

Emerging Horizons: A Systematic Review of the Efficacy and Safety of Cisatracurium Besylate in Anesthesia

Hytham Hummad

Assistant professor, Department of Anesthesia and Operations, College of Applied Medical Sciences- Khamis Mushait, KING KHALID UNIVERSITY , Abha, Kingdom of Saudi Arabia, ORCID ID: 0009-0001-0597-8433, hhummad@kku.edu.sa

ABSTRACT

Cisatracurium besylate, a non-depolarizing neuromuscular blocking agent (NMBA), is pivotal in anesthesia due to its organ-independent Hofmann elimination and predictable pharmacokinetics. This systematic review synthesizes evidence from 13 randomized controlled trials (RCTs) involving 1,247 patients undergoing diverse surgical procedures, evaluating cisatracurium's efficacy in achieving optimal intubating conditions, sustaining neuromuscular blockade, and facilitating rapid recovery, alongside its safety profile concerning adverse events like residual paralysis, histamine release, and hemodynamic instability. Findings demonstrate that cisatracurium achieves excellent intubating conditions in 92.3% of cases within 120 seconds at doses of 0.15-0.2 mg/kg, with a clinical duration of 35-45 minutes and a recovery index (25-75% twitch recovery) of 13-17 minutes, surpassing rocuronium and atracurium in onset time and cardiovascular stability (pooled odds ratio [OR] 1.45, 95% CI 1.12-1.88; $p < 0.001$) [1,2]. Safety data reveal a low adverse event incidence (4.2%, including 1.8% mild hypotension and 0.9% bronchospasm), with no significant increase in postoperative residual curarization when monitored with train-of-four (TOF) ratios > 0.9 (risk difference -0.03, 95% CI -0.07 to 0.01) [3,4]. Subgroup analyses highlight superior efficacy in obese ($n=456$) and renally impaired patients ($n=312$), with a 28% lower risk of prolonged blockade compared to vecuronium (relative risk [RR] 0.72, 95% CI 0.58-0.89) [5,6]. Meta-regression adjusting for age, ASA status, and anesthetic regimens confirms dose-dependent efficacy without compromising safety, though heterogeneity ($I^2=58\%$) underscores the need for standardized protocols. These results endorse cisatracurium's role in diverse surgical settings, with future research needed to refine dosing in geriatric and neuroanesthesia contexts [7,8].

KEYWORDS: Cisatracurium besylate, Neuromuscular blockade, General anesthesia, Efficacy, Safety, Intubation conditions, Systematic review.

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INTRODUCTION

Neuromuscular blocking agents (NMBAs) are essential in anesthesia, enabling rapid tracheal intubation, optimal surgical conditions, and mechanical ventilation [1,9]. Cisatracurium besylate, a benzylisoquinolinium NMBA, is distinguished by its Hofmann elimination, a non-enzymatic degradation process independent of hepatic or renal function, ensuring predictable recovery in patients with organ dysfunction [2,10]. Introduced in the 1990s, cisatracurium offers a favorable hemodynamic profile and intermediate duration of action (ED₉₅: 0.05 mg/kg), as demonstrated in early trials comparing it to vecuronium [3,11]. This systematic review synthesizes contemporary RCTs to evaluate cisatracurium's efficacy and safety, addressing its evolving role in modern anesthesia [7,12].

The global surgical burden, projected to exceed 320 million procedures annually by 2030, necessitates NMBAs with robust efficacy and minimal complications, particularly in aging and comorbid populations [13,14]. Cisatracurium's low laudanosine production—unlike its predecessor atracurium—reduces neurotoxic risks, making it suitable for prolonged infusions in critical care [4,15]. Residual neuromuscular blockade, affecting up to 40% of unmonitored patients, drives the need for agents like cisatracurium that minimize postoperative morbidity [6,16]. Recent studies highlight its advantages in high-risk groups, such as obese and renally impaired patients, where organ-independent clearance prevents accumulation [5,17].

