

Mathematical Modeling of Drug Delivery Methods for HIV Treatment

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Abstract

Drug delivery methods for treating patients, especially those with compromised immune systems due to human immunodeficiency virus (HIV), are widely studied to provide doctors with a variety of options. In this study, differential equation calculations were used to analyze both instantaneous and time-dependent methods of drug delivery. My findings showed that the critical dose (d_{cr}), the dosage that will eliminate the infection, for the instantaneous method was 2.3 mg, while for the time-dependent methods it was 3.5 mg. If a pill or injection with a drug dose greater than 2.3 mg is administered, there will be an initial decrease in virus amount, giving doctors more time to evaluate treatment options or allow the immune system to act. Overall, my study provides valuable insights into the optimal drug delivery methods for treating patients, particularly those with compromised immune systems. These findings may help doctors make more informed decisions about treatment options and ultimately improve patient outcomes.

Human immunodeficiency virus (HIV) is a sexually transmitted infection characterized by a weakened immune system. The virus attacks the immune system, causing those who have HIV to be more susceptible to further illness compared to the average person (CDC, 2022). HIV without proper treatment can progress to acquired immunodeficiency syndrome (AIDS), a chronic and potentially deadly infection. A common disparity between HIV-positive and negative patients is the infection and colonization of *Staphylococcus aureus* in the nasal cavity, which can spread to the rest of the body causing severe illness. *Staphylococcus aureus* is a type of staph infection, a

common genus (biological classification that ranks above the species and is comprised of multiple similar species) of germs, that is present in the noses of 30% of the population (CDC, 2011). Usually staph germs are harmless, but they can cause staph infections in various areas of the body, such as sepsis, pneumonia, and endocarditis. All of these infections can be deadly, especially in immunocompromised individuals. The most well-known type is methicillin-resistant *Staphylococcus aureus* (MRSA), which is an antibiotic-resistant strain of the bacteria, causing it to be extremely dangerous to those with HIV. The other types, however, are susceptible to a

variety of drugs, which can be used to both lessen the severity and cure the virus.

There are a variety of drug delivery methods that can be used to treat infections. Mathematical modeling has been used for over 50 years to help doctors understand the way these methods work, but also to save money and time by better understanding dosages and time to cure. While there are currently no universal math models for drug delivery, models for certain scenarios or types of drug delivery have been developed (Elmas et al., 2020, pp. 327-350).

When doctors are deciding on treatment options for bacterial infections, two main types of drug delivery are instantaneous (intravenous) and time dependent (pill/shot). The differences between these methods can be modeled graphically and mathematically and the decay of bacteria due to drug treatment can also be modeled using an initial value exponential growth equation. These mathematical models can be used by doctors to determine the critical dose necessary to eradicate the germs, as well as the time it will take to completely remove the germs if a million bacteria are initially present. It can also be used to determine a range in which the bacteria will initially decrease before increasing again.

There are three main variables when analyzing drug delivery: the bacteria count (x) in millions of cells, the dosage of drug in milligrams (d), and the time (t) to remove the infection in minutes. The initial equation given was the exponential formation of *Staphylococcus aureus*, signified by the growth of cells with respect to time, with the number of cells starting at 1 million [$x(0)=1$].

Discussion

In order to better understand treatment options for *Staphylococcus aureus* in HIV-positive patients, mathematical

models of intravenous and pill drug delivery methods were formulated. While these models do not factor in variables of the biological environment that the bacteria will be in such as the immune system, body temperature, and drug resistance of the bacteria, the model does help doctors to understand how the bacteria count changes as a function of drug dose and time. These equations stemmed from the differential equations describing how the cell count of *Staphylococcus aureus* changed with time. $x = 0.4329d + (1 - 0.4329d)e^{0.02310t}$ was the equation found for the intravenous method, and

$x = 0.2886de^{-0.01155t} + (1 - 0.2886d)e^{0.02310t}$ was the equation for the pill method. From these equations, the critical dose to eliminate the infection was determined. The critical dose for the intravenous method was 2.31 mg and 3.465 mg for the pill method. This shows that direct delivery (intravenous) requires a lower dosage in order to eliminate the infection compared to a time-dependent (pill) release of the drug. The time-dependent method, however, has a second dosage that will cause the bacteria count to initially decrease, allowing for the body to catch up, or giving doctors more time to determine alternative options. It was found that at dosages between 2.311 mg and 3.465 mg, the cell count will initially decrease, then increase exponentially. Both delivery methods were graphed to show the relationship between the time to cure the infection and the drug dosage. It was discovered that as the dosage increases, the critical time decreases.

Conclusion

Doctors can use this information to determine what the best dosage is that won't harm the patient or give harmful side effects while still eliminating the infection in a reasonable amount of time. Using these models, doctors will have a better

understanding for prescribing medication, as well as the method for delivering the drug to the system. It is important to understand what treatment options are available to HIV-positive patients with staph infections, as they are disproportionately affected by MRSA (Cole & Popovich, 2013, pp. 244–253). While the model is not comprehensive and does not factor in the body's immune system, nutritional and environmental effects, etc., future studies can include this information to build a more wide-reaching and accurate model for staph infection elimination using various drug delivery methods. With this research, doctors can make more informed decisions about which method and dosage to give, leading to increased chances of survival and lower chances of side effects in HIV-positive patients suffering from staph infections.

References

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