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Intranasal Dexmedetomidine in Termination of First Trimester Pregnancy of Suction Evacuation

Hang Shi[1], **Duo Yang**[2] **and Jie Liu**[3*]

[1]*Department of Dermatology, The First Hospital of Dalian Medical University, China*

[2]*Department of Anesthesiology, Qingdao Women and Children's Hospital, China*

[3]*Department of Anesthesiology, The Second Hospital of Dalian Medical University, China*

[*]**Corresponding author:** Jie Liu, Department of Anesthesiology, The Second Hospital of Dalian Medical University, China, Tel: 86-411-84671291-5066; Fax: 86-411-84671291; E-mail: liujaye@hotmail.com

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Abstract

Background and aim: Deep sedation without intubation for termination of first trimester pregnancy of suction evacuation entails use of sedatives such as propofol or a combination of propofol and sulfentanil, with unwanted complications. Dexmedetomidine is a α_2-adrenorecepter agonist which provides sedation, anxiolysis and analgesia, without any of the complications associated with the popular sedatives.

Methods: A total number of 90 patients were randomized to three groups: 1. Group P, treated with intranasal saline, intravenous saline and propofol; 2. Group DP, treated with intranasal dexmedetomidine, intravenous saline and propofol; and 3. Group SP, treated with intranasal saline, intravenous sulfentanil and propofol. The primary outcome was the consumption of propofol, and the secondary outcomes were numeric rating scale (NRS) anxiety score, NRS pain score of uterine cramping, amount of blood loss, use of oxytocin and NRS satisfaction scores of obstetric and gynecological (ob/gyn) physicians and patients.

Results: The consumption of propofol, NRS pain score of uterine cramping after surgery, NRS anxiety score, and amount of blood loss in group DP were significantly lower than those in group P and group SP. Ob/gyn physicians' satisfaction score in group DP was significantly higher compared with group SP and group P. Registry number for clinical trials: ChiCTR-IPR-14005654.

Conclusion: Sedation with intranasal dexmedetomidine (1 μg/kg) provided effective analgesia and anxiolysis, reduced consumption of propofol and lower blood loss in termination of first trimester pregnancy of suction evacuation. Compared with propofol or the combination of propofol and sulfentanil, intranasal dexmedetomidine was associated with higher satisfaction score of ob/gyn physicians. No unforeseen perioperative respiratory and cardiovascular adverse events occurred.

Keywords: Suction evacuation; First trimester pregnancy; Intranasal dexmedetomidine; Sedation.

Introduction

Termination of first trimester pregnancy of suction evacuation is a minor surgical procedure in gynecology and obstetrics with associated perioperative pain and anxiety. In USA, many women experience significant pain although obstetric and gynecological (ob/gyn) physicians usually provide a paracervical block of 10-20 mL of 1% lidocaine to relief the pain during suction evacuation [1]. Conscious sedation with combination of intravenous midazolam 1-3 mg and fentanyl 50–100 μg is often used [1], but available studies do not support the efficacy of this practice [2,3]. Deep sedation without intubation is feasible in termination of first trimester pregnancy of suction evacuation in the outpatient setting [4]. Propofol and combination of propofol and sulfentanil are widely used for termination of first trimester pregnancy of suction evacuation with satisfactory deep sedation and surgical condition in China [5]. However, these sedatives are associated with the risk of respiratory depression, hypoxemia, infusion pain, postoperative nausea and vomiting [5]. Dexmedetomidine is a highly selective α_2-adrenoceptor agonist with sedative, anxiolytic and analgesic effects [6]. Dexmedetomidine has been used as a sedative agent in intensive care unit and an anesthetic adjunct in surgery [7-9]. Recently, more and more studies propose it as a sedative agent in moderate sedation for clinical surgeries/procedures [10-13]. Intravenous infusion of dexmedetomidine is commonly used, but rapid administration or bolus might cause bradycardia and hypotension [14]. In addition, the analgesic effect of intravenous dexmedetomidine is inconsistent [15-18]. Therefore, different routes of administration and multimodal analgesia are suggested in future studies. Intranasal dexmedetomidine is convenient and non-invasive, and it provides sedative and analgesic effects during surgery/procedure for both children and adults without any adverse effects of respiratory depression, bradycardia, or discomfort of intranasal drips [10,11,19,20]. The number of clinical trials those have evaluated the clinical use of intranasal dexmedetomidine in sedation for surgery and clinical procedures is limited. To date, however, no study has been conducted to explore the clinical use of intranasal dexmedetomidine in termination of first trimester pregnancy of suction evacuation, the purpose of this study. Consumption of propofol was used as a measure of efficacy. In this

double-blind, randomized, placebo-controlled study, we hypothesized that total consumption of propofol would be significantly less for patients receiving intranasal dexmedetomidine when compared with two other mainly used medications in China, propofol and combination of propofol and sulfentanil.

