A Decision Support Tool for Antibiotic Therapy

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ABSTRACT

We developed a decision support tool to assist physicians anticipating the need for antibiotic therapy. The initial screen alerts physicians of pertinent patient information, provides direct access to other essential medical information, and stimulates clinical judgment by suggesting an antibiotic regimen. The decision support tool also suggests the dose and interval for any ordered antibiotics selected by the physicians. During a 7-month pilot study, all antibiotics for patients admitted to the Shock/Trauma/Respiratory Intensive Care Unit (STRICU) were ordered using the decision support tool. Clinical data from the study period and a 12-month control period (the previous year) were collected and compared.

The decision support tool was used to order antibiotics 588 times during the study period and the suggested antibiotics were used 218 (37%) times. The computer suggested dosages were used over 90% of the time. The mean cost of antibiotics was \$87.00 ($p < 0.04$) less per patient during the study period as compared to the control period. Prospective assessment revealed only 3 antibiotic adverse drug events (ADEs) (0.9%) among 336 study patients as compared to 15 ADEs (2.4%) among 626 control patients ($p = 0.164$).

INTRODUCTION

Antibiotics are one of the most widely used classes of drugs in hospitals and account for one-third of total pharmacy costs [1]. Patients with infections have improved chances for survival with appropriate antimicrobial therapy [2]. There are three principal indications for antibiotic use: 1) to treat identified pathogens with known susceptibilities (therapeutic), 2) to treat suspected pathogens with unknown susceptibilities (empiric), and 3) to avert infection with potential pathogens (prophylactic). Studies have shown that misuse of antibiotics is frequent in each of these categories (3-5). Improper ordering of antibiotics can result in an increase in patient morbidity and mortality. Inappropriate antibiotic use has been shown to cause adverse drug events (ADEs), drug-resistant bacteria, and increased hospital costs [6-9]. Antibiotics as a group are the second leading cause of ADEs at LDS Hospital [10].

The selection of appropriate antibiotics has become more complex due to the introduction of new antibiotics, shifts in bacterial pathogens [11], as well as increases in antibiotic resistance. The antibiotic of choice for the treatment of an infection should either be the most active drug against the pathogen(s) or the least toxic antibiotic selected from several equally effective agents [12]. In addition to wise selection of antibiotics, the correct dosage, route, and interval must be used, and physicians must be aware of possible drug-allergy, drug-drug, and drug-laboratory incompatibilities. Moreover, today's cost driven healthcare systems demand the use of the most cost-effective treatments. In this paper we describe the development and initial evaluation of a decision support tool to improve the use of and reduce the cost of antibiotics.

METHODS

The computerized medical record on the HELP System [13] was an essential component that enabled us to develop the decision support tool for the treatment of infections. Our goal was to develop a tool that could provide the essential information for therapeutic, empiric, and prophylactic antibiotic therapy. The decision support tool is a computer program that can be accessed from computer terminals at different Intermountain Health Care Hospitals and from physician's offices and homes that are connected to the HELP System.

Physicians gain access to the program by selecting the "Antibiotic Assistant" option from the physician's main menu on the HELP System. The physicians use standard HELP System screens to identify the patient. The Antibiotic Assistant program accesses the patient's computerized medical record to produce a screen similar to figure 1. The amount and type of patient information displayed varies depending on the specific data and condition of the patient. The first line displays the patient number, name, room, age, sex, and admit diagnosis. The second line shows the patient's admission date and time and displays the patient's maximum 24 hour white blood count

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and maximum temperature and indicates whether these values are increasing or decreasing. The program then calculates the renal function of the patient using formulas for ideal body weight and estimated creatinine clearance. A decrease in liver function and a left shift in the patient's differential leukocyte count also is detected and displayed. The patient's antibiotic allergies and current antibiotic therapy is then displayed. If the patient is receiving amphotericin, the total amphotericin dosage received by the patient is calculated and displayed.

