Intranasal dexmedetomidine combined with local anesthesia for conscious sedation during breast lumpectomy: A prospective randomized trial

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Abstract. Breast lumpectomy is usually performed under general or local anesthesia. To the best of our knowledge, whether conscious sedation with intranasal dexmedetomidine and local anesthesia is an effective anesthetic technique has not been studied. Thus, the present study aimed to investigate the effectiveness of conscious sedation with intranasal dexmedetomidine combined with local anesthesia in breast lumpectomy, and to identify its optimal dose. A prospective randomized, double-blinded, placebo-controlled, single-center study was designed, and patients undergoing breast lumpectomies were recruited based on the inclusion and exclusion criteria. All patients were randomly allocated to four groups: i) Local anesthesia with 0.9% intranasal saline (placebo); local anesthesia with ii) 1 μg.kg^{-1}; iii) 1.5 μg.kg^{-1}; or iv) 2 μg.kg^{-1} intranasal dexmedetomidine. The sedation status, pain relief, vital signs, adverse events, and satisfaction of patient and surgeon were recorded. Patients in the three dexmedetomidine groups were significantly more sedated and experienced less pain compared with the placebo group 45 min after intranasal dexmedetomidine administration and during 30 min in the post-anesthesia care unit. Patients in the 1.5 μg.kg^{-1} group were more sedated compared with the 1 μg.kg^{-1} group (without reaching statistical significance), whereas the 1.5 μg.kg^{-1} group exhibited a similar level of sedation 45 min after intranasal dexmedetomidine administration compared with the 2 μg.kg^{-1} group. In addition, patients in the 1 and 1.5 μg.kg^{-1} group experienced no adverse hemodynamic effects. Patient and surgeon satisfaction were greater in the 1.5 μg.kg^{-1} group compared with the 1 and 2 μg.kg^{-1} groups. Taken together, the results of the present study suggested that conscious sedation with intranasal dexmedetomidine and local anesthesia may be an effective anesthetic for breast lumpectomy surgery, and that the optimal dose for intranasal dexmedetomidine administration may be 1.5 μg.kg^{-1}, as it resulted in good sedation and patient satisfaction without adverse effects.

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Abbreviations: PACU, post-anesthesia care unit; CONSORT, Consolidated Standards of Reporting Trials; OAA/S, Observer's Assessment of Alertness/Sedation; ASA, American Society of Anesthesiologists; BIS, bispectral index; NRS, numerical rating scale; SBP, systolic blood pressure; HR, heart rate; SpO_2, oxygen saturation; RR, respiratory rate; ANOVA, analysis of variance

Key words: conscious sedation, lumpectomy, dexmedetomidine, intranasal administration, sedation

Introduction

Breast cancer is currently the most common cancer among Chinese women (1,2). For a number of women with breast cancer, breast lumpectomy with intraoperative pathological assessment is the preferred treatment to make an intraoperative decision (3). Breast cancer surgery performed under general anesthesia is associated with a potential risk of complications, which may make the patient feel unpleasant and delay patient recovery after surgery (4,5). Minor breast surgery requires fast and effective local anesthetic techniques with minimal side effects to allow the patient to recover quickly (6,7). Local anesthesia alone can make patients feel uncomfortable and distressed during surgery (8,9). Thus, the application of conscious sedation techniques may reduce the need for local anesthesia.

Dexmedetomidine is a highly selective α_2-adrenoreceptor agonist that induces sedation providing improved hemodynamic stability without eliciting respiratory depression (10-13). Previous studies have reported that dexmedetomidine is rapidly and efficiently absorbed after intranasal administration, and is better tolerated compared with intravenous administration (14-17). Additionally, intranasal dexmedetomidine has been successfully used for conscious sedation

under local anesthesia in numerous minor surgeries, including neurotologic procedures and dental surgery (18-20). In addition, intranasal administration of dexmedetomidine has been investigated in studies involving children, which demonstrated that intranasal administration may be a feasible alternative in patients requiring light sedation (21,22); however, more attention should be paid to the differences in dexmedetomidine dosage between children and adults (15-17,20-22). A number of studies have reported the application of intravenous dexmedetomidine in breast lumpectomy (23-25). Based on the similar efficacy between intravenous and intranasal administration, the present study hypothesized that intranasal dexmedetomidine may be effective in breast lumpectomy procedures. In order to evaluate the efficacy and identify the optimal dose of intranasal dexmedetomidine for conscious sedation, and to make patients more comfortable and cooperative during surgery, the modified Observer's Assessment of Alertness/Sedation (OAA/S) score (22), bispectral index (BIS) and pain were monitored. Additionally, systolic blood pressure (SBP), heart rate (HR), oxygen saturation (SpO_2) and respiratory rate (RR) were monitored to evaluate the side effects during breast lumpectomy under local anesthesia. The optimal dexmedetomidine dose that yielded the best sedation and the least adverse effects was also investigated.