Methods

The study protocol was approved by Institutional Review Board of the second hospital of Dalian Medical University and the registry number was ChiCTR-IPR-14005654.

We recruited 90 nulliparous pregnant (gestational age 8-10 weeks, determined by last menstrual period, and intrauterine pregnancy confirmed by ultrasound) ASA I-II patients, aged 18-35 years who were undergoing elective termination of first trimester pregnancy of suction evacuation at the second hospital of Dalian Medical University. Patients with known dead fetus, multi fetus, ectopic pregnancy, cornual pregnancy, cervical pregnancy, incomplete abortion, allergy or regular use of dexmedetomidine, opioids, propofol and sedatives, and history of abortion or labor, miscarriage or cesarean delivery, impaired liver or renal function, alcohol consumption in excess of 28 units per week, known psychological disorders, asthma, heart disease, BMI>24 kg/m^2, sleep apnea syndrome and patient refusal were excluded. After obtaining written informed consent, patients were randomized to three groups. A computer-generated random sequence was used for drug allocation, and this was prepared by a statistician who was unaware of the clinical nature of the study.

This statistician was the one who prepared intranasal drugs (saline or dexmedetomidine) and intravenous drugs (saline or sulfentanil) before sedation according to the sequence. Neither patients nor ob/gyn physicians knew the sequence. An attending anesthesiologist who did not know the sequence was in charge of sedation, giving drug and discharge.

A nurse in Post Anesthesia Care Unit (PACU) who was in charge of patients after surgery did not know the sequence either. No premedication was given. In group P, patients received intranasal saline, intravenous saline and propofol; in group DP, patients were given intranasal dexmedetomidine, intravenous saline and propofol; while the group SP patients were administered intranasal saline, intravenous sulfentanil and propofol. Vital signs including HR, BP, pulse Oxygen Saturation (SpO_2) and respiratory rate (RR) (S/5 Anesthesia Monitor, Datex-Ohmeda, WI, USA) were monitored as baseline parameters. Patients received saline (0.01 ml/kg) or dexmedetomidine (200 μg/2 mL) 1 μg/kg intranasally. The intranasal drug was stored in one 1 ml syringe.

Before intranasal drug administration, patients gently blew their noses. The attending anesthesiologist administered equal volume of intranasal drug to each naris as drops. Numeric rating scale (NRS) score of discomfort of intranasal drips (0=no discomfort, 10=worst discomfort) was recorded. Vital signs were recorded every 5 min, while Observer's Assessment of Alertness/Sedation (OAA/S) and NRS anxiety score (0=no anxiety, 10=worst anxiety) were obtained every 15 min. If $SpO_2 \leq 92\%$ or RR<10 beat per minute (bpm), patient was given oxygen delivery on intermittent positive pressure with facial mask until patient's SpO_2 was 100% or RR ≥ 10 bpm. The oxygen flow was 5 L/min when connected with facial mask by tube.

In previous study, 1 μg/kg intranasal dexmedetomidine provided adequate sedation within 30-45 min [4,19]. Thus, in this clinical trial, patients were transferred to the operation bed 45 min later and placed in the lithotomy position.

Oxygen inhalation was administrated through nasal catheter with oxygen flow 2 L/min. A 22G intravenous catheter was inserted into the right median cubital vein, and 0.04 ml/kg saline or 0.1 μg/kg sulfentanil (2.5 μg/mL) was injected after recording the NRS pain score of IV insertion (0=no pain, 10=worst pain). One minute later, 2 mg/kg propofol was infused into the patient's vein, and the NRS pain score of propofol injection (0=no pain, 10=worst pain) was obtained. When the patient's OAA/S ≤ 3, surgery was initiated. If the patient's OAA/S exceeded 3 or patients moved, a bolus of 20 mg propofol was injected as a rescue repeatedly until the patient was still or OAA/S ≤ 3, as needed. The electric suction machine (6000 XL electric vacuum aspiration machine, Andelu, Nanjing, China) was used for this surgery.