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IHC ANTIBIOTIC ASSISTANT & ORDER PROGRAM
11111111 Doe, Jane Q.  E613  55yr F  Dx: Morbid obesity, hypertension
Max 24hr WBC= 28.5↓  Admit: 03/22/95.15.37  Max 24hr Temp= 38.6↓
RENAL FUNCT: Impaired, CrCl= 40,  Max 24hr Cr= 1.3→  IBW: 52kg
Patient's Diff shows a left shift, Max 24hr Bands = 13↑
ANTIBIOTIC ALLERGIES: Penicillin
CURRENT ANTIBIOTICS:
1. 03/31/95.22:47 AMPHOTERICIN B, VIAL 45              Q 24hrs
2. 04/03/95.16:32 IMIPENEM/CILASTATIN, VIAL 500        Q 12hrs
3. 04/03/95.16.32 GENTAMICIN, VIAL 130                 Q 24hrs
Total amphotericin given = 316mg
IDENTIFIED PATHOGENS          SITE               COLLECTED
 Pseudomonas aeruginosa       Sputum             04/03/95.01:00
 Candida albicans             Peritoneal Fluid   03/30/95.14:00
ABX SUGGESTION          DOSAGE  ROUTE  INTERVAL
 Imipenem               500mg   IV     *q12h (infuse over 1hr)
 Gentamicin            *130mg   IV      q24h (infuse over 1hr)
 Amphotericin B          45mg   IV      q24h(infuseover2-4hr)
 Pentoxifylline         800mg   PO      q  8h
Suggested Antibiotic Duration: 10 days
* Adjusted based on patient's renal function
<0>EXIT, <1>Micro, <2>Antiblo, <3>Empiric, <4>Mono, <5>Explain
<6>Abx Hx, <7>ID Rnds, <8>Lab/Abx levels, <9>Xray, <+>New Pat
ORDER:<*>Suggested Abx, <Enter>Other Abx, </>D/C Abx, <->Modify Abx,
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Figure 1. Example of the initial screen from the Antibiotic Assistant program.

The program uses the patient's admission diagnosis, white blood cell count, temperature, surgical operation, and chest radiograph information to suggest the need for and type of antibiotic therapy. The program then scrutinizes the patient's microbiology, serology and pathology data and identifies any pathogens that should be treated. The program accesses the computerized antibiograms and empiric logic for identified pathogens that do not have antibiotic susceptibility results. For example, empiric logic from infectious disease specialists is evoked as soon as a gram negative bacillus is identified from a blood culture whereas the antibiograms are used once the pathogen is identified.

Computerized logic is used to suggest an antibiotic regimen that would cover the identified and potential pathogens. In addition to infection information, the logic uses patient allergies, drug-drug interactions, toxicity, and cost in the selection of suggested antibiotics. The logic uses the patient's renal and hepatic function to calculate the dose and interval for each suggested antibiotic. The Antibiotic Assistant program was designed to suggest an "ID Consultation" whenever antibiotics could not be found to cover all identified and potential pathogens or when the patient's condition was beyond the logic domain of the program. The first screen was designed to identify any important information that should be known in the selection of antibiotics.

The bottom of the first screen contains a number of options physicians can use to obtain more detailed information. The program was devised so that the user only needs to use the number pad on the keyboard. Typing 0, for example, exits the program. Option 1 allows direct access to the complete microbiology culture and antibiotic susceptibility results for the patient. Option 2 allows the review of computerized antibiograms for pathogens with antibiotic susceptibility results. The antibiograms are automatically updated each month. Option 3 contains the empiric module which was designed to identify the most likely pathogens and the cost of the most active antibiotic regimens based on patient specific information. Option 4 displays antibiotic monographs for each of the formulary antibiotics. The development, use, and evaluation of options 2, 3 and 4 have been described in detail in previous publications [14,15]. Option 5 is the explain module. When the computer logic is selecting the suggested antibiotics, key decision steps that were influential in the selection are flagged. Option 5 allows the review of these rules (Figure 2).

Logic Used to Help Select Suggested Antibiotics

Patient should receive IV antibiotics.
Renal function dictates that dosage should be adjusted.
Cultures show fungi or yeast that were not considered pathogens.
Cultures show isolated bacteria that were not considered pathogens.
Aminoglycosides potentiate ototoxicity if given w/ loop diuretics.
*Serious Pseudomonas infections need combo Rx, gent + B'lactam.
Amphotericin B is suggested for serious fungus infections.
Suggested Abx will cover possible aspirated anaerobes (Xray 3/29).
Positive respiratory culture was supported by Xray on 3/29.
Suggested antibiotics will cover likely pathogens from dirty surgery.
Suggest imipenem because of dirty surgery and positive Xray.
Suggest pentoxifylline to minimize renal toxicity of amphotericin B.
Identified pathogens are covered by the suggested antibiotics.
Suggested antibiotics are least expensive of appropriate antibiotics.

