On-Line Computer Pharmacokinetics Program: Lessons Learned from Its Failure

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Decision support computer technology (DST) embedded in laboratory or hospital information systems has great potential but has rarely been successful. Through studying a pharmacokinetic program that automatically extracted data without requiring manual data entry, we have identified several barriers to the successful implementation of DST. Manual data entry is a major barrier, but so is the entry of erroneous data such as heights, weights, drug dosing times, and specimen collection times. In such a system, unanticipated changes of clinical practice and software changes in the system's component modules can be incompatible with the decision-support program, necessitating software revisions. We also noted that clinicians increased their ordering of laboratory tests and changes in drug doses but without improvement in patients' outcomes. This suggests that information output from the program can be misinterpreted by clinicians. In summary, DST programs should be validated in an actual working environment.

Indexing Terms: laboratory management/monitoring therapy/aminoglycoside antibiotics

Decision Support Technology

Reasons for Implementation

Decision support computer technology has been available in medical settings for >30 years (1, 2). Computers appeared to be ideal tools to assist medical professionals in solving problems with complex relationships, especially those requiring mathematical calculations, or reminding care-givers to perform tasks at periodic intervals. Many expert systems and other forms of decision support technology have been proposed and demonstrated, but few have been successful in an actual clinical environment. Use of this technology is often limited because the user must manually enter data (2–5).

We used a pharmacokinetic (PK) model to study whether by automating the data entry such a system could be made more generally available. We designed a study to determine whether a PK system that had previously produced favorable patient outcomes could be successfully automated to operate without human data entry. Earlier testing of a similar computer program operated by clinical pharmacologists had been highly successful in decreasing toxicity and improving the length of stay of patients (6). Our present study, however, found that the PK system failed to produce an improved patient outcome and, in fact, the study patients had more drug dose changes, a greater number of laboratory tests, and for a significant subgroup of patients, an even longer hospital stay than a similar group of control patients. The brief description of the study and its results is not intended as a detailed report of our work. Rather, here we analyze the factors that resulted in the failure of a fully automated computer program for calculating PK data and for providing dosing advice and therapeutic drug monitoring (TDM) reminders. We believe this may provide some lessons for developers of other types of decision support technology. As will be discussed, we found several barriers to the automation of this complex computer program placed in the adverse environment of a tertiary-care hospital staffed with house officers.

Computer Setup and PK Program

Our study used the VA-developed Decentralized Hospital Computer Program (DHCP; Department of Veterans Affairs, Washington, DC) (7). This MUMPS-based integrated hospital information system is used in >170 VA Medical Centers, the Indian Health Service, and other private-sector hospitals. Modules in DHCP include admission, transfer, discharge, pharmacy, laboratory, dietetics, nursing, surgery, and clinic scheduling, among others. A unique feature of the DHCP system is the ability of users to modify programs and design new routines. We investigated the ability of the integrated hospital information system to extract data from different functional modules, such as laboratory, admissions, and pharmacy, and to use the information without needing any additional data entry to provide physicians with dosing advice and TDM reminders that could favorably affect their care of a patient. The study was performed in two Veterans Affairs Medical Centers, with use of the "same" DHCP hospital information system in slightly different versions.

Our PK program was embedded in the DHCP system and was inapparent to the user. In this study, we used the aminoglycoside antibiotics (gentamicin, tobramycin, and vancomycin) as models of a drug with a narrow

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therapeutic index. When an order was placed for gentamicin, tobramycin, or vancomycin, the program searched data already in the computer such as the patient's predose values for serum creatinine (renal function), weight, and height, and calculated a predicted initial dose by using population-based PK formulas (Fig. 1). If the required data for dose calculation were absent, the program alerted the physician of the need to obtain these data. To avoid a failure of the program to operate, the program inserted a temporary average height and weight if none was present in the database; these were corrected on the next working day by our research assistant. If no serum creatinine value was available, the program defaulted to a value of 88 mmol/L (10 mg/L) to calculate the initial recommendations, and initiation of therapy was allowed, pending acquisition of the required data. The computer reminded the physician to order serum creatinine assays and our research assistant to enter height and weight, if not available initially.

