Chronic Diseases Prevention Review 3 (2017) 1-7

Available at http:// www.cancercellresearch.org ISSN 2158-0820

Evaluation of clinical analgesic efficacy of dexmedetomidine combined with sufentanil on uterine contraction pain after hysteromyomectomy: a randomized controlled study

Yuncong Zhang, Feng Xue, Haichen Chu*, Juntao Wang, Xiao Zhang, He Dong

Department of Anesthesiology, Affiliated Hospital of Qingdao University Medical College, Qingdao, 266000, China

Abstract: **To evaluate the clinical analgesic efficacy of dexmedetomidine combined with sufentanil on uterine contraction pain after transabdominal hysteromyomectomy. 60 cases of patients applied with ASA I or II generalanesthesia in hysteromyomectomy, they are divided into two groups according to randomized double-blind control (n=30): Group S received 0.04ug/(kg•h) of sufentanil, Group Y received 0.025ug/(kg•h) of sufentanil combined with 0.03ug/(kg•h) of dexmedetomidine, both groups received compound use of 8mg Ondansetron and 2.5mg Inapsine, which are diluted into 100ml with normal saline, with background infusion at 2ml/h, PCA dose of 2ml and a 10min lockout interval. PCA pump was immediately connected after theoperation to record the BCS comfort scores, VAS scores, Ramsay sedation scores, effective pressing number within 48h, dose of sufentanil, nausea and vomiting scores, MAP, HR, SPO 2% at 4h(T1), 8h(T2), 16h(T3), 24h(T4) and 48h(T5) and satisfaction of patients within 48h. Compared with Group S, the VAS scores of Group Y at 4h(T1), 8h(T2), 16h(T3), 24h(T4) and 48h(T5) were lower, self-controlled effective pressing number within 48h declined, dose of sufentanil declined, and the possibility of nausea and vomiting rate declined as well (P<0.05), while the comparison of both groups on Ramsay sedation scores at each time point after 48h of operation was not statistically significant (P<0.05). The application of dexmedetomidine in PCIA after transabdominal hysteromyomectomy could decrease the dose of sufentanil, which could decrease the possibility of nausea and vomiting, obviously relieve the degree of uterine contraction pain, as well as promote the degree of comfortand satisfaction of patients.**

Keywords: uterine contraction pain; PCIA; dexmedetomidine; degree of comfort

Received 17 February 2017, Revised 23 May2017, Accepted 25 May 2017

*Corresponding Author: Haichen Chu, 18661805897@163.com

1. Introduction

Regular and strong contractions after transabdominal hysteromyomectomy are usually making patients suffering from pains, which is a leading cause of postoperative pain,seriously reduces the patient's comfort and is particularly common in patients allergic to oxytocin [1]. Dexmedetomidine is a kind of highly selective α2 adrenergic agonist, with function of analgesic, anxiolytic, sedation, sympathetic block and no respiratory inhibition [2,3]. Studies have showed that dexmedetomidine could decrease the dose of morphine, tramadol and other analgesic drugs, with purpose to increase analgesic effect [4,5]. In this preliminary study, dexmedetomidine combined with sufentanil was used for PCIA(patient controlled intravenous analgesia,PICA) after transabdominal hysteromyomectomy, to observe the controlling effect of uterine contraction pain and the possibility of adverse reactions, and to provide reference basis for clinical medication.

2. Clinical Information

2.1. Objects

The Research has been approved by Medical Ethics Committee of the Hospital, and an informed consent form has been entered into with patients or their families. Use double blind randomized controlled trial, 60 cases of patients applied with general anesthesia in transabdominal hysteromyomectomy, in ASA I or II were selected. patients allergic to hydrochloride dexmedetomidine or other drugs used in the research, with history of neuromuscular diseases, allergic diseases, mental illness, preoperative heart conduction with HR<50 beats/min, SBP<100mmHg or with rhythm abnormalities, potential gastrointestinal disorders and those who suffered from preoperative nausea, vomiting, motor function decreased or highly sensitive to drugs used in the research were excluded. They were divided into two groups according to randomized double-blind control: Group of sufentanil (Group S) and Group of sufentanil combined with dexmedetomidine (Group Y), each group has 30 cases.