The antibiotic suggestions should not replace clinical judgement.
Press <Enter> to return to previous screen

Figure 2. The "explain" screen showing some of the logic used to generate the suggested antibiotics in figure 1.

Option 5 not only helps to explain the logic for the suggested antibiotics, but also identifies patient information such as aspiration pneumonia from chest radiographs that may support the decision to suggest antibiotics. Option 6 displays the complete antibiotic history for the patient's entire admission including order and stop times, dosages, routes, and intervals. Option 7 displays a screen called "Infectious Disease Rounds". This option arranges the patient's temperature, blood culture results, white blood cell counts, serum creatinine, and given antibiotics by each day of hospitalization. Option 8 provides direct access to any laboratory test results including antibiotic blood levels and serology results. Option 9 allows the user to read radiologist's dictated reports of patient radiographs. Since the date is displayed in the explain option of any radiographs used to help suggest antibiotics, the user can go directly to the radiograph of interest. The "+" key is used to select a new patient.

The Antibiotic Assistant program was made available to all physicians in July, 1994. Any physician could use the program but all antibiotics for patients in the Shock/Trauma/Respiratory Intensive Care Unit (STRICU, a 12 bed unit) had to be ordered through the Antibiotic Assistant program. Thus, the patient information presented on the initial screen of the program was always presented before the physicians in the STRICU made their antibiotic decisions. Physicians can order the suggested antibiotics as displayed (including the dose, route, and interval) by entering the "*" key from the initial screen. Pressing the "Enter" key displays an alphabetical list of antibiotics on the hospital formulary. Physicians who do not wish to order the suggested antibiotics can order any therapy they choose. When physicians choose an antibiotic from the list, the computer automatically calculates the dose and interval. The physicians can then order that antibiotic using the "*" key or they can change the dose and/or interval. If the physician selects an antibiotic to which the patient is allergic or that interacts with other current drugs, the program alerts the physician. The physician can still order the antibiotic but must hit the "*" key to override the alert. When physicians order antibiotics other than the suggested antibiotics, an override screen appears and they must enter the reason from a list or type in their reason. Antibiotics not contained on the formulary list can be ordered by selecting "other drugs" from the list and typing in all or part of the antibiotic name. This also allows physicians to order non-antibiotic drugs such as pentoxifylline that are commonly used with antibiotics. Physicians use their social security numbers as an electronic signature and for final verification of the order and are not required to sign the computer generated order placed in the patient's chart. Thus, only valid physician social security numbers can be used to order antibiotics. The "/" key on the number pad puts the physicians in the D/C antibiotic mode. The first screen lists the numbered antibiotics the patient is currently receiving. Physicians identify the antibiotics they wish to discontinue by entering the number listed in front of the antibiotic. Physicians have to verify any antibiotics chosen to be discontinued before they are actually discontinued. The "-" key can be used to modify a current antibiotic. This option allows the physician to simply change the dose or interval of a current antibiotic and the program automatically discontinues the old order and orders the new antibiotic.

The Antibiotic Assistant program keeps a log each time it is used. The log contains information such as the user, patient number, time used, patient room, electronic signature used, suggested antibiotics, options used, drug-drug and allergy alert overrides, and reasons for antibiotic selection overrides. Almost all antibiotics are ordered in the STRICU by housestaff physicians who are supervised by a rotating intensive care specialist on the service. We chose to introduce the Antibiotic Assistant program during July to coincide with the arrival of new housestaff. New housestaff rotate through the STRICU from July through June and are generally not present during the next year. We selected all patients admitted to the STRICU from July, 1993, through June, 1994, as control patients. All patients admitted from July, 1994, through February, 1995, were used as study patients. The computerized medical records for all patients in the control and study periods were used to calculate patient and antibiotic information during their stay in the STRICU. Antibiotic costs in 1994 were used for all antibiotics ordered during the control and study periods. The Mann-Whitney U test was used to detect statistically significant differences in antibiotic costs between the control and study periods. Prospective ADE surveillance was used to identify ADEs to antibiotics during the control and study periods [16]. A chi-squared test was used to detect statistically significant differences in ADE rates between control and study periods.

