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Case Report

Anaesthesia Section

Inadequate Neuromuscular Blockade Due to Donepezil During General Anaesthesia for Cataract Surgery: A Case Report

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ABSTRACT

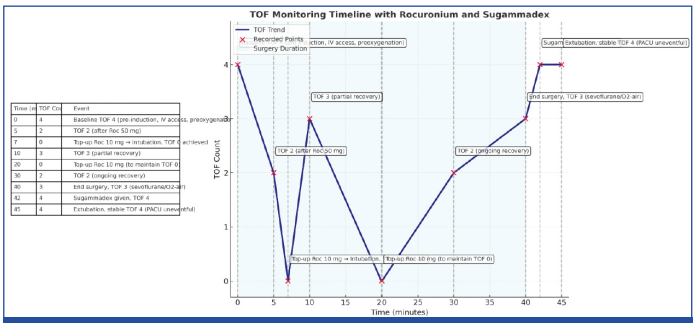
Donepezil, an acetylcholinesterase inhibitor used to treat dementia and Alzheimer's disease, can interfere with non-depolarising neuromuscular blockers by increasing synaptic acetylcholine, potentially leading to inadequate neuromuscular blockade. A 57-year-old male with Down syndrome, dementia, and chronic donepezil therapy underwent elective cataract surgery under general anaesthesia. Despite standard dosing of rocuronium, neuromuscular blockade was delayed and incomplete, requiring repeated boluses. Quantitative Train of Four (TOF) monitoring revealed resistance to non-depolarising muscle relaxants, likely due to donepezil-induced acetylcholinesterase inhibition. Rapid recovery occurred despite Chronic Kidney Disease (CKD) Stage 3, and reversal with sugammadex was successful. This case highlights the importance of neuromuscular monitoring and tailored anaesthetic planning in patients on cholinesterase inhibitors.

Keywords: Acetylcholinesterase, Dementia, Donepezil, Rocuronium

CASE REPORT

A 57-year-old male with Down syndrome (Trisomy 21) with a history of dementia and depression for the last 7 years was scheduled for elective bilateral cataract surgery under general anaesthesia. He lived in a residential care facility and was assessed as the American Society of Anaesthesiologists (ASA) Class III. He had no prior anaesthetic exposure or family history of anaesthesia-related complications. He has also been diagnosed with borderline diabetes, hypertension and chronic kidney disease for the last 5 years, which was managed non pharmacologically. His medication for dementia was donepezil 10 mg nocte with escitalopram 20 mg OD and mirtazapine 7.5 mg nocte for depression for the last 7 years. He took the last dose of donepezil the night before surgery. Hypercholesterolaemia was managed with rosuvastatin 10 mg nocte. He was also on caltrate 600 mg/400 units twice a day and prolia injection every 6 months for osteoporosis. On examination, he was able to follow the instructions and seemed cooperative. His weight was 83 kilograms and height 162 cms. On auscultation, there was no murmur and clear air entry on both sides. Laboratory parameters were normal, except for the creatinine of 153 micromol/L. The Electrocardiogram (ECG) revealed sinus bradycardia with a heart rate of 54 beats per minute (bpm), without any ST segment changes. Airway examination revealed an edentulous jaw, a Mallampati I score, a thyromental distance of 7 cm, and a normal neck range of motion.

After intravenous access and preoxygenation, anaesthesia was induced using propofol (2 mg/kg) and fentanyl (2 micrograms/kg). When the patient lost consciousness, Train of Four (TOF) stimulation of the left ulnar nerve was initiated using a peripheral nerve stimulator. The initial TOF count was 4, and the patient then received a bolus injection of rocuronium 0.6 mg/kg (approximately 50 mg). The TOF count decreased at an unusually slow rate, and a TOF count of 2 was detected approximately 5 min after the administration of rocuronium. Despite the full dose, TOF monitoring revealed only partial neuromuscular blockade. A further 10 mg of rocuronium was administered to facilitate intubation to achieve a TOF count of 0. After successful endotracheal intubation, however, a TOF count of 3 was detected at 10 min and needed an additional bolus of 10 mg to keep the TOF count 0. Adequate relaxation was eventually achieved, though the onset was delayed and laryngeal reflexes persisted initially, requiring careful titration and a cautious airway approach. Anaesthesia was maintained with sevoflurane and an oxygen/air mixture. The surgical procedure lasted 40 minutes. Intraoperatively, TOF recovery was faster than expected, with a TOF count of 3 noted by the end of the procedure (see [Table/Fig-1]). Reversal was achieved using sugammadex (2 mg/kg). The patient was successfully extubated after confirming adequate respiratory efforts, obeying verbal commands, and the ability to lift the head for five seconds with a TOF count of 4. The patient remained stable in the Post-Anaesthesia Care Unit (PACU).



[Table/Fig-1]: TOF monitoring timeline showing delayed onset and accelerated recovery of neuromuscular blockade in a patient on chronic donepezil therapy.

DISCUSSION

Donepezil, a reversible acetylcholinesterase inhibitor, is known to alter the pharmacodynamics of neuromuscular blocking agents. By increasing synaptic acetylcholine concentrations, it can antagonise the effects of non-depolarising muscle relaxants such as rocuronium [1].