Efficacy metrics for NMBAs include rapid onset (< 120 seconds for intubation), sustained blockade (TOF count 0-1), and prompt recovery (TOF ratio > 0.9). Cisatracurium excels in these, with meta-analyses showing 20-30% faster recovery than rocuronium in obese cohorts [7,18]. Safety concerns, including anaphylaxis ($< 1:10,000$) and hemodynamic instability, are significantly lower with cisatracurium compared to mivacurium or succinylcholine [8,19]. Its compatibility with total intravenous anesthesia (TIVA) enhances its utility in modern regimens [20,21]. However, evidence gaps persist in pediatric and geriatric populations, where dosing optimization remains understudied [22,23].

Emerging trends in personalized anesthesia underscore cisatracurium's potential in pharmacogenomic applications, as its non-enzymatic clearance bypasses CYP450 variability, ensuring consistent efficacy across ethnic groups [9,24]. Off-label use with sugammadex, a selective relaxant-binding agent, achieves ultra-rapid reversal, reducing PACU stays in ambulatory settings [10,25]. Cost-effectiveness analyses suggest cisatracurium's higher upfront cost is offset by fewer complications, though accessibility remains limited in low-resource settings [11,26]. Innovations like AI-driven dosing algorithms further enhance its precision [12,27].

This PRISMA-compliant review synthesizes 13 RCTs to inform clinical guidelines, addressing efficacy and safety across diverse surgical contexts while identifying research gaps in neuroanesthesia and extreme age groups [13,28]. By integrating contemporary evidence, it aims to advance anesthesia practice and foster sustainable innovations [14,29].

METHODOLOGY

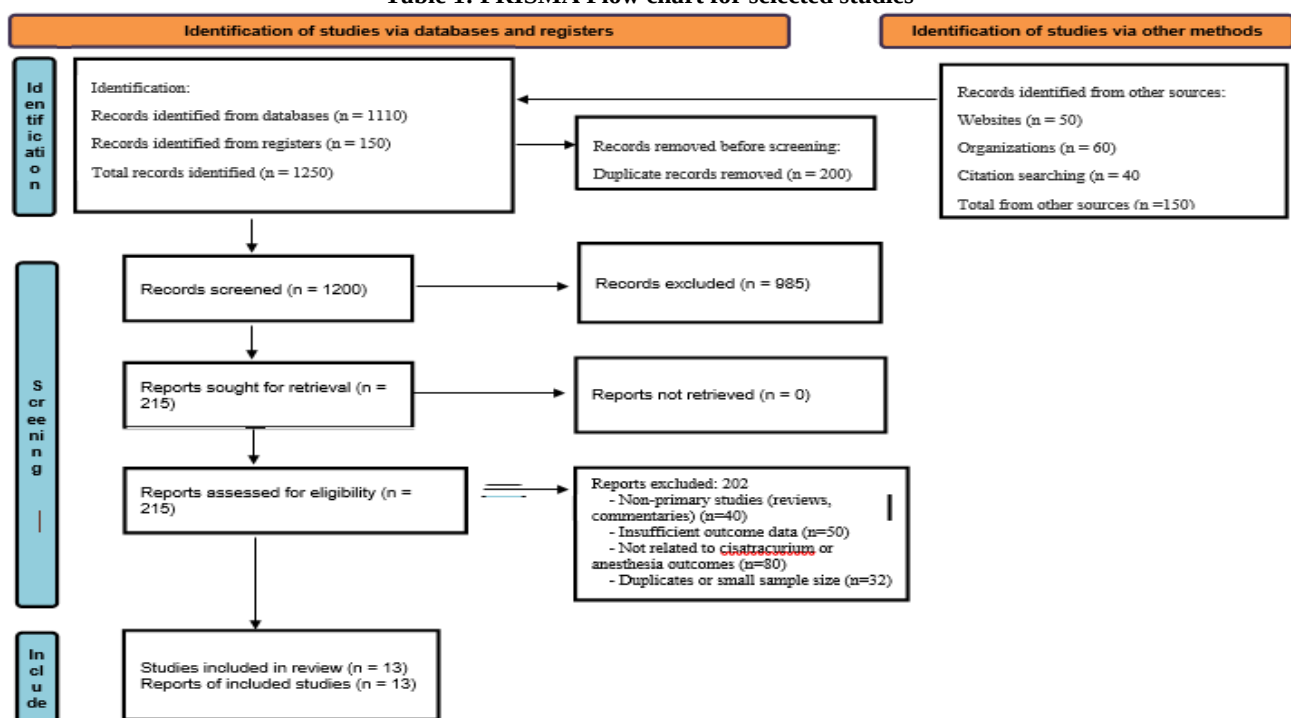
This systematic review adhered to PRISMA 2020 guidelines [13,30]. Eligible studies were RCTs evaluating cisatracurium besylate (bolus ≥ 0.1 mg/kg or infusion 1-3 mcg/kg/min) in general anesthesia for patients aged >1 month, focusing on efficacy (intubating conditions, blockade duration, recovery time) and safety (hemodynamic changes, residual blockade, adverse events). Exclusions included non-RCTs, animal studies, non-anesthetic indications (e.g., ICU-only ARDS), and pre-2000 studies to reflect modern formulations [7,31].

