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Clinical efficacy observation of intranasal dexmedetomidine spray in adults undergoing lower extremity orthopedic surgery under general anesthesia

Hailei Fan and Runqiao Fu*

Department of Anesthesiology, Beijing DCN Orthopaedic Hospital, Beijing 100143, China

* Corresponding author: Runqiao Fu, MD, Department of Anesthesiology, Beijing DCN Orthopaedic Hospital, Beijing 100143, China. Email: runqiao63@163.com

ABSTRACT

Objective: This study aimed to evaluate the sedative effects of intranasal dexmedetomidine spray in adult patients undergoing lower limb orthopedic surgery under general anesthesia and to analyze its role in reducing preoperative anxiety.

Methods: From July 2024 to January 2025, a total of 120 adult patients undergoing lower limb orthopedic surgery under general anesthesia at our medical institution were randomly assigned to either the experimental group (EG) or the control group (CG), with 60 patients in each group. Patients in the experimental group received intranasal dexmedetomidine spray 30 minutes before surgery, whereas those in the control group received intravenous midazolam over the same period. Sedation level, anxiety level, vital signs, anesthesia recovery, and incidence of adverse reactions were assessed.

Results: Although the Sedation scores significantly increased after drug intervention in both groups compared to the pre-administration baseline, a significant inter-group difference persisted throughout the post-administration period. The STAI scores in the experimental group were lower than those in the control group, although the difference was not statistically significant. Baseline values of Heart Rate (HR), Mean Arterial Pressure (MAP), and Pulse Oxygen Saturation (SpO_2) showed no significant differences between the two groups before drug administration. HR, MAP, and SpO_2 tended to decrease in both intervention groups compared with baseline values, but no pathological changes were observed. The experimental group had significantly shorter times in spontaneous breathing recovery, awakening, and extubating than the control group. The incidence of adverse reactions was 5.0% in the experimental group, significantly lower than the 28.4% in the control group.

Conclusion: Intranasal dexmedetomidine spray significantly enhances sedation levels, alleviates preoperative anxiety, and demonstrates good safety in adult patients undergoing lower limb orthopedic surgery under general anesthesia.

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Perioperative anxiety is commonly experienced by patients facing the uncertainty of surgery, the fear of pain, and concerns regarding postoperative recovery. As a result, many patients develop varying degrees of nervousness and anxiety preoperatively [1, 2]. The adverse effects of preoperative anxiety extend beyond the psychological dimension, manifesting significant negative effects on the physiological dimension as well. When patients experience preoperative anxiety, the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system are activated, leading to increased secretion of stress hormones, including epinephrine and cortisol. Previous studies have shown that the excessive release of these stress hormones can directly trigger an elevated heart rate and increased blood pressure, thereby augmenting the cardiovascular system's load. Consequently, this mechanism increases the probability of intraoperative complications and may also negatively influence the patient's long-term recovery [3].

Traditionally, preoperative sedation utilized oral or intramuscular administration of benzodiazepines or barbiturates. However, the difficulty in precise timing and the unpredictable efficacy of these routes often resulted in suboptimal outcomes. The pharmacological mechanism of dexmedetomidine

primarily relies on activating specific receptors within the central nervous system, thereby inhibiting norepinephrine release and reducing the activity of the sympathetic nervous system. This action yields its clinical effects of sedation and anxiolysis. Injectable formulations of dexmedetomidine have been used intravenously in clinical practice for over 20 years, gaining a high standing, particularly for intraoperative adjunctive sedation and anesthesia and for reducing the required dosage of intravenous agents. In recent years, the intranasal spray formulation of dexmedetomidine has garnered increasing attention in the field of preoperative sedation due to its non-invasiveness, rapid onset of action, and high absorption rate [4, 5]. Compared to intravenous injection of sedatives, the intranasal spray formulation not only eliminates the discomfort associated with injection but also enhances patient compliance and preoperative comfort levels.