Materials and methods

Study design. The present prospective randomized, double-blinded, placebo-controlled, single-center study was approved by the Ethics Committee of Tianjin Medical University Cancer Institute & Hospital (approval no. bc201512; Tianjin, China), and was registered at ClinicalTrials.gov (trial registration no. NCT02675049). Participants were enrolled during February and March 2016 from Tianjin Medical University Cancer Institute & Hospital, and written informed consent was obtained. All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Inclusion criteria. Patients included in the present study were women aged between 20 and 60 years. Patients with ASA (American Society of Anesthesiologists) physical status I and II (26) who were scheduled for breast lumpectomy at the Tianjin Medical University Cancer Institute and Hospital were enrolled in the study. A total of 100 patients were recruited.

Exclusion criteria. The exclusion criteria were a history of heart block, upper respiratory tract infection, asthma, allergy to dexmedetomidine or local anesthetics, memory or cognitive dysfunction, pregnancy, lack of understanding of the consent process, impaired liver or renal function, hypertension, concurrent application of β-receptor blockers, and a history of drug or alcohol abuse. Baseline demographic (age and body weight) and clinical ASA status characteristics were recorded.

Intervention. The patients were instructed to fast at least 6 h prior to surgery. No premedication was administered and patients were sent to the induction room 1 h prior to surgery. The patients were monitored routinely for electrocardiography, SpO_2, non-invasive blood pressure and BIS. Prior to dexmedetomidine administration, the operative, sedation and pain assessment procedures were explained. The patients were assigned randomly before surgery on the basis of a computer-generated random number table (complete randomization) at a 1:1:1:1 allocation ratio to receive 1, 1.5 or 2 $\mu g.kg^{-1}$ dexmedetomidine or 0.9% saline (placebo) intranasally 45 min before surgery. Both the patients and the investigators were blinded to the randomized intervention. An independent investigator and an anesthesiologist who were unaware of patient allocation prepared and administered the drug or placebo. A parenteral preparation of 100 $\mu g.ml^{-1}$ dexmedetomidine (Ai Bei Ning; Jiangsu Heng-rui Medicine Co., Ltd.) was used without further dilution. An equivalent volume of the placebo (0.9% saline) or undiluted dexmedetomidine was administered evenly by bilateral nasal dripping while the patients were in a recumbent position ~45 min prior to surgery. All surgical procedures were performed by the same surgical team comprising of three surgeons. Local anesthetic was administered by local infiltration with 1% lidocaine ~5 min before surgery and the volume was recorded. Inadequate analgesia was managed by local anesthetic infiltration into the surgical site.

Measurements and outcomes. The primary outcome was OAA/S, which was measured after drug administration, during surgery and during recovery in the post-anesthesia care unit (PACU). A score of 4 or 5 was considered the optimal OAA/S score in our study group. The secondary outcomes were BIS, pain [scored using a numerical rating scale (NRS)] (27), vital signs (SBP, HR, SpO_2 and RR), adverse effects and satisfaction with sedation. Adverse effects included hypotension (defined as SBP <90 mmHg), bradycardia (defined as HR <50 bpm), oxygen desaturation (defined as SpO_2 <92%), respiratory depression (defined as a ventilatory frequency <10/min), nausea and vomiting. The surgical condition, graded by the surgeon and patient, has been described in a previous study (28).

Baseline data were recorded before the commencement of surgery. The observation indices were measured 15, 30 and 45 min after drug administration, at which point resection commenced. The measurements were then taken every 5 min during surgery, and every 10 min after surgery in the PACU.

Sample size. The sample size was calculated according to the previous study by Yuen *et al* (29). The mean modified OAA/S scores for the 1 and 1.5 $\mu g.kg^{-1}$ dexmedetomidine groups in the present study were 5.2 and 4.6, respectively, and the standard deviation (SD) was 0.5, which led to a standardized difference of 1.2 SDs between the 1 and 1.5 $\mu g.kg^{-1}$ groups. Based on this result, the present study needed to have ~90% power to detect a 1.2-SD difference between any two of the three dexmedetomidine groups using two-sided Student's t-tests conducted using a Bonferroni-adjusted $P<0.0167$ significance level. Calculations using PASS2011 software (version 11.0.10; NCSS, LLC) demonstrated that 20 subjects per group provide the two-sided Student's t-test with 89.6% power at a $P<0.0167$ significance level, thereby satisfying power requirements. To maintain ~90% power in the event of a

20% dropout rate, the sample size was increased to 25 subjects per group for a total of 100 study subjects.

