Comparative Study of 4-Compartmental PK-PD Model with Effective Site Compartment for Different Parameter Set

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ABSTRACT

Target-controlled infusion pumps are for patients to control pain or to infuse sedations and anesthesia, typically those who underwent surgery. The pump has a programmable syringe device used to control the injection level of drugs. These pumps are even used in the ICU or operating theaters to manage patient’s pain after surgery or sedation. PK-PD Models are used to obtain the drug concentrations levels of the patient. The model depends on the drug flow rates in different parts of the body. There are many parameter sets available to measure the amount of drugs in the patients. This article presents a three compartmental patient model through Simulink to obtain concentrations levels from different parts of the body. The model is checked for a seven parameter set and suggests the set with the best results.

KEYWORDS

3-compartmental model, Anesthesia, PK-PD model, Target Controlled Infusion(TCI)

INTRODUCTION

Based on severity of disease (Khanday et al., 2016) the drug can be given to the patient either through oral or intravenous (IV). When a drug is infused through IV line, it will be distributed among different parts of the body. According to pharmacokinetics studies, the infused medicine passed through human body is absorbed, distributed and eliminated. The mathematical modeling of drug concentration is a predictive tool for analysis of biological processes. Modeling the drug infusion helps to add intelligence to infusion device and interoperability feature to the device. For example, Patient Controlled Infusion (PCA) is a self-controlled infusion pump used to infuse high alert sedations or drugs to patients. Once the drug is administrated, the microcontroller programmed pump will automatically infuse the medicine in to the patient. The infusion of too much drug into the patient may cause adverse events like death, respiratory depression and coma. The pump even involves many medical errors like programmable errors and prescription errors etc. With these abnormalities in infusion pumps, more attention of continuous monitoring of physiological parameter of patients is needed to control overdosed high alerts (like respiratory depression) while infusing through IV fluids (Shola & V, 2017).

Anesthesia is a drug is used before surgery through infusion pumps. This is used to provide painless surgery to the patient and smooth operation. When infusing these kinds of drugs administrator may use different ranges of infusions. However, providing the optimum drug delivery levels and steady state blood concentrations while infusing, is important for safest use of pump. This paper presents the patient model for drug delivery, how this model varies with different sets of pharmacokinetic (PK) parameters. The model is simulated through a MATLAB Simulink model, results are given and best models in targeting the drug at effective site compartment are suggested.

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BACKGROUND

The patient model for drug infusion is the process of administrating drug into the patient body through mathematical model. There are basically two patient models involved for knowing the drug interaction with human body.

Pharmacokinetic Model

The absorption, distribution and metabolism study of the drug (Wheatley, 2003) and the changes of drug concentration rate during drug administration through mathematical modelling is called pharmacokinetic. Young patients can dissolve the drug more rapidly (Ilyas et al., 2017) than elders and the metabolism of drug is in exponential form in human bodies. Therefore, it evaluates the drug status in a body through different mathematical models. The effect of drug levels can be measured through its concentration levels at different receptor levels like tissues of the body. The pharmacokinetic patient model is a mathematical tool that helps the clinician to measure the drug concentration levels into human body and to adjust the values for abnormal situations. Different mathematical models for pharmacokinetic models are available to understand the levels of the drug administration levels.

The compartmental model is mathematical representation of the body or a part of the body to study physiological or pharmacokinetic characteristics. Here the body is represented with a series of compartments arranged either in serial or in parallel based on the process of material.

Compartmental Models

The process of analyzing the drug concentration of a particular part, or compartment, through a mathematical model is known as compartmental model. In this model the body is represented as a series of parts or compartments. It is used to understand the physio or pharmacokinetic parameters of the patient during drug infusion. The compartment represents the group of similar tissues or fluids (Spruill et al., 2014). Organs and tissues with similar group of distribution are considered as one compartment. For example, the drug diffusion from lung organ is different from heart compartment. Based on the density of perfusion of drug through different organs, the compartments are categorized as central compartments and peripheral compartments. Peripheral compartments are further divided into highly perfused blood compartments like heart, lungs, liver, kidney and blood, and low perfused or peripheral compartments such as fat tissue, muscle tissues, etc.

Based on the seriousness of disease the drug can administrate to patient either orally or intravenously. Through oral process, the entire body is considered as one compartment. The rate of drug movements is described by first order kinetics. If the disease status is higher, the drug will be administrated through IV line. For example, the control of pain to post-surgical patients cannot be treated through orally. Obviously, the clinicians need IV administration since the effect of drug orally is less efficient than IV. Through IV administration, the drug directly enters into blood streams, then to different parts of the tissues and leaves from the body through liver and kidneys. Based on drug administration and number of compartments considered for the administration process the compartmental models are divided as follows: 1-compartment model, 2-compartment model and 3-compartment model.

The compartmental model shown in Figure 1 is single compartment model where the whole body is treated as single homogeneous compartment and the drug diffuses directly into blood. Here the input to the model is drug infusion and output is drug elimination. For example, oral drug administration or taking tablet can be represented using 1-compartment model and drug elimination through kidney is the output.

The compartmental model given in Figure 2 represents the diffusion of drug through two different homogeneous parts like blood and tissues. The input of the model is either through arterial blood, or through venous blood. For example, IV line drug infusion could be considered for this model.
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