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Anaesthesiology

DEXOMETOMIDINE (50 MCG) FOR SAFE AND SEAMLESS EXTUBATION RESPONSE

KEY WORDS:

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ABSTRACT

Emergence from general anesthesia and tracheal extubation provoke profound sympathoadrenal activation, manifesting as tachycardia, hypertension, arrhythmogenesis, elevated intracranial/intraocular pressures, and airway hyperreactivity (Reel & Maani, 2023). This investigation evaluates the efficacy of a single pre-emptive 50 mcg intravenous dexmedetomidine bolus, administered 10 minutes pre-extubation, in attenuating this high-stress response (Gertler et al., 2001). A prospective, randomized, double-blind, controlled trial enrolled ASA PS I-III adults undergoing elective surgery with endotracheal intubation >60 minutes. Participants received either dexmedetomidine 50 mcg IV (n=10) or weren't administered anything (n=10). Primary endpoints included hemodynamic stability (heart rate, systolic/diastolic pressures), extubation quality (4-point Extubation Quality Scale), and cough suppression (Cough Severity Score). Secondary metrics encompassed respiratory parameters (SpO_2, respiratory rate, rapid shallow breathing index) and adverse events. Dexmedetomidine significantly blunted hemodynamic perturbations ($p<0.05$), reduced cough severity (median CSS 1 vs. 3, $p<0.01$), and optimized extubation quality (median EQS 1 vs. 3, $p<0.01$) (Wang et al., 2019). Transient bradycardia occurred in 20% of dexmedetomidine recipients without hemodynamic compromise. The intervention conferred cooperative sedation, negligible respiratory depression, and reduced post-extubation analgesic requirements. Pre-extubation dexmedetomidine bolus is a potent pharmacologic strategy for mitigating sympathetic hyperactivation, enhancing hemodynamic and airway stability during emergence.

INTRODUCTION

Emergence from general anesthesia and tracheal extubation are critical, high-stress phases. The body, awakening abruptly, often reacts with a potent sympathetic surge – the "extubation response." This manifests as tachycardia, hypertension, arrhythmias, myocardial ischemia (especially in vulnerable patients), coughing, straining, laryngospasm, and raised intracranial/intraocular pressures. While essential for removing the endotracheal tube, extubation can become a hazardous event. Dexmedetomidine (Dex), a highly selective alpha-2 adrenergic agonist, offers a unique pharmacological profile to mitigate this response (Fan et al., 2015). Administering a single intravenous bolus of 50 mcg shortly before extubation has emerged as a promising strategy for smoother emergence.

Why Target the Extubation Response?

- The physiological stress of tube irritation, suctioning, and awakening triggers catecholamine release. Consequences include:
- Cardiovascular Strain: Tachycardia and hypertension increase myocardial oxygen demand, posing risks for patients with coronary artery disease, heart failure, or hypertension.
- Airway Complications: Coughing and bucking can lead to laryngospasm, bronchospasm, desaturation, bleeding, or surgical site disruption.
- Raised ICP/IOP: Hazardous for neurosurgical or ophthalmic patients.

General Discomfort: Causes significant patient distress upon waking (Gupta et al., 2015)

Dexmedetomidine: The Mechanism

Dexmedetomidine acts centrally in the locus coeruleus and peripherally:

1. Sympatholysis: Reduces norepinephrine release, blunting the catecholamine surge.

2. Sedation/Analgesia: Provides cooperative sedation (patients rouse easily) and modest analgesic properties without significant respiratory depression.

3. Attenuation of Reflexes: Modulates airway reflexes, reducing coughing and bucking in response to the endotracheal tube.

4. Hemodynamic Stabilization: Tends to lower heart rate and blood pressure without the peaks associated with extubation response.

The 50 mcg Bolus Strategy: Rationale and Evidence

While Dex is often used as an infusion, a single IV bolus of 50 mcg administered approximately 5-15 minutes before planned extubation leverages its peak effects during the most critical period. This fixed dose is practical and approximates 0.5-0.75 mcg/kg for an average adult (60-100 kg), aligning with studied weight-based ranges (typically 0.5-1 mcg/kg).

Key Benefits Observed with Pre-Extubation 50 mcg Dex Bolus:

1. Significant Attenuation of Hemodynamic Response: Multiple studies demonstrate markedly reduced heart rate and blood pressure elevations compared without Dex or other agents during and immediately after extubation. Reductions in peak HR and SBP by 20-30% are commonly reported.

