Anesthesia Optimization of Post-Surgery Wake Up Time Providing Adequate Analgesia

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Abstract

What is the best drug concentration during anesthesia?

We are creating algorithms to minimize pain and shorten wake up time after surgery. This will be used by anesthesiologist during surgery to continuously provide optimal drug cocktails with surgery and patient specificity.

Introduction

In anesthetics multiple drugs are used to ensure a patient's well being during the surgical procedure. Certain drug to drug relationships react antagonistically, synergistically, while others have no effect at all. It is difficult for the anesthesiologist to know exactly how the patient will react, or is reacting to the drugs during a surgery. The anesthesiologist can only perceive the responsive cues from the patient during the surgery: pulse rate, blood pressure, and muscle functionality. By monitoring these responses the anesthesiologist ensures that the patient is kept far from recovery during the surgery to prevent side effects. To aid the anesthesiologist simple visualizations are displayed to show a history of administered drugs.

Background

Past research has found optimum recovery tracts, to reduce wake up time by accounting for the patient's individual co-variables: size, weight, age, sex, etc.[1] Studies by Vuyk and Manyam created two drug models, examining an opioid and a sedation drug.[1,2] Their results include the quickest recovery time from anesthesia and the corresponding drug concentrations, for static surgeries. Analgesia, adequate pain relief, is required for a truly successful surgery, and was not taken into account during previous studies. More recent research, dealing with the adequate analgesia problem, from Kern et al., has found drug to drug synergistic effects for various drugs.[3] Some unanswered questions remain: can recommended doses be found for specific surgeries? Can models predict effects of three or more drugs?

Method

The goal of this research is to optimize surgery anesthetically, by recommending efficient doses, accounting for adequate analgesia, and minimizing post-surgery wake time. Three drugs which will be taken into account, each having a specific advantage; Fentanyl, Remifentanil, and Propofol. Fentanyl, an opioid for analgesia, is a slow acting drug-thus prolonging time until effect and time to wear off. Fentanyl's characteristics are not ideal for short surgeries,

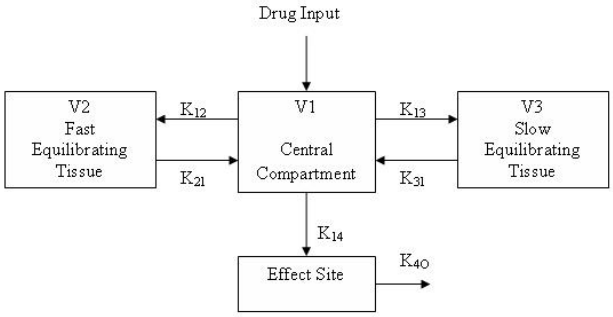
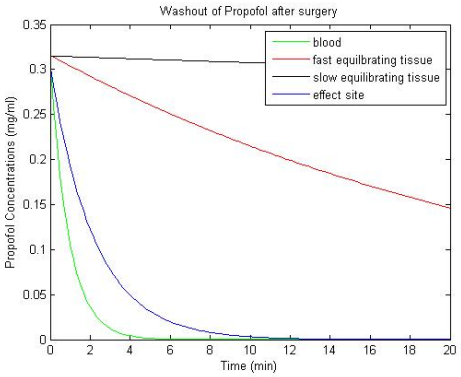
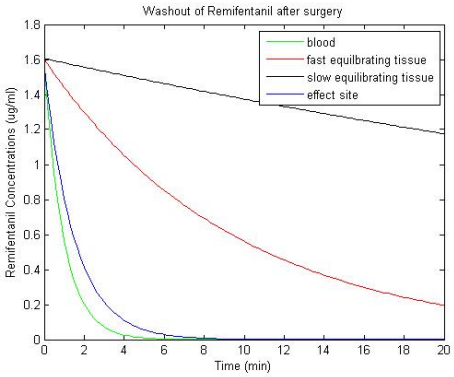


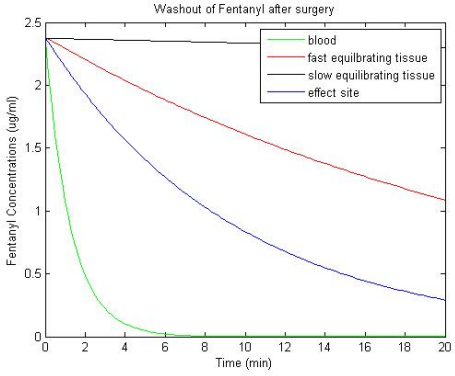
Figure 1: Three compartment pharmacokinetic model