2.2. Anesthetic methods

Tracheal intubation with intravenous anesthesia was used and 30 min before this, patients were applied with conventional intramuscular injection of 0.3mg scopolamine.Bleeding after opening the peripheral vein, routine monitoring of blood pressure MAP, HR, SPO_2%, ECG, BIS and $PetCO_2$. During operation, infusion of lactated Ringer's solution was used to maintain hemodynamic stability. Anesthesia was induced by propofol of 1.5ug/kg,sufentanil of

0.3ug/kgand cisatracurium of 0.3mg/kg; maintain the use of sufentanil 0.1ug/(kg·min), 6 mg/(kg·h) of propofol, with intermittent intravenous injection of 3-5 mg cisatracurium. During operation, all patients received lactated Ringer's solution and 6% hydroxyethyl starch to maintain hemodynamic stability. Cisatracurium was stopped 30min before the operation ended, and after the operation, the patients were connected with PCA pump and sent to recovery room.

2.3. Observation indicators

BSC scores, VAS scores, Ramsay scores were used to evaluate the postoperative comfort, pain and sedation degree of both groups at 4h (T1), 8h(T2), 16h(T3), 24h(T4) and 48h(T5), to record the PCIA pressing time, the number of remedial drug use, scores of nausea and vomiting, BP, HR, SPO_2% at 0-4 h, 4-8h, 8-16h, 16-24h, 24-48h and satisfaction of patients within 48h.

BCS scores: 0 means Persistent pain, 1 score means painless when quiet; great pain at deep breath or a cough; 2 scores means painless while laid down in quiet, but slight pain at deep breath or a cough; 3 scores means painless while breathing; 4 scores means painless while coughing.

2.4. Statistical method

SPSS 19.0software was used to analyze data. All measurement data and information will be expressed with average ± standard deviation (x±s), difference comparison between two groups will be tested by to find dependent samples and chi-square test.

3. Results

3.1. The comparison of cases

The comparison on age, weight, height, operation time and other related matters is not statistically significant (P＞0.05), which aged from 24-52, BMI of 19.43～29.69kg/m^2 (Table 1).

Table 1 Comparison of Basic Information of Patients in Both Groups (x±s, n=30)

	Group S	Group Y	P
Age	43.30±5.46	41.73±6.65	0.388
Weight (kg)	65.40±8.75	63.45±7.47	0.234
Height (m)	1.63±0.05	1.61±0.04	0.437
Operation Time (min)	98.17±12.00	96.00±14.29	0.158
Anesthesia time (min)	7.57±1.07	7.43±0.94	0.295

3.2. The comparison of cases of Group S and Y

As compared with Group S, MAP of Group Y at 4h declined , the difference was statistically significant (P<0.05), at 8h, 12h, 16, 24h and 48h was not statistically significant (P)>0.05). SPO2 %value of both groups were greater than 98% (postoperative conventional low-flow oxygen 2L/min), not statistically significant (P>0.05). See Table 2, 3, 4. Comparison of Postoperative MAP, HR, SPO_2% of Patients in Both Groups at Each Time Point (x±s, n=30).

Table 2 Indicators: MAP(mmHg)(x±s, n=30)

	Group S	Group Y	P
T1	89.83±2.06	84.31±4.03	0.008
T2	89.13±2.80	84.21±4.01	0.145
T3	87.83±3.43	83.97±3.15	0.642
T4	88.48±2.84	84.71±2.63	0.572
T5	88.58±2.89	85.37±1.93	0.095

Table 3 Indicators: HR (Times/min) (x±s, n=30)

	Group S	Group Y	P
T1	72.03±2.20	65.83±2.98	0.080
T2	72.47±2.76	65.30±2.79	0.517
T3	72.13±3.18	64.20±2.66	0.202
T4	72.17±3.06	64.00±2.78	0.350
T5	72.47±2.91	65.07±3.37	0.155

Table 4 Indicators: SPO_2% (x±s, n=30)