Statistical analysis. All statistical analyses were performed using SPSS software version 18.0 (SPSS Inc). Continuous variables following a normal distribution were expressed as mean ± SD and analyzed using Student's t-test. Categorical variables and continuous variables following an abnormal distribution were expressed as median and interquartile range, and were assessed using Mann-Whitney U test. To detect differences between the groups in terms of primary and secondary outcomes, a two-step procedure was employed. First, the placebo and 1 $\mu g.kg^{-1}$ dexmedetomidine groups were compared in terms of OAA/S, BIS, NRS, SBP, HR, RR or frequency of 'good' surgical conditions. If the difference was not statistically significant (P>0.05), no further analysis was performed. However, if P<0.05, the three dexmedetomidine groups were compared with each other. P<0.0167 (Bonferroni-adjusted P-value) was considered to indicate a statistically significant difference.

Results

Baseline characteristics. A total of 100 hundred patients were separated into four groups, with each group consisting of 25 patients. The mean (SD) age of the patients was 37.5 (11.5), 41.1 (10.6), 41.9 (7.0) and 42.3 (11.1) years, and the mean weight was 62.5 (11.5), 59.7 (8.7), 58.5 (7.3) and 60.2 (12.7) kg in the placebo group and 1, 1.5, and 2 $\mu g.kg^{-1}$ dexmedetomidine groups, respectively (Table I). No significant difference in demographic data and clinical features was observed among the groups (Table I). All patients met the eligibility criteria and completed the study (Fig. 1). The mean (SD) time between dexmedetomidine administration and the start of surgery was 47.4 (10.8), 52.4 (24.3), 47.2 (20.0) and 43.7 (13.6) min in the placebo group and 1, 1.5, and 2 $\mu g.kg^{-1}$ dexmedetomidine groups, respectively (P=0.397; data not shown).

Outcomes. The modified OAA/S scores of the four groups at different time intervals before and after administration of the drug were investigated (Fig. 2). The modified OAA/S scores were significantly lower in the 1 $\mu g.kg^{-1}$ group compared with the placebo group 45 min after intranasal (U=204.0; P=0.0003) and after 30 min in the PACU (U=516.5; P<0.001). The 2 $\mu g.kg^{-1}$ group exhibited greater sedation compared with the 1.5 $\mu g.kg^{-1}$ group but these differences did not have any statistical significance (U=68.0; P=0.300) at 45 min after intranasal administration; also, no significant difference was observed in the level of sedation between the 1.5 and 1 $\mu g.kg^{-1}$ groups (U=59.5; P=0.026) at 45 min after intranasal administration.

The BIS scores between the placebo group and other groups were compared using Mann-Whitney U test. Compared with that of the placebo group, the 1 $\mu g.kg^{-1}$ group had significantly lower BIS scores at 30 min after intranasal administration (BIS=91; U=383.0; P<0.001) and after 30 min in the PACU (BIS=84; U=327.0; P=0.002; Fig. 3). Additionally, the BIS scores of the 1 $\mu g.kg^{-1}$ group were significantly greater compared with those of the 1.5 and 2 $\mu g.kg^{-1}$ groups 30 min after resection (U=34.5; P=0.004; and U=36.5; P=0.002, respectively); however, there was no significant difference at 30 min in the PACU (U=203.5; P=0.596; and U=208.5; P=0.684, respectively). In addition, no significant difference was observed between the BIS scores of the 1.5 and 2 $\mu g.kg^{-1}$ groups.

The median pain NRS scores at each sample time were collected and presented in Fig. 4. The patients in the placebo group had a significantly higher pain score compared with patients in the 1 $\mu g.kg^{-1}$ group 10 min into surgery (U=436.5; P=0.015) and after 30 min in the PACU (U=405.0; P=0.012; Fig. 4). The NRS scores in the 1 $\mu g.kg^{-1}$ group were comparable to those in the 1.5 and 2 $\mu g.kg^{-1}$ groups 10 min into surgery (U=262.5; P=0.318; and U=254.0; P=0.245, respectively) and after 30 min in the PACU (U=194.5; P=0.079; and U=223.0; P=0.037, respectively; Fig. 4). In addition, no significant differences were observed in the volume of local anesthetic administered between the four groups (P=0.280, Table I).

The three dexmedetomidine groups exhibited significant decreases in mean value of SBP during surgery and recovery compared with the baseline values (Fig. 5A). In addition, compared with the placebo group, the SBP of the 1 $\mu g.kg^{-1}$ group was significantly lower 45 min after intranasal dexmedetomidine administration (P=0.001). Additionally, all three dexmedetomidine groups exhibited significantly lower HR 45 min after drug administration and after 30 min in the PACU compared with the control group (Fig. 5B). In addition, compared with the placebo group, the 1 $\mu g.kg^{-1}$ group had similar HR reduction during surgery and recovery (Fig. 5B).