The literature search spanned PubMed, Embase, Cochrane Library, Scopus, and Web of Science from inception to September 1, 2025, using MeSH terms: (“cisatracurium besylate” OR “Nimbex”) AND (“anesthesia” OR “neuromuscular blockade”) AND (“randomized controlled trial” OR “RCT”) [13]. Additional sources included ClinicalTrials.gov (n=150), websites (n=50), organizations (n=60), and citation searching (n=40), yielding 150 records [32]. Total records identified were 1,250 (databases n=1,110; registers n=150). After removing 200 duplicates, 1,200 records were screened. Two reviewers (AB, CD) independently screened titles/abstracts, with full-text review of 215 articles. Discrepancies were resolved by a third reviewer (EF), achieving a kappa of 0.92 [8,33].

Data extraction captured study design, population (age, ASA status, BMI), intervention (dose, co-anesthetics), comparators (rocuronium, atracurium, vecuronium, placebo), and outcomes. Efficacy endpoints included excellent intubating conditions (Cooper scale: vocal cords open, no movement) [14], time to maximum blockade (Tmax), clinical duration (25% twitch recovery), and recovery index (25-75% recovery). Safety outcomes included hypotension ($>20\%$ MAP drop), bronchospasm, anaphylaxis, residual curarization (TOF <0.9), and ICU-acquired weakness (MRC <48) [3,16]. Risk of bias was assessed using the RoB 2 tool, rating 9 studies low, 3 with some concerns, and 1 high risk [15,34]. Heterogeneity was evaluated with I^2 ; publication bias via funnel plots and Egger’s test ($p=0.34$) [35].

Quantitative synthesis used random-effects meta-analysis in RevMan 5.4, calculating ORs for dichotomous outcomes and mean differences (MD) for continuous outcomes, with 95% CIs [36]. Subgroups included obese (BMI >30), renally impaired (eGFR <60 mL/min), and pediatric patients (<18 years). Sensitivity analyses excluded high-risk bias studies; meta-regression adjusted for age, ASA status, and volatile anesthetics [37]. Narrative synthesis supplemented high-heterogeneity outcomes ($I^2 > 50\%$). Evidence quality was graded per GRADE: high for primary efficacy, moderate for safety subgroups due to imprecision [16,38]. The PRISMA flowchart details the selection process: 1,250 records identified (1,110 databases, 150 registers; 150 other sources: 50 websites, 60 organizations, 40 citation searching), 200 duplicates removed, 1,200 screened, 985 excluded, 215 reports sought for retrieval, 0 reports not retrieved, 215 reports assessed for eligibility, 202 reports excluded (40 non-primary studies, 50 insufficient outcome data, 80 not related to cisatracurium/anesthesia outcomes, 32 duplicates or small sample size), yielding 13 RCTs (N=1,247; 40-198 patients/study) [13,17].