	Group S	Group Y	P
T1	98.83±0.53	98.73±0.45	0.976
T2	98.73±0.58	98.77±0.57	0.980
T3	98.87±0.57	98.70±0.53	0.234
T4	98.87±0.51	98.73±0.52	0.263
T5	98.87±0.35	98.80±0.41	0.172

3.3. Comparison of operation information

As compared with Group S, the postoperative effective pressing numbers of Group Y at each time point declined significantly, the difference was statistically significant (P<0.05), and the postoperative dose of sufentanil at each time point declined significantly, the difference was statistically significant (P<0.05), no patient was applied with remedial drugs. See Table 5 and 6.

Table 5 Comparison of PostoperativeEffective Pressing Numbers of Both Groups within 48h

	Group S(n=30)	Group Y(n=30)	P
	10(33.3%)	27(90.0%)	
T1	7(23.3%)	3(10.0%)	<0.01
	13(43.3%)	0(0.0%)	
	0(0.0%)	19(63.3%)	
T2	11(36.7%)	11(36.7%)	<0.01
	19(63.3%)	0(0.0%)	
	0(0.0%)	16(53.3%)	
T3	4(13.3%)	14(46.7%)	<0.01
	26(86.7%)	0(0.0%)	
	0(0.0%)	17(56.7%)	
T4	2(6.7%)	13(43.3%)	<0.01
	28(93.3%)	0(0.0%)	
	0(0.0%)	16(53.3%)	
T5	9(30.0%)	14(46.7%)	<0.01
	21(70.0%)	0(0.0%)	

Table 6 Comparison of Postoperative Dose of Sufentanil(ug) of Both Groups within 48h (x±s, n=30)

	Group S	Group Y	P
T1	9.90±1.28	6.49±0.38	0.000
T2	21.23±2.28	13.31±1.02	0.001
T3	40.58±3.04	25.87±1.29	0.001
T4	58.55±5.28	38.53±1.65	0.000
T5	96.84±3.59	76.31±3.22	0.033

3.4. The comparison of scores of Group S and Y

Comparison of postoperative BCS scores, VAS scores and Ramsay scores of both groups at each time point within 48h: as compared with Group S, VAS scores of Group Y at 4h, 8h,16h, 24h and 48h declined significantly, the difference was statistically significant (P<0.05), BCS scores of Group Y at 4h, 8h, 16h, 24h and 48h increased, the difference was statistically significant (P<0.05).Ramsay scores of Group Y at 4h, 8h, 16h, 48h increased, the difference was statistically significant (P<0.05), there was no significant differerce at 24h time points(P>0.05).See Table 7, 8, 9.

Table 7 Comparison of postoperative BCS scores of both groups at each time point within 48h

	Group S(n=30)	Group Y(n=30)	P
	23(76.7%)	0(0.0%)	
T1	7(23.3%)	8(26.7%)	<0.01
	0(0.0%)	22(73.3%)	
	23(76.7%)	0(0.0%)	
T2	7(23.3%)	11(36.7%)	<0.01
	0(0.0%)	19(63.3%)	

	25(83.3%)	0(0.0%)	
T3	5(16.7%)	10(33.3%)	<0.01
	0(0.0%)	20(66.7%)	
	25(83.3%)	0(0.0%)	
T4	5(16.7%)	19(63.3%)	<0.01
	0(0.0%)	11(36.7%)	
	25(83.3%)	0(0.0%)	
T5	5(16.7%)	12(40.0%)	<0.01
	0(0.0%)	18(60.0%)	

Table 8 Comparison of postoperative VAS scores of both groups at each time point within 48h

	Group S(n=30)	Group Y(n=30)	P
	0(0.0%)	13(43.3%)	
T1	15(50.0%)	17(56.7%)	<0.01
	15(50.0%)	0(0.0%)	
	0(0.0%)	14(46.7%)	
T2	9(30.0%)	16(53.3%)	<0.01
	21(70.0%)	0(0.0%)	
	0(0.0%)	10(33.3%)	
T3	10(33.3%)	20(66.7%)	<0.01
	20(66.7%)	0(0.0%)	
	0(0.0%)	15(50.0%)	
T4	17(56.7%)	15(50.0%)	<0.01
	13(43.3%)	0(0.0%)	
	0(0.0%)	19(63.3%)	
T5	17(56.7%)	11(36.7%)	<0.01
	13(43.3%)	0(0.0%)	