All the suction was collected and filtrated by a filter screen. The filtrated fluid was the blood loss and was counted by mL. The rest of suction, which was solid and called suction tissue, was weighted. Oxytocin of 10 U was injected intravenously if blood loss was greater than or equal to 10 mL. Vital signs were recorded every 3 min during the surgery. If $SpO_2 \leq 92\%$ or RR<10 bpm, patient was given oxygen delivery on intermittent positive pressure with facial mask until patient's SpO_2 was 100% or RR ≥ 10 bpm. The oxygen flow was 5 L/min when connected with facial mask by tube. If HR<50 bpm, atropine 0.5 mg was given intravenously and if mean arterial pressure (MAP)<60 mmHg, 5 mg intravenous ephedrine was given. After the surgery, patients were monitored on the operation bed until they were awake (OAA/S=4).

Patients were moved to the bed of PACU and their vital signs and OAA/S were monitored and recorded by nurse every 5 min. NRS pain score of uterine cramping (0=no pain, 10=worst pain) was obtained from patients every 15 min in the next 30 min. If patients got nausea, vomiting, dizziness, drowsiness and dry mouth, the nurse in PACU would record.

Patients were discharged when reached the criteria of post-anesthesia discharge scoring system (PADSS, Appendix 1), after recording their blood loss, oxytocin injection, amount of suction tissue, surgical condition (Appendix 2), duration of surgery, duration from end of surgery to awake, duration from awake to getting off the bed, duration from awake to discharge and NRS satisfaction scores (0=completely unsatisfied, 10=completely satisfied) of the ob/gyn physician and patient respectively.

The primary endpoint was the dosage of propofol. We considered a clinically significant difference in propofol dosage in group DP to be 0.5 mg/kg, and previous study showed that the mean dosage of propofol used in abortion was 3.56 ± 0.98 mg/kg [5].

To obtain 85% power of test at the 5% level of significance, the requested sample size was 29 per group. The total sample size was 90 with 30 per group, to allow for possible patient dropouts. The secondary outcomes were NRS anxiety score, NRS pain scores of uterine cramping, amount of blood loss, use of oxytocin and NRS satisfaction scores of ob/gyn physicians and patients. Graphpad Prism version 6.05 for Windows (GraphPad Software, La Jolla California USA) was used to perform the statistical analysis. Categorical data were analyzed by Fishers exact test.

Perioperative vital signs, NRS pain scores of anxiety, uterine cramping, propofol injection and IV insertion, duration of surgery, duration from end of surgery to awake, duration from awake to getting

off the bed, duration from awake to discharge, amount of suction tissue and blood loss, dosage of propofol, NRS satisfaction scores of ob/gyn physicians and patients were analyzed by Wilcoxon signed rank test. The surgical condition, use of oxytocin and adverse events were analyzed by Fishers exact test. P<0.05 was considered statistically significant.

Results

Ninety patients were recruited. Patients' clinical demographics and surgical profile were listed in Tables 1 and 2. No significant difference was found in demographic data, duration of pregnancy, duration of surgery, duration from end of surgery to awake, duration from awake to getting off the bed, duration from awake to discharge, amount of suction tissue, NRS score of discomfort of intranasal drip or NRS satisfaction scores of patients' among three groups.

Amount of blood loss in group DP was significantly lower than that in group P (5 ml versus 7.5 ml, p<0.05) and group SP (5 ml versus 10 ml, p<0.05). Usage of oxytocin in group DP was significantly lower than that in group P (5U versus 10U, p<0.05) and group SP (5U versus 12U, p<0.05). NRS pain scores of propofol injection in groups DP (0.7 versus 2.8, p<0.001) and SP (1.4 versus 2.8, p<0.05) were significantly lower than that in group P.

The NRS satisfaction score of ob/gyn physicians in group DP was significantly higher than in group P (9.7 versus 8.4, p<0.001) and group SP (9.7 versus 9.1, p<0.05). The surgical condition ranked as good in group DP was significantly more than that in group P (26 versus 18, p<0.05) and group SP (26 versus 20, p<0.05), while surgical condition ranked as fair in group P (12 versus 4, p<0.001) and group SP (10 versus 4, p<0.001) were significantly more than that in group DP, no difference was found between group P and group SP.

