Clinical Pharmacokinetics of Rocuronium Bromide

Karin S. Khuenl-Brady and Harald Sparr

Department of Anaesthesia and Intensive Care Medicine,
Leopold-Franzens-University of Innsbruck, Innsbruck, Austria

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Summary

A new aminosteroidal neuromuscular blocking agent, rocuronium bromide, has recently been introduced into clinical practice. Its main advantage over other currently used drugs of this kind is its fast onset of action, which could render rocuronium the muscle relaxant of choice for rapid facilitation of tracheal intubation. A further advantage of the new compound over vecuronium bromide is the less extensive formation of breakdown products, reducing the contribution of active metabolites to the neuromuscular blocking effects of the parent compound.

Thorough knowledge of the pharmacokinetics of any new drug is highly desirable for the anaesthesiologist because absorption, distribution to the tissue, as well as elimination by biotransformation and excretion, are closely related to its effects. Due to its chemical relationship to other aminosteroidal neuromuscular blocking agents such as pancuronium bromide or vecuronium, rocuronium is expected to display pharmacokinetic behaviour similar to that of its predecessors. Hepatic and renal disease may prolong the effect of rocuronium, but to a lesser extent than seen with pancuronium or vecuronium, because the plasma clearance of rocuronium is not significantly influenced by dysfunction of the liver or kidneys. On the contrary, in elderly or hypothermic patients the reduction in plasma clearance results in a prolonged duration of the action of rocuronium.

All information on the pharmacokinetics of this new nondepolarising neuro-
During recent years, research into the field of neuromuscular blocking drugs has been focused on finding a nondepolarising agent that could replace suxamethonium chloride (succinylcholine) for rapid intubation. Securing the airway is one of the most important goals during general anaesthesia. An adverse or fatal outcome is likely if this is not successfully achieved within a few minutes.

Providing good intubation conditions rapidly is, therefore, a very desirable characteristic of drugs used to facilitate tracheal intubation. Among all available agents, suxamethonium chloride is currently the drug of choice for rapid intubation. However, its depolarising mode of action can lead to a number of serious adverse effects, including arrhythmia, muscle pains, an increase in serum potassium and the triggering of malignant hyperthermia. Nevertheless, suxamethonium chloride is still widely used because of its rapid onset of action, exposing patients to risks which would be avoidable with a nondepolarising agent. Recent studies indicate that rocuronium bromide has the fastest onset of action of all nondepolarising muscle relaxants, leading to expectations that it might replace suxamethonium chloride in the future.

As with most other drugs, the pharmacokinetic behaviour of neuromuscular blocking agents is closely bound to its effects. Knowledge of the disposition, excretion and biotransformation of any newly developed compound is therefore indispensable for its rational use in various surgical procedures. More importantly, the influence of renal and hepatic impairment, age, hypothermia or pregnancy is essential for adequate administration. Deviations from normal response (prolongation of effect or increased sensitivity, in the case of muscle relaxants) do not appear unexpectedly if the underlying mechanisms are understood and kept in mind during application. Therefore the effects of rocuronium have been investigated in healthy adults, various diseases and extremes of age, as well as under different clinical conditions. This review will discuss all information currently available on the clinical pharmacokinetics of rocuronium.

1. Pharmacology and Adverse Effects

Rocuronium bromide is the 2-morpholino-3-hydroxy-16-N-allyl-pyrrolidino analogue of vecuronium (fig. 1). In contrast with the latter it is stable in aqueous solution and 6 times less potent, with a dose to produce 95% depression of twitch tension (muscle force) \( [\text{ED}_{95}] \) of approximately 0.23 to 0.36 mg/kg.\(^{[1-3]}\) 0.6 mg/kg, a dose that is also used in most pharmacokinetic studies, is usually administered to facilitate tracheal intubation. The onset time (time from injection to development of maximum blockade) ranges between 40 and 180 seconds. Good to excellent intubating conditions, however, are almost always present 60 seconds after the injection of rocuronium\(^{[4,5]}\) because of the fast development of neuromuscular blockade at the laryngeal muscles.\(^{[6]}\) The clinical duration of action (time from injection to recovery of 25% of initial twitch height) ranges from 15 to 40 minutes under intravenous anaesthesia, and is slightly longer under inhalational agents.\(^{[1]}\)

Several clinical studies have demonstrated the absence of cardiovascular adverse effects\(^{[7,8]}\) and