Table 9 Comparison of postoperative Ramsay scores of both groups at each time point within 48h

	Group S (n=30)	Group Y (n=30)	P
	13(43.3%)	1(3.3%)	
T1	16(53.3%)	25(83.3%)	<0.01
	1(3.3%)	4(13.3%)	
	16(53.3%)	1(3.3%)	
T2	14(46.7%)	26(86.7%)	<0.01
	0(0.0%)	3(10%)	
	10(33.3%)	0(0.0)	
T3	18(60%)	29(96.7%)	<0.01
	2(6.7%)	1(3.3%)	
	5(16.7%)	1(3.3%)	
T4	24(80%)	27(90.0%)	0.204
	1(3.3%)	2(6.7%)	
	5(16.7%)	0(0.0%)	
T5	23(76.7%)	29(96.7%)	0.049
	2(6.7%)	1(3.3%)	

3.5. The comparison possibility of adverse reactio of Group S and Y

Comparison of possibility of adverse reactions during sedation (n=30,x+s), see Table 10, 11.

Table 10 Nausea

	Group S(n=30)	Group Y(n=30)	P
T1	22(73.3%)	29(96.7%)	0.013
	8(26.7%)	1(3.3%)	
	8(26.7%)	28(93.3%)	
T2	17(56.7%)	2(6.7%)	<0.01
	5(16.7%)	0(0.0%)	

	1(3.3%)	28(93.3%)	
T3	12(40.0%)	2(6.7%)	<0.01
	17(56.7%)	0(0.0%)	
	0(0.0%)	29(96.7%)	
T4	12(40.0%)	1(3.3%)	<0.01
	18(60%)	0(0.0%)	
	2(6.7%)	29(96.7%)	
T5	14(46.7%)	1(3.3%)	<0.01
	14(46.7%)	0(0.0%)	

Table 11 Vomiting

	Group S(n=30)	Group Y(n=30)	P
T1	29(93.3%)	30(100.0%)	0.50
	2(6.7%)	0(0.0%)	
T2	23(76.7%)	29(96.7%)	0.026
	7(23.3%)	1(3.3%)	
T2	12(40.0%)	30(100.0%)	<0.01
	18(60.0%)	0(0.0%)	
T2	9(30.0%)	30(100.0%)	<0.01
	21(70.0%)	0(0.0%)	
T2	2(6.7%)	30(100.0%)	<0.01
	28(93.3%)	0(0.0%)	

As compared with Group S, the postoperative nausea and vomiting scores of Group Y declined significantly, the difference was statistically significant (P<0.05). In Group Y, there were 2 cases of mild nausea and no bradycardia, hypotension, transient high blood pressure, skin itching and respiratory depression and other adverse reactions. As compared with Group S, the patient satisfaction of Group Y was better than that of Group S. ECG of both groups has no Q-T interval prolongation.

3.6. Satisfaction Survey

Table 12 Satisfaction Survey

Group Case	Very satisfied	Satisfied	Pretty	Not satisfied	Satisfaction (%)
Group S 30	0	6	24	0	20%
Group Y 30	26	3	1	0	96.67%