	Group P (n=30)	Group SP (n=30)	Group DP (n=30)
Age (yrs)	26.7 (4.8) (20-35)	28 (4.1) (21-35)	27.3 (4.5) (21-35)
Body weight (kg)	56.3 (5.3) (50-65)	56.6 (5.5) (50-65)	55.3 (5.1) (48-65)
BMI (kg/m^2)	20.8 (1.7) (19-24)	21.0 (1.6) (19-23.5)	20.6 (1.5) (19-23)
ASA status I	30 (100%)	30 (100%)	30 (100%)
II	0 (0%)	0 (0%)	0 (0%)
Duration of pregnancy (weeks)	9.2 (1.1) (8-10)	9.1 (1.0) (8-10)	9.1 (0.9) (8-10)
*No significant difference was found among three groups. Data shown are number (percentage) or means (SD) (range) within the group			

Table 1: Preoperative patients' characteristics and data.

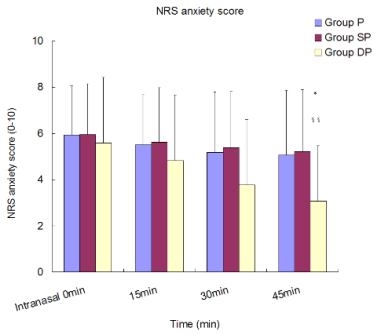

Figure 1: NRS anxiety score from intranasal Dex/Saline start to 45 min (X ± SD).

NRS anxiety score from intranasal dexmedetomidine/saline start to 45 min was shown as Figure 1. Forty-five min after intranasal Dex/saline, the NRS anxiety score in group DP was significantly lower compared with group P (3.2 versus 5.0, p<0.05) and group SP (3.2 versus 5.2, p<0.01). No difference was found at other time points among the three groups.

At 45 min after intranasal Dex/Saline, NRS anxiety score in group DP was significantly lower compared with group P and group SP (P<0.05 and P<0.01, respectively). (*P<0.05 when group P compared with group DP, §§P <0.01 when group SP compared with group DP).

Figure 2 showed rescue and total dosage of propofol. Both rescue and total dosage of propofol used in group DP were significantly lower than in group P and SP (P<0.001 and P<0.01, respectively). No difference was found between group P and group SP. Rescue and total dosage of propofol used in group DP was significantly lower compared with group P and SP (P<0.001 and P<0.01, respectively). (***P<0.001 when group P compared with DP, §§ P <0.01 when group SP compared with group DP).

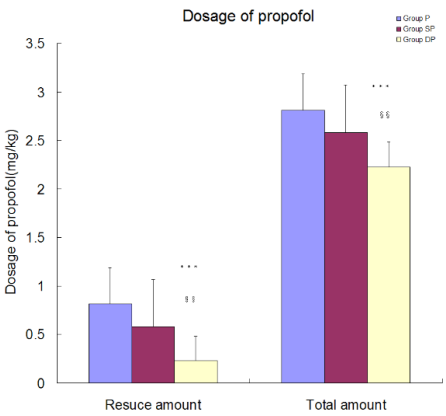

Figure 2: Rescue and total dosage of propofol (X ± SD).

	Group P (n=30)	Group SP (n=30)	Group DP (n=30)
Surgical condition Good	18 (60%)	20 (67%)	26 (87%)*§
Fair	12 (23%)	10(27%)	4 (13%)***§§§
Poor	0	0	0
Very poor	0	0	0
Duration of surgery (min)	4.8 (1.6) (3-8)	4.6 (1.6) (3-8)	4.0 (1.2) (3-7)
Duration from end of surgey to awake (min)	3.5 (1.4) (1-7)	4 (1.4) (2-7)	3 (1.2) (1-6)
Duration from awake to getting off the bed (min)	4.5 (1.5) (2-9)	5.2 (2.2) (2-10)	4.5 (2.5) (2-12)
Duration from awake to discharge (min)	35 (2.5) (28-40)	34.5 (6.8) (30-40)	34 (2.1) (30-40)
Amount of suction tissue (g)	3 (1.5) (1-6)	2.75 (2.2) (1-8)	3 (1.1) (1-6)
Blood loss (mL)	7.5 (4.3) (5-20)	10 (4.6) (5-20)	5 (2.2) (5-10) §
Oxytocin (U)	1033%	1243%	517%*§
NRS score of discomfort of intranasal drip (0-10)	1.2 (0.8) (0-2)	1.1 (0.9) (0-2)	1.0 (0.8) (0-2)
NRS score of IV insertion (0-10)	2.8 (2.4) (0-8)	1.9 (1.3) (0-7)	2.6 (2.5) (0-5)
NRS pain score of propofol injection (0-10)	2.8 (2.2) (0-8)	1.4 (2.2) (0-5)	0.7 (1.2) (0-5)***
NRS satisfaction score of ob/gyn physicians (0-10)	8.4 (1.4) (3-10)	9.1(1.1) (7-10)	9.7 (0.6) (8-10)*§
NRS satisfaction score of patients (0-10)	9.7 (0.3) (9-10)	9.8 (0.3) (9-10)	9.8 (0.3) (9-10)

