

## The cisatracurium besilate – A short review

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### Abstract

Various neuromuscular blocking agents are used in the routine anesthesia practice. Cisatracurium besilate is a nondepolarising neuromuscular blocking agent which has an intermediate duration of action. Due to the high molecular weight and high polarity the volume of distribution is low. Cisatracurium besilate undergoes Hofmann elimination which makes this as a drug of choice in organ failure patients.

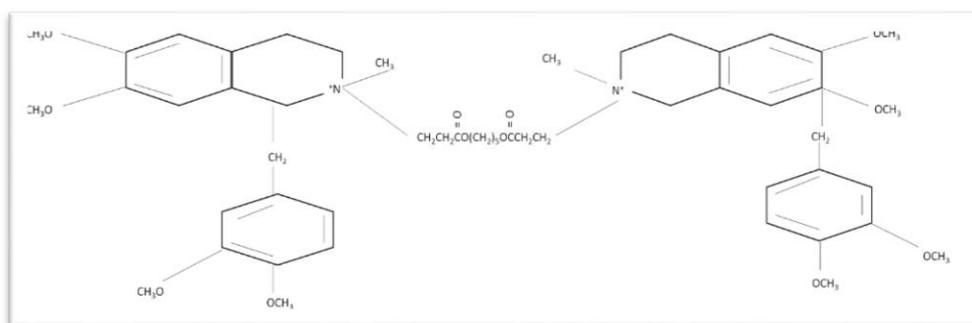
**Keywords:** Cisatracurium, Neuromuscular blocking agent, Nondepolarizing.

### Introduction

General anesthesia (GA) is commonly practiced due to various disadvantages seen with regional techniques. With the newer research molecules of anesthetic drugs and the safety margins, the GA can be conducted safely. GA has five components that are analgesia, amnesia, paralysis, hypnosis, immobility. Though achieving all the components are challenging, the use of muscle relaxant is very tricky and a thorough knowledge of the drugs before the use is very important. Muscle relaxants are used to facilitate endotracheal intubation, ensure patient immobility and improve surgical exposure along with adequate hypnosis and analgesia. Two types of neuromuscular

blockers are available i.e., non-depolarizing and depolarizing. Cisatracurium Iew benzyloisoquinoline which was introduced for clinical use since 1995. It is a recently launched product in India with nondepolarising neuromuscular blocking property and has an intermediate duration of action.

**Chemical formulation:** Cisatracurium is an intermediate-acting bis-benzyloisoquinolinium skeletal muscle relaxant. The chemical name is cisatracurium besylate and has the molecular weight of 1243.487 g/mol. The molecular formula of cisatracurium is C<sub>65</sub>H<sub>82</sub>N<sub>2</sub>O<sub>18</sub>S<sub>2</sub>. It is one of the 10 isomer of the atracurium which has the similar profile.<sup>(1)</sup> The chemical structure is shown in Fig.1.



**Fig. 1: Chemical structure of Cistatracurium**

**Pharmacodynamics:** Cisatracurium is a new skeletal muscle relaxant which mainly acts on the cholinergic receptors leading to blocking of impulses which are transmitted to skeletal muscle. The onset of action and the duration of action are intermediate in nature when compared to other skeletal muscle relaxant drugs. The action is mainly reversed by the acetyl cholinesterase inhibitors like neostigmine thus antagonizing the action of cisatracurium.

### Pharmacokinetics

**Route of administration:** Intravenous

**Dosage and formulation:** Injection cisatracurium besylate is available in solution formulation which is a sterile, non-pyrogenic solution provided in 5, 10 and 20 ml vials. Each ml contains 2mg of cisatracurium. Many manufacturers provide 20ml vial which is mainly for the ICU use, equivalent to 10mg/ml, intended for infusion. The single use vials contain 0.9% benzyl alcohol as a preservative. Initial dose for tracheal intubation in adults is 0.15 or 0.2 mg/kg; then 0.03 mg/kg I.V every 40 to 50 minutes. Infusion dose of 3 mcg/kg/minute can be considered for prolonged surgery. In children 0.1mg/kg as a initial dose.

**Onset, peak and duration:** Onset of action is 1-3 min and with the peak of 2-5 min and duration of action is 25-45 minutes.