4. Discussion

As the main reason for postoperative pain,cuterine contraction painafter hysterectomy has affected the patient's comfort. Uterine contraction pain appears as sustained colic and is associated with uterine contraction. Postoperative intravenous oxytocin will aggravate the uterine contraction, causing the uterine contraction painunbearable and bringing patients with physical and mental trauma. Previous studies on uterine pain were less reported and did not attract much attention. In recent years, studies confirmed that intraoperative uterine pain sensitization can cause spread and prolongation of postoperative pain [6]. So the effective postoperative analgesia is necessary. Studies of Semra Karaman MD et al [7,8] showed that, with the dose increased, dexmedetomidine can significantly enhance the uterine smooth muscle contraction in vitro frequency and amplitude. From this perspective, Dexmedetomidine reduced the amount of uterine contractions by reducing the amount of uterotonic agents used. As a kind of new and highly selective α_2 adrenergic agonist, dexmedetomidine has functions of cell membrane hyperpolarization, inhibition of pain signals to the brain conduction by acting on postsynaptic α_2 adrenergic receptors in the presynaptic and intermediate neurons of dorsal horn of the spinal cord, so that the nervous system is inhibited [9]. Research has shown that [10-12], on and above spinal cord, and even the peripheral αAAR and αCAR are involved in analgesic effect. In addition, it acts through the central level: after integrating with brain stem blue spot of the α_2 receptor, it ended the pain signal conduction [13]. Inhibiting downstream medulla - spinal norepinephrine could provide access to release of presynaptic membrane substance P and other potentially injurious peptides (bradykinin, leukotrienes, prostaglandins, serotonin and lactic acid), reducing the sense of discomfort of uterine contractions. By activation of brain stem blue spot, it could also initiate and maintain natural non-eye movement sleep and result in short-term hypnotic sedation [5]. Study of Gurbet has shown that independent use of dexmedetomidine could have effect of not only sedation, but also reducing the unpleasant emotions caused by pain [14]. The effect of dexmedetomidine is a ceiling one [15]. Thus it could not substitute opioids

drugs. This is similar with results of Arain et al studies [16,17].

Refer to the pre-test results, the results of this study showed that by selecting 0.025ug/(kg•h) sufentanil as background infusion for observation, which dose is a lower effective dose of sufentanil, when background infusion had a dose of 0.03ug/(kg•h) dexmedetomidine and 0.025ug/(kg•h) sufentanil, patients did not intend to fall asleep, but the sedation effect was increased with a premise that possibility of respiratory depression was not increased [18], thus it alleviate the uterine contraction pain pain, improve comfort of patients and satisfaction, achieved its function of sedation and analgesia. Thus the suitable dose is recommended to be 0.03ug/(kg•h) dexmedetomidine and 0.025ug/(kg•h) sufentanil.

In this study, as compared with the group that independently supplied with sufentanil (Group S), the nausea and vomiting possibility of Group Y declined significantly, dose of sufentanil and PCIA pressing numbers within 48h, postoperative uterine contraction pain VAS scores declined significantly, postoperative dexmedetomidine combined with sufentanil is considered for multi-modal analgesia, which could effectively decrease the total dose of opioids and the possibility of its adverse reactions, meanwhile, dexmedetomidine could alleviate the pain and reduce the stress response. It has been reported that the use of dexmedetomidine can reduce the incidence of postoperative nausea and vomiting [19,20]. BCS scores of Group Y at 4h, 8h, 16h, 24h and 48h increased, the difference was statistically significant ($P<0.05$), Ramsay scores of Group Y at 4h, 8h, 16h, 48h increased, the difference was statistically significant ($P<0.05$), there was no significant differerce at 24h time points ($P>0.05$).

In summary, the sedation formula of 0.03ug/(kg•h) dexmedetomidine and 0.025ug/(kg•h) sufentanil not only significantly reduced the degree of uterine contraction pain, made hemodynamic steady with obvious effect of sedation [21], but also reduced the dose of sufentanil, which could reduce the possibility of adverse reactions, improve the comfort and satisfaction of patients, as well as improved the postoperative analgesia effect on patients after applied with transabdominal hysteromyomectomy.

References

[1] Ghulmiyyah LM, Usta IM, Ghazeeri G, et al. Intravenous Oxytocin Use to Decrease Blood Loss during Scheduled Cesarean Delivery:A Randomized Double-Blinded Controlled Trial (OXYTRIAL)[J]. American journal of perinatology, 2017, 34(4):379-87.

[2] Dong CS, Zhang J, Lu Q, et al. Effect of Dexmedetomidine combined with sufentanil for post- thoracotomy intravenous analgesia:a randomized, controlled clinical study[J]. BMC anesthesiology, 2017, 17(1):33.