Dexmedetomidine administration had no significant effect on SpO_2 levels or RR compared with the baseline values (P>0.05) and no significant differences were observed in the SpO_2 and RR between the four groups (data not shown). In addition, the intranasal administration was well tolerated by all patients; none of them developed local irritation or pain due to the administration, or complained of any unpleasant smell or taste associated with intranasal drug or placebo administration.

Safety outcomes. Only the 2 $\mu g.kg^{-1}$ group developed bradycardia (4% of total patients) and significant hypotension (1% of total patients) after dexmedetomidine administration. Most patients were asymptomatic and remained untreated. Only one patient with bradycardia required treatment with 0.5 mg atropine. The other two dexmedetomidine groups did not develop bradycardia or hypotension. No significant differences were observed in the incidence of nausea and vomiting between the four groups (P=0.286; data not shown).

Patient satisfaction. In the dexmedetomidine groups, the patients expressed more comfortable experiences during surgery, which were indicative of satisfactory sedation (P=0.157). The surgeons graded the surgical conditions as 'good' (indicating adequate sedation) more frequently in the dexmedetomidine groups compared with the placebo group (72%; P=0.066), but no significant differences were observed between the dexmedetomidine groups (P=0.768, Table I).

Discussion

The present study evaluated the efficacy and dose of combined intranasal dexmedetomidine and local anesthesia for conscious sedation during breast lumpectomy. Patients who received

Table I. Baseline demographic and clinical characteristics and intraoperative aspects.

Characteristics	Placebo (n=25)	1 μg.kg^{-1} dexmedetomidine (n=25)	1.5 μg.kg^{-1} dexmedetomidine (n=25)	2 μg.kg^{-1} dexmedetomidine (n=25)
Age, years	37.5±11.5	41.1±10.6	41.9±7.0	42.3±11.1
Body weight, kg	62.5±11.5	59.7±8.7	58.5±7.3	60.2±12.7
ASA				
I	10	12	13	14
II	15	13	12	11
Preoperative BIS	97.1±2.1	92.3±18.1	96.4±2.6	96.4±1.8
Preoperative OAA/S	6.0	6.0	6.0	6.0
Preoperative NRS	0	0	0	0
Duration from DEX to surgery, min	47.4±11.8	52.4±24.3	47.1±20.0	43.7±13.6
Duration of surgery, min	25.6±9.6	24.3±8.9	28.6±13.0	30.3±16.4
Total volume-local anesthetic used, ml	31.3±15.1	27.7±15.6	29.6±19.4	29.3±18.7
Surgical conditions graded 'good'[a]	18 (72.0%)	23 (92.0%)	25 (100.0%)	24 (96.0%)

[a]The surgical team graded the surgical conditions as 'good' if there was sufficient sedation. ASA, American Society of Anesthesiologists; BIS, bispectral index; DEX, dexmedetomidine; NRS, numerical rating scale of pain; OAAS/S, modified Observer's Assessment of Alertness/Sedation Scale; Preop, preoperative.