**Distribution:** The volume of distribution is small due to relative large molecular weight and high polarity.

**Metabolism & Elimination:** The cisatracurium is eliminated by both biliary and urinary route. The drug undergoes Hofmann elimination which is a pH and temperature dependent process. The metabolic products are laudanosine and monoquaternary acrylate. Laudanosine is metabolized into desmethyl metabolites and gets conjugated with glucuronic acid and excreted through urine. The later undergoes into hydrolysis to form monoquaternary alcohol which intern undergoes Hofmann elimination. Approximately 77% if the drug injected undergoes Hofmann elimination which is an organ independent elimination process. The elimination half-life of cisatracurium besilate in patients with normal organ function is 25 minutes. Raise in temperature either body or room temperature will reduce the potency of cisatracurium as its metabolism is temperature and pH dependent. The increased in metabolism of Cisatracurim seen in patients having fever and prolonged action is seen in case of cardiac surgeries where hypothermia was induced.<sup>(2,3)</sup> The drug should not be administered with the same line where patient is receiving warm intravenous fluids.

**Special population:** There is no drug dosage adjustment is required for renal failure patient receiving this drug. But it is recommended to have neuromuscular

junction monitoring while receiving.<sup>(4,5)</sup> The pharmacokinetics of cisatracurium differ marginally in elderly patients. Onset is also delayed in elderly due to slower biophase equilibration.<sup>(6,7)</sup> But certain studies have shown, clinically the onset time is not significantly different between the adults and elderly population.<sup>(8,9)</sup>

**Pregnancy & lactation:** The cisatracurium metabolite laudanosine crosses the placental barrier which is about 14% of maternal blood concentrations.<sup>(10)</sup> There are no specific studies exists on usage of this drug in patient with lactation.

**Drug interaction:** Synergistic effects are seen with other muscle relaxants like, atracurium, vecuronium and rocuronium.<sup>(11)</sup>

### Indications

This drug is used as a muscle relaxant for tracheal intubation during general anesthesia. It is successfully used in critical care where patient were put on mechanical ventilation that were requiring complete skeletal muscle paralysis. The dosage requirement will be higher for the patients who are on mechanical ventilation for prolonged duration. This may be due to degradation of the receptors. Thus there is a need for neuromuscular monitoring in such patients.<sup>(12)</sup>

**Contraindications:** Patients with known hypersensitivity to this drug, malignant hyperthermia and neuromuscular disorders.

**Table 1: Comparison with Atracurium and Vecuronium**

Feature	Cisatracurium	Artacurium	Vecuronium
Duration	Intermediate	Intermediate	Intermediate
Metabolite	Laudanosine	Laudanosine	3-desacetylvecuronium
Elimination half life	22 minutes	20 minutes	65-75 minutes
Metabolism	Hofmann	Hoffman	By liver
Cost effectiveness (In comparison with Atracurium)	No	-	Yes
Hypotension and bradycardia due to histamine release	Insignificant	Significant	Insignificant

**Storage:** The drug should be stored at 2-8°C to preserve the potency of the drug.

**Safety and tolerability:** This drug has been studied in patients with severer sepsis and receiving prolonged mechanical ventilation and the results showed that standard dosing of this drug may result in slower patient response with reduced effect. The author recommended to use larger dose to overcome the delayed effect.<sup>(13)</sup> The accumulation of metabolite laudanosine after prolonged infusion of cisatracurium causes seizures in animals. This may not be true with the humans as reported earlier.<sup>(14)</sup> Various studies have shown insignificant cardiovascular and cerebral parameter changes when given bolus and maintenance dose. This drug is preferred in patients with instability

of hemodynamic. Cisatracurium when compared with the vecuronium in coronary artery disease patients the author found that there was a clinically insignificant change in the hemodynamics.<sup>(15-17)</sup> There is no systemic or cutaneous histamine release when the drug injected in either bolus or as continuous infusion method.<sup>(18)</sup>

### Conclusion

Cisatracurium is a newer intermediate onset and duration skeletal muscle relaxant. This drug can be safely be used in hepatorenal impairment. Like other muscle relaxants it can be used in both elective surgical procedures under general anesthesia and in patients

who receive the prolonged controlled mechanical ventilation. The only concern could be the cost effectiveness in comparison with available skeletal muscle relaxants.