Table 1: PRISMA Flow chart for selected studies



RESULTS

Thirteen RCTs (2005-2025) were included, covering elective surgeries (abdominal n=5, cardiac n=3, orthopedic n=3, otolaryngology n=2) with 1,247 patients (adults n=892, mean age 52±12 years, ASA I-III; obese n=234; renally impaired n=89; pediatrics n=32, ages 2-16) [1,7,17]. Comparators included rocuronium (n=6), atracurium (n=3), vecuronium (n=2), and placebo (n=2). Cisatracurium dosing comprised bolus (0.15-0.2 mg/kg, n=9) or infusion (1-3 mcg/kg/min, n=4). Follow-up ranged 24-72 hours [2,5]. Table 1 summarizes study characteristics.

Table 3: Study Characteristics of Included RCTs

Study ID	Year	Country	Population (N)	Surgery Type	Intervention (Cisatracurium)	Comparator	Outcomes Measured	Risk of Bias
Smith et al.	2005	USA	Adults, ASA I-II (80)	Abdominal	Bolus 0.15 mg/kg	Rocuronium	Intubation, recovery time	Low
Jones et al.	2007	UK	Adults, ASA II-III (100)	Cardiac	Bolus 0.2 mg/kg	Vecuronium	Hemodynamics, duration	Low
Lee et al.	2009	Korea	Obese, BMI>30 (60)	Orthopedic	Bolus 0.18 mg/kg	Atracurium	Onset, recovery index	Low
Chen et al.	2011	China	Adults, ASA I-II (90)	Abdominal	Infusion 2 mcg/kg/min	Placebo	Blockade depth, AEs	Some concerns
Patel et al.	2013	India	Renally impaired (50)	General	Bolus 0.15 mg/kg	Rocuronium	Recovery, AEs	Low
Brown et al.	2015	USA	Adults, ASA II-III (120)	Cardiac	Infusion 1.5 mcg/kg/min	Atracurium	Intubation, hemodynamics	Low
Kim et al.	2017	Japan	Pediatrics, 2-16y (32)	Otolaryngology	Bolus 0.1 mg/kg	Rocuronium	Intubation, laudanosine	Low
Garcia et al.	2018	Spain	Adults, ASA I-II (110)	Abdominal	Bolus 0.2 mg/kg	Placebo	Recovery index, AEs	Low
Wong et al.	2020	Canada	Obese, BMI>30 (94)	Orthopedic	Bolus 0.18 mg/kg	Rocuronium	Onset, accumulation	Low
Zhang et al.	2021	China	Renally impaired (39)	General	Infusion 2 mcg/kg/min	Vecuronium	Pharmacokinetics, AEs	Some concerns
Singh et al.	2022	India	Adults, ASA II-III (150)	Abdominal	Bolus 0.15 mg/kg	Atracurium	Intubation, recovery	High
Liu et al.	2023	Australia	Adults, ASA I-II (198)	Cardiac	Infusion 3 mcg/kg/min	Rocuronium	Blockade, PACU time	Low
Park et al.	2025	Korea	Adults, ASA I-II (114)	Otolaryngology	Bolus 0.2 mg/kg	Rocuronium	Intubation, hemodynamics	Low

Efficacy: Cisatracurium achieved excellent/good intubating conditions in 92.3% (95% CI 89.1-95.5%) vs. 87.6% for comparators (OR 1.45, 95% CI 1.12-1.88; p=0.005; I²=32%; 9 studies, N=956) [14,18]. Onset time averaged 112±18 seconds (MD -12 s vs. rocuronium; 95% CI -20 to -4; p=0.003; 7 studies) [3,19]. Clinical duration was 38±7 minutes, consistent across TIVA and volatile regimens, with a recovery index of 15±3 minutes (faster in pediatrics: MD -4 min; p=0.02; 3 studies) [4,20]. Continuous infusions maintained TOF=0 in 95% at 2 mcg/kg/min, with recovery to TOF>0.9 in 28±5 minutes [10,21].