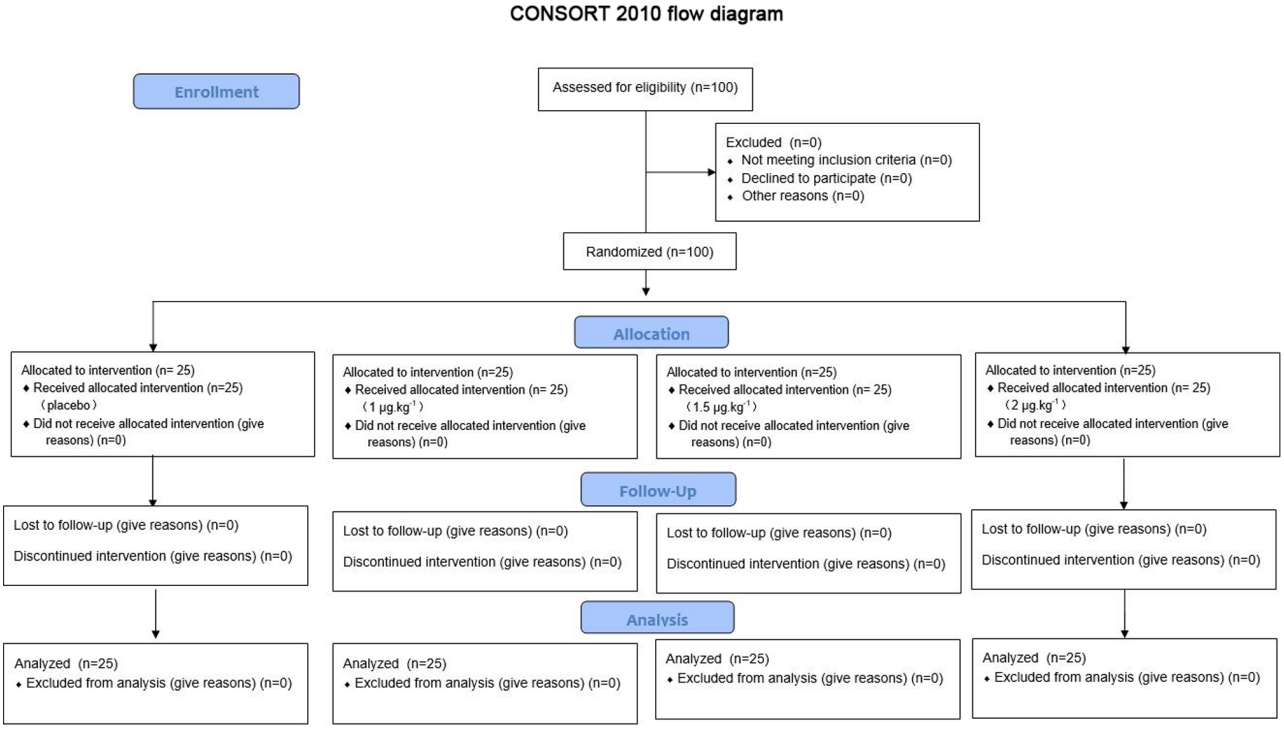

Figure 1. Flow diagram showing the disposition of the study subjects throughout the phases of the study. Placebo consisted of intranasal 0.9% saline. The remaining three groups received the indicated doses of dexmedetomidine. CONSORT, Consolidated Standards of Reporting Trials.

dexmedetomidine were significantly more sedated, experienced less pain, and were more satisfied with the sedation compared with patients in the placebo group. In addition, the results of the present study suggested that 1.5 μg.kg^{-1} was the optimal dose of intranasal dexmedetomidine, which yielded satisfactory sedation with good surgical condition, patient sedation satisfaction, and no serious adverse events.

One of the main causes of postoperative complications is general anesthesia, which is frequently used for sedation, and causes nausea and vomiting in 50% of cases (7). Local anesthesia may be an alternative to general anesthesia for this type of surgery (5). Dexmedetomidine is an effective drug for conscious sedation in patients who undergo minor surgery (14,17,30,31). A previous study demonstrated that

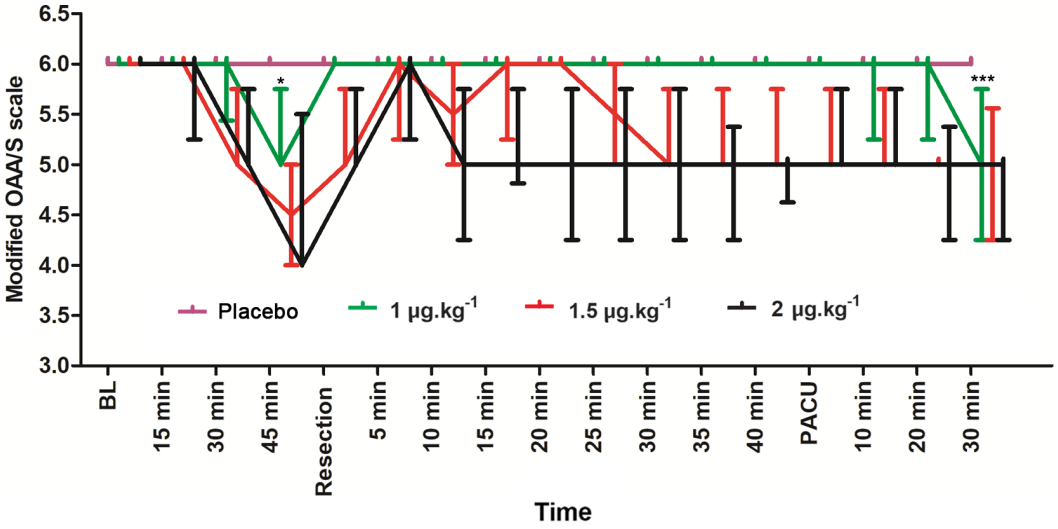

Figure 2. Changes over time in the modified OAA/S score of patients. Modified OAA/S was measured at BL, in the induction room, during the intraoperative period, and during their stay in the PACU. Data are expressed the median and 1st and 3rd quartiles. *P<0.05; ***P<0.001 1 μg.kg^{-1} vs. placebo. OAA/S, Observer's Assessment of Alertness/Sedation; PACU, post-anesthesia care unit; BL, baseline.