## References

- Correa, Claudia Maria Nogueira, Sudo, Gisele Zapata, and Sudo, Roberto Takashi.. Hemodynamic effects of atracurium and cisatracurium and the use of diphenhydramine and cimetidine. *Revista Brasileira de Anestesiologia*, (2010),60(1),52-63.
- Sharma V, Verma S, Biyani G, Bhatia PK. Temperature and cisatracurium degradation: So what is new? *Indian Journal of Anaesthesia*. (2015), 59(11):763.
- Tewari P, Sikora R. Shortened duration of action of atracurium in a patient with pyrexia. *Indian Journal of Anaesthesia*. (1998), 42, 61–4.
- Soukup J Czeslick E Bunk S Clausen T Menzel M Radke J Cisatracurium in patients with compromised kidney function. Pharmacodynamic and intubation conditions under isoflurane-nitrous oxide anesthesia. *Anaesthesist*. (1998), 47(8), 669-76.
- Della Rocca G, Pompei L, Coccia C, Costa MG, Cecchini V, Vilardi V, Pietropaoli P Atracurium, cisatracurium, vecuronium and rocuronium in patients with renal failure. *Minerva Anestesiologica*. (2003), 69(7-8):605-11, 612, 5.
- Sorooshian SS, Stafford MA, Eastwood NB, Boyd AH, Hull CJ, Wright PM. Pharmacokinetics and pharmacodynamics of cisatracurium in young and elderly adult patients. *Anesthesiology*. (1996), 84(5), 1083-91.
- The effect of blood flow upon the activity of gallamine triethiodide. Goat VA, Yeung ML, Blakeney C, Feldman SA *British Journal of Anaesthesia* (1976), 48(2), 69-73.
- Kim JH, Lee YC, Lee SI, et al. Effective doses of cisatracurium in the adult and the elderly. *Korean Journal of Anesthesiology* (2016), 69(5), 453-459.
- Clinical pharmacokinetics of cisatracurium besilate. Kisor DF, Schmith VD *Clinical Pharmacokinetics*. (1999), 36(1), 27-40.
- Fodale V, Santamaria LB Laudanosine, an atracurium and cisatracurium metabolite. *European Journal of Anaesthesiology*. (2002), 19(7), 466-73.
- Kim KS Chun YS Chon SU Suh JK. Neuromuscular interaction between cisatracurium and mivacurium, atracurium, vecuronium or rocuronium administered in combination. *Anaesthesia*. (1998), 53(9), 872-8.
- Dieye E, Minville V, Asehnoune K, et al. Pharmacodynamics of cisatracurium in the intensive care unit: an observational study. *Annals of Intensive Care*. (2014), 4, 3.
- Liu X, Kruger PS, Weiss M, Roberts MS. The pharmacokinetics and pharmacodynamics of cisatracurium in critically ill patients with severe sepsis. *British Journal of Clinical Pharmacology*. (2012), 73(5), 741-9.
- Grigore AM, Brusco L Jr, Kuroda MKoorn R. Laudanosine and atracurium concentrations in a patient receiving long-term atracurium infusion. *Critical Care Medicine*. (1998), 26(1), 180-3.
- Movafegh A Amini S Sharifnia H Torkamandi H Hayatshahi A Javadi M. Cost analysis and safety comparison of Cisatracurium and Atracurium in patients undergoing general anesthesia. *European Review for Medical and Pharmacological Sciences*. (2013), 17(4), 447-50.
- Soukup J, Doenicke A, Hoernecke R, Vorhammer B, Seebauer A, Moss J. Cardiovascular effects after bolus administration of cisatracurium. A comparison with vecuronium. *Anaesthesist* (1996), 45(11), 1024-9.
- Reich DL, Mulier J, Viby-Mogensen J, Konstadt SN, van Aken HK, Jensen FS, DePerio M, Buckley SG. Comparison of the cardiovascular effects of cisatracurium and vecuronium in patients with coronary artery disease. *Canadian Journal of Anaesthesia*. (1998), 45(8), 794-7.
- Selcuk M Celebioglu B Celiker V Basgul E Aypar U. Infusion and bolus administration of cisatracurium - effects on histamine release. *Middle East Journal of Anaesthesiology*. (2005), 18(2), 407-19.