RESULTS

From July, 1994, through February, 1995, the Antibiotic Assistant program was used 6,664 times (32/day) not counting use by infectious disease specialists. Of the 6,664, 3,061 (46%) were for patients in the STRICU. Antibiotics were ordered through the program 588 times and physicians used the suggested antibiotics for 218 (37%) times. Thus, 370 times physicians selected other antibiotics and their reasons were logged (Table 1). The physicians stated that the most common reason to select other antibiotics was because the patient had an infection not identified by the computer. Forty-four times the physicians agreed with the suggested antibiotics but did not agree with the recommended dosage. The physicians selected "other" as their reason to override the suggested antibiotics 89 times. However, 9 times the physicians typed in that they did agree with the suggested antibiotics but not the dosage. Other frequent reasons included were that the patient was on dialysis, or that there was an attending physician preference, or infectious disease consultation.

During the control period (7/93 through 6/94) 626 patients were admitted to the STRICU compared to 336 during the study period (7/94 through 2/95, Table 2). There were 403 (64%) patients who received antibiotics during the control period compared to 233 (69%) during the study period. The cost of antibiotics was $87.03 less per patient for patients who received antibiotics during the study period compared to the control period ($p < 0.04$). Thus, the average cost of antibiotics in the STRICU was $61.72 per day during the control period compared to $50.97 during the study period. In addition, there were only three (0.9%) ADEs due to antibiotics in the study period compared to 15 (2.4%) during the control period ($p = 0.164$).

TABLE 1
REASONS STATED BY PHYSICIANS FOR NOT USING SUGGESTED ANTIBIOTICS

Reason	No.
1. Pat had infection not identified by computer.	134
2. Suggested antibiotics not adequate for patient's therapy.	38
3. Patient had positive cultures before admission.	10
4. Patient had positive Xray taken before admission.	0
5. Patient's Xray suggested antibiotic therapy was needed.	10
6. Patient's admit diagnosis warranted antibiotic therapy.	20
7. Patient needed antibiotics for surgical prophylaxis.	12
8. Patient needed antibiotics due to dirty surgery.	10
9. Did not agree with suggested dosage.	44
10. Computer identified pathogens were incorrect.	1
11. Did not believe computer identified respiratory infect.	1
12. Patient's Xrays did not warrant antibiotic therapy.	1
13. Other (Free text).	89
TOTAL	370

TABLE 2
COMPARISON BETWEEN STUDY AND CONTROL PATIENTS

Category	Control	Study
No. of patients	626	336
No. pats receiving antibiotics	403/64%	233/69%
Av. antibiotic cost	$382.68	$295.65*
Av. STRICU LOS (days)	6.2	5.8**
Av. STRICU-Dsch LOS (days)	13.4	12.2**
No. antibiotic ADEs	15	3**

* $p < 0.04$, Mann-Whitney U.
** Not statistically significant.

DISCUSSION

Concern over the rising costs of medical care has been expressed frequently by patients, legislators, and members of the health care community. Hospitals are now pressed to find ways to provide appropriate patient care and remain financially solvent. The cost of antibiotics contributes to the expenses incurred by both hospitalized and ambulatory patients. This study supports the theory that quality patient care can reduce cost. Another study has shown reduced charges by displaying the charges of laboratory tests and drugs on workstations when physicians made orders [17]. Physicians have told us that they had no idea of the relative cost differences between certain antibiotics. The difference in the cost of antibiotics is based on the dosage and interval which are dependent on the specific patient's renal function.

We did not expect the physicians to use the suggested antibiotics every time. All the information that is critical for the decision to use antibiotics is not available in computerized medical records and so the Antibiotic Assistant can only facilitate clinical judgment. This study included the most severely ill patients in our hospital. Physicians reluctance to change from the broad spectrum antibiotics they normally use may have been justified. The computer logic does not examine cost until the last step in the antibiotic suggestion process. Selecting appropriate antibiotic therapy for the identified and potential pathogens was the main goal of the program. Cost was only used when two or more equally effective antibiotics were available.

We have found that the primary cause of ADEs at our hospital was drug doses that were too high for the patient's renal function. This was especially true for antibiotics. We found that the physicians followed the computer suggested dose and interval over 90% of the time. The automatic calculation of renal function and antibiotic dosage was a feature of the program that was readily accepted. The physicians usually changed the antibiotic dosages when the Antibiotic Assistant alerted them of a change in renal function and suggested a dosage change. We believe that this feature of the program will be an effective tool for the prevention of ADEs. Since the attributable cost of an ADE is almost $2,000 [18], this will not only improve patient care but also further reduce the cost of health care.