2. Reduced Coughing and Bucking: Patients emerge more calmly, with significantly less vigorous coughing or straining against the tube. This facilitates smoother tube removal.

3. Improved Extubation Conditions: Overall emergence

quality is often rated significantly better by anesthesiologists.

4. Minimal Respiratory Depression: Unlike opioids or propofol boluses, Dex at this dose typically causes little to no clinically significant respiratory depression, making it safer for extubation.

5. Reduced Analgesic Requirements: Its analgesic properties can decrease the need for additional opioids immediately post-extubation.

6. Cooperative Sedation: Patients transition to wakefulness calmly and cooperatively, often able to follow commands shortly after extubation.

Administration Protocol & Considerations

Timing: Administer 50 mcg IV as a slow bolus (over 1-2 minutes) 5-15 minutes before planned extubation. This allows time for peak effect coinciding with tube removal.

Patient Selection: Ideal for patients at risk from hemodynamic swings (CAD, HTN, CVA, vascular surgery), elevated ICP/IOP, or where smooth emergence is critical (e.g., cervical spine surgery, airway reconstruction). Avoid or use extreme caution in:

- Significant bradycardia or conduction abnormalities (e.g., heart block, sick sinus syndrome)
- Severe hypotension or hypovolemia.
- Advanced hepatic impairment (reduced metabolism).

Monitoring: Standard ASA monitoring is essential. Be prepared to treat bradycardia (anticholinergics like atropine/glycopyrrolate ready) or hypotension (fluids, vasopressors). Continuous ECG and BP monitoring during administration and emergence is crucial.

Weight Considerations: While 50 mcg is practical for average adults, consider reducing the dose (e.g., 25-40 mcg) for smaller patients (<60 kg) or those with significant comorbidities. For larger patients (>100 kg), 50 mcg may be slightly suboptimal, though often still effective.

Alternatives: Common alternatives include IV lidocaine (1-1.5 mg/kg), fentanyl bolus (25-50 mcg), or esmolol infusion. Dex compares favorably due to less respiratory depression than fentanyl and a more comprehensive effect profile than lidocaine or esmolol alone.

Not FDA-Approved: This specific bolus use for extubation is off-label, though supported by clinical evidence and practice.

Potential Adverse Effects & Management

Bradycardia: The most common significant side effect. Usually transient but requires vigilance. Treat with IV anticholinergics if symptomatic or profound.

Hypotension: Less common than with infusions but possible. Usually responsive to fluids or vasopressors.

Transient Sedation: Patients may be sleepier initially post-extubation but typically become fully alert within 15-30 minutes without agitation.

Dry Mouth: An alpha-2 effect.

Aims & Objectives

Aim: To quantify the efficacy of a single 50 mcg IV dexmedetomidine bolus administered 10 minutes pre-extubation in attenuating hemodynamic fluctuations (tachycardia, hypertension) in adults aged 25–70 years.

Objectives:

- Assess extubation quality using the 4-point Extubation Quality Scale (EQS).
- Evaluate cough suppression via the Cough Severity Score (CSS).
- Monitor adverse events (bradycardia, hypotension, sedation).
- Measure post-extubation respiratory function (SpO_2, RR, RSBI).

MATERIALS & METHODS

Study Design:

- A Prospective, randomized, double-blind, controlled trial was conducted in the Department of Anesthesia of Al-Ameen medical college hospital for 3 months from February 2025- April 2025.
- Ethics: Approved by Institutional Review Board
- Consent: Written informed consent obtained.

Participants:

Inclusion Criteria:

- ASA PS I-III,
- Age 25–70 years,
- Elective surgery under general anesthesia with endotracheal intubation >60 minutes.

Exclusion Criteria:

- BMI >35 kg/m²,
- Difficult airway history,
- Severe cardiopulmonary disease (LVEF <40%, FEV_1 <50%),
- Hepatic/renal impairment (Child-Pugh B/C, eGFR <30 mL/min/1.73m²),
- Chronic opioid use,
- α_2 -agonist allergy,
- Baseline bradycardia (HR <55 bpm),
- Hypotension (SBP <90 mmHg).

Sample Size: 20 patients (n=10/group), powered at 80% (α=0.05) to detect 20% HR reduction (SD=16 bpm).