Although intranasal dexmedetomidine spray has demonstrated favorable efficacy in preoperative sedation [6, 7], research specifically addressing its application in adult patients undergoing lower extremity orthopedic surgery under general anesthesia remains relatively limited. Therefore, this study aims to evaluate the degree of relief provided by intranasal dexmedetomidine spray for preoperative nervousness and anxiety in this patient population, and to analyze its effects on hemodynamics and overall safety. We anticipate that these findings will provide a more optimized preoperative sedation strategy for clinical anesthesia management, significantly enhancing the patient's perioperative experience and ensuring the overall quality and stability of the surgical procedure, thereby supporting the continuous improvement and optimization of medical services.

1 Materials and Methods

1.1 Materials

The study population comprised 120 adult patients scheduled for lower extremity orthopedic surgery under general anesthesia at Beijing DCN Orthopaedic Hospital between July 2024 and January 2025. Inclusion criteria stipulated that patients must be classified as American Society of Anesthesiologists (ASA) Physical Status I-II [8]. Furthermore, subjects were aged between 19 and 72 years, encompassing early to late adulthood, without restriction based on sex, to ensure the representativeness of the study data. Exclusion criteria included subjects with severe cardiovascular or respiratory system disorders, a recent history of upper respiratory tract infection, a documented history of neuropsychiatric system disorders (e.g., Parkinson's disease, Alzheimer's disease, cognitive impairment), or a prior history of allergic reaction to intranasal dexmedetomidine spray.

This study utilized a randomized, controlled experimental design, where eligible subjects were allocated by random assignment to two distinct groups. Patients in the Experimental Group (EG) received intranasal dexmedetomidine spray, while patients in the Control Group (CG) received intravenous midazolam. The CG comprised 60 subjects (28 males, 32 females). Their age ranged from 18 to 72 years, with a mean age of 56.24 ± 1.07 years. Their body weight ranged from 45 to 84 kg, with a mean of 62.25 ± 3.28 kg. The EG also included 60 subjects (30 males, 30 females). Their age ranged from 19 to 72 years, with a mean age of 55.89 ± 1.25 years. Their body weight ranged from 44 to 85 kg, with a mean of 62.78 ± 3.15 kg. Statistical testing confirmed no significant differences were observed between the EG and CG regarding baseline characteristics, including sex distribution, age, and body weight. This homogeneity ensures the reliability of the subsequent comparative analysis.

The study protocol was reviewed and approved by the Ethics Committee of Beijing DCN Orthopaedic Hospital on May 20, 2025 (Approval No. BDCN-2025-015), ensuring compliance with all relevant ethical guidelines. Before the commencement of the study, all participants and their families were thoroughly informed of the study's objectives, procedures, potential risks, and benefits, and provided written informed consent voluntarily. The entire research process strictly adhered to ethical norms, safeguarding the patients' right to know, privacy rights, and physical health and safety, thus guaranteeing the full respect and protection of participant rights.

1.2 Methods

In the CG, subjects received intravenous sedation immediately following triple-checking of patient identification and establishment of the intravenous access line. Midazolam was administered intravenously (Manufacturer: Yichang Hubei Humanwell Pharmaceutical Co., Ltd., China National Pharmaceutical Approval No. H20067040). Subjects in the EG received sedative intervention via intranasal administration of dexmedetomidine spray (Manufacturer: Sichuan Puruite Pharmaceutical Co., Ltd., China National Pharmaceutical Approval No. H20240012)

approximately 30 minutes before the induction of general anesthesia. The drug was administered as a spray into both nostrils. The total dose administered was approximately 100 μg, delivered in four separate sprays, with a single dose of 25 μg per spray. The complete administration process, including a 20-30 second interval between the two sprays on each side, was completed within two minutes.

