J Med Sci 2025;45 (4):166-168
DOI: 10.4103/jmedsci.jmedsci_72_25

CASE REPORT

Anaphylactic Shock Induced by Higher Doses But Not Lower Doses of Cisatracurium

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A 49-year-old female experienced recurrent anaphylactic shock triggered by higher doses of cisatracurium during multiple surgeries. Anaphylaxis occurred with doses higher than 6 mg. Lower doses or complete avoidance prevented shock recurrence. Elevated serum tryptase levels confirmed IgE-mediated mast cell activation. This case highlights the dose-dependent nature of cisatracurium-induced anaphylaxis and emphasizes the importance of effective communication, accurate documentation, and prompt management to prevent re-exposure and mitigate this life-threatening complication. Skin testing may provide evidence of causative allergen.

Key words: Anaphylactic shock, case report, cisatracurium, communication, IgE, tryptase

INTRODUCTION

Anaphylaxis is a life-threatening hypersensitivity reaction requiring immediate intervention. Neuromuscular blocking agents (NMBAs) are among the most common triggers of perioperative anaphylaxis.[1,2] Cisatracurium's quaternary ammonium groups contribute to its anaphylactic potential.[3,4] We report a case of recurrent anaphylactic shock occurring in two hospitals, triggered by higher doses, but not lower doses, of cisatracurium. This case underscores the importance of effective communication and accurate documentation in ensuring perioperative safety.

CASE REPORT

A 49-year-old female (156 cm, 56 kg) with type 2 diabetes mellitus sustained multiple injuries in a traffic accident. During surgery under general anesthesia at an external hospital (first anesthesia), she developed anaphylactic shock, leading to the procedure's cancellation. After stabilization, she was transferred to our hospital.

Upon arrival, she underwent a second general anesthesia for orthopedic surgery. Since the specific anaphylactic trigger had not been identified, our team proceeded without muscle relaxants, given that NMBAs are common culprits. No adverse events occurred during this anesthetic course. One week later, she underwent further surgery for wound reconstruction. A different anesthesiologist administered 4 mg of cisatracurium to facilitate laryngeal mask airway (LMA) insertion. No adverse events were observed.

One year later, the patient underwent a fourth surgery for a scaphoid fracture. Given the absence of prior adverse reactions to cisatracurium, 6 mg was administered during induction, resulting in immediate shock with tachycardia (100–123 bpm), hypotension (72/46 mmHg), and desaturation (SpO_2: 72–83%). Despite fluid resuscitation and ephedrine administration, there was no significant improvement. Suspecting anaphylactic shock, diphenhydramine, hydrocortisone, and epinephrine were administered, stabilizing her hemodynamic status and allowing surgery to proceed.

Received: April 07, 2025; Revised: April 15, 2025; Accepted: May 27, 2025; Published: July 21, 2025
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How to cite this article: Wu TS, Liu YH, Wu ZF, Tse J. Anaphylactic shock induced by higher doses but not lower doses of cisatracurium. J Med Sci 2025;45:166-8.

After surgery, the LMA was replaced with an endotracheal tube before transferring the patient to the intensive care unit (ICU). For this purpose, 16 mg of cisatracurium was administered. Shortly after, a second episode of shock developed, with a further increased heart rate (156 bpm), hypotension (56/32 mmHg), and the appearance of a maculopapular rash on the abdomen and arms. Despite hemodynamic compromise, airway pressure, end-tidal carbon dioxide levels, and oxygen saturation remained stable. The arterial blood gas analysis under an FiO_2 of 70% showed the following results: PH - 7.323, $PaCO_2$ - 44.6 mmHg, PaO_2 - 94.4 mmHg, HCO_3^- - 21.4 mmol/L, base excess - 3.5 mEq/L, K+ - 2.8 mEq/L, sugar - 256 mg/dL, and lactate - 3.75 mmol/L. The patient was treated with repeated epinephrine boluses and infusion before ICU transfer. She was extubated 1 h later and discharged 2 days postoperatively. A blood sample collected immediately after the shock revealed an elevated tryptase level (15.1 ng/mL), which decreased to 1.21 ng/mL after 24 h. Elevated serum IgE levels (159 IU/mL) and leukocytosis (32,570/μL) were also observed.