In the present case, donepezil was possibly responsible for the seemingly inadequate muscle relaxation intra-operatively. The increased dose requirement of Non-depolarising Muscle Relaxants (NDMR) can be due to the increased availability of acetylcholine at the neuromuscular junction.

A comparable case by Jang EA et al., described a patient receiving donepezil who exhibited inadequate neuromuscular blockade with rocuronium despite appropriate dosing under Total Intravenous Anaesthesia (TIVA) [2]. The authors proposed that acetylcholinesterase inhibition increases acetylcholine concentration at the neuromuscular junction, competitively antagonising non-depolarising agents. They

noted that the absence of volatile anaesthetic potentiation during TIVA may accentuate this resistance.

Similarly, Bhardwaj A et al., reported a patient on chronic donepezil therapy who required excessive doses of rocuronium and vecuronium yet developed residual neuromuscular weakness and delayed recovery post-operatively, necessitating ventilatory support [3].

This variability is likely multifactorial, involving receptor-level adaptations, altered pharmacokinetics in renal dysfunction, and individual variability in drug metabolism [4]. Adverse neuromuscular signs associated with donepezil therapy, including relative insensitivity to neuromuscular blockers, are likely due to the inhibition of acetylcholinesterase at NMJs, which prolongs the action of acetylcholine on postsynaptic nicotinic acetylcholine receptors without substantially impairing evoked acetylcholine release [5].

In contrast, the present case demonstrated resistance to rocuronium despite sevoflurane anaesthesia, which typically enhances neuromuscular blockade. The onset was markedly delayed, requiring repeated 10 mg boluses to achieve a TOF count of 0, and accelerated recovery occurred with TOF 3 by the end of surgery. This bidirectional alteration with reduced onset potency but shortened duration differs from the delayed recovery seen by Bhardwaj et al., suggesting interindividual variability in donepezil-NMBA interactions [3].

In the present case, the patient's CKD was an additional factor potentially influencing the altered neuromuscular response. Rocuronium is primarily eliminated by the hepatobiliary route, but renal clearance contributes to approximately 10% of total elimination. In CKD, reduced plasma clearance and prolonged elimination half-life have been reported, which can theoretically lead to delayed recovery from neuromuscular blockade [6]. However, the current case paradoxically demonstrated rapid recovery and resistance, suggesting that the predominant mechanism was pharmacodynamic antagonism from chronic donepezil therapy, which overshadowed any kinetic prolongation related to renal impairment.

Moreover, recent studies have highlighted an increased risk of adverse events, including respiratory complications, heart failure, and hypertensive crises in CKD patients receiving rocuronium and sugammadex compared to cisatracurium-neostigmine combinations. Despite this, sugammadex was deliberately chosen in this case because of its superior and predictable reversal of aminosteroid relaxants, even in the presence of donepezil-related receptor competition. This systematic review and meta-analysis conclude sugammadex may effectively and safely reverse rocuronium-induced NMB in patients with ESRD [6]. Several prospective case-control studies on the administration of sugammadex in patients with ESRD have been reported [7,8].

Neostigmine, by further inhibiting acetylcholinesterase, might have worsened cholinergic effects and produced an unreliable reversal. Thus, although CKD may prolong rocuronium elimination, the dominant clinical manifestation in this patient was functional resistance rather than delayed clearance. The use of quantitative TOF monitoring and sugammadex provided a controlled and safe reversal, minimising residual paralysis risk and avoiding the unpredictable response that could follow neostigmine administration in the context of both CKD and donepezil therapy [8].

Niruba et al. reported the case of an elderly male with dementia on chronic donepezil therapy who demonstrated resistance to atracurium, which is a non-depolarising neuromuscular blocker, during general anaesthesia for orthopaedic surgery [9]. The case illustrated that acetylcholinesterase inhibition from donepezil leads to increased acetylcholine levels at the neuromuscular junction, competitively antagonising the effect of atracurium, which undergoes organ-independent Hofmann elimination. The authors described a prolonged onset time, incomplete muscle relaxation, and shortened duration of action despite repeat boluses, necessitating adjustments in anaesthetic technique and airway management.

Given these findings, perioperative strategies must be tailored to account for possible resistance or sensitivity. Some authors have suggested withholding donepezil for 2-3 weeks before surgery to reduce cholinergic tone [4]; however, this must be balanced against the risk of worsening cognitive function [10]. Where surgery cannot be delayed, quantitative neuromuscular monitoring becomes essential for accurately titrating relaxant dosing and guiding reversal decisions. This case reinforces that anaesthesiologists must remain vigilant when managing patients on cholinesterase inhibitors, particularly those with multiple comorbidities. Individualised planning and intraoperative monitoring can help avoid complications related to inadequate or prolonged neuromuscular blockade.

CONCLUSION(S)

In patients on chronic donepezil therapy, especially those with intellectual disability or comorbidities like CKD, the response to neuromuscular blockers may be significantly altered. Anaesthetic management should be individualised, and TOF monitoring should be standard practice. Awareness of these interactions is essential to avoid complications during induction and emergence from anaesthesia.

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