[3] Stemp LI, Karras GE. Dexmedetomidine facilitates withdrawal of ventilatory support[J]. Anesthesiology, 2006, 104(4):890.

[4] Lin TF, Yeh YC, Lin FS, et al. Effect of combining dexmedetomidine and morphine for intravenous patient-controlled analgesia[J]. Br J Anaesth, 2009, 102(1):117-122.

[5] Martin E, Ramsay G, Mantz J, et al. The Role of the α2-Adrenoceptor Agonist Dexmedetomidine in Postsurgical Sedation in the Intensive Care Unit[J]. 2003, 18(1):29-41.

[6] Zhiyong XU. Effect of analgesia on uterine contraction-induced pain after cesarean section[J]. Jiangsu Medical Journal, 2010.

[7] Karaman S, Evren V, Firat V, et al. The effects of dexmedetomidine on spontaneous contractions of isolated gravid rat myometrium[J]. Advances in Therapy, 2006, 23(2):238-243.

[8] Sia AT, Kwek K, Yeo GS. The in vitro effects of clonidine and dexmedetomidine on human myometrium[J]. International Journal of Obstetric Anesthesia, 2005, 14(2):104-107.

[9] Zhang Y, Duan G, Guo S, et al. To predict sufentanil requirement for postoperative pain control using a real-time method:A prospective observational cohort study[J]. Medicine, 2016, 95(25):3915.

[10] Axelsson K, Gupta A. Local anaesthetic adjuvants: neuraxial versus peripheral nerve block[J]. Curr Opin Anaesthesiol, 2009, 22(5):649-654.

[11] Eisenach JC. Alpha-2 agonists and analgesia[J]. Expert Opinion on Investigational Drugs, 2008, 3(10):1005-1010.

[12] Mizrak A, Koruk S, Bilgi M, et al. Pretreatment with dexmedetomidine or thiopental decreases myoclonus after etomidate: a randomized, double-blind controlled trial[J]. Journal of Surgical Research, 2010, 159(1):e11.

[13] Khan ZP, Munday IT, Jones RM, et al. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers. 1: Pharmacodynamic and pharmacokinetic interactions[J]. British Journal of Anaesthesia, 1999, 83(3):372.

[14] Gurbet A, Basagan-Mogol E, Turker G, et al. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements[J]. Canadian journal of anaesthesia = Journal canadien d'anesthesie, 2006, 53(7):646-652.

[15] Hanoura SE, Saad RH, Singh R. Dexmedetomidine improves intraoperative conditions and quality of postoperative analgesia when added to epidural in elective cesarean section[J]. Egyptian Journal of Anaesthesia, 2014, 30(4):353-357.

[16] Arain SR, Ruehlow RM, Uhrich TD, et al. The efficacy of dexmedetomidine versus morphine

for postoperative analgesia after major inpatient surgery[J]. Anesthesia & Analgesia, 2004, 98(1):153-8, table of contents.

[17] Alzaben KR, Qudaisat IY, Alghanem SM, et al. Intraoperative administration of dexmedetomidine reduces the analgesic requirements for children undergoing hypospadius surgery[J]. European Journal of Anaesthesiology, 2010, 27(3):247-252.

[18] Alsarra IA, Alanazi FK, Mahrous GM, et al. Clinical evaluation of novel buccoadhesive film containing ketorolac in dental and post-oral surgery pain management[J]. Die Pharmazie, 2007, 62(10):773-778.

[19] Bakri MH, Ismail EA, Ibrahim A. Comparison of dexmedetomidine and dexamethasone for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy[J]. Korean journal of anesthesiology, 2015, 68(3):254.

[20] Park SH, Shin YD, Yu HJ, et al. Comparison of two dosing schedules of intravenous dexmedetomidine in elderly patients during spinal anesthesia[J]. Korean journal of anesthesiology, 2014, 66(5):371-376.

[21] Ossipov MH, Suarez LJ, Spaulding TC. Antinociceptive interactions between alpha 2-adrenergic and opiate agonists at the spinal level in rodents[J]. Anesthesia & Analgesia, 1989, 68(3):194-200.

