Sugammadex: will it change anaesthetic practice?

Non-depolarizing neuromuscular blocking drugs are widely used to facilitate intubation of the trachea, mechanical ventilation, and provide muscle relaxation during surgery. Reversal of non-depolarizing neuromuscular blocking drugs is performed commonly using neostigmine combined with glycopyrrolate. However, partial spontaneous recovery from neuromuscular block is required before the reversal drugs can be given to successfully restore normal neuromuscular activity; attempted reversal of profound neuromuscular block will usually result in incomplete recovery and residual weakness. Postoperatively, residual weakness is common and often poorly recognized, occurring in up to 45% of patients (Debaene et al, 2003) and may lead to significant respiratory complications. Neostigmine is also associated with a number of side effects.

Suxamethonium, a depolarizing neuromuscular blocking drug, undergoes rapid metabolism in the plasma by pseudocholinesterase, and recovery occurs without use of an anticholinesterase. At 1–1.5 mg/kg its rapid onset provides optimal conditions for intubation of the trachea within 1 minute and it is the drug of choice during rapid sequence induction. However, its short duration of action renders it little use for maintaining neuromuscular blockade.

Suxamethonium is also limited by a number of serious side effects, including malignant hyperpyrexia. Despite its swift offset, usually within 4–5 minutes, this is not sufficiently rapid to allow the return of spontaneous ventilation to prevent hypoxic brain injury time in the 'can't intubate, can't ventilate' scenario.

Sugammadex (Bridion, Schering-Plough, Kenilworth, N.J.) is a novel selective relaxant binding agent with the potential to change the practice of clinical neuromuscular pharmacology, as it appears to be able to reverse rapidly any degree of neuromuscular blockade produced by giving the non-depolarizing drug rocuronium.

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Sugammadex is a modified gamma cyclodextrin, an oligosaccharide. Three-dimensionally it is a hollow doughnut shape, comprised of a ring of eight negatively-charged sugars with a hollow, lipophilic core. This enables sugammadex to attract and encapsulate rocuronium molecules. Once administered, it rapidly removes free rocuronium molecules from the plasma via excretion in the urine.

The case for sugammadex

Sugammadex 2–4 mg/kg can rapidly reverse moderate rocuronium-induced neuromuscular block in a mean time of less than 2 minutes. No residual paralysis or significant adverse effects have been reported, suggesting it is an important new alternative to neostigmine.

High-dose rocuronium (1–1.2 mg/kg) is widely used as an alternative to suxamethonium in rapid sequence induction. Gijsenbergh et al (2005) suggested sugammadex 8 mg/kg can reverse the profound neuromuscular block produced by such doses in a mean time of 1–1.2 minutes. This raises the exciting prospect of sugammadex providing rescue therapy in the 'can't intubate, can't ventilate' scenario where rocuronium has been used, as well as the complete reversal of profound neuromuscular block at the end of surgery, without the risk of residual paralysis. It has also been shown that vecuronium can be effectively reversed by sugammadex (Suy et al, 2007).

The case against sugammadex

The most common adverse effect of using sugammadex is dysgeusia (metallic taste). Hypotension and a prolonged QT interval on the electrocardiogram have been reported, the significance of which is unclear. Flushing, an erythematous rash and two cases of bronchospasm in patients with pulmonary complications have occurred, but no cases of anaphylaxis.

Perhaps the greatest weakness is its inability to reverse the effects of suxamethonium, which a recent Cochrane review found to provide better intubating conditions than rocuronium during rapid sequence induction (Perry et al, 2008). It is also ineffective against the benzylisoquinolinium neuromuscular blocking drugs which are commonly used in clinical practice. In patients with normal renal function, the terminal half life of sugammadex is 1–2 hours and the return of a normal response to rocuronium is expected to take several half-lives and be dose dependent. This raises the question of scenarios in which reintubation of the trachea or repeat surgery is required following recent sugammadex use.

Disposition of sugammadex in patients with diminished or absent renal function is unclear. A study of 30 patients investigated the efficacy and safety of sugammadex in patients with end-stage renal failure and reported the drug was well tolerated (Staals et al, 2008) but further safety studies are indicated. Questions remain over the potential for sugammadex to encapsulate both endogenous and exogenous steroids. Finally expense may prove prohibitive if large doses (4–16 mg/kg) are required to reverse profound degrees of neuromuscular block.

Conclusions

Sugammadex is a novel, exciting drug with the potential to radically alter the practice of anaesthesia. However, it is not without its limitations; whether it will spell the end of conventional reversal drugs and use of suxamethonium remains to be seen. **BJHM**

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