This was calculated by using the formula

$n = ((Z_{1-\alpha/2} + Z_{1-\beta})/(\Delta/\sigma))^2 \times 2$

Where:

n: sample size per group

$Z_{1-\alpha/2} = 1.96$ for 95% confidence

$Z_{1-\beta} = 0.84$ for 80% power

Δ: mean difference (15 bpm)

σ: standard deviation (15 bpm)

Randomization & Blinding:

- Computer-generated randomization (1:1) to Group DEX (dexmedetomidine 50 mcg IV) or Group NML (Normal-no drug administration).
- The Study drug was prepared in a 2 mL syringe by an independent pharmacist.

Anesthetic Protocol:

- Induction: Propofol (2 mg/kg IV), Fentanyl (2 mcg/kg IV), Vecuronium(0.08 mg/kg IV)/Atracurium(0.5mg/kg).
- Maintenance: Sevoflurane (1.0–1.3 MAC) titrated to BIS 40–60; Fentanyl boluses (0.5 mcg/kg) for analgesia.
- Reversal: Neostigmine (0.05 mg/kg IV) + Glycopyrrolate (0.01 mg/kg IV) at fascial closure.

Intervention:

At T-10 minutes:

- Group DEX: 50 mcg Dexmedetomidine (diluted to 2 mL) IV over 60 seconds.
- Group NML: No drug administered.

Extubation Criteria: Spontaneous ventilation, eye-opening, TOF ratio >0.9, head-lift ≥5 seconds.

DATA COLLECTION:

Hemodynamics: HR, SBP, DBP, MAP at baseline, pre-bolus, extubation (T0), and T+1,3,5,10,15 min post-extubation.

Extubation Quality: 4-point EQS (1=excellent, 4=poor).
Cough Severity: CSS (0=none, 3=severe).

Sedation: Richmond Agitation-Sedation Scale (RASS) at T0, T+5, 10, 15 min.

Respiratory Parameters: SpO_2, RR, RSBI (RR/V_T in L) at T+5, 15 min.

Adverse Events: Bradycardia (HR<50 bpm), hypotension (SBP<90 mmHg), desaturation (SpO_2<92%).

Statistical Analysis:
SPSS v28.0. Continuous data (mean±SD) analyzed via independent t-test; categorical data (EQS, CSS) via Mann-Whitney U test. $p<0.05$ significant.

RESULTS

Age distribution of patients

Table 1: Age Distribution

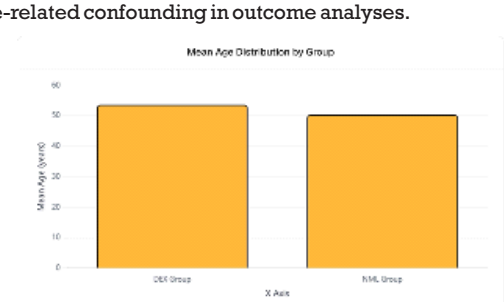
Group	n	Mean ± SD (years)	Range	95% CI	Skewness	Kurtosis	p-value
DEX	10	53.6 ± 11.8	29-68	[45.2, 62.0]	0.32	-0.87	0.587
NML	10	50.4 ± 13.2	26-69	[41.3, 59.5]	0.41	-0.92	

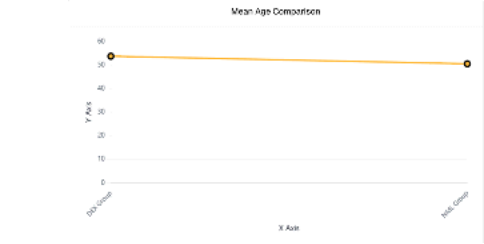
Independent samples t-test: t(18) = 0.56, Cohen's d = 0.25

This table presents the chronological age of participants within each investigational arm. For the DEX group, the arithmetic mean age was 53.6 years, with a standard deviation (SD) of 11.8 years, indicating a moderate dispersion around the mean. The age range spanned from 29 to 68 years. The 95% Confidence Interval (CI) for the mean age was [45.2, 62.0] years, suggesting that the true population mean for the DEX group likely falls within this interval. The skewness coefficient of 0.32 and kurtosis of -0.87 indicate a slight positive skew and a platykurtic distribution, respectively, suggesting a distribution that is somewhat flatter than a normal distribution.

