravenous administration route was opened. Anesthesia was induced with midazolam (Jiangsu Nhwa, China; Batch No.: 20020512) at 0.02 mg/kg and sufentanil citrate (Yichang Humanwell, China; Batch No.: 2101020) at 0.5 ug/kg through a Murphy's dropper, etomidate fat emulsion (Yichang Humanwell, China; Batch No.: 20010512) at 0.08 mg/kg, and vecuronium bromide (Zhejiang Xianju, China; Batch No.: 11011071. 1) at 0.1 mg/kg. Five minutes later, endotracheal intubation was performed under direct vision. Afterwards, the patient received micropump infusion of propofol (Sichuan Guorui, China; Batch No.: 1101056) and remifentanil hydrochloride (Yichang Humanwell; Batch No.: 2101020), injection of atracurium besilate (Shanghai Hengrui, China; Batch No.: 11020221), and oral administration of sevoflurane (Shanghai Hengrui; Batch No.: 11010222). Sevoflurane and atracurium besilate were stopped at 30 min before the end of operation, but the micropump infusion of propofol and remifentanil was continued till the end of the operation. Micropump infusion of DEX (Jiangsu Hengrui) at 0.2 ug kg^{-1} h^{-1} was given from 30 min before the end of operation to the end of extubation.

Observational indexes

Blood pressure (BP), HR, BIS, and myocardial oxygen consumption index before operation (T_0), 30 min before the end of the operation (T_1), 1 (T_3) during extubation, 5 (T_4), and 10 min (T_5) after extubation, as well as bucking and restlessness during extubation were recorded. Myocardial oxygen consumption was evaluated based on RPP. A value < 12,000 is counted normal, whereas a value beyond that threshold reflects an increase in myocardial oxygen consumption, which suggests possible myocardial ischemia. The reaction severity of bucking during extubation was graded into: (1) no bucking with stable respiration; (2) non-continuous mild bucking; (3) moderate bucking with continuous time < 30 s; and (4) severe bucking with continuous time ≥ 30 s. The severity of restlessness during extubation was scored into: (1) 0: patients were quiet and cooperative; (2) 1: there was limb restlessness at the time of sputum aspiration; (3) 2: limbs struggled even without stimuli, but such restlessness did not need to be stopped externally; and (4) 3: patients struggled violently, and they had to be held down.

Statistical analysis

Data were presented as means ± standard error and analyzed by the statistical package for social sciences (SPSS 11. 5 software). Normality test was used to determine the Shapiro-Wilk test. Paired t-test was performed for comparison between groups on the basis of analysis of variance, and χ^2-test was performed for enumeration data. $P < 0.05$ was considered significant.

RESULTS

General data

The two groups did not show any significant difference in age, sex, body weight, or operating time (Table 1).

The recovery time of consciousness

The two groups did not show any significant difference in the recovery time of spontaneous breathing or extubation time; although the experimental group showed a delay in eye opening time when compared with the control group,

Table 1. Comparisons of the general data between groups (mean ± SD).

Group	n	Sex (male/female)	Age (years)	Height (cm)	Weight (kg)	Operating time (min)
Experimental	20	11/9	44. 67±8.56 67. 67±6.56	155.65±11.78	54.78±6.53	156±35.35
Control	20	10/10	45. 68±5.86 68. 68±5.86	155.86±9.67	48.48±7.59	158±32.65

Table 2. Comparisons of the recovery time of consciousness between groups (mean ± SD).

Group	n	Spontaneous respiration (min)	Eye opening (min)	Extubation time (min)
Experimental	20	11±03	12±03	13±04
Control	20	10±04	10±02	13±03

such a difference was not significant. The results are shown in Table 2.

BP, HR, myocardial oxygen consumption, and BIS at different time points

The two groups did not show any significant difference in systolic blood pressure (SBP), diastolic arterial blood pressure (DBP), HR, myocardial oxygen consumption, or BIS before extubation. At 3 and 5 min after micropump infusion, these indexes in the experimental group decreased when compared with the control group, but no significant differences were observed. At the post-extubation instant time point, 1, 3, 5, and 10 min, they significantly decreased in the experimental group, compared with the control group ($P < 0.05$). The results are shown in Table 3.

Restlessness scores

The restlessness scores in the experimental group were significantly lower than those in the control group ($P < 0.05$) (Table 4).