PK calculation of the appropriate aminoglycoside dose was automatically performed and compared with the physician's order. If the dose was projected to result in a subtherapeutic or toxic blood concentration, the computer sent this information to the physician. It also sent a reminder to the physician to request orders for peak and trough serum drug assays for the first day of drug administration and every 3 days thereafter. When the assay results were available to the computer, the PK program recalculated the dose, sending a new reminder to the physician. If the new dose recommendation did not agree with the prescribed dose (within ±20%) and no dose adjustment was made, a reminder notice was initiated. Serum creatinine and drug assays were required at 3-day intervals. If they were not ordered by the physician, the computer printed a reminder notice for the physician. In the event of an increase in serum creatinine or the report of a nontherapeutic concentration of drug, a change in drug dose was expected. The computer checked for these, alerting the physician if they did not occur or were inappropriate according to the PK calculations. We delivered these computer-generated reminders and recommendations to ward personnel, who placed them at the front of the patients' charts but did not make them part of the permanent medical record.

The software initiated reminders or recommendations for only those patients who had inappropriate drug doses ordered, or who lacked an appropriate follow-up examination. The PK data input and calculations were inapparent to physicians. When the calculated blood concentration projections were above or below the recommended range, the computer sent an appropriate comment. Reminders were also generated to suggest that the physician could request a PK consultation, if needed.

Barriers Identified

Software Design

The software implementation process proved to be much more complex than we had anticipated. Even when two institutions used the "same" computer software, the version differences, local modifications, and election of user-configurable options greatly restricted the transportability of the software.

The software was based on assumptions of clinical practice as it existed at the time that the idea of the study was conceived. In subsequent years, several changes in the administration of antibiotic drugs invalidated the software by imposing the following practices:

1) Administration of drugs at times other than the standard 4-, 6-, 8-, 12-, or 24-h intervals; e.g., every 19 h.
2) Drawing of TDM specimens at "random" times other than peak or trough times.
3) Administration of more than one aminoglycoside drug at a time.
4) Administration of many single-dose orders rather than a stable maintenance dose (the computer handles each dose change as a new initial drug order).
5) Implementation of a clinical pharmacy consultation service.

Although these site-specific clinical practice changes could be accommodated by changes in the computer program, some would require major revisions. Because changes in clinical practice occur as an evolving process, computer program changes also need to occur continuously. In designing such a program successfully, one would need to be able to anticipate those clinical practice changes necessitating program alterations and to give the end user the option to reconfigure the system.
Not only do clinical practice changes introduce problems, but in a large integrated hospital information system, various modules are continuously being modified, either by the vendor or by the user, who may be able to select user-configurable options. We found that changes in some modules had a profound, and sometimes disabling, effect on our program.

Errors in Data Input

Manual data entry is a major barrier to the use of decision support technology (2–5). It is our belief that physicians, given free access to such programs, rarely use them because of the time and bother of entering the required data. Thus, we elected to design a program that relied on data already in the DHCP system (5). We also redesigned laboratory systems to ensure that such data as the times of drug administration and specimen collection would always be entered into the system. As it turned out, however, many of these data were erroneous. Anecdotal experience suggests that this is a common problem.

Most medical centers have difficulty in obtaining accurate drug-administration and specimen-collection times. Frequently, even the times recorded in the patient’s chart at the bedside are erroneous. When the output of the computer is based on inaccurately recorded times, errors are probable. In a successful PK system (6), the users of the output information manually entered the times of dosing and specimen collection; accordingly, there was “ownership” in the accuracy of the input data.

We saw a similar problem in the input of heights and weights. One of our institutions had no standardization of the tables used. Although the computer program was able to accept and use either metric or avoirdupois units, data were not always entered with the correct unit, resulting in erroneous calculations. Only an elaborate error-checking routine e.g., involving concordance between a subject’s age and height and weight, would be likely to detect such errors.

Errors in Integration of Information

The intervention-group physicians in our study changed their patients’ aminoglycoside doses more frequently than did the control group. Although this was of borderline statistical significance (P = 0.08), the data suggested that they made better use of the TDM assays or the computer-generated reminder notices.

The intervention-group patients’ drug assay trough values were significantly lower than in the control group (P <0.05) and more of their peak concentrations were subtherapeutic (not statistically significant). When the control-group drug trough assay values deviated from the therapeutic range, they were more likely to be in the high toxic range than in the subtherapeutic range. This difference in physician behavior did not translate into an improvement in patient outcomes. Data analysis from the study indicated no renal function differences or differences in the number of febrile days between the study groups.

