A Brief Treatise on the Area Under the Curve

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Abstract

This chapter briefly discusses the pharmacologic parameter, commonly referred to as the Area Under the Curve, that describes the distribution and elimination of drugs from the body.

The "area under the curve" graph classically describes the plasma concentration of a drug as a function of time after an intravenous (IV) bolus of a medication plotted on *x* and *y* coordinates. Although an oversimplification, this visualization assists in estimating plasma medication levels.

In a one-compartment model, one must assume that all medication remains within the plasma compartment and does not redistribute to other body partitions. With an IV injection, the concentration of the drug is very elevated immediately after injection; however, the concentration drops exponentially as a constant fraction undergoes metabolism (Fig. 4.1). After four elimination half-lives, the level of medication approaches zero and changes minimally as time progresses.

In a two-compartment model, there is the presumption that all the drug does not remain within the plasma. It is assumed that medication distributes between the central plasma compartment and a "peripheral" partition. This imagery becomes clinically informative in relation to highly lipophilic drugs such as propofol. After a

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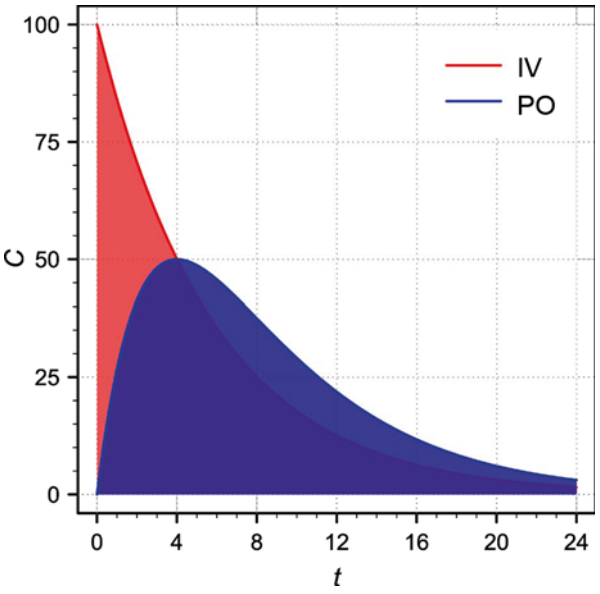

Fig. 4.1 Area Under the Curve, concentration vs. time: One-compartment model for bolus IV and PO administration [Reprinted from http://en.wikipedia.org/wiki/Bioavailability Last accessed on July 20, 2012. With permission from the Creative Commons License]

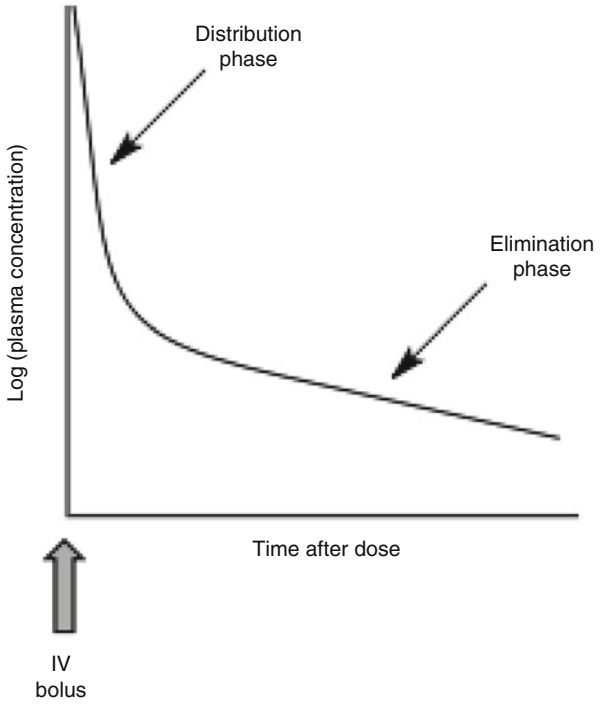

Fig. 4.2 Area Under the Curve, concentration vs. time: Two-compartment model for bolus IV administration [Reprinted from http://en.wikipedia.org/wiki/Pharmacokinetics Last accessed on July 20, 2012. With permission from the Creative Commons License]

single bolus, the concentration exponentially decreases as medication redistributes to the peripheral compartment (Fig. 4.2). With time, the concentration between the two compartments equalizes, and drug diffusion reverses. In other words, medication now moves from the peripheral to the central compartment. The concentration of medication gradually decreases within the central partition secondary to metabolism, highlighting another important assumption of the two-compartment model. Drug can only be metabolized from the central compartment; medication within the periphery is not subject to degradation. Graphically, this pharmacokinetic phenomenon is characterized by two curves. An initial distribution phase reflects diffusion of medication to the periphery. The second curve, or elimination phase, describes gradual metabolism from the central compartment. The slope of the distribution phase is much steeper than the slope of the elimination phase, indicating that drug concentration drops precipitously after injection, then more slowly due to elimination.