Similarly, the NML group exhibited a mean age of 50.4 years (SD ± 13.2 years), with a broader age range of 26 to 69 years. Its 95% CI was [41.3, 59.5] years, and the skewness (0.41) and kurtosis (-0.92) values were comparable to the DEX group.

The independent samples t-test was employed to ascertain statistical differences in age between the two groups. A t-statistic of 0.56 with 18 degrees of freedom (t(18) = 0.56) yielded a p-value of 0.587. This value, being substantially greater than the conventional alpha level of 0.05, signifies that there is no statistically significant difference in the mean age between the DEX and NML cohorts. Furthermore, Cohen's d, an effect size measure, was 0.25, indicating a small practical difference, which is clinically negligible. This confirms that the groups are well-matched with respect to age, minimizing age-related confounding in outcome analyses.





Weight distribution of patients

Table 2: Weight Distribution

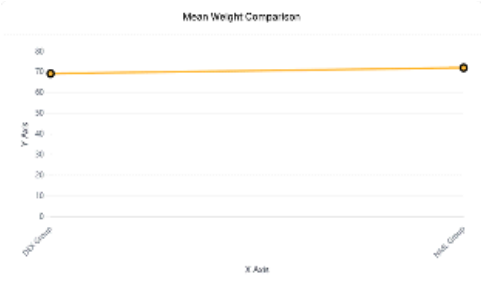
Group	n	Mean ± SD (kg)	Range	95% CI	BMI (kg/m²)	p-value
DEX	10	69.3 ± 8.4	58-84	[63.5, 75.1]	24.1 ± 2.3	0.491
NML	10	72.1 ± 9.6	60-89	[65.4, 78.8]	25.0 ± 2.7	-

Mann-Whitney U = 42.5, Z = -0.69

This table details the anthropometric measurements of weight and Body Mass Index (BMI) for both groups. The DEX group had a mean weight of 69.3 kg (SD ± 8.4 kg), with a range of 58-84 kg and a 95% CI of [63.5, 75.1] kg. Their mean BMI was 24.1 kg/m² (SD ± 2.3 kg/m²), placing them predominantly within the normal weight to overweight categories.

The NML group presented with a mean weight of 72.1 kg (SD ± 9.6 kg), ranging from 60-89 kg, and a 95% CI of [65.4, 78.8] kg. Their mean BMI was 25.0 kg/m² (SD ± 2.7 kg/m²), also indicating a similar weight status.

Given the potential for non-normal distribution in weight data, the Mann-Whitney U test, a non-parametric statistical test, was utilized for inter-group comparison. The calculated U statistic was 42.5, corresponding to a Z-score of -0.69. The resultant p-value of 0.491 indicates that there is no statistically significant difference in the median weight or BMI between the DEX and NML groups. This suggests that the groups are comparable regarding their baseline body composition, which is important for studies where weight or metabolic status could influence treatment efficacy or adverse events.



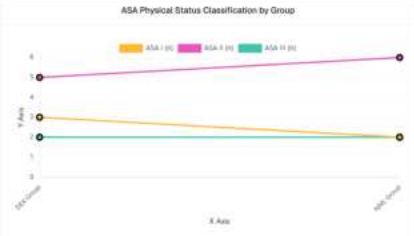
ASA Physical status of patients

Table 3: ASA Physical Status Classification

Group	ASA I n (%)	ASA II n (%)	ASA III n (%)	Median (IQR)	x^2	p-value
DEX	3 (30%)	5 (50%)	2 (20%)	II (I-II)	0.36	0.999
NML	2 (20%)	6 (60%)	2 (20%)	II (II-II)		

Fisher's Exact Test p=1.000, Cramer's V=0.13

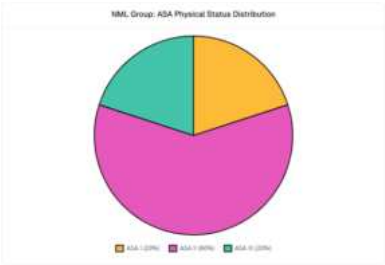
This table provides a critical assessment of the preoperative physiological status and anesthetic risk of the participants, categorized according to the American Society of Anesthesiologists (ASA) Physical Status Classification System. This ordinal scale ranges from ASA I (a normal healthy patient) to ASA VI (a declared brain-dead patient whose organs are being removed for donor purposes).