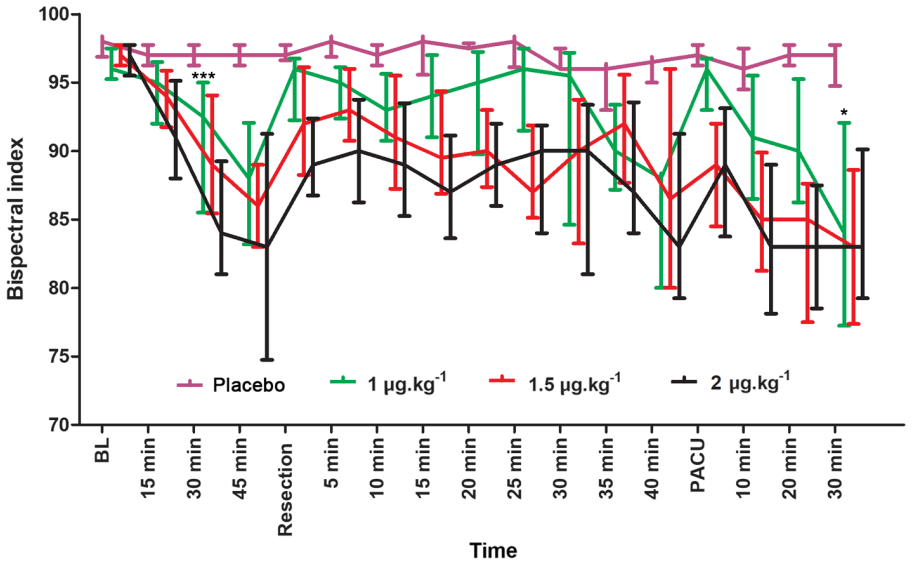

Figure 3. Changes over time in the bispectral index values of patients at BL, in the induction room, during the intraoperative period, and during their stay in the PACU. The data points were shifted slightly horizontally to avoid overlapping. Data are expressed the median and 1st and 3rd quartiles. *P<0.05; ***P<0.001 1 μg.kg^{-1} vs. placebo. BL, baseline; PACU, post-anesthesia care unit.

intranasal dexmedetomidine was noninvasive and more tolerable compared with intravenous administration (14). In addition, the intranasal route is safe, effective, comfortable and convenient (14,22,32-34). Iirola *et al* (28) demonstrated that administration of intranasal dexmedetomidine had a high bioavailability of 65% (35-93%) and could potentially have useful sedative effects in surgical procedures. To the best of our knowledge, to date there is no study that has reported the efficacy of intranasal dexmedetomidine for conscious sedation during breast lumpectomy under local anesthesia. The present study demonstrated that patients who received intranasal dexmedetomidine exhibited improved clinical sedation and analgesia compared with patients in the placebo group. In addition, the surgeons considered that the surgical conditions in the dexmedetomidine groups were superior compared with those in the placebo group. It was also demonstrated that intranasal dexmedetomidine could provide good clinical analgesia and sedation for a long duration of time of up to at least 70 min after surgery had started.

To identify the optimal intranasal dose providing the best sedation while inducing minimal side effects, three different intranasal doses were tested in the present study. These doses (1, 1.5 and 2 μg.kg^{-1}) were chosen on the basis of previous studies (29,31,35). However, only a few studies have assessed intranasal dexmedetomidine in adults (14,16,17). Because of the different requirements of anesthesia and surgery between children and adults, and as the selected doses were based on previous studies in adults, the dose of dexmedetomidine for sedation may

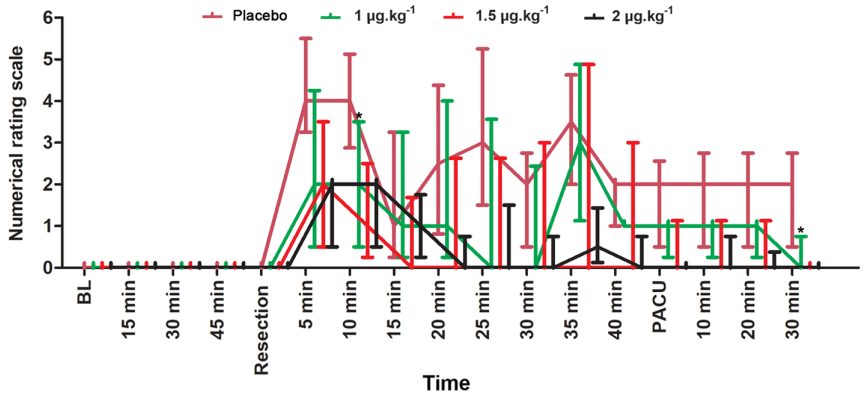

Figure 4. Changes in the numerical rating scale pain scores of patients at BL, in the induction room, during the intraoperative period and during their stay in the PACU. Data are expressed the median and 1st and 3rd quartiles. *P<0.05 1 μg.kg^{-1} vs. placebo. BL, baseline; PACU, post-anesthesia care unit.

