DEVELOPMENT AND IMPLEMENTATION OF A DECISION SUPPORT TOOL TO ASSIST PHARMACISTS TO DETERMINE PRECISE DOSING AND INTERVALS OF AN AMINOGLYCOSIDE (ANTIBIOTIC)

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ABSTRACT

The focus of this paper is to describe the development and implementation of a decision support tool to assist pharmacists in the management of dosing and intervals of an aminoglycoside. The development effort successfully created an end solution needed by pharmacists in a timely manner and provided the required portability of an application of this type. The project was completed in a community hospital located in southwest Virginia.

INTRODUCTION

An aminoglycoside is a molecule composed of a sugar group and an amino group, and several aminoglycosides function as antibiotics. Some of the common aminoglycoside antibiotics include Gentamicin, Amikacin, Tobramycin, Vancomycin, and Neomycin. It is critical that these antibiotics be carefully dosed based on numerous patient parameters to avoid damage to the kidneys, and to a lesser extent the auditory system. Precise dosing of an aminoglycoside can be a rather painstaking process since there are numerous difficult calculations that must be performed and the process is prone to error. Our goal in the creation of the this decision support tool was to automate much of this process and free the clinician up to do what they do best and leave the binary decisions and labor intensive calculations to the computer.

Pulaski Community Hospital located in southwest Virginia typically uses two different aminoglycosides in the course of disease treatment for patients. The first, Gentamicin, was being dosed using an excel spreadsheet that was deployed on a single aging laptop that sat in an office in the corner of the department. The second, Vancomycin, was dosed using a nomogram that was used to determine approximate dosing values based on only two parameters. Both of these drugs require careful monitoring for peak and trough concentrations of the drug within the body so as to adhere to the pulse dosing methodology in which the body is allowed to enjoy a drug free period after reaching the maximum therapeutic levels.

PURPOSE

The purpose of this project was twofold, first was to create an end to end solution in which the clinical pharmacist would be able to enter in a number of patient parameters into the program and receive back a number of calculated values as well as the recommended dose in milligrams as well as the dosing interval in hours. Our second aim was to make the program small enough to be sent as an email attachment, as straightforward to use as possible, not require an internet connection to operate, and able to run on modest hardware on any platform. To facilitate our goals toward those points we chose to write the program in JAVA, since it is a ubiquitous language and an executable jar file could be created that would run in any operating environment that would support the JAVA virtual machine.

NEED

The need for an application such as this stemmed from the fact that not all the computers that were available to the pharmacists had the Microsoft Office suite installed on them, thus restricting them to a single computer within their department. Additionally, pharmacists are on call at night after pharmacy hours, and many of the staffing pharmacists live in rural areas where they do not have access to internet connection which would allow them to avail themselves to an online calculator. Finally, our program would be able to utilize the comprehensive formulas, and return results that are accurate to two decimal places.

PROJECT DEVELOPMENT

Our first step toward facilitating our initial goal was to make sure we fully understood the problem, and that began with understanding exactly what information the program would need as input in order to perform the necessary calculations. After examining the existing spreadsheet, interviewing several of the staffing pharmacists, and experimenting with several online calculators, we narrowed it down to eight essential pieces of information.

1. Gender
2. Height
3. Weight
4. Age
5. Serum Creatinine
6. Desired Peak
7. Desired Trough
8. Infusion Time

The first four fields are self explanatory, but we will briefly describe what the last four refer to. Serum creatinine is a measure of the quantity of a waste product called creatinine which is present in the human body. The desired peak and trough are numbers that represent what maximum and minimum levels that the clinician is aiming for in terms of the concentration of the drug in the body. These ideal levels vary from drug to drug, and can vary for a single drug based on the organism that is being targeted and various complicating factors involved with the patient such as renal failure, congestive heart Failure (CHF), hypotension, etc. The infusion time refers to how long it will take the drug to infuse into the patient, i.e. 30 minutes for Gentamicin, or 2 hours for Vancomycin.

Once these parameters have been passed to the program, along with information as to which of the two supported drugs a dosing regimen is being sought for, we can begin the calculations. The first calculation was one of the easiest and most straight forward. The patient’s weight is still collected in pounds, and our first task was to transform this value into kilograms since all calculations that follow require the weight to be in that form.

$$\text{Weight in Kilograms} = \text{Weight in Pounds} / 2.2$$

Two additional weights are also required for further calculations, and these are the ideal body weight, and the adjusted body weight.

$$\text{Ideal Body Weight (Males)} = 50\text{kg} + 2.3 * \text{each inch over 5 feet}$$

$$\text{Ideal Body Weight (Females)} = 45.5\text{kg} + 2.3 * \text{each inch over 5 feet}$$

$$\text{Adjusted Body Weight} = \text{Ideal Body Weight} + 0.4(\text{Actual Body Weight} - \text{Ideal Body Weight})$$

The adjusted body weight is used in some of the calculations if the actual body weight is greater than 25% of the calculated ideal body weight.