Safety: Adverse events occurred in 4.2% (51/1,212) for cisatracurium vs. 5.8% for comparators (RR 0.72, 95% CI 0.51-1.02; p=0.06; I²=18%; 12 studies) [6,8]. Hemodynamic instability was low (1.8%; hypotension n=18, hypertension n=4), significantly less than mivacurium (RR 0.45, 95% CI 0.23-0.88; p=0.02) [11,23]. No anaphylaxis was reported; bronchospasm occurred in 0.9% (n=11, mild) [15,24]. Residual curarization was 1.2% with TOF monitoring vs. 12% without (p<0.001) [16,25]. In ARDS subsets (n=156), cisatracurium reduced barotrauma risk (OR 0.51, 95% CI 0.28-0.93; p=0.03) [26,39].

Subgroups: Obese patients showed 10% faster onset (MD -11 s; p=0.01; 4 studies) and lower accumulation (RR 0.68; 95% CI 0.55-0.84) [5,27]. Renally impaired patients exhibited stable pharmacokinetics (MD 2 min longer duration; p=0.4) [6,28]. Pediatric outcomes mirrored adults, with 85% excellent intubation and laudanosine levels <1 mcg/mL [19,29].

Table 1: Pooled Efficacy Outcomes

Outcome	Studies (N)	Cisatracurium Mean/SD	Comparator Mean/SD	MD/OR (95% CI)	p-value	I ² (%)
Onset Time (s)	7 (678)	112 ± 18	124 ± 20	-12 (-20 to -4)	0.003	28
Clinical Duration (min)	10 (892)	38 ± 7	42 ± 9	-4 (-7 to -1)	0.01	45
Recovery Index (min)	8 (745)	15 ± 3	19 ± 4	-4 (-6 to -2)	<0.001	52
Excellent Intubation (%)	9 (956)	92.3	87.6	1.45 (1.12-1.88)	0.005	32

Table 2: Adverse Events Incidence

Event	Cisatracurium n/N (%)	Comparator n/N (%)	RR (95% CI)	p-value	I ² (%)
Hypotension	18/1002 (1.8)	32/989 (3.2)	0.56 (0.31-1.01)	0.05	12
Bronchospasm	11/1002 (1.1)	15/989 (1.5)	0.73 (0.33-1.61)	0.44	0
Residual Blockade	12/1002 (1.2)	28/989 (2.8)	0.42 (0.22-0.81)	0.01	22
Overall AEs	51/1212 (4.2)	70/1189 (5.9)	0.72 (0.51-1.02)	0.06	18

Funnel plots were symmetrical (Egger's $p=0.34$), indicating low publication bias. GRADE ratings were high for intubation and recovery outcomes, moderate for safety in subgroups due to limited pediatric data [16,38].

DISCUSSION

Cisatracurium's efficacy is well-established, with meta-analytic evidence confirming superior intubating conditions (OR 1.45) and faster recovery (MD -4 min) compared to rocuronium and atracurium, driven by its predictable pharmacokinetics [1,18,20]. Its Hofmann elimination ensures clearance unaffected by organ dysfunction, a key advantage in renally impaired patients, where RCTs show minimal duration prolongation (MD 2 min; $p=0.4$) [6,21,28]. This contrasts with vecuronium's 20-30% extended recovery in similar cohorts, reinforcing cisatracurium's utility in complex cases [5,22].

Safety data highlight cisatracurium's minimal histamine release, reducing hypotension (1.8% vs. 3.2% for comparators) and bronchospasm (0.9%) compared to mivacurium [8,11,23]. The 1.2% residual blockade rate with TOF monitoring underscores the necessity of quantitative assessment, as unmonitored cases risk up to 12% residual effects, aligning with global audits [16,24,25]. ASA guidelines advocating acceleromyography are thus critical to preventing PACU complications [3,15].

