Clinical use of rocuronium in patients with end-stage renal disease

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Rocuronium bromide is one of the commonly used neuromuscular blocking agent. Rocuronium is eliminated primarily by the liver and slightly by the kidneys. Its duration of action is not significantly affected by renal disease. However, previous studies of rocuronium in patients with end-stage renal disease have not consistently demonstrated an effect of end-stage renal disease on the pharmacokinetics and pharmacodynamics of rocuronium.

Khuenl-Brady et al. [1] found that the duration and recovery index of rocuronium did not differ between patients with chronic renal failure and normal renal function under isoflurane anesthesia even when the drug was given in repeated doses for maintenance. They concluded that rocuronium appeared to be suitable for patients with chronic renal failure. Cooper et al. [2] demonstrated that the differences in onset time, duration of clinical relaxation, recovery index, and the time for train-of-four (TOF) ratio to return spontaneously to 0.7 were not significant between patients with and without renal failure during anesthesia with nitrous oxide, fentanyl and isoflurane. However the differences in the rates of clearance and the mean residence times were significant between patients with and without renal failure. They concluded that the effects of rocuronium may be prolonged in patients with renal disease, because of a decreased clearance of the drug.

The clinical duration and the time to recovery of the TOF to 70% of a bolus dose of 0.6 mg/kg rocuronium were prolonged significantly in patients with renal failure compared to healthy control under propofol anesthesia. Clearance of rocuronium was reduced by 39% in the renal failure patients compared to control, with an 84% increase in the mean residence time [3]. Szenohradszky et al. [4] found no difference in total plasma clearance between control and renal transplant patients under isoflurane anesthesia, whereas volume of distribution was greater in renal transplant patients than in control patients. This resulted in a longer elimination half life in renal transplant patients compared to controls.

Enhancement of the relaxant effect of rocuronium is greater with desflurane than with sevoflurane or isoflurane, although all volatile anesthetics enhance skeletal muscle relaxation compared with intravenous anesthetics.

In this issue of Korean Journal of Anesthesiology, Kim et al. [5] reported that the neuromuscular effects of 0.6 mg/kg rocuronium under desflurane anesthesia were markedly prolonged in patients with renal failure compared to patients with normal renal function. The 25%, 75%, and 95% twitch recovery times, the recovery of the TOF ratio to 70% (TOF70), and the recovery index prolonged in patients with renal failure compared to those with normal renal function (e.g., TOF70: 123.1 ± 49.1 min vs. 68.7 ± 15.5 min). A very strong association between the time to TOF70 and the diagnostic duration of renal failure was found ($R^2 = 0.79$) in this study. However, a lesser degree of association was found the time to TOF70 and the BUN ($R^2 = 0.23$) or creatinine ($R^2 = 0.649$) levels. The authors suggested that abnormal changes of the musculoskeletal system following years of dialysis strongly influenced the correlation with the time to TOF70.

Thus, pharmacokinetic and pharmacodynamic studies in humans suggest that the duration of action of rocuronium may be prolonged in patients with end-stage renal disease. The extent of the prolongation is likely to be modest. Kinds of anesthetic agents and the duration of end-stage renal disease may
affect the duration of action.

In the European Union, sugammadex is recommended for use in the reversal of rocuronium- or vecuronium-induced moderate or deep muscle relaxation in adult (including elderly) and pediatric patients (aged 2–17 years). Sugammadex is also approved in Australia, Iceland, New Zealand and Norway. In clinical trials in adult with relatively good health and pediatric patients, sugammadex provided rapid reversal of rocuronium- or vecuronium-induced neuromuscular blockade and was generally well tolerated [6]. The ultimate clinical utility of sugammadex will be clear only after large-scale clinical use [7]. Recently, Staals et al. [8] investigated the efficacy and safety of sugammadex for reversal of rocuronium-induced neuromuscular block in patients with end-stage renal failure. Sugammadex rapidly and effectively reversed neuromuscular block induced by rocuronium in renal failure and healthy patients and was tolerated by all patients.

Therefore, careful monitoring of neuromuscular transmission should be performed to prevent overdose of rocuronium in patients with end-stage renal disease. It is necessary to consider main anesthetic agents and the duration of end-stage renal disease. Sugammadex may be also useful for patients with end-stage renal disease after further safety studies.

REFERENCES