Due to this critical event, our team contacted the external hospital for a comprehensive review of her first anesthesia record. It was revealed that tachycardia (80–100 bpm), hypotension (70/40 mmHg), and desaturation (SpO_2: 89–92%) developed immediately after anesthesia induction, which included 12 mg of cisatracurium. The patient was stabilized with multiple norepinephrine and epinephrine boluses. During the perioperative period, three additional doses of 4 mg were administered, each worsening the shock, requiring a continuous infusion of epinephrine throughout the remainder of the procedure. The arterial blood gas analysis under an FiO_2 of 50% yielded the following results: PH - 7.21, $PaCO_2$ - 52 mmHg, PaO_2 - 59 mmHg, HCO_3^- - 20.8 mmol/L, base excess - 7.1 mEq/L, K+ - 2.7 mEq/L, sugar - 168 mg/dL, and lactate - 1.2 mmol/L. She was transferred to the ICU, extubated 3 hours later, and later transferred to our hospital for further management. Postshock tryptase levels were also elevated (10.9 ng/mL) and decreased to 3.2 ng/mL after 24 h.

In summary, the patient experienced anaphylactic shock during her first anesthesia at the external hospital. Among the three subsequent anesthetic procedures at our institution, another episode occurred. A detailed list of the medications administered during her anesthetic management is presented in Table 1.

Table 1: Medications administrated during the patient's four anesthesia sessions

	1st anesthesia	2nd anesthesia	3rd anesthesia	4th anesthesia
Fentanyl	✓	✘	✓	✓
Lidocaine	✓	✓	✓	✓
Propofol	✓	✓	✓	✓
Cisatracurium (mg)	12+12 mg	✘	4 mg	6+16 mg
Sevoflurane	✓	✓	✘	✘
Desflurane	✘	✘	✓	✓
Dexamethasone	✓	✓	✓	✓
Cefazolin	✓	✓	✓	✓

✓ indicates the medication was administered; ✘ indicates the medication was not administered

DISCUSSION

Based on the patient's history and the sequence of events, cisatracurium is suspected as the anaphylactic trigger, with reactions occurring at induction doses ≥6 mg but not at 4 mg. Furthermore, additional doses of 4 mg during the first anesthesia and 16 mg for endotracheal intubation during the fourth anesthesia exacerbated the shock, suggesting a dose-dependent response. Che *et al*.[5] demonstrated that cisatracurium activates mast cells via the MRGPRX2 receptor, leading to dose-dependent histamine release and subsequent hypersensitivity reactions. Higher doses increase the risk of pseudoallergic and anaphylactic reactions.

Re-exposure also plays a significant role in allergic reactions. Research suggests that re-exposure to NMBAs can lead to severe hypersensitivity reactions, even in cases where the initial administration did not result in anaphylaxis or when a skin test was negative. Jeong *et al*.[6] reported that 20% of patients who received skin test-negative NMBAs still experienced hypotension, highlighting the risks of re-exposure. Zhou *et al*.[4] further demonstrated that prior exposure to NMBAs increases the likelihood of severe allergic reactions upon subsequent administration, potentially due to IgE-mediated hypersensitivity or pseudoallergic mechanisms. A sensitization phase may prime the immune system, leading to allergic reactions upon later exposure (late sensitization).

The patient declined further testing after discharge. If she agrees to additional testing, skin testing with incremental doses of cisatracurium could confirm the suspected dose-dependent anaphylactic reaction.

Identifying the allergen is crucial for preventing future episodes, but immediate treatment is paramount. Delayed intervention risks cardiovascular collapse. Epinephrine is the first-line therapy, alongside hemodynamic stabilization and airway management. While diagnostic tests, such as skin testing or specific IgE testing, help identify allergens, acute management should prioritize rapid resuscitation.

Effective communication and documentation are critical in preventing recurrent events. Had the external hospital provided a record of potential allergenic drugs, subsequent events might have been avoided. The patient's medical records should be updated to indicate a cisatracurium allergy, ensuring safer future anesthetic management.

CONCLUSION

This case highlights the dose-dependent nature of cisatracurium-induced anaphylaxis and the increased risk upon re-exposure. Effective interinstitutional communication and thorough documentation of suspected allergies are essential for safe perioperative management.

Declaration of patient consent

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its amendments. The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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