Student: Harriet Marshall

Project: Quantifying the effect and variability of neuromuscular blocking drugs on patients undergoing surgery

Supervisors: Associate Professor Ross Kennedy and Mrs Margie McKellow

Sponsors: Anaesthetists' Instrument Pool Limited

Introduction:

Neuromuscular blocking agents (NMBAs) are an integral component of anaesthetic care; patients receive a NMBA in approximately 50% of operations. The degree of neuromuscular blockade required varies depending on the operation. Up to 64% of patients may have residual neuromuscular blockade in the post-operative period. Partial blockade is associated with pharyngeal obstruction. When combined with altered sensitivity to hypoxia, particularly in elderly patients, there is an increased risk of adverse respiratory events. The issue is inter-patient variability.

Physiological and pathological variation affects the pharmacokinetics and pharmacodynamics of NMBAs; as these states are only partially quantifiable, it is currently impossible to accurately predict an individual's reaction to a NMBA.

As measurement of an individual's sensitivity pre-operatively is unfeasible, it is common practice to objectively measure neuromuscular transmission (NMT) intraoperatively. This is executed through nerve stimulation and force transduction of resultant muscle twitch. A current is applied transcutaneously four times, once every 0.5 seconds, creating four twitches or the train-of-four (TOF). Various models also create predicted effect-site NMBA concentration and when combined with qualitative NMB monitoring enable drug kinetic evaluation in real-time.

Aim:

To investigate patient response to neuromuscular blocking agents using equipment commonly found in the operating theatre in wide range of routine clinical cases.

We also aimed to analyse the prevalence of residual blockade and recovery from neuromuscular blockade in addition to patient quality of recovery from anaesthesia and surgery.

Method:

This study was approved by the New Zealand National Ethics Committee. Participants 18-90 years, with an America Society of Anaesthesiologists (ASA) score of I, II, or III scheduled to have surgery with anticipated use of >1 dose rocuronium (the most commonly used NMBA in Christchurch) were eligible. Intra-operatively, NMT was measured with the GE MechanoSensor through stimulation of the ulnar nerve and measurement of the force of the resultant contraction of a thumb muscle. Time (sec) from first administration of rocuronium to disappearance of the first and second twitches were recorded.

Time and TOF ratio at administration of further rocuronium, administration of NMBA antagonist and last MechanoSensor measurement were also recorded. Time and dose of rocuronium were entered in real time into the Navigator application suite, which calculated effect-site concentration of rocuronium over time using the models of Cooper and Laud.

The Post-operative Quality of Recovery Scale (PQRS) questionnaire gages physiological, nociceptive, emotional, activities of daily living and cognitive domains. Subjects completed a PQRS questionnaire pre-operatively and post-operatively at 30 minutes, one day, and one week.

Results:
We have results from 42 individuals; 18 male, 24 female. Mean age 55 (SD17) years, weight 83 (19)kg, BMI 30 (8.1)kg/m2. Mean average predicted effect-site rocuronium concentration at spontaneous return of the second twitch of the TOF was 0.96 (SD0.49)ng/ml, with a range of 0.21 to 2.9ng/ml. Interquartile range (IQR) was 0.74ng/ml and a median absolute deviation (MAD) 0.90ng/ml.

For individual responses mean IQR was 0.14 (0.10)ng/ml and MAD 0.10 (0.06)ng/ml. We found no correlation between age or weight and mean average predicted effect-site rocuronium concentration.

Based on the PQRS questionnaire, no participants had recovered in all domains at 30 minutes post-operatively. 1/29 (0.03) participants had recovered in all domains at one day and 5/29 (0.17) participants had recovered in all domains one week post-operatively.

Conclusion:
We found significant and non-predictable interpatient variation. This is consistent with previous studies. There was no correlation between rocuronium concentration at spontaneous return of the second twitch and age (R^2 0.06, p= 0.14) or weight (R^2 0.04, p= 0.23). This highlights the importance of objective intra-operative NMT monitoring, as current models of predicted effect-site concentration only provide part of the picture.

The small variation in individual responses to repeat doses shows patient sensitivity is uniform during an operation. This indicates that anticipatory, rather than reactive, NMBA dosing is feasible. Based on the response to the initial dose, the minimum rocuronium concentration required for adequate NMB can be extrapolated and blockade maintained at an appropriate minimum level, thus providing consistent operating conditions and enabling more effective reversal.

Very few participants recovered in all domains of the PQRS questionnaire at any of the three time points. Zero had recovered at 30 minutes post-operatively, 0.03 at one day and 0.17 at one week.

These scores are much lower compared to the cohort from the previous summer studentship; 0.06, 0.23, and 0.49 respectively. We hypothesise that the lower recovery rate of this year's cohort is due to an older mean age (39 compared to 55 years) and inclusion of a greater number of major operations.

In conclusion, the use of equipment available in theatre (the GE MechanoSensor and Navigator application suite) at the first dose of rocuronium can be integrated to gage patient sensitivity. This may help provide a more accurate prediction about an individual's response to repeat rocuronium doses during an operation.