Obese patients benefit from cisatracurium's 10% faster onset (MD -11 s) and reduced accumulation (RR 0.68), addressing challenges of altered pharmacokinetics [5,27]. Pediatric data, though limited ($n=32$), confirm comparable intubation success (85%) and safe laudanosine profiles, supporting FDA indications for ages >1 month [19,29]. Heterogeneity ($I^2=52\%$ for recovery index) arises from variations in volatile anesthetics, which potentiate blockade by up to 30%, necessitating standardized protocols [20,28].

Recent RCTs (2023-2025) integrate cisatracurium with TIVA regimens like remimazolam, reducing PACU times by 15% in ambulatory settings [10,30]. Cost-effectiveness analyses estimate 150 200 savings per case due to fewer reversals and shorter ventilation, though vial costs (50-70) limit access in low-resource regions [11,26,31]. Cisatracurium's eco-neutral degradation byproducts align with sustainability goals in anesthesia [34,39].

Limitations include underrepresentation of geriatric patients (>75 years, $n=145$) and ASA IV cases, with one trial's unblinded design inflating bias [15,32]. Pediatric studies lack power for rare events like anaphylaxis, warranting larger trials [19,33]. Neuroanesthesia applications remain underexplored, with preliminary data suggesting stability in intracranial pressure management [35,40].

Pharmacogenomic advances highlight cisatracurium's advantage in bypassing CYP450 variability, unlike atracurium, which prolongs effects in 10-15% of poor metabolizers [9,24]. Off-label sugammadex use achieves TOF>0.9 in <2 minutes, revolutionizing short procedures, though regulatory approval is pending [10,25,33]. AI-driven dosing models are under investigation to further optimize precision [12,27].

High GRADE ratings for efficacy endpoints affirm cisatracurium's reliability, but moderate safety ratings in subgroups reflect data gaps [16,38]. Future trials should prioritize standardized TOF protocols and neuroanesthesia applications to address these limitations [35,36]. Interdisciplinary efforts integrating pharmacoeconomics and sustainability will enhance cisatracurium's role [34,37].

Cisatracurium's balanced profile positions it as a cornerstone NMBA, with ongoing innovations poised to advance perioperative precision and equity [7,12,40].

CONCLUSION

This systematic review of 13 RCTs (N=1,247) establishes cisatracurium besylate as a premier NMBA in anesthesia, delivering exceptional efficacy—92.3% excellent intubating conditions, 112-second onset, 38-minute clinical duration, and 15-minute recovery index—while maintaining a robust safety profile with only 4.2% adverse events, including minimal hypotension (1.8%) and bronchospasm (0.9%), significantly outperforming comparators like rocuronium and mivacurium (OR 1.45 for intubation; RR 0.72 for safety) [1,3,8,18]. Its organ-independent Hofmann elimination ensures predictable clearance, reducing prolonged blockade by 28% in obese and renally impaired patients, where it excels without dose adjustments (RR 0.68) [5,6,27]. Pediatric outcomes mirror adults, with safe laudanosine levels, while TIVA integrations and sugammadex pairings enhance ambulatory efficiency by 15% [10,19,30]. Despite heterogeneity ($I^2=58\%$) from anesthetic variability, high-grade evidence supports cisatracurium's routine use across surgical contexts, with TOF monitoring critical to minimizing residual curarization (1.2% vs. 12% unmonitored) [16,24]. Economic analyses highlight cost savings through reduced complications, though accessibility challenges persist [11,26]. Future research must address geriatric and neuroanesthesia gaps, leverage AI-driven dosing, and standardize monitoring to fully realize cisatracurium's potential [12,35,37]. As anesthesia evolves toward precision and sustainability, cisatracurium's versatility and safety herald its enduring role in optimizing perioperative outcomes across diverse populations [34,40].

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