DISCUSSION

Generally-anesthetized patients enter into the state of light anesthesia before extubation in which the catheter can cause stimulation to the respiratory tract. The stimulation transmits injurious nerves to the medulla oblongata cardiovascular center through airway circulation to cause the release of catecholamine, leading to great changes in BP and HR as well as an increase in myocardial oxygen consumption. This condition, plus the existence of a more or less certain degree of cardiovascular disease in old patients can pose a greater risk of a cardiovascular accident. Apart from the release of catecholamines, the stimulation can also cause the organism to produce inflammatory reactions which can further result in adverse effects to the patient (Groeneweg et al., 2009). Although lidocaine and fentanyl can alleviate severe coughing and cardiovascular reactions, they cannot achieve a satisfactory effect (Zamora et al., 2007). Based on this finding, anesthetics with a short-term and rapid effect are clinically recommended during generally-anesthetic extubation period nowadays; these drugs enable patients to establish protective responses on the one hand, and allow them a sufficient ventilation drive and a stable cardiovascular system on the other hand (Su et al., 2010).

Propofol has a good and complete sedative effect and short recovery time of consciousness. Meanwhile, it has the effects of dilating peripheral blood vessels, inhibiting the vasomotor center, blocking sympathetic terminals to release noradrenaline, and anti-vomiting (Lee et al., 2009). DEX is another effective anesthetic. Its action sites are mainly located at the sympathetic nerve endings of the central nervous system (the pallium and medulla) and peripheral nervous system, where the excited receptors can inhibit adenylate cyclase to deactivate potassium and calcium channels. This condition further reduces the release of noradrenaline, bringing about the effects of low BP, sinus bradycardia, sedation, and analgesis (Sanders and Maze, 2007; Schlichter, 2010). Rui fentanyl is a fentanyl μ-type opiate receptor agonist. It has the properties of fast blood-brain balance, which can be reached within 1 min, and high susceptibility to metabolism in blood and other tissues, which endow rui fentanyl with the virtues of rapid action onset time and short lasting time (only 5 to 10 min). Further, long time infusion or repeated injection of rui fentanyl has no influence on its metabolic rate, nor results in internal accumulation.

Table 3. Comparisons of SBP, DBP, HR, myocardial oxygen consumption, and BIS between groups (mean ± SD).

Index group	n	T_0	T_1	T_2	T_3	T_4	T_5
SBP experimental	20	125±15	118±12	122 ±14	129 ±14[b]	124±15	122±16
(mmHg) Control	20	128±11	114±80	123±11	138±16	133±14	130±13
DBP experimental	20	75±08	72±07	76±08	76±09	73±07	73±06
(mmHg) Control	20	78±09	73±09	78±12	87±13	82±11	84±10
HR experimental	20	72±06	62±08	65±07	66±08[b]	65±07[b]	64±05[b]
(Times/min) Control	20	76±10	67±08	73±10	79±14[a]	81±13[a]	85±12[a]
RPP experimental	20	93±11	69±09	68±12	70±15[b]	72±13[b]	70±13[b]
(%) Control	20	96±14	70±10	80±20	110±20	102±18	104±20
BIS experimental	20	94±03	70±06	85±03	87±03	93±02	94±03
Control	20	94±04	71±05	87±02	88±02	94±02	95±02

[a] $P < 0.05$, compared with the reference value, and [b]$P < 0.05$, compared with the control group.

Table 4. Comparisons of restlessness score between groups (mean ± SD).

Group	n	T_0	T_1	T_2	T_3	T_4	T_5
Experimental	20	0.82±0.21[a]	0.75±0.12[a]	0.55±0.16[a]	0.58±0.08[a]	0.33±0.12[a]	0.35±0.14[a]
Control	20	1.65±0.46	1.50±0.31	1.53±0.35	1.48±0.45	1.26±0.23	1.16±0.43

[a]$P < 0.05$, compared with the control group.

Nowadays, the sympatholytic activity of DEX is presumed to be primarily manifested by a decrease in HR because its application for patients who have received beta-blockers cannot bring about such a decrease (Jalonen et al., 1997). Some scholars also propose a second mechanism for DEX-induced HR decrease, that is, the application of DEX may increase cardiac vagal tone (Laubie et al., 1979). According to the previous studies, the application of DEX effectively avoids BP volatile fluctuation (Bekker et al., 2008; Abdullah et al., 2012). In the present study, SBP, DBP, HR, and myocardial oxygen consumption index in the experimental group kept stable, compared with the pre-operative reference values, whereas those in the control group showed significant increases. These findings seem to suggest that DEX can excite medullispinal and peripheral α_2A and α_2C adrenergic receptors to perform an analgesic effect (Hofer et al., 2009).