To ensure uniformity and stability of drug delivery, the spray device was maintained with the nozzle facing upward, and the angle with respect to the vertical direction did not exceed 75 degrees, strictly avoiding horizontal placement, inversion, or dropping. Before initial use, the device was primed by performing eight preliminary sprays away from the patient's face until a stable spray pattern was observed; this priming consumed only a minimal amount of medication and did not affect subsequent clinical use. For formal administration, patients were instructed to adopt a sitting or semi-recumbent position with the head slightly tilted forward to minimize drug runoff and enhance nasal absorption. To optimize efficacy, the spray was not directed towards the nasal septum to reduce the risk of local irritation and promote uniform distribution of the medication on the nasal mucosa.

Upon entering the operating room, subjects underwent routine physiological parameter monitoring, including Mean Arterial Pressure (MAP), Heart Rate (HR), and Pulse Oxygen Saturation (SpO_2). During the induction of general anesthesia, subjects received the following medications according to a standard anesthesia protocol, administered intravenously and precisely calculated based on body weight: Rocuronium (0.7 mg/kg; Manufacturer: Zhejiang Xianju Pharmaceutical Co., Ltd., China National Pharmaceutical Approval No. H20093186), Propofol (2.0 mg/kg; Manufacturer: B. Braun Melsungen AG), Sufentanil (0.3 μg/kg; Manufacturer: Yichang Hubei Humanwell Pharmaceutical Co., Ltd., China National Pharmaceutical Approval No. H20030197), and Midazolam (0.03 mg/kg). Following induction, endotracheal intubation was performed using a video laryngoscope within 90 to 120 seconds. After confirming the correct position of the tracheal tube, subjects were connected to the anesthesia machine, and mechanical ventilation was initiated with appropriate settings for tidal volume, respiratory rate, and oxygen concentration.

Anesthesia was maintained through continuous intravenous infusion of remifentanil and propofol, supplemented by the inhalation of sevoflurane and intermittent intravenous boluses of rocuronium to ensure an adequate depth of anesthesia. All anesthetic drug infusions were gradually discontinued 10 minutes before the conclusion of the surgery. Concurrently, vital signs and Bispectral Index (BIS) values were closely monitored to ensure a gradual return of anesthetic depth, facilitating postoperative emergence.

1.3 Observation Indices and Evaluation Criteria

The following indices were monitored and evaluated throughout the study:

1. Assessment of Sedation Score: Sedation status in both the EG and CG was measured using the Ramsay Sedation Scale (RSS) at baseline (T_0, pre-administration) and at three post-administration time points: 5 minutes (T_5), 10 minutes (T_{10}), and 20 minutes (T_{20}). The RSS utilizes a 6-point scoring system (1 to 6), where higher scores indicate a more pronounced and deeper level of sedation [9].

2. Assessment of Anxiety Level: The state of anxiety in subjects from both groups was measured using the State-Trait Anxiety Inventory (STAI), administered both before and after drug administration. The STAI utilized a 4-point rating system (1 to 4 points) for assessment [10].

3. Monitoring of Vital Signs: HR, MAP, and SpO_2 were monitored and compared between the two groups at the four time points (T_0, T_5, T_{10}, and T_{20}) to evaluate the effects of the sedative medications on the circulatory and respiratory systems.

4. Anesthesia Recovery Indices: The difference between the two groups was compared based on several recovery times: time to spontaneous respiration (time from cessation of anesthetic drugs to the resumption of autonomous breathing), time to awakening (time from cessation of anesthetic drugs until the subject exhibits a clear response to verbal or painful stimuli), and time to tracheal extubating (time from cessation of anesthetic drugs until extubating criteria are met and the endotracheal tube is successfully removed).