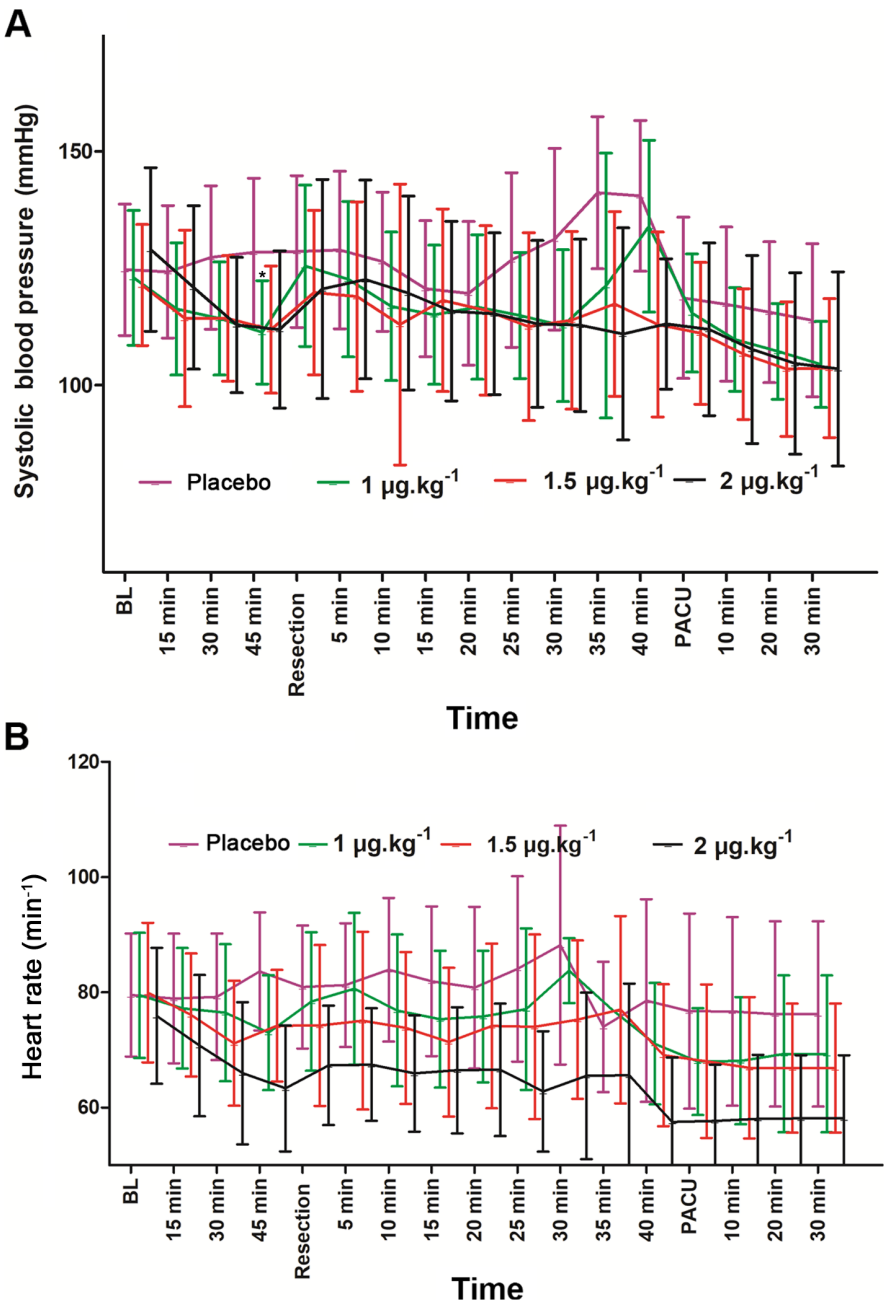

Figure 5. Changes in (A) systolic blood pressure and (B) heart rate of patients at BL, in the induction room, during the intraoperative period and during their stay in the PACU. *P<0.05 1 μg.kg^{-1} vs. placebo. Data are expressed as mean ± SD. BL, baseline; PACU, post-anesthesia care unit.