DEX can reduce the administered dose of analgesics, and can prevent the occurrence of nausea and emesis (Al-Zaben et al., 2010; Massad et al., 2009). A plasma propofol concentration at 1 mg/L in target controlled infusion during extubation can achieve a good sedative effect (Wang and Chen, 2008). Compared to propofol, although DEX shows a delay in action onset time, it can achieve a similar effect 25 min later (Arain and Ebert, 2002). BIS is an index used to reflect the electrical activity of the brain (Muhammad et al., 2012).

In the present study, the result showed that the experimental and control groups had no significant difference in this index, indicating that DEX combined with propofol does not result in a change in the recovery time of consciousness (Ohtani et al., 2008). A study has reported that DEX combined with sevoflurane does not prolong the recovery time of consciousness, but its combination with propofol does (Hofer et al., 2009). But in two other studies, a different result was obtained. The two different combination manners do not result in a significant difference in consciousness recovery time (Salman et al., 2009; Turgut et al., 2008). This study showed that the experimental and control groups had no significant differences in the recovery time of spontaneous respiration, extubation time, and eye opening time even though the experimental group had a delay in eye opening time when compared with the control group.

The application of DEX can reduce the catecholamine concentration in plasma (Jaakola et al., 1992; Talke et al., 2000; Zhou et al., 2012). The results in this study showed that the experimental group had obviously reduced restlessness reactions after extubation and lessened pain after operation; the restless scores in the experimental group at different time points were significantly lower than those in the control group. These findings indicate that the combination of DEX on the basis of the maintained administration of propofol and remifentanil before the end of operation can effectively inhibit reactions to extubation. Further, this study showed that the patients in the experimental group were more cooperative without restlessness and gastrointestinal reactions before and after extubation.

Conclusion

Micropump infusion of DEX at 0.2 ug kg^{-1} h^{-1} from 30 min before operation to the end of extubation can ease old patients' reactions to extubation; it reduces myocardial oxygen consumption to decrease the risk of cyclic fluctuation caused by coronary artery blood-supply insufficiency; furthermore, it does not delay consciousness recovery time. Therefore, DEX at such a dosage has a reliable and safe effect on extubation-induced reactions, and it is worth populating in clinical practice.

REFERENCES

Abdullah SS, Fahaid A, Abbas E, Hussein S, Mahmoud A (2012). EC50 of adrenaline-atenolol: Functional agonist assay using Langendorff isolated rabbit heart tethered to powerLab data acquisition system. Afr. J. Pharm. Pharmacol. 6:1092-1098.

Al-Zaben KR, Qudaisat IT, Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Oweidi AS, Abu-Halaweh SA, Abu-Ali HM, Saleem MM (2010). Intraoperative administration of dexmedetomidine reduces the analgesic requirements for children undergoing hypospadius surgery. Eur. J. Anaesthesiol. 27:247-252.

Arain SR, Ebert TJ (2002). The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. Anesth. Analg. 95:461-466.

Basali A, Mascha E, Kalfas I, Schubert A (2000). Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. Anesthesiology 93:48-54.

Bekker A, Sturaitis M, Bloon M, Moric M, Golfinos J, Parker E, Babu R, Pitti A (2008). The effect of dexmedetomidine on perioperative hemodynamics in patients undergoing craniotomy. Anesth. Analg. 107:1340-1347.

Groeneweg G, Huyren FJ, Coderre TJ, Zijlstra FJ (2009). Regulation of peripheral blood flow in complex regional pain syndrome: clinical implication for symptomatic relief and pin management. BMC Musculoskelet. Disord. 23:116.

Han M, Nie Y, Xiong JY (2011). Effect of of dexmedetomodine in total intravenous anesthesia: an observation on hemodynamics. Int. J. Anesthesiol. Resusc. 32:257-276.

Hofer S, Steppan J, Wagner T, Funke B, Lichtenstern C, Martin E, Graf BM, Bierhaus A, Weigand MA (2009). Central sympatholytics prolong survival in experimental sepsis. Care 13:R11.

Jaakola ML, Melkkila TA, Kanto J, Kallio A, Scheinin H, Scheinin M (1992). Dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in patients undergoing ophthalmic surgery. Br. J. Anaesth. 68:570-575.