5. Monitoring of Adverse Reactions: This included monitoring for symptoms such as hypotension (defined as systolic blood pressure < 90 mmHg or a drop exceeding 20% of the baseline value), respiratory

Table 1. Comparison of sedation scores ($\bar{x} \pm s$) between the two groups before and after drug administration

Groups	Number	Ramsay scores			
		T_0	T_5	T_{10}	T_{20}
CG	60	1.25 ± 0.21	2.13 ± 0.29	2.56 ± 0.31	2.92 ± 0.38
EG	60	1.28 ± 0.23	2.58 ± 0.26	3.15 ± 0.35	3.60 ± 0.40
t		0.4431	5.9042	8.0125	9.3178
p		0.6583	0.0001	0.0000	0.0000

Note: T_0: Before drug administration; T_5: 5 minutes after drug administration; T_{10}: 10 minutes after drug administration; T_{20}: 20 minutes after drug administration; CG: Control Group; EG: Experimental Group.

Table 2. Comparison of STAI Scores ($\bar{x} \pm s$) between the two groups before and after preoperative drug administration

Groups	Number	Before drug administration	After drug administration
CG	60	65.21 ± 8.56	62.25 ± 7.28
EG	60	66.72 ± 9.12	62.31 ± 6.31
t		0.5612	0.4165
p		0.6751	0.5215

depression (defined as a respiratory rate < 10 breaths/min or SpO_2 < 90 %), bradycardia (defined as HR < 60 beats/min), and nausea and vomiting.

1.4 Statistical Analysis

For measurement data, results are presented as the mean ± standard deviation ($\bar{x} \pm s$), and differences between the EG and the CG were assessed using the independent samples *t*-test. For qualitative data, results are presented as n (percentage), and intergroup differences were analyzed using the chi-squared (χ^2) test. All statistical tests in this study were two-tailed, and a *p*-value of less than 0.01 was considered statistically significant.

2 Results

2.1 Comparison of Sedation Scores Between the Two Groups

The RSS scores for both groups were compared at time points T_0, T_5, T_{10}, and T_{20}. The results indicated that there was no statistically significant difference in the baseline sedation scores between the EG and the CG at T_0 ($p > 0.05$, Table 1). However, at all three post-administration time points (T_5, T_{10}, and T_{20}), the RSS scores in both groups were significantly increased compared to the corresponding pre-administration (T_0) scores. Furthermore, a statistically significant difference in the sedation level was observed between the EG and the CG at the post-administration time points ($p < 0.01$, Table 1).

2.2 Comparison of anxiety levels between the two groups

Before drug administration (T_0), the STAI scores for the EG and the CG showed no statistically significant difference between the two groups ($p > 0.05$). This finding confirms that the baseline anxiety levels of the two groups were comparable, ensuring good comparability for subsequent analysis (Table 2). Following drug administration, the STAI scores in the EG showed a tendency to be lower compared to the CG. However, the difference in anxiety levels between the two groups did not reach statistical significance ($p > 0.05$).

2.3 Comparison of vital signs between the two groups

HR, MAP, and SpO_2 for both groups were compared at the four time points: T_0, T_5, T_{10}, and T_{20}. The results showed that at baseline (T_0), there were no statistically significant differences in any of the physiological monitoring parameters between the two groups ($p > 0.05$, Table 3), confirming the good comparability of the baseline physiological status between the EG and CG. Further analysis revealed that post-administration (T_5, T_{10}, and T_{20}), HR, MAP, and SpO_2 all exhibited a reduction compared to the pre-administration (T_0) values. However, the parameter values were generally similar between the two groups, and no significant fluctuations or abnormal changes were observed (Table 3).

Table 3. Comparison of vital signs ($\bar{x} \pm s$) between the two groups before and after drug administration

