Pharmacologic Reversal of Neuromuscular Blockade in Patients with Cardiac Disease: A New Age

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ABSTRACT

Postoperative residual curarization is one of the most clinically significant complications of the use of muscle relaxants. Prevention of residual paralysis depends on judicious neuromuscular blockade management, monitoring, and use of reversal agents. Administration of anticholinesterase agents is particularly problematic in patients with cardiac diseases. Thus, the use of neostigmine should be individualized based on a risk/benefit analysis. Clinical data suggest that sugammadex is the drug of choice for the reversal of neuromuscular blockade in the patient with cardiac disease.

INTRODUCTION

Neuromuscular blockade (NMB) is used routinely to enable tracheal intubation and maintain good surgical conditions. In addition to facilitating airway management, clinical guidelines recommend NMB use as an adjuvant for managing mechanical ventilation, decreasing oxygen consumption, managing status asthmaticus, increasing intracranial pressure, and treating muscle spasms. It has also been used to manage increased intra-abdominal pressure and for therapeutic hypothermia after out-of-hospital ventricular fibrillation-associated cardiac arrest. Neuromuscular blocking agents (NMBAs) cause skeletal muscle relaxation by blocking the transmission of nerve impulses at the neuromuscular junction. Non-depolarizing NMBAs competitively antagonize the nicotinic acetylcholine receptors and prevent depolarization on the postsynaptic motor endplate. Postoperative residual curarization is one of the most clinically significant complications of the use of muscle relaxants. It may lead to severe respiratory complications in the postoperative period including airway obstruction, increased risk of aspiration, attenuation of the hypoxic ventilatory response, the need for reintubation, as well as pneumonia oratelectasis, and thus prolong hospitalization. It suggests that NMB is an important patient safety issue.

Prevention of residual paralysis depends on judicious NMB management, monitoring, and use of reversal agents. The degree of neuromuscular block can be assessed by applying a supramaximal stimulus to a peripheral nerve, and then measuring the associated muscular response. Train-of-four (TOF) monitoring, which involves a series of four electrical impulses (2 Hz) delivered to a peripheral nerve, has become popular in the context of detecting residual paralysis postoperatively. Thus, residual block is defined as a TOF ratio less than 0.90. Pharmacologic reversion is required if the spontaneous reversal of NMB by metabolism and elimination of the NMBAs is insufficient to reach a TOF more than 0.9. Anticholinesterase agents (e.g., neostigmine) with concomitant use of antimuscarinic agents such as atropine and glycopyrrolate, to prevent the clinical effects of the parasympathetic activation, maybe used to reverse paralysis. Neostigmine acts by increasing the level of acetylcholine (Ach) at the neuromuscular junction. Ach potentiates the neurotransmission in both nicotinic and muscarinic receptors affecting the cardiovascular system through both central and peripheral pathways. Cardiac side effects include atropine-resistant bradycardia (high doses), nodal rhythm disturbances, atrioventricular block, Q-Tc interval prolongation, or other non-specific electrocardiographic alterations. Other side effects are anaphylaxis, convulsions, nausea and vomiting or fetal bradycardia. Anticholinergic agents such as atropine are used in combination with neostigmine to minimize neostigmine-associated bradycardia, excessive airways secretions. However, atropine may cause nodal rhythm and atrial arrhythmias. Therefore, administration of neostigmine might be particularly problematic in patients with cardiac diseases. Thus, the use of anticholinesterase agents should be individualized based on a risk/benefit analysis. Table 1 shows the main cardiac diseases in which the use of neostigmine implies a significant risk.

Several case reports of asystole preceded by bradycardia and sinus arrest after administration of neostigmine for reversal of NMB have been reported in several heart transplant patients. In the past, it was thought that drugs acting at the level of the sympathetic and parasympathetic system had no effect on the transplanted heart. The transplanted heart is denervated from parasympathetic and sympathetic innervation, while
preserving intrinsic cardiac mechanism, making the heart strictly dependent on Starling’s pressure-volume relationship. However, some degree of sympathetic and parasympathetic reinnervation has been shown to occur several months to years after heart transplantation, but is likely not complete until 15 years after transplantation.12–15

Likewise, neostigmine (1) can trigger fatal arrhythmias in patients with Wolff–Parkinson–White syndrome causing serious hemodynamic disorders;16 (2) may lead to QT prolongation, then their use should be done with caution in QT syndrome;17 (3) can produce hypotension, cardiac arrhythmia, and congestive heart failure in patients with chronic heart failure. On the other hand, atropine causes an increase in the heart rate increasing the consumption of oxygen in the myocardium, reason why it could be poorly tolerated in the patient with coronary artery disease.18–21 Caution should be exercised in the anesthetic management of patients with these cardiac diseases when reversing neuromuscular block with the anticholinesterase even when a muscarinic antagonist is co-administered. Avoidance of neuromuscular block if possible, use of short-acting drugs if paralysis is required, and use of new reversal agents are strategies to avoid a potentially catastrophic response to neostigmine.

In 2006, sugammadex, a new drug was described.19 It acts by forming tight complexes with aminosteroidal NMBAs in the plasma20 and can provide immediate reversal of deep block.2 The use of this agent has several advantages: (1) Sugammadex reverts immediately moderate (1.3–1.7 minutes) to deep (2.7 minutes) NMB in a safe way and it is useful when intubation has failed.21 (2) It does not involve direct interaction with cholinergic system. Therefore, its effects on the cardiovascular system, respiratory function, and thermoregulation are not clinically significant.19,21,22,23 (3) Alone or in combination with rocuronium or vecuronium, sugammadex does not cause QT prolongation.19,24 It is safe and effective for the reversal of rocuronium-induced NMB in patients with cardiovascular disease undergoing non-cardiac surgery.19,25 (4) It is safe in patients with pulmonary diseases or with hepatic impairment.26 (5) No dose adjustment is recommended in elderly patients with normal organ function or patients with mild to moderate renal impairment.19,26 Its clearance is not affected by gender, race, or body weight.

Despite the absence of well-designed multicenter clinical trials, clinical data suggest that sugammadex is the drug of choice for the reversal of NMB in the patient with cardiac disease. In any case, its introduction into clinical practice has meant a new age in reversal of NMB, especially in the anesthetic management of high-risk populations such as the patient with cardiac disease.

REFERENCES