*P<0.05 when compared with group P; §P<0.05 when compared with group SP; §§§P<0.001 when compared with group SP; P<0.001 when compared with group P; P<0.05 when compared with group P; ob/gyn=obstetrics and gynecology; Data shown are number (percentage) or means (SD) (range) within the group.

Table 2: Intraoperative and postoperative data.

NRS pain score of uterine cramping after abortion at PACU is shown in Figure 3 (mean ± standard deviation, X ± SD).

NRS pain score of uterine cramping in group SP was significantly lower than that in group P in PACU at 0 min (3.6 versus 5.1, p<0.05), 15 min (3.4 versus 5.0, p<0.05)and 30 min (3.1 versus 5.0, p<0.001). NRS pain score of uterine cramping in group DP was also significantly lower than that in group P in PACU at 0 min (3.6 versus 5.1, p<0.05), 15 min (3.5 versus 5.0, p<0.05) and 30 min (2.8 versus 5.0, p<0.001). No difference was found between group SP and group DP.

NRS pain score of uterine cramping in group SP was significantly lower compared with group P in PACU, at 0 min, 15 min and 30 min (P<0.05, P<0.05 and P<0.01, respectively) (Figure 3).

NRS pain score of uterine cramping in group DP was also significantly lower in group P in PACU at 0 min, 15 min and 30 min (P<0.05, P<0.05 and P<0.001, respectively). (*P<0.05 when group P compared with group DP, ***P<0.001 when group P compared with group DP, #P<0.05 when group SP compared with group P, ##P<0.01 when group SP compared with group P).

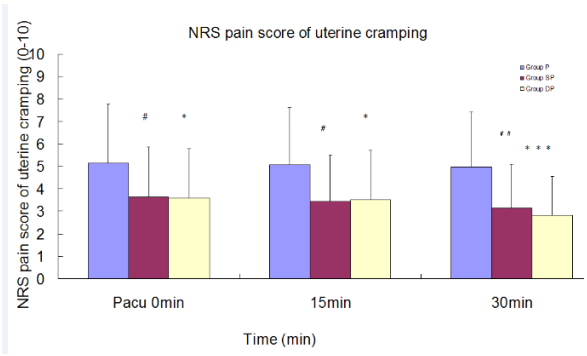

Figure 3: NRS pain score of uterine cramping after abortion at PACU (X ± SD).

Figure 4 illustrated the heart rate in the induction room, during surgery and in the PACU. The heart rate in group DP was significantly lower than that in group P and group SP (P<0.001, all) during the whole procedure. No difference was found between group P and group SP. Compared with group P and group SP, heart rate in group DP was lower during the whole procedure (P<0.001). (***P<0.001 when group P compared with group DP, §§§P<0.001 when group SP compared with group DP).

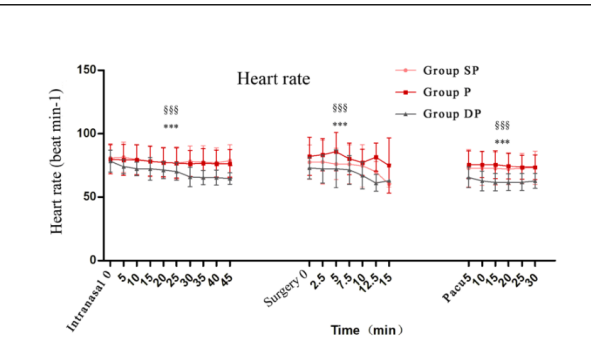

Figure 4: Heart rate of patients during induction, intraoperative period and at the PACU. Data shown are mean ± SD).