Appropriate statistical tests were performed to ensure that the study groups were comparable. We believe that the consequence of computer intervention in increasing the number of dose changes may have had an adverse effect on the length of stay (but not the number of febrile days) for patients with a primary discharge diagnosis of infection (for whom the infection, presumably, was responsible for the hospital length of stay). This finding contradicts the findings and conclusions of Burton et al. (6), who used a similar computer intervention but filtered it through clinical pharmacists. It is tempting to believe that the clinical pharmacists made better use of the computer intervention than did resident physicians, who may have used the PK information less critically. The quality of the data entry in the computer system in the study by Burton et al. was better because of being reviewed by the pharmacists prior to computer entry.

Conclusions and Recommendations

The lack of success of computer-assisted decision-making models is fundamentally due to the tendency to confuse thinking with computing. We often overlook how many tiny variables contribute to the overall decision and are involved even in very narrow areas such as a PK calculation. These variables are all critical to ensuring accuracy and eliminating erroneous data. For example, in a patient with an amputation, how should the height and weight be adjusted? In the model involved in this study, the computer would not question this, but a human would probably make adjustments. That is, a simple glance at the patient would convey a tremendous amount of information not available to the computer. These data are used by the human professional to ensure that the input variables used in this decision process were appropriate.

Apparently, each patient is sufficiently different to require human review of all the input data to avoid errors that would seriously compromise the reliability of a computer-generated decision or calculation. We cannot merely assume that because someone has entered some data into the computer that the data are current, accurate, or validated for its intended purpose.

Time is the other fundamental problem area in using computer-generated decisions, where data from several different disciplines are required to make a decision. Each discipline in the healthcare setting has its own work pattern, and all the various data needed for a given task may not become available in the computer simultaneously for any given patient. When the data are available, they may not coincide with the time schedule of the physician or other provider who will ultimately carry out the computer’s recommendations. Healthcare providers also tend to move around throughout the day, working out of several offices in different facilities. This makes it logistically difficult to make sure that the correct individual in any given case will see the reminder, warning, or assistance from the computer at the earliest possible time. The provider may not know if the computer decision arrived before
or after she or he updated orders on a given patient. Also uncertain is how much time it takes for updated orders to be acted upon and whether any or all of the updated data have been incorporated into the computer's latest decision. Thus the automatic feature of having the computer notify the physician requires a human intervention, much like that of "critical value" notification—which has defied all attempts to assure automatic alerting of a physician at the earliest possible time.

A major barrier to the use of computer-based decision support technology has been the need to enter data and interact with the computer over an extensive time period. In designing our system, we attempted to avoid these impediments and to provide automatic data entry from files already in the system. In doing so, we discovered other barriers to the successful use of the system. Some were apparent at the time of the program's installation and led to visible failure of the computer to operate as designed. Other barriers were inapparent until outcome data from the study were analyzed.

Complex decision support programs involving the guiding of therapy are based on patterns of clinical practice that are subject to change. In designing the computer software, it is not possible to anticipate these practice changes. Perhaps we are asking too much of a computer program to be able to continuously adapt to unanticipated practice changes.

Notification of measured or projected TDM values outside an accepted optimal range leads to increased attention to dose adjustments, but may not lead to improved patient outcomes as measured by length of stay, number of febrile days, or renal function. In fact, in the subgroup of patients whose length of hospitalization was due primarily to infection, this intervention appears to have an adverse effect on the length of stay.

We conclude that when a successful PK computer program using manual data input is automated to extract input data without human intervention, the program may not have the desired effect. Human intervention by an experienced individual, both at the data-input stage and when computer reminders and recommendations are given, is important.

More worrisome is the finding that a well-validated PK dose calculation program, already shown to improve patient outcomes such as hospital length of stay, actually had an adverse effect when automated. This was probably due to a combination of poor input data and improper interpretation of the computer's output by physicians. In the previous study of a similar computer program, all input data and the output from the program were evaluated by an experienced clinical pharmacist. These observations lead us to recommend that decision support programs that have been validated in one setting with individuals with special qualifications should not be placed in general use by nonspecialists without further validation in the new setting. Not only must it be shown that the program operates as intended, but also one must prove that it achieves the desired patient outcome.

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References