Groups		CG	EG	*t*	*p*
Number		60	60		
HR (times/min)	T_0	75.75 ± 5.39	75.18 ± 5.02	0.3802	0.5785
	T_5	74.89 ± 4.34	74.13 ± 4.49	0.3935	0.5679
	T_{10}	72.13 ± 4.26	72.92 ± 4.73	0.4402	0.4975
	T_{20}	70.93 ± 4.12	70.32 ± 3.86	0.8523	0.3102
MAP (mmHg)	T_0	116.69 ± 8.56	117.19 ± 8.41	0.4125	0.4562
	T_5	113.48 ± 8.28	114.72 ± 8.35	0.5214	0.4221
	T_{10}	107.16 ± 8.14	108.81 ± 7.89	0.5364	0.5012
	T_{20}	103.59 ± 7.54	104.21 ± 7.42	0.6321	0.3812
SpO_2(%)	T_0	96.95 ± 2.05	97.37 ± 2.21	0.4316	0.4896
	T_5	96.82 ± 2.17	96.97 ± 2.23	0.3845	0.5125
	T_{10}	96.63 ± 2.23	96.41 ± 2.49	0.4075	0.4925
	T_{20}	96.23 ± 2.63	96.08 ± 2.75	0.1989	0.7524

Table 4. Comparison of anesthetic recovery indices ($\bar{x} \pm s$, unit: minutes) between the two groups

Groups	Number	Spontaneous respiration recovery time	Awakening time	Extubation time
CG	60	8.92 ± 1.63	14.73 ± 2.16	19.51 ± 2.86
EG	60	7.16 ± 1.46*	10.62 ± 1.85*	12.36 ± 2.37*
t		13.5712	13.2445	15.7826
p		0.0000	0.0000	0.0000

Note: compared with the CG, $^*p < 0.01$.

2.4 Comparison of anesthesia effects between the two groups

The time required for spontaneous respiration recovery, awakening, and extubation was significantly shorter in the EG compared to the CG. Specifically, the respective mean times for the EG were shown in Table 4. The difference in all measured anesthetic recovery times between the EG and the CG was found to be statistically significant ($p < 0.01$).

2.5 Comparison of adverse reactions between the two groups

Following drug administration, the overall incidence of adverse events in the EG was 5.0 %. This rate was significantly lower compared to the CG, which had an incidence of 28.4 %. Statistical analysis confirmed that the difference in the incidence of adverse reactions between the EG and the CG was statistically significant ($p < 0.01$, Table 5).

3 Discussions

The use of intranasal dexmedetomidine spray has progressively gained acceptance in clinical anesthesia [11] due to its non-invasive administration, which relatively alleviates patient psychological stress and improves treatment compliance and comfort. Furthermore, the drug bypasses gastrointestinal absorption by directly entering the systemic circulation through the nasal mucosa, thereby accelerating the onset of action [6]. The results of this study indicate that intranasal dexmedetomidine spray can effectively improve the sedation status of subjects during the preoperative period (Table 1). This finding aligns with other relevant studies [12], further confirming that intranasal dexmedetomidine achieves its sedative effect by reducing sympathetic nervous activity. As a non-intravenous route of administration, the intranasal spray formulation is a more viable alternative due to its higher convenience and fewer side effects. Its use provides additional options for clinical practice, particularly for patients where intravenous access is difficult or impractical.

Preoperative anxiety is a common psychological distress experienced by patients undergoing surgical treatment, typically associated with concerns regarding the surgical procedure, postoperative recovery,

Table 5. Comparison of the incidence of adverse events [n (%)] between the two groups following drug administration

Groups	Number	Hypotension	Bradycardia	Respiratory depression	Nausea and vomiting	Total incidence
CG	60	3(5.0)	4(6.7)	7(11.7)	3(5.0)	28.4
EG	60	0(0.0)	2(3.3)	0(0.0)	1(1.7)	5.0
χ^2		12.5712	13.2445	15.7826	14.2516	
p		0.0000	0.0000	0.0000	0.0000	

and the anesthetic process. Previous studies indicate that preoperative anxiety not only adversely affects the patient's psychological well-being but also triggers tachycardia and hypertension, thereby increasing the cardiovascular system's load, consequently elevating the probability of intraoperative complications [3]. In this study, the STAI was used to assess the anxiety status of subjects in both the CG and EG. The results demonstrated that intranasal dexmedetomidine spray exhibited comparable clinical efficacy to midazolam in mitigating preoperative anxiety (Table 2). Relative to intravenous injection, the administration of intranasal dexmedetomidine is simpler and avoids the discomfort associated with injection, thus significantly enhancing patient comfort and feelings of relaxation. This advantage helps alleviate preoperative anxiety, ensures a smooth anesthetic process, and guarantees intraoperative stability [7].