Systolic blood pressure was significantly lower in the induction room and PACU for patients from group DP compared with group P and group SP (P<0.001, both Figure 5). No difference was found between group P and group SP. Compared with group P and group SP, systolic blood pressure in group DP was lower at induction and PACU (P<0.001). No difference was found between group P and group SP. (***P<0.001 when group P compared with group DP, §§§P<0.001 when group SP compared with group DP) (Figure 5).

OAA/S in group DP was significantly lower in the induction room and PACU when compared with group P and group SP (P<0.001 and P<0.05, respectively) (Figure 6).

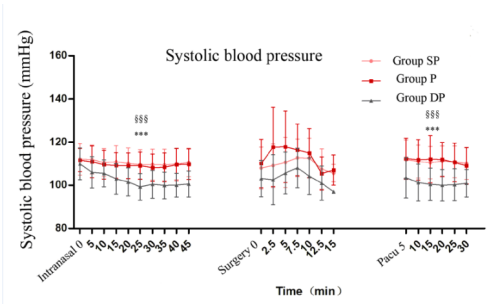

Figure 5: Systolic blood pressure of patients at induction, intraoperative period, and at the PACU. Data shown are mean ± SD).

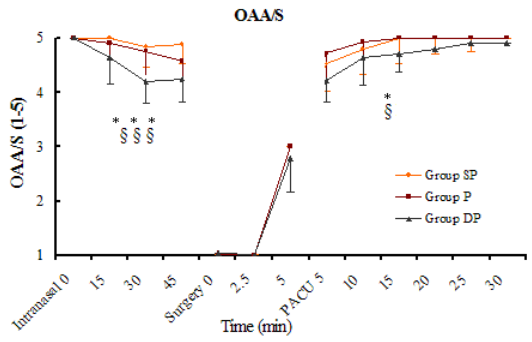

Figure 6: OAA/S at induction, intraoperative period and at PACU.

Adverse events occurring perioperatively were listed in table 3.

	Group P (n=30)	Group SP (n=30)	Group DP (n=30)
Bradycardia	0 (0%)	0 (0%)	0 (0%)
Hypoxia	0 (0%)	0 (0%)	0 (0%)
Hypotension	0 (0%)	0 (0%)	0 (0%)
Nausea	2 (6.7%)	2 (6.7%)	2 (6.7%)
Vomiting	0 (0%)	0 (0%)	0 (0%)
Dizziness	1 (3.3%)	1 (3.3%)	1 (3.3%)
Drowsiness	0 (0%)	2 (6.7%)	2 (6.7%)
Dry mouth	1 (3.3%)	2 (6.7%)	1 (3.3%)
Data shown are number (percentage) within the group. No significant difference was found among three groups.			

Table 3: Perioperative adverse events.

In Figure 6 data are medians with IQR. Compared with group P and group SP, AUC of OAA/S in group DP was significantly lower at induction room, (P<0.001, both). Compared with group SP and DP, AUC of OAA/S in group P was significantly higher at PACU (P<0.05, both). (*P<0.05 when group P compared with group DP, §P<0.05 when group SP compared with group DP, ***P<0.001 when group P compared with group DP, §§§P<0.001 when group SP compared with group DP).

Two patients in group DP and 2 patients from group SP experienced drowsiness at the PACU, but there was no significant difference among three groups. None of these patients developed clinically significant decreases of vital signs that required vasopressor or anticholinergic support. SpO_2 and respiratory rate were similar among the three groups during surgery. No respiratory depression (defined as a RR<10 bpm), or oxygen saturation less than 92% occurred (Table 3).

Discussion

This is the first study evaluating intranasal dexmedetomidine in termination of first trimester pregnancy of suction evacuation. We demonstrated that intranasal dexmedetomidine (1 μg/kg) reduced the consumption of propofol. Compared with propofol alone or propofol and sulfentanil combination which are mainly used for termination of first trimester pregnancy of suction evacuation in China, patients administered with intranasal dexmedetomidine showed anxiolysis, less consumption of propofol, decreased blood loss, lower NRS pain score of uterine cramping and higher NRS satisfaction score of ob/gyn physicians.