Estimating the creatinine clearance is the next step, and as indicated earlier, the creatinine clearance is a measure of how quickly the body is able to clear creatinine from the blood. This formula is called the Cockcroft and Gault equation, and has a rule built into it that states if the patient is over 65 years of age, and their creatinine clearance is less than 1, the value of 1 is used in the serum creatinine field for the purposes of calculation.

$$\text{Creatinine Clearance} = [(140 - \text{age}) * \text{Ideal Body Weight}] / (\text{Serum Creatinine} * 72)$$

Note: If the patient is female, the calculated value is further multiplied by 0.85

Once the creatinine clearance has been obtained, it is then possible to calculate the estimated kel, or elimination constant, also sometimes referred to the coefficient of elimination. This equation allows the clinician to estimate the elimination rate of the drug by the body.

$$\text{Gentamicin Kel} = (0.00285 * \text{Creatinine Clearance}) + 0.015$$

$$\text{Vancomycin Kel} = (0.00083 * \text{Creatinine Clearance}) + 0.0044$$

The next calculation needed is the estimated half life of the drug; this value represents the estimated value in hours at which the drug levels will drop by half within the body.

$$\text{Half Life} = 0.693 / \text{Elimination Constant}$$

The last sub result we needed to obtain to perform the final calculations was the estimated volume of distribution. This is the calculation that is sensitive to the patient's obesity status; we also included an option to force the calculation to be performed using the patient's actual body weight when dosing Vancomycin since there are certain situations in which the clinician may choose to only use actual body weight for that drug. The normal acceptable range for the volume of distribution for Gentamicin is 0.25 to 0.3 Liters per Kilogram, and 0.6 to 0.7 for Vancomycin. Based on standard practice for the pharmacists at Pulaski Community Hospital, 0.3 and 0.7 respectively were chosen and hard coded into the system.

The final three equations are the most difficult, require the most calculator manipulations, and are the main reasons that this process was ripe for automation. The dosing interval is a calculated value in hours that represents how long the patient should go between doses.

$$\text{Dosing Interval} = \text{Ln} (\text{Desired Peak} / \text{Desired Trough}) / \text{Elimination Constant} + \text{Time of Infusion}$$

Calculating the desired dose, the second of the two actionable calculated values, is also a very complex formula to solve.

$$\text{Dose} = [\text{Elimination Constant} * \text{Volume of Distribution} * \text{Time of Infusion} * \text{Desired Peak} * (1 - e^{-\text{elimination constant} * \text{dosing interval}})] / (1 - e^{-\text{elimination constant} * \text{time of infusion}})$$

Having finally reached our answer, there is a final step to perform where we can essentially check our work. We have two final formulas which allow us to predict the peak and trough; these two calculated values should always match the desired peak and trough values entered by the clinician during the data entry phase of using our application.

$$\text{Calculated Peak} = [\text{Dose} * (1 - e^{-\text{elimination constant} * \text{time of infusion}})] / [\text{Elimination Constant} * \text{Volume of Distribution} * \text{Time of Infusion} * (1 - e^{-\text{elimination constant} * \text{dosing interval}})]$$

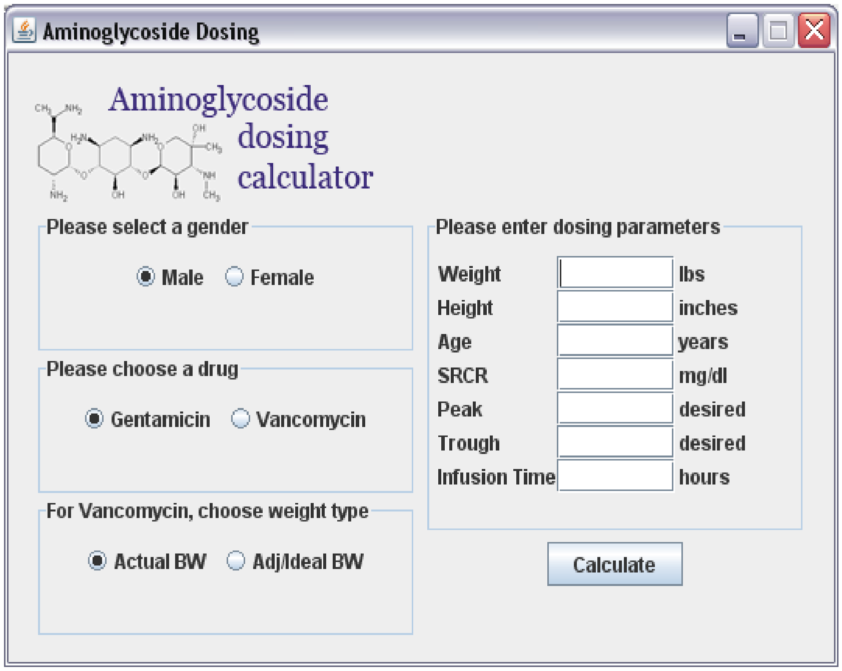
$$\text{Calculated Trough} = \text{Calculated Peak} * e^{-\text{elimination constant}(\text{dosing interval} - \text{time of infusion})}$$