(a) Depletion of Propofol



(b) Depletion of Remifentanil



(c) Depletion of Fentanyl

Figure 2: Drug Characteristics

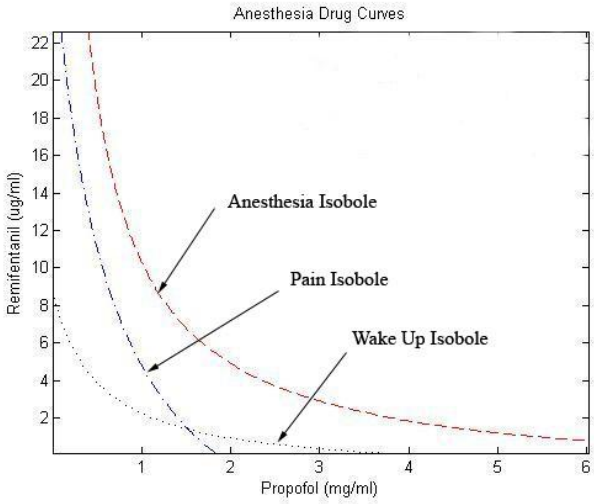


Figure 3: Levels of Anesthesia

but more ideal to use in longer operations.[4] Remifentanil, also an opioid for analgesia, is a quick acting drug. Remifentanil provides a quick effect in the body and is excreted from the body quickly; therefore its effectiveness is best for rapid short term effects.[5] These two opioids produce a similar effect and their concentrations can be combined at any moment to find an overall opioid effect. Propofol, a sedation drug for anesthesia, is highly synergistic with Fentanyl and Remifentanil, reducing needed concentrations.[3] These three drugs have a highly synergistic behavior and are common anesthetic drugs.

The pharmacokinetic model is seen in figure 1. This model describes the kinetics of the each drug throughout the body. Drugs are first introduced to the blood system typically via intraveneously or orally. The drug circulates the blood till it is absorbed by the tissues. Various tissues absorb the drug quickly while other tissues are saturated at a slower rate. An imaginary effect site is proportional to the drug amount in the blood. Each of the drugs have different kinetics, as shown in figure 2, and must be tracked individually. Remifentanil eliminates from all of the compartments in the body rapidly. Fentanyl, also an opioid, has a slower elimination rate from the body in all compartments. Propofol's elimination characteristics is similar to fentanyl except the depletion in the effect site is faster like remifentanil.

The model can also be described in differential equations.

$$\frac{dC_1}{dt} = -(k_{12} + k_{13} + k_{14})C_1 + k_{21}C_2 + k_{31}C_3 + I \tag{1}$$

$$\frac{dC_2}{dt} = k_{12}C_1 - k_{21}C_2 \tag{2}$$

$$\frac{dC_3}{dt} = k_{13}C_1 - k_{31}C_3 \tag{3}$$

$$\frac{dC_4}{dt} = k_{14}C_1 - k_{40}C_4 \tag{4}$$

Where C is the concentration in the specific compartment. K is the correpsonding rate constant different for each drug. I is the infusion or bolus of the drug administered. The system is complex due to the I, which is a piece-wise step function. I is not linear beacuse surgeries demand different levels of anesthesia at different times, i.e. at highly invasive points in surgery,

higher anesthesia is required.

When the surgery is finished I goes to 0. The system of differential equations is easily solvable without the I term. Let M be the matrix of the coefficents from the differential equations 2 - 4. Also let λ be the eigen values and t be the time after end of infusion.

$$\frac{dC}{dt} = MC \tag{5}$$

$$\Rightarrow \tag{6}$$

$$\frac{dC_1}{dt} = C_1(0)e^{\lambda_1 * t} \tag{7}$$

$$\frac{dC_2}{dt} = C_2(0)e^{\lambda_2 * t} \tag{8}$$

$$\frac{dC_3}{dt} = C_3(0)e^{\lambda_3 * t} \tag{9}$$

$$\frac{dC_4}{dt} = C_4(0)e^{\lambda_4 * t} \tag{10}$$

$$\tag{11}$$

These specific concentrations calculate the concentrations of the drugs as they are elimnated from the body. Comparing the washout time of the different possible concentrations we will be able to determine wake times and pain levels. This concept is shown in figure 3. During the procedure the patient will be in a state above the *Anesthesia Isobole*, as the drug eliminates from the body the patient will begin to feel pain. They will probably feel pain when their drug combination crosses the *Pain Isobole* and they will probably wake when they cross the *Wake Up Isobole*.

Discussion

We are presently working to find the algorithm to find the best drug cocktail. The algorithm produced from this method will be able to be used by the anesthesiologist during surgery. The anesthesiologist can administer the anesthetic drugs, concurrently the algorithm will calculate the expected anesthetic level of the patient and give recommended doses with equal anesthetic levels, with the quickest wake up time and sufficient analgesia levels. This research will become a educated guide to reassure and help the anesthesiologist during surgeries. This algorithm will be validated through clinical studies this summer.

References

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