Dexmedetomidine is a α_2 adrenoceptor agonist, with a α_2:α_1 selectivity ratio of 1, 620:1, which is eight times that of clonidine [6]. Dexmedetomidine is an effective sedative, anxiolytic and analgesic drug [6]. Yuen et al reported that significant sedation in healthy volunteers within 45 min of intranasal administration of 1 μg/kg dexmedetomidine, with the sedative effect lasting 3 h [19]. Zhang et al. found that adequate sedation was achieved within 30 to 45 min after intranasal dexmedetomidine in patients during electrochemotherapy for facial vascular malformation [4]. Lirola et al. demonstrated that the median times to reach peak plasma concentration and the elimination half-life were 38 and 114 min, respectively, with the median absolute bioavailability of 65% following intranasal dexmedetomidine of 84 μg/kg [21]. We obtained similar results of sedation and anxiolysis with intranasal dexmedetomidine 45 min before abortion. In the induction room, OAA/S in group DP was significantly lower than in group P and group DP (P<0.001, both). The NRS anxiety score in group DP was also significantly lower than in group P and group SP (P<0.05 and P<0.01, respectively). Our study was the first one to evaluate anxiolysis following intranasal dexmedetomidine in termination of first trimester pregnancy of suction evacuation and we demonstrated that intranasal dexmedetomidine (1 μg/kg) might alleviate the anxiety of patients undergoing termination of first trimester pregnancy of suction evacuation.

As a α_2 adrenoceptor agonist, dexmedetomidine is also an effective analgesic drug. For healthy volunteers, a single bolus of dexmedetomidine lead to a 50% reduction in pain scores when compared with placebo in an ischemic pain model in Jaakola's study [16], and intravenous dexmedetomidine 1 μg/kg over 10 min followed by an infusion of 0.2 to 0.6 μg/kg/h reduced pain by ~30% using the cold pressor test in Hall's study [17]. However, Angst et al found that dexmedetomidine of target controlled infusion at concentrations ranging from 0.09 to 1.23 ng/ml had no analgesic effect in human volunteers on heat and electrical pain test [18]. In the third molar

surgery under local anesthesia, intravenous dexmedetomidine was shown to offer a comparable sedative effect to midazolam, without better analgesia [15]. These studies showed that the analgesic effect of intravenous dexmedetomidine was inconsistent [15-18]. Intranasal dexmedetomidine was effective and well tolerated without affecting the pain pressure threshold in healthy volunteers [19]. In Cheung's study, intranasal dexmedetomidine offered sedative and analgesic effects during surgery in adults, and 1 μg/kg of intranasal dexmedetomidine was proven to provide patients under unilateral third molar surgery with local anesthesia more sedation perioperatively with better postoperative pain relief [10]. Similar results happened in our study. The NRS pain score of uterine cramping after surgery in group SP and DP was significantly lower compared with group P after 30 min in PACU. In contrast to a study reporting that dexmedetomidine failed to reduce the injection pain of propofol [22], our study found a significantly lower NRS pain score associated with propofol injection in group DP compared with group P ($P<0.001$). The difference might be related to the increased duration (45 min) and dosage of dexmedetomidine (1 μg / kg) administered in our study. No differences were found between groups P and SP or groups SP and DP. Our results showed that intranasal dexmedetomidine (1 μg/kg) provided effective analgesia for propofol injection and uterine cramping after termination of first trimester pregnancy of suction evacuation.

In Cheung's study, intranasal dexmedetomidine 1.5 μg/kg with patient-controlled-sedation (PCS) of propofol and alfentanil offered deeper perioperative clinical sedation with significantly less use of additional sedatives during upper gastrointestinal endoscopy [11]. Similarly, in our study, consumption of propofol in group DP was significantly lower than that in group P and group SP ($P<0.001$ and $P<0.01$, respectively). Therefore we demonstrated that intranasal dexmedetomidine reduced the propofol requirement during termination of first trimester pregnancy of suction evacuation. Our result was also consistent with other previous studies that dexmedetomidine might reduce the anesthetic dosages [8,9,23]. Guan et al showed that the mean consumption of propofol for termination of first trimester pregnancy of suction evacuation was 3.56 ± 0.98 mg/kg for propofol and 2.11 ± 1.08 mg/kg for propofol combined with sulfentanil5. In our study, consumption of propofol was 2.8 ± 0.4 mg/kg and 2.6 ± 0.5 mg/kg respectively, probably due to the differences in study protocol. Compared with the rescue with propofol of 1 mg/kg in Guan's study, our study used a bolus of 20 mg propofol [5]. Both studies showed no significant differences with propofol sedation versus propofol and sulfentanil.