Once we had completed the work of entering our formulas into our JAVA application, we began the process of testing our results. A number of previous dosage calculations were made available to us, in which we compared the results of the spreadsheet and nomogram, as well as online calculators, to results that our application provided. After a few refinements, our application calculated exact matching answers to industry standard calculators available on the internet, as well as falling closely to the values that the pharmacists were obtaining using their old system in the hospital.

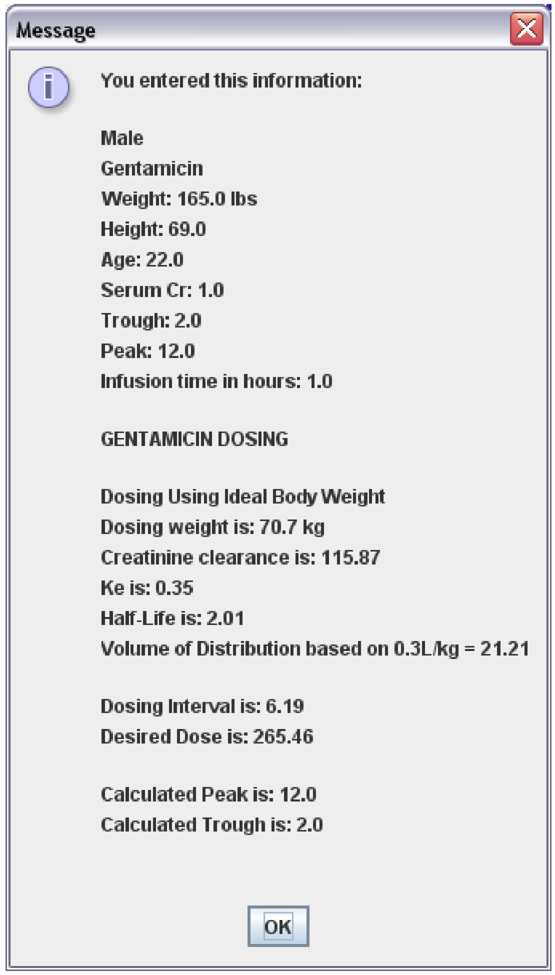
Graphical User Interface Development

Upon completing numerous tests to verify the validity of the calculations, the dosing calculator required a facelift to increase its usability and overall appearance. The current state of the dosing calculator is a basic command prompt in which the user is prompted with a series of input questions and enters a response for each. An additional goal for this project was to design a graphical user interface (GUI) that would be easy to use as well as provide a familiar screen layout pharmacists are used to seeing on the office computers.

Java provides the ability to design a graphical user interface utilizing the Swing library which allows a sophisticated set of GUI components to be implemented. Our interface design makes consistent use of text boxes and radio buttons placed within panels that hold a group of components together. The group of panels is placed in a frame which holds the entire interface intact. Interface design standards were followed by ensuring that text boxes were aligned and did not vary in size to create a non-interrupted navigation of screen components. An example of the design follows:



The results of the calculations are presented to the user in a new window. First, the input variables are displayed to the user as a confirmation that the correct numbers were submitted. This is followed by an identification of the specific drug the dosage is being sought after. Thirdly, the results reveal whether the dosage is calculated using the ideal or adjusted body weight. Lastly, the calculations are presented to the user based upon their body weight which has been converted to kilograms. An example of the output follows:



SUMMARY

Upon setting out to develop an application intended to ease the workload of pharmacists in a hospital environment, we have accomplished our desired goals for the project. We created a program that empowered a user to receive calculations based on specific information entered about a patient with minimal effort as opposed to working out complex math calculations with far less advanced technology. Specifically, this decision support tool provides aminoglycoside dosing recommendations within industry standards while at the same time minimizing adverse risks to patients. Our dosing calculator also proved to be extremely lightweight and portable while being completely functional on any computer system capable of running a JAVA virtual machine. Efforts to increase the usability with a graphical user interface have diminished any confusion or hardship the previous command prompt may have caused. With the dosing calculator already placed in a live hospital environment, pharmacists are nothing less than grateful that the old, paper weight of a laptop can be retired from that office corner.