While STRICU length of stay and length of stay from admission to the STRICU to discharge was reduced during the study period (Table 2), it was not statistically significant. This decrease is encouraging, however, we hesitate to accredit the role of the Antibiotic Assistant program for this reduction since both of these two length of stay measurements have been declining in recent years. A decrease in length of stay in the STRICU could have had an impact on the cost of antibiotics used in the STRICU.

However, the 6% (6.2 days to 5.8 days) decrease in length of stay could not have reduced the cost of antibiotics from $382.68 to $295.65 (23%).

Prescribing guides that have been assembled by authorities to offer physicians assistance in ordering antibiotics do not include patient-specific information and cannot recognize geographical variation in occurrence of microbes or antibiotic resistance. Every major class of bacterial pathogens has demonstrated the ability to develop resistance to one or more commonly used antibiotics and experience indicates that resistance will eventually become a problem for every newly developed antibiotic [7,8]. The Antibiotic Assistant program relies on empiric knowledge if antibiogram and antibiotic susceptibilities are not available. However, as pathogens become identified and antibiotic susceptibilities become available, this information is used in place of the empiric logic. Thus, further development of the computer-based medical record is an essential step to further the development and implementation of computer-aided decision support. However, physicians themselves must use and apply the computer provided information in the appropriate clinical context. This study was designed to determine the effect of displaying pertinent patient information at the time antibiotics decisions were being made. Accordingly, the computer enhanced but did not replace clinical judgment.

References

1. Miwa LF, Kennedy DL, Freidman JP. US hospital anti-infective use from 1985 to 1990.P&T 1992;17:983-85,989-90,993.
2. Bryan CS, Reynolds KL, Brenner ER. Analysis of 1,186 episodes of gram negative bacteremia in non-university hospitals: The effects of antimicrobial therapy. Rev Infect Dis 1983;5:629-638.
3. Maki DG, Schuna AA. A study of antimicrobial misuse in a university hospital. Am J Med Sci 1978;275:271-282.
4. McGowan JE, Improving antibiotic use has become essential - Can surgery lead the way? Infect Control Hosp Epidemiol 1990;11:575.
5. Yu VL, Stoehr GP, Starling RC, Shogan JE. Empiric antibiotic selection by physicians: Evaluation of reasoning strategies. Am J Med Sci 1991;301:165-172.
6. Faich GA. Special Report: Adverse drug reaction monitoring. N Engl J Med 1986;314:1589-1592.
7. Ma MY, Goldstein EJC, Friedman MH, Anderson MS, Mulligan ME. Resistance of gram-negative bacilli as related to hospital use of antimicrobial agents. Antimicrob Agents Chemother 1983;24:347-352.
8. McGowan JE. Antimicrobial resistance in hospital organisms and its relation to antibiotic use. Rev Infect Dis 1983;5:1033-1048.
9. Dunagan WC, Woodward RS, Medoff G, et al. Antimicrobial misuse in patients with positive blood cultures. Am J Med 1989;87:253-259.
10. Classen DC, Pestotnik SL, Evans RS, Burke JP. Computerized surveillance of adverse drug events in hospital patients. JAMA 1991;266:2847-2851.
11. McGowan JE, Finland M. Infection and antibiotic usage at Boston City Hospital:Changes in prevalence during the decade 1964-73, J Infect Dis 1974;129:421.
12. Choice of antimicrobial drug. Med Lett 1992;34:21-28.
13. Pryor TA, Gardner RM, Clayton PD, Warner HR. The HELP System, J Med Sys 1985;7:87-102.
14. Evans RS, Pestotnik SL, Classen DC, Burke JP. The development of an automated antibiotic consultant. MD Comp 1993;10:17-22.
15. Evans RS, Classen DC, Pestotnik SL, Lundsgaarde HP, Burke JP. Improving empiric antibiotic selection using computer decision support. Arch Intern Med 1994;154:878-884.
16. Evans RS, Pestotnik SL, Classen DC, et al. Development of a computerized adverse drug event monitor. SCAMC. Washington, DC,IEEE Computer Society Press, pp 23-27 (1991).
17. Tierney WM, Miller ME, Overhage JM, McDonald CJ. Physicians inpatient order writing on microcomputer workstations. JAMA 1993;269:379-383.
18. Evans RS, Classen DC, Stevens LE, et al. Using a hospital information system to assess the effects of adverse drug events. SCAMC. Washington, DC,IEEE Computer Society Press, pp 161-165 (1993).