There was no difference on duration of pregnancy, duration of surgery or amount of suction tissue among three groups, while the amount of blood loss in group DP was significantly lower compared with groups P and SP ($P<0.05$ and $P<0.05$, respectively). This difference might due to the lower BP caused by dexmedetomidine in group DP. The usage of oxytocin in group DP was also significantly lower than in groups P and SP ($P<0.05$ and $P<0.05$, respectively). The surgical condition in group DP was better than in group P and SP ($P<0.05$ and $P<0.05$, respectively). These inspiring results showed the reason why NRS satisfaction scores of ob/gyn physicians in group DP were significantly higher compared with group P and group SP ($P<0.001$ and $P<0.05$, respectively).

Intravenous infusion of dexmedetomidine is commonly administrated with a loading dose followed by a maintenance infusion, and rapid intravenous administration or bolus has been associated with bradycardia and hypotension due to peripheral α_2-receptor stimulation [14]. Aantaa found that intravenous dexmedetomidine (0.5 μg/kg) as premedication on minor gynecologic surgery decreases thiopental anesthetic requirements, but patients' systolic and diastolic blood pressure were moderately reduced after dexmedetomidine administration [24]. Our study showed that the patients were healthy and tolerated these minor side effects with no cardiovascular morbidity requiring intervention. Similar results were reported in Cheung's study [10]. Hypoxia was reported with dexmedetomidine during third molar surgery intravenously [15] and with propofol and combination of propofol and sulfentanil during termination of first trimester pregnancy of suction evacuation in Guan's study [5], while no case happened in our study. This inconsistency might result from that the oxygen inhalation was administrated to patient through nasal catheter with oxygen flow 2 L/min when patient was transferred to the operation bed, and till she was moved to the bed of PACU after surgery. There was no difference on nausea or vomiting caused by propofol or combination of propofol and sulfentanil among three groups and those adverse effects did not decrease in the group DP, even though the dosage of propofol decreased. This might because the amount of propofol decreased in group DP was not big enough to eliminate those adverse effects.

In our study, the duration of intranasal dexmedetomidine in the induction room (45 min) was much longer compared with duration of surgery (3-8 min). In 2013, there were an estimated 13 million abortions performed in China, and approximately 10 million abortion pills sold. Of these, the number of artificial abortions induced by suction evacuation is substantial. Nearly 20 patients undergo elective termination of first trimester pregnancy of suction evacuation at our hospital every morning, and each patient has to wait for 30-60 min (including preoperative examine and payment) for the operation. The onset of intranasal dexmedetomidine (1 μg/kg) is compatible with this waiting time and might help to alleviate pre-surgery anxiety. However, intranasal dexmedetomidine (1 μg/kg) is contra-indicated for emergency artificial abortion. No differences were found at any time points between the end of surgery and discharge among the three groups. These results showed that intranasal dexmedetomidine (1 μg/kg) was not associated with any postoperative delays or hospital discharge. Furthermore, although intranasal dexmedetomidine required longer time (45 min in induction room) and alternative space (from induction room to operation bed) if compared with intravenous dexmedetomidine (15-20 min for onset of sedation [4] and operation bed only), the using time of operation bed would be much shorter than that in intravenous route, which means more efficient utilization of operation bed and is adapted for the substantial number of patients every day.

Our study was associated with a few limitations. First, all the patients recruited were nulliparous with normal BMI. In the future, we suppose to investigate the effect of intranasal dexmedetomidine on patients with a history of pregnancy and labor and on patients who are overweight or obesity. Secondly, bed shortage in the induction room prevented sedation of a higher number of patients. In the future, we will evaluate ambulatory patients in an effort to sedate larger patient population so that we can get higher efficiency of the operating bed and induction room. Third, the attending anesthesiologist, instead of patient, was the one who evaluate whether the sedation was ready for surgery. This might influence the use of rescue of propofol. In the future, we might evaluate the effect of intranasal dexmedetomidine combined with PCS of propofol in termination of first trimester pregnancy of suction evacuation in large population.

Conclusion

Intranasal dexmedetomidine (1 μg/kg) is a noninvasive way to provide effective sedation, anxiolysis and analgesia in termination of first trimester pregnancy of suction evacuation. It reduced the consumption of propofol and lowered the amount of blood loss. Therefore, compared with propofol sedation or use of combined propofol and sulfentanil, intranasal dexmedetomidine sedation contributed to a higher satisfaction score among ob/gyn physicians. No untoward perioperative cardiovascular and respiratory events occurred.

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