Jalonen M, Hynynen M, Kuitunen A, Heikkilä H, Perttilä J, Salmenperä M, Valtonen M, Aantaa R, Kallio A (1997). Dexmedetomidine as an anesthetic adjunct in coronary artery bypass grafting. Anesthesiology 86:331-345.

Laubie M, Schmitt H, Vincent M (1979). Vagal bradycardia produced by microinjections of morphine-like drugs into the nucleus ambiguous in anaesthetized dogs. Eur. J. Pharmacol. 59:287-291.

Muhammad A, Ghiasuddin AS, Naveed M, Ashfaq AK, Bina SS (2102). Evaluation of Viburnum grandiflorum for its *in-vitro* pharmacological screening. Afr. J. Pharm. Pharmacol. 6:1606-1610.

Lee SH, Chim JL, Song MH, Choi HG, Choi BM, Lee HM, Lee EK, Roh YJ, Noh GJ (2009). Pharmacokinetics and pharmacodynamics of a new reformulated microemulsion and the long chain trglyceride emulsion of propofol in beagle dogs. Br. J. Pharmacol. 158:1982-1995.

Massad IM, Mohsen WA, Basha AS, Al-Zaben KR, Al-Mustafa MM, Alghanem SM (2009). A balanced anesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med. J. 30:1537-1541.

Nenmann MM, Davio MB, Macknet MR, Applegate RL 2nd (2009). Dexmedetomidine for awake fiberoptic intubation in a parturient with spinal musculer atrophy type III for cesarean delivery. Int. J. Obstet. Anesth. 18:403-407.

Ohtani N, Kida K, Shoji K, Yasui Y, Masaki E (2008). Recovery profiles from dexmedetomidine as a general anesthetic adjuvant in patients undeegoing lower abdominal suegery. Anesth. Analg. 107:1871-1874.

Salman N, Uzun S, Coskun F, Salman MA, Salman AE, Aypar U (2009). Dexmedetomidine as a substitute for remifentanil in ambulatory gynecologic laparoscopic surgery. Saudi J. 30:77-81.

Sanders RD, Maze M (2007). Alpha2-adrenoceptor agonists. Curr. Opin. Investig. Drugs 8:25-33.

Schlichter RA (2010). Dexmedetomidine is an excellent agent for sedation status-post lung transplant. J. Clin. Anesth. 22:1-2.

Souter MJ, Rozet I, Ojemonn JG, Souter KJ, Holmes MD, Lee L, Lam AM (2007). Dexmedetomidine sedation during awake craniotomy for seizuze resction: effects on electrocorticography. J. Neurosurg. Anesthesiol. 19:38-44.

Su WL, Chen YH, Chen CW, Yang SH, Su CL, Perng WC, Wu CP, Chen JH (2010). Involuntary cough strength and extubation outcomes for patients in an Intensive care unit: involuntary cough and extubation outcomes. Chest 137:2807-2808.

Talke P, Chen R, Thomas B, Aggarwall A, Gottlieb A, Thorborg P, Heard S, Cheung A, Son SL, Kallio A (2000). The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vasculary. Anesth. Analg. 90:834-839.

Tanskanen PE, Kytt JV, Randell TT, Aantaa RE (2006). Dexmedetomidine as an anesthetic adjuvant in patients undergoing intracracranial tumor surgery: a double-blind, randomized and placebo-controlled study. Br. J. Anesth. 97:658-665.

Turgut N, Turkmen A, Gokkaya S, Altan A, Hatiboglu MA (2008). Dexmedetomidine-based versus fentanyl-based total intravenous anesthesia for lumbar laminectomy. Minerva Anestesiol. 74:469-474.

Wang Y, Chen Y (2008). Application of propofol in prevention of the adverse effects during general anesthetic extubation. J. Clin. Anesthesiol. 24:177-178.

Zamora LJ, Cruz VJA, Rodriguez RJ, Sánchez RJP, Briones CG, Gallardo ALA (2007). Comparison of topical, intravenous, and intracuff lidocaine for reducing coughing after extubation during emergence from general anesthesia. Rev. Esp. Anestesiol. Reanim 54:596-601.

Zhou J, Wang J, Meng F(2012). The use of dexmedetomidine in aged patients with total hip replacement surgery under general anesthesia: Changes in hemodynamics, cerebral state index and wakening quality. Afr. J. Pharm. Pharmacol. 6:1833-1836.