Short communication

The fish tank model of first-order elimination: An effective pharmacokinetic teaching tool

Daniel Brown, PharmD*

Lloyd L. Gregory School of Pharmacy, Palm Beach Atlantic University, FL

Abstract

Objective: This report describes student perceptions of the fish tank model of first-order elimination as a learning aid in a clinical pharmacokinetics course.

Fish tank model: The model is based on a large rectangular fish tank filled with goldfish that are equally distributed throughout the tank. The elimination of fish results from passing an aquarium net through the water with a consistent motion at a constant rate, such that the number of fish removed per pass of the net consistently declines as the concentration of fish in the tank declines. Volume of distribution is the size of the tank, clearance is the volume of water that passes through the net per unit of time as fish are removed, and the elimination rate constant is the fraction of the volume of the tank compared to the volume of water that has fish cleared from it per unit of time.

Assessment: Two cohorts of students voluntarily participated in an online survey that called for Likert-type responses to indicate agreement with statements about whether the fish tank model helped them to understand first-order elimination concepts. Survey response rates were 77% and 94%. Both cohorts demonstrated approximately 70–80% agreement that the fish tank model enhanced their learning of clearance, volume of distribution, elimination rate constant, and protein binding.

Conclusion: The fish tank model appears to be an effective learning aid that helps students to develop a deeper conceptual understanding of basic pharmacokinetic principles.

© 2013 Elsevier Inc. All rights reserved.

Keywords: Pharmacokinetics; Fish tank; First-order elimination; Learning model; Teaching tool

Introduction

Pharmacokinetics is a mainstay field of study in PharmD curricula. Of the 65 (out of 82) colleges/schools of pharmacy that responded to a 2002 survey, 74% reported having more than one stand-alone course in pharmacokinetics.[1] The survey further revealed that an average of 5.8 credit hours were devoted to pharmacokinetics with about three credit hours devoted specifically to clinical pharmacokinetics.[1]

Pharmacokinetic concepts have proven to be elusive to the understanding of many pharmacy students. The complexities of logarithmic relationships between the physiologic and pharmacodynamic processes related to first-order drug elimination can be difficult to grasp. From an educational perspective, any new learning tool or teaching strategy that has the potential to reduce the mystery or dissipate some of the confusion surrounding fundamental pharmacokinetic concepts—that might better enable students to understand and apply pharmacokinetic principles and relationships—is worth pursuing. It is one thing to perform calculations by plugging numbers into an equation or memorizing and recalling factual definitions, but reconciling the intricate dynamics at play as a drug is being absorbed, distributed, metabolized, or excreted, can be particularly challenging.

Most pharmacokinetic resources describe fundamental first-order processes without applying an illustrative model. One textbook uses a novel illustration of a man shoveling gravel into a box filled with sand while another man clears

* Correspondence to: Daniel Brown, PharmD, Lloyd L. Gregory School of Pharmacy, Palm Beach Atlantic University, P.O. Box 24708, West Palm Beach, FL 33416-4708.

E-mail: daniel_brown@pba.edu

the gravel out of a different box of sand and then returns it to be refilled with gravel.[2] The model depicts the relationship between maintenance dose, clearance, and elimination rate constant. The fish tank model represents a different metaphor by which to illustrate the impact of physiologic processes that affect drugs within the body and the mathematical relationships between the pharmacokinetic parameters involved. This report describes one instructor's experience teaching applied clinical pharmacokinetics using the fish tank model as a conceptual foundation.

The fish tank model

The PharmD curriculum of the Lloyd L. Gregory School of Pharmacy at Palm Beach Atlantic University includes two courses in pharmacokinetics. Biopharmaceutics and Pharmacokinetics is a three-credit course taught by pharmaceutical science faculty members in the second semester of the first professional year. It covers the scientific and mathematic foundations of pharmacokinetics. Clinical Applications of Pharmacokinetic Dosing and Monitoring is a two-credit course taught by a pharmacy practice faculty member in the first semester of the second professional year. This course focuses on practical applications of clinical pharmacokinetics that are used by pharmacists when dosing and monitoring drugs. It was originally developed as a lecture-based course but was modified into a team-based learning format in 2011.

The fish tank model is introduced to students at the start of the second course to review principles that they have already learned from a mathematical perspective and facilitate a deeper understanding by engaging students in a more conceptual, application-oriented approach to the material. The intent is to both reinforce and deepen students' understanding of pharmacokinetic processes so that later in the course, when learning to apply drug-specific methods of pharmacokinetic dosing and monitoring, they will be better prepared to critically think their way to logical decisions rather than relying on the mere execution of equations to derive a "correct" answer.

Assumptions and abbreviations

Abbreviations used in describing the fish tank model correspond to those used in the recommended textbook of the course.[3]

V: volume of distribution
Cl: clearance
K: elimination rate constant
F_p: fraction of unbound drug in plasma
C: concentration of drug in the plasma
C_{ss}: concentration of drug at steady state
$C_{ss(total)}$: total concentration of drug at steady state
$C_{ss(unbound)}$: concentration of free (unbound) drug at steady state

The fish tank model assumes 100% bioavailability and instantaneous absorption and distribution, so as to eliminate the need to consider either the extent or rate of drug absorption and distribution. The model is based on elimination being the only process taking place within the context of a first-order, one-compartment system.

First-order design

The model is based on a large rectangular fish tank—the type found in a pet shop—with hundreds of goldfish equally distributed throughout the tank. Elimination of fish results from passing a typical aquarium net through the water with a consistent motion at a constant rate. According to this scenario, the number of fish removed per pass of the net will consistently decline, which means that the rate of elimination of fish is dependent on the concentration of fish in the tank. As long as fish are not being added to the tank, the elimination rate will continue to decline over time with every pass of the net. If fish are added to the tank, the rate of elimination will suddenly increase proportionately because the net would then capture a greater number of fish as it passes through the tank. That is what first-order drug elimination (which applies to most drugs) is all about.

Any physiologic mechanism by which drugs are eliminated from the blood as a first-order process can be represented by a "net" that is being used to remove fish from the tank. As long as the volume of water that passes through the net per unit of time is constant, it does not matter whether a moveable net is being pulled through a stationary tank or the water in the tank is flowing through a stationary net—as blood flows through a liver or kidney.

Volume of distribution

According to the fish tank model, the human body can be thought of as a large container filled with blood, much like a fish tank is a large container filled with water. When a dose of drug is administered, it is as if the drug is being placed into a tank of unknown volume. A higher concentration results if the size of the tank is small and a lower concentration results if the tank is large. When the "tank" is a human body, the apparent size of the body's "tank" relates to the plasma concentration that results from a given dose, just as the size of a fish tank could be determined by the concentration of fish that results from placing a known quantity of fish into the tank. Volume "of distribution" indicates the relative "size" of a patient's "tank" (the central compartment) based on the drug concentration that results from a given dose, which in turn, depends not on the patient's volume of blood, but on the extent to which the drug remains in the blood or distributes out of the blood.

A drug that tends to distribute out of the blood will characteristically produce a low plasma concentration that is reflective of a large volume. Therefore, anything that increases a drug's distribution (such as tissue binding)