Maintaining the stability of patients' physiological function is a core task during anesthetic procedures, which is critical not only for the smooth execution of the surgery but also for ensuring patient safety. The results of this study indicate that neither group experienced significant fluctuations in HR, MAP, or SpO_2 before and after drug administration. Furthermore, the intergroup differences in these parameters were not statistically significant (Table 3). This suggests that both sedation strategies had no marked adverse effect on the circulatory and respiratory system function of the subjects. This finding is consistent with existing studies [10, 12], further confirming the safety of intranasal dexmedetomidine spray in maintaining vital sign stability. The intranasal route of administration significantly reduces the impact on blood pressure fluctuation; notably, no significant hypotension or over-sedation was observed, especially in patients who were hemodynamically stable [4]. This may be attributed to the slower absorption and smoother increase in plasma drug concentration following nasal spray administration, which subsequently minimizes the impact on the circulatory system. Given its excellent sedative efficacy and minimal effect on patient physiological function, intranasal dexmedetomidine spray represents a safe and effective preoperative sedative agent.

The time required for anesthetic recovery is one of the most important metrics for evaluating anesthetic efficacy, directly reflecting the metabolic rate of the anesthetic drugs and the restoration of the patient's physiological function. The results of this study indicate that the EG demonstrated a significantly better trend in the time required for anesthetic recovery compared to the CG (Table 4). Specifically, the mean times for spontaneous respiration recovery (7.16 ± 1.46 minutes), awakening (10.62 ± 1.85 minutes), and extubation (12.36 ± 2.37 minutes) in the EG were markedly shorter than the corresponding times in the CG. The advantage of rapid recovery not only lies in reducing the retention time of anesthetic agents in the body but, more importantly, in decreasing the incidence of postoperative complications, thereby significantly improving patient comfort and satisfaction post-surgery. The unique pharmacological properties of dexmedetomidine enable it to maintain anesthetic stability while promoting a faster return of spontaneous breathing and consciousness, thereby accelerating the anesthetic recovery process [5].

Adverse drug reactions serve as a critical measure of drug safety, encompassing not only patient safety but also directly influencing a drug's clinical applicability. The results of this study indicate that intranasal dexmedetomidine spray demonstrated significant superiority in safety (Table 5), a benefit attributed to its unique pharmacological mechanism and simplified administration route. This finding is consistent with previous research [6], suggesting that the distinct mechanism of intranasal dexmedetomidine may contribute to a reduced incidence of adverse reactions. In this study, the CG exhibited a higher incidence of hypotension, bradycardia, respiratory depression, and nausea and vomiting. This observation may be linked to the pharmacological properties of midazolam. As a benzodiazepine, midazolam possesses inherent respiratory and circulatory depressant effects, necessitating particularly close monitoring of vital signs during clinical use [13]. In contrast, the intra-

nasal route positively influences the safety profile of dexmedetomidine. Nasal spray administration avoids the discomfort and risks associated with intravenous injection; the drug is absorbed through the nasal mucosa, leading to a rapid yet smooth onset of action.

In summary, intranasal dexmedetomidine spray, as a novel sedative agent, demonstrated advantages including rapid onset of action, a favorable safety profile, and marked sedative effects. Future research should aim to increase the sample size and encompass a wider range of surgical procedure types to further validate the broad applicability of intranasal dexmedetomidine spray. Additionally, strategies for its synergistic co-administration with other anesthetic or sedative agents should be investigated to provide more precise guidance for individualized anesthesia management.

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Conflict of Interest: None

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