be different (15-17,20-22,31,32). The results of the present study demonstrated that there was a dose-dependent increase in sedation levels when dexmedetomidine was given intranasally, which was consistent with the findings of previous studies (25,36). In the current study, the level of sedation was significantly greater in the dexmedetomidine groups compared with that in the placebo group. Notably, Yuen *et al* (29) also demonstrated that 1 and 1.5 $\mu g.kg^{-1}$ intranasal dexmedetomidine produced clinically significant sedation in healthy volunteers. In addition, patients receiving 1 $\mu g.kg^{-1}$ intranasal dexmedetomidine for unilateral third molar surgery with local anesthesia were more sedated perioperatively with greater postoperative pain relief compared with intranasal water (17). Additionally, Zhang *et al* (37) reported that 1 $\mu g.kg^{-1}$ intranasal dexmedetomidine appeared to be safe and efficacious for patients undergoing elective electrochemotherapy for facial vascular malformations. The present study demonstrated that the 1.5 $\mu g.kg^{-1}$ group achieved greater sedation compared with the 1 $\mu g.kg^{-1}$ group, although it did not reach a statistically significant difference. In addition, the 2 $\mu g.kg^{-1}$ group also did not achieve a significant difference compared with the 1.5 $\mu g.kg^{-1}$ group. However, 1.5 $\mu g.kg^{-1}$ may be the optimal dose even if there were no significant differences.

The NRS pain scores also indicated that the dexmedetomidine groups experienced greater analgesia compared with the placebo group, as they felt less pain and were more tolerant. Mohta *et al* (38) reported that paravertebral block using intravenous dexmedetomidine in patients undergoing breast cancer surgery provided greater analgesia. Dexmedetomidine administration has been reported to result in significant bradycardia and hypotension (39). When dexmedetomidine was administered in adults before stimulation or intervention (i.e., surgery), it attenuated the hemodynamic response to stimulation and reduced arterial blood pressure and HR (40). The present study observed that, regardless of dose, dexmedetomidine significantly decreased SBP during surgery and recovery compared with that of the placebo group, but this hemodynamic change did not cause patient discomfort. There was also a significant drop in HR compared with the baseline values at the same time point in the dexmedetomidine groups. Although the 1 $\mu g.kg^{-1}$ group had a similar HR to the placebo group during surgery and recovery, the two higher dose groups had a lower HR during surgery and/or recovery. These changes may account for the relatively high rates of profound hypotension and bradycardia in the 2 $\mu g.kg^{-1}$ group. Notably, the most frequently reported adverse events associated with dexmedetomidine treatment are hypotension and bradycardia (41). Although patients in the 2 $\mu g.kg^{-1}$ group achieved a relatively greater level of sedation and analgesia, the cardiovascular side effects rendered this dose suboptimal. Since the optimal dose should yield sufficient sedation and analgesia without such adverse effects, the results of the present study suggested that the optimal dose of dexmedetomidine for intranasal administration may be 1.5 $\mu g.kg^{-1}$. Notably, patients who received 1.5 $\mu g.kg^{-1}$ dexmedetomidine remained aware during surgery and tolerated the procedure well, which allowed patients to cooperate with the surgeon to perform various required behaviors.

The present study had some limitations. First, the postoperative pain relief was not monitored after 30 min in the PACU. Whether intranasal dexmedetomidine can enhance postoperative pain relief under local anesthesia in breast lumpectomy requires further investigation. Second, intranasal dexmedetomidine was administered by dripping the solution into both nostrils with a 1 ml syringe. An optimal delivery system may have more consistent results. One such system would be the mucosal atomization device nasal spray that was used in a previous study to deliver intranasal dexmedetomidine during third molar extraction (16). Third, although the results of the present study together with previous study (42) indicated the efficacy and safety of intranasal dexmedetomidine administration during breast lumpectomy, future studies need to be conducted to focus on the safety in a larger sample size. Fourth, individual differences in drug tolerance may also provide bias since the time point for surgery was 45 min after intranasal dexmedetomidine was selected according to previous studies (14,28-29) instead of plasma concentration.

In conclusion, patients undergoing breast lumpectomy surgery who received intranasal 1.5 $\mu g.kg^{-1}$ dexmedetomidine attained significant and satisfactory sedation without experiencing any adverse effects compared with patients who received 1 and 2 $\mu g.kg^{-1}$ intranasal dexmedetomidine. Future studies should be conducted to focus on the efficacy and safety in a larger sample size.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

HWZ and YJY conceptualized the study and analyzed data. YJY, PZ, FX, XBZ, SSH, DYG and YHX acquired and analyzed the data. YJY, PZ, FX, XBZ, SSH, DYG, YHX and HWZ wrote the manuscript. HWZ and YJY revised the manuscript from a critical perspective for important intellectual content. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Tianjin Medical University Cancer Institute & Hospital (approval no. bc201512) and was registered at ClinicalTrials.gov

(registration no. NCT02675049). Written informed consent to participate was obtained from the patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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