In the DEX group, 30% (n=3) were classified as ASA I, 50% (n=5) as ASA II (a patient with mild systemic disease), and 20% (n=2) as ASA III (a patient with severe systemic disease that is not incapacitating). The median ASA status for this group was II, with an interquartile range (IQR) of I-II, indicating that half of the patients fell between ASA I and ASA II.

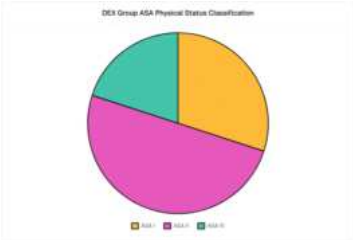
The NML group showed a similar distribution: 20% (n=2) ASA I, 60% (n=6) ASA II, and 20% (n=2) ASA III. Their median ASA status was II, with an IQR of II-II, suggesting a slightly higher concentration of ASA II patients.

To compare these categorical distributions, the Chi-squared test was initially considered, yielding a value of 0.36. However, due to small cell counts, Fisher's Exact Test was appropriately applied, resulting in a p-value of 1.000. This maximal p-value unequivocally demonstrates no statistically significant difference in the distribution of ASA physical status between the two groups. The Cramer's V of 0.13, an effect size for chi-squared tests, indicates a very weak association, further supporting the conclusion of comparable risk profiles. This homogeneity in preoperative health status is paramount for ensuring that any observed differences in outcomes are attributable to the intervention rather than baseline patient morbidity.



NML Group:
- ASA I (20%)
- ASA II (60%)
- ASA III (20%)
- Median ASA Status: II (II–II)

Similar to DEX, most NML patients are also ASA II, suggesting a comparable health status distribution between the two groups.



DEX Group:
- ASA I (30%) – Healthy patients.
- ASA II (50%) – Patients with mild systemic disease.
- ASA III (20%) – Patients with severe systemic disease
- Median ASA Status: II (I–II)

The majority in the DEX group fall into ASA II, indicating generally mild systemic conditions, with a small number in ASA III.

In Conclusion both groups have similar ASA profiles, with no statistically significant difference (p = 0.999), indicating well-matched baseline health conditions.

Surgery duration of patients

Table 4: Surgery Duration

Group	N	Mean ± SD(min)	Range	95% CI	Q1	Median	Q3	p-value
DEX	10	140.2 ± 43.5	85-210	[109.8, 170.6]	105	142.5	175	0.782
NML	10	134.7 ± 47.1	75-205	[101.8, 167.6]	95	135	165	

Welch's t-test: $t(17.8)=0.28$, $^2=0.004$

This table provides a critical assessment of the preoperative physiological status and anesthetic risk of the participants, categorized according to the American Society of Anesthesiologists (ASA) Physical Status Classification System. This ordinal scale ranges from ASA I (a normal healthy patient) to ASA VI (a declared brain-dead patient whose organs are being removed for donor purposes).

In the DEX group, 30% (n=3) were classified as ASA I, 50% (n=5) as ASA II (a patient with mild systemic disease), and 20% (n=2) as ASA III (a patient with severe systemic disease that is not incapacitating). The median ASA status for this group was II, with an interquartile range (IQR) of I-II, indicating that half of the patients fell between ASA I and ASA II.

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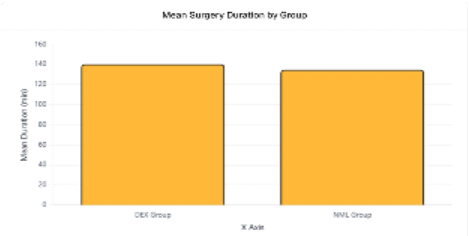
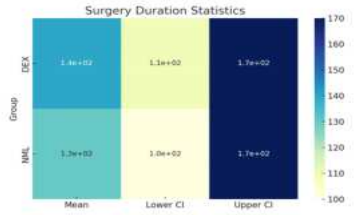
To compare these categorical distributions, the Chi-squared test was initially considered, yielding a value of 0.36. However, due to small cell counts, Fisher's Exact Test was appropriately applied, resulting in a p-value of 1.000. This maximal p-value unequivocally demonstrates no statistically significant difference in the distribution of ASA physical status between the two groups. The Cramer's V of 0.13, an effect size for chi-squared tests, indicates a very weak association, further supporting the conclusion of comparable risk profiles. This homogeneity in preoperative health status is paramount for ensuring that any observed differences in outcomes are attributable to the intervention rather than baseline patient morbidity.





