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Mathematical Model for the Effective Medicine Dosage and its Concentration in Blood Stream of a Patient

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Abstract: For most drugs there is a minimum concentration below which the drug is ineffective and a maximum concentration above which the drug is dangerous. This study presents a mathematical model for the effective medicine dosage and its concentration in bloodstream of a patient. Two mathematical tools, the exponential decay and geometric series are used to find the dose concentration of a drug in bloodstream of a patient.

Key words: Dose concentration, exponential decay, geometric series, mathematical model, patient, series

INTRODUCTION

Mathematical models simulate complex systems in a relatively fast time without the enormous costs of laboratory experiments and the biological variations. particularly for oncology, such models can be calibrated using experimental or clinical data (Wang *et al*., 2009; Gao *et al*., 2013) and competing hypotheses of tumor progression can be evaluated and treatment options thoroughly analyzed before clinical intervention (Powathil *et al*., 2012; Rockne *et al*., 2010). The application of mathematics in pharmacokinetics by using one and two compartment models is discussed by Koch-Noble (2011).

One of the physician's responsibilities is to give medicine dosage for a patient in an effective procedure. The search considers a model for a drug being given to a patient at regular intervals. When the drug is broken dowen by the body, its concentration in the bloodstream decreases. Also, it doesn't disappear completely before the next dose is given. Thus there is a tendency for the average drug concentration to increase over time.

MATERIALS AND METHODS

Exponential decay model and effective medicine dosage: An exponentialdecay model for the concentration of a drug in a patient's bloodstream is described in this study. Suppose that the drug is administered intravenously, so that, the concentration of the drug in the bloodstream jumps almost immediately to its highest level. The concentration of the drug then decays exponentially. If we letbe the concentration at time t and be the concentration just after the first dose is administered then an exponential decay model would be given by:

$$C(t) = C_0 e^{-kt}$$

where, k is the decay constant and is a property of the particular drug being used. It is usually obtained experimentally.

Now assume that an additional dose of the drug is given to the patient. Since, we are assuming that when the drug is administered it is diffused so rapidly throughout the bloodstream that, for all practical purposes, it reaches its highest concentration instantaneously, we would see a jump in the concentration of the drug when the new dose is given.

After the additional dose is given, the concentration again decays over time. A problem facing physicians is the fact that for most drugs, there is a concentration, m, below which the drug is ineffective and a concentration, M, above which the drug is dangerous. Thus, the physician would like the concentration C(t) satisfy:

$$m \le C(t) \le M$$

This requirement helps determine the initial dose of a drug and when the next dose should be administered. Note that, many factors could be important in determining the time between doses that is actually used including practical considerations like hospital schedules and shift changes.

RESULTS AND DISCUSSION

Equal, regularly-spaced doses: Consider next what happens if equal doses of the drug are given at regular time intervals. Recall that a drug has a maximum safe concentration and a minimum effective concentration. A treatment program of equal, regularly-spaced doses is safe and effective if the concentration of the drug satisfies:

$$m \le C(t) \le M$$

during the treatment. For the concentration of the drug after the first dose we presented the expression $C(t) = C_0e^{-kt}$. This expression is valid as long as only a single dose is given. However, suppose that at t = L a second dose is given and that the amount of the drug administered is the same as the first dose. According to our model, the concentration will jump immediately by an amount equal to C_0 when the second dose is given. However, when the second dose is given, there is still some of the drug in the bloodstream remaining from the first dose. This means that to compute the concentration just after the second dose, we have to add the value C_0 to the concentration remaining from the first dose. During the time between the second and third doses, the concentration decays exponentially from this value. To find the concentration after the third dose, we would have to repeat this process but now we have contributions from the first and second doses to include. We can calculate the concentration just before the second dose is administered by setting t = L in our equation:

$$C(t) = C_0e^{-kt}$$

to get:

$$C(L-) = C_0e^{-kL}$$

where, by C(L-) we mean the:

$$\lim_{t\to L^-} C(t)$$

Now, when the second dose is administered the concentration jumps by an increment, so that, the concentration just after the second dose is given is:

$$C_0+C(L-) = C_0+{}_0e^{-KL} = \left(1+e^{-KL}\right)$$

The concentration then decays from this value according to our exponential decay rule but with a slight twist. The twist is that the initial concentration is at t = L, instead of the more familiar case of t = 0. Our way to handle this is to write the exponential term as:

$$e^{-K(t-L)}$$

so that, at t = L, the exponent is 0. If we do this, then we can write the concentration as a function of time as:

$$C(t) = C_0\left(1+e^{-KL}\right)e^{-k(t-L)}$$

This function is only valid after the second dose is administered and before the third dose is given. That is, for $L\le t<2L$. Now, suppose that a third dose of the drug is given at t = 2L. The concentration just before the third dose is given is C(2L) which is:

$$C(2L-) = C_0\left(1+e^{-KL}\right)e^{-KL}$$

which, we can also write as:

$$C(2L-) = C_0\left(e^{-KL}+e^{-2KL}\right)$$

when the third dose is given, the concentration would jump again by and the concentration just after the third dose would be:

$$C(2L) = C_0\left(1+e^{-KL}+e^{-2KL}\right)$$

This process can be continued and leads to the following two formulas. The first is the concentration just before the Nth dose of the drug. This is:

$$C\left((N-1)L-\right) = C_0\sum_{i=1}^{N-1}e^{-ikL}$$

The second result, we need is the concentration just after the Nth dose which is:

$$C\left((N-1)L\right) = C_0\sum_{i=1}^{N-1}e^{-ikL}$$

Geometric series: We define a parameter r by:

$$r = e^{-KL}$$

where, $0<r<1$, k and L are positive constants. The properties of the exponential function can be used to show that:

$$r^i = e^{-ikL}$$

where, i is a non-negative integer. We can write our two formulas for the concentration just before and after the dose in terms of r as:

$$C\left((N-1)L^-\right) = C_0\sum_{i=1}^{N-1}r^i = C_0\frac{r-r^N}{1-r}$$

And:

$$C\left((N-1)L\right) = C_0\sum_{i=1}^{N-1}r^i = C_0\frac{r-r^N}{1-r}$$

where, the formula for the partial sum of a geometric series has been used to obtain the last equality in each of the equations above.

Now, assume a treatment program is to be continued indefinitely. The formulas above show that C((N-1) L^{-}) and C((N-1) L) both increase with This means that the minimum concentration is the concentration just before the second dose or:

$$C_{min} = C_0 r$$

and that the maximum concentration occurs just after the last dose. Thus, we have that:

$$C_{max} \leq \lim_{N\to\infty} C_0 \frac{1-r^N}{1-r} = \frac{C_0}{1-r}$$

Example: A patient is injected a particular drug. The concentration is 1.5 mg/mL (milligrams per milliliter), just after the drug is injected. After 4 h the concentration has dropped to 0.25 mg/mL. Here, C (4) = 0.25 at t = 4 and C_0 = 1.5 at t = 0.

$$C(t) = C_0 e^{-kt}$$

$0.25 = 1.5\, e^{-4k}$. Thus, the decay constant k is 0.4479398673 h^{-1}.

CONCLUSION

In this study, the exponential decay model and geometric series presents in detail the effective medicine dosage. Also, these techniques have been used for analysis of dose concentration in bloodstream of a patient and modeling of minimum and maximum concentration of a drug administered intravenously.

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