FINAL PROJECT REPORT

Name:

R R Kennedy

Project Title:

Determination of Effect Site Targets for Sevoflurane

Please copy the "Outcome(s)" statement, entered on your application form, in the space below.

The overriding aim of this research is to facilitate more rational use of inhalational anaesthetics by validating the concept of effect-guided delivery.

This approach enables the anaesthetist to use the optimum amount of anaesthetic for each stage of the procedure. This allows the anaesthetic "recipe" to be better balanced, potentially producing faster wake up and reduced stays in the Recovery ward.

The ability to optimise delivery, especially with reduced flows has the potential for considerable cost saving. Inhalational anaesthetic agents commonly appear in the top 10 drugs by cost, partly because they are intrinsically expensive and partly because of the large number of patients receiving these drugs. This means that relatively modest decreases in the total amount administered to each patient have the potential for quite large savings overall.

The specific outcomes of this project are to determine the effect site rate constant for various noxious stimuli and to compare this with the values determined for the hypnotic component of anaesthesia. This information will allow more accurate titration of anaesthesia delivery and levels to patient needs at different stages of anaesthesia and surgery.

Will your work contribute to this outcome(s) in the manner you envisaged? If not, what has changed?

We believe we have completely achieved the outcomes outlined above.

We have determined the levels of sevoflurane required for two common airway manipulations (insertion of laryngeal mask airway and endotracheal tube) using an approach based on real-time estimation of "effect-site" levels. As well as determining the EC50, as outlined in the proposal we have derived dose response curves for these interventions. This allows estimation of EC95 values (the concentration required for 95% of the population), which is of more practical clinical value than the level required for 50% of the population. In addition the steepness of the dose response curve provides a useful guide to inter-individual varaition.

As part of the study we also determined the concentrations in the blood and brain at the time patients lost consciousness. These results further confirmed the value of using brain (or effect site levels) as these are more reliable and have a steeper dose response curve.

We were able to demonstrate that the time constant (or delay) for transfer between blood and brain for the "effect" of airway manipulation is faster than for the effect of "hypnosis". The implication of this result, supported by our recent work on eeg changes, is that anaesthetic agents affect different parts of the CNS at different rates. This has practical implications for the delivery and titration of these agents.

From our results we have data to guide administration of sevoflurane in a number of settings: if effect site guidance is available we have defined EC50 & EC95 levels for loss of

consciousness and insertion of various airways; for when these systems are not available we have derived time and delivery rate guidelines that achieve similar levels.

There is increasing evidence that there are subtle, unwanted effects of administering too much anaesthetic agents and that, with intravenous agents, effect-site rather than plasma level based dosing, provides significant advantages. We believe the results of this project help extend these concepts to the administration of inhaled agents and that in addition to defining underlying concepts we have derived practical clinical endpoints.

Please copy the "Specific Objective(s)" statement, entered on your application form, in the space below.

1. To determine the effect site concentration required for insertion of a laryngeal mask airway or an endotracheal tube.
2. To determine the effect site concentration required for IV cannulation.
3. To further validate the concept of effect site control.
4. Develop Guidelines for the time at which manipulations can be performed when Sevoflurane is the sole agent.

Briefly describe how successful you were in achieving the stated objective(s). If the objective(s) was not achieved, explain why that is the case and describe what you did manage to achieve.

As outlined in the outcomes section, we have completely achieved objectives 1, 3, and 4.

The study outlined in objective 2 has yet to commence, although it is our intention to do so. We have approached the various studies making up the project serially, and undertook comprehensive data analysis of the "LMA" component before moving on the "ETT" component which has extended the time for completion. In addition, recruitment rates were less than anticipated.

Based on this experience we have revised our planned study for objective 2, in particular we plan to use both fast and slow wash-in groups rather than comparison with published data. We are preparing this study.

Please confirm delivery of the outputs listed on your application form. If these outputs were not to be delivered, please explain why.

Two meeting presentations, with published abstracts.

Paper in preparation which will be submitted to a major international anaesthesia journal.

Data analysis has strengthened collaborative links with other workers in this field (Waikato, Sydney & Switzerland)