A PHARMACOKINETIC APPROACH TO RAPID TITRATION OF PROPOFOL TO MODERATE OBSTRUCTION FOR DIAGNOSIS OF SLEEP APNEA

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Introduction: Sleep nasendoscopy employs propofol titrated to moderate obstruction to permit anatomic identification of the site of airway obstruction[1]. While airway obstruction and loss of consciousness are fellow travelers[2], the ability to reliably achieve and maintain moderate obstruction can be challenging[3]. We describe a pharmacokinetic approach to rapid titration to an endpoint of moderate obstruction.

Methods: The pharmacokinetic model of Masui [4]was employed in conjunction with the pharmacodynamic model of Johnson [5]. The Masui model includes a LAG model that does not account for changes in infusion rate. To circumvent this limitation, a control sequence was implemented that utilized one bolus, an initial infusion rate, and a secondary infusion rate. This sequence was designed to minimize a loss function:

$$L = \left|P_{sleep}(90) - 0.05\right| + \left|P_{sleep}(195) - 0.5\right| + \left|P_{sleep}(390) - 0.995\right|$$

where $P_{sleep}(N)$ is the probability of sleep at N seconds. For any given age and weight, this sequence can be obtained, as shown in figure 1:

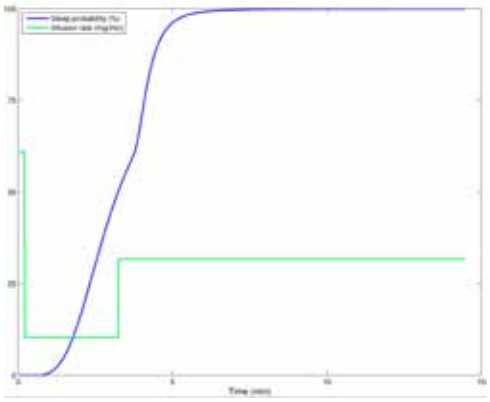

Figure 1

At some point during the interval 90 – 390 seconds, the patient will exhibit the desired level of obstruction. At that instant, the infusion rate necessary to maintain that effect site, and the period that the pump must be stopped to achieve this smoothly are calculated, as shown in figure 2:

The software, implemented in MATLAB, performs these calculations in real-time.

The software was employed in a prospective study of sleep nasendoscopy for screening patients undergoing transoral robotic tongue base reduction. To date, 12 patients have been evaluated with the lowest recorded saturation being 96%, and with 11/12 patients completing endoscopy with no chin lift or jaw thrust.

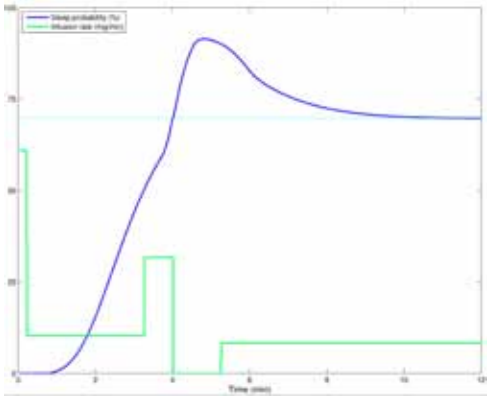

Figure 2

Discussion: Titration of propofol to precise pharmacodynamic endpoints shows promise in simplifying challenging tasks such as sleep nasendoscopy. The proposed system employs an anesthesiologist in the loop for titration, and may overcome the reluctance of the US FDA to permit target controlled infusion in clinical practice.

References:

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4. Masui K, Kira M, Kazama T, Hagihira S, Mortier EP, Struys MM. Early phase pharmacokinetics but not pharmacodynamics are influenced by propofol infusion rate. *Anesthesiology*. 2009;111:805-817.
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