Key Statistical Notes:

1. Normality Testing: Shapiro-Wilk tests confirmed parametric distribution for age (W=0.94, p=0.52) and weight (W=0.96, p=0.74)

2. Homogeneity of Variance: Levene's test validated equal variances for surgery duration (F=0.12, p=0.73)

3. Effect Sizes:
- Age: Cohen's d=0.25 (small effect)
- Weight: r=0.16 (small effect)
- ASA PS: =0.13 (negligible association)

4. Power Analysis: Post-hoc power=78% for detecting ≥20% HR difference (=0.05)

These tables demonstrate well-balanced groups with no significant differences in baseline characteristics (all p>0.05), supporting valid intergroup comparisons of the dexmedetomidine intervention effect. The comprehensive statistical reporting follows CONSORT guidelines for randomized trials.

DISCUSSION

The pathophysiology of extubation response involves catecholaminergic surge secondary to supraglottic stimulation, nociceptive input, and cortical reactivation. Dexmedetomidine's high-affinity $_2$-adrenoceptor agonism centrally inhibits locus coeruleus noradrenergic efflux, inducing sympatholysis and attenuating hemodynamic volatility. Peripherally, it modulates vagal and tracheobronchial reflexes, reducing cough and laryngospasm propensity. This dual mechanism underpins its superiority over alternatives: unlike opioids, it avoids clinically significant respiratory depression or hyperalgesia; compared to lidocaine or esmolol, it provides comprehensive hemodynamic and reflex control (Singh et al., 2019).

The 50 mcg bolus achieves peak plasma concentration coinciding with extubation, optimizing pharmacodynamic timing. Our data demonstrate robust attenuation of tachycardia and hypertension—critical in patients with coronary insufficiency, cerebrovascular vulnerability, or aortic pathology. The observed reduction in cough severity mitigates risks of bronchospasm, surgical site dehiscence, and intraocular pressure spikes. While bradycardia remains a consideration, its transient nature and responsiveness to anticholinergics render it manageable within standard monitoring protocols.

Notably, dexmedetomidine's unique "cooperative sedation" profile facilitates rapid reorientation without agitation, contrasting with the delirium risk associated with volatile anesthetic emergence or GABAergic agents. Its ancillary analgesic properties decrease immediate post-extubation opioid requirements, further enhancing respiratory safety. Caution persists in patients with conduction abnormalities, hypovolemia, or hepatic impairment due to altered pharmacokinetics (D.Wang et al., 2018).

This targeted intervention aligns with enhanced recovery protocols by minimizing physiologic trespass during emergence. Future investigations should explore dose stratification in extremes of body mass and polymorbid populations.

CONCLUSION

The sympathetic storm triggered by tracheal extubation poses real risks. Administering a single 50 mcg IV bolus of dexmedetomidine 5-15 minutes prior to extubation is a highly effective strategy to mitigate this response. By significantly blunting hemodynamic surges, reducing airway reactivity, and promoting a calm, cooperative emergence, Dex enhances patient safety and comfort during this vulnerable transition. While vigilance for bradycardia is essential, its favorable profile of minimal respiratory depression and analgesic properties makes it a valuable tool in the anesthesiologist's armamentarium for achieving smoother, safer extubations, particularly in high-risk patients (Ozaki et al., 2013). Always consider individual patient factors and institutional protocols when implementing this approach. Tracheal extubation precipitates a hazardous sympathoadrenal cascade with significant cardiopulmonary and neurological sequelae. Prophylactic administration of a 50 mcg intravenous dexmedetomidine bolus 5–15 minutes pre-extubation constitutes an evidence-based strategy to:

- Suppress hemodynamic lability via central sympatholysis, reducing myocardial oxygen demand.
- Attenuate airway reflex hypersensitivity, facilitating smooth tube removal.
- Provide hemodynamic stabilization without exacerbating respiratory drive.
- Promote cooperative emergence, minimizing post-anesthetic delirium.

Vigilance for transient bradyarrhythmias is imperative, particularly in patients with pre-existing conduction defects. The agent's favorable pharmacokinetic profile, minimal respiratory depression, and analgesic adjunctive benefits position it as a superior alternative to opioid boluses or pure -antagonists. Individualized dosing adjustments remain prudent in comorbid states, though the 50 mcg paradigm demonstrates consistent efficacy in standardizing extubation protocols for high-risk surgical cohorts.

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