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Reduction of Incorrect Antibiotic Dosing Through a Structured Educational Order Form

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- Antibiotics are often used inappropriately in hospitals. We created a structured antibiotic order form designed to guide physicians toward correct therapeutic decisions without restricting their clinical options. Educational messages and graphic reminders were incorporated into a new form required to order parenteral antibiotics at a teaching hospital. Pharmacokinetic considerations were emphasized. The forms were supplemented with brief literature reviews and appropriate references. Before introduction of the form, pharmacokinetically incorrect orders for clindamycin, cefazolin sodium, and metronidazole hydrochloride accounted for 90%, 60%, and 75% of patient-days of therapy for these drugs, respectively. Immediately after implementation of the form, nonrecommended dosing schedules dropped to under 6% of patient-days for all three antibiotics. Savings from these drugs alone accounted for over $76,000 annually. We conclude that in a period of increasing constraints on hospital budgets and proliferating restrictions on physicians' clinical choices, educational intervention at the time orders are written can provide a cost-effective and noncoercive means of improving some forms of acute-care clinical decision making.

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The era of effective antimicrobial therapy is now a half-century old, during which time these medications have resulted in some of the greatest therapeutic triumphs in the history of medicine. Perhaps inevitably, this class of drugs has also been the subject of less-than-ideal prescribing practices. The widespread perception that antibiotics are, in general, low-cost, low-risk therapeutic agents has been associated with patterns of inappropriate use that have been well documented in settings ranging from tertiary-care teaching centers to ambulatory practice. While they are among the safer therapeutic agents currently available, antibiotics are, of course, not risk free, with negative consequences of misuse running the entire clinical spectrum from rash to severe end-organ damage and anaphylaxis. Widespread antibiotic use is also associated with the development of bacterial resistance, a problem of increasing concern. In an era of cost containment, it is not surprising that this class of drugs has also received increased scrutiny because of the extraordinarily high costs of many of its newer members; antibiotics currently constitute the costliest drug category in most hospitals. Of the more than $4 billion spent by hospitals on medications in the United States in 1986, some $1.4 billion, about a third, was used for antibiotics.

With the advent of prospective payment systems, economic issues have gained importance as additional reasons for attempting to improve the precision of use of antibiotics. If the level of improper use of antibiotics were even half as high as the published estimates of 50%, reduction of such misuse could result in potential savings of hundreds of millions of dollars per year in the United States alone. Thus, new economic factors combined with older concerns about adverse clinical effects and the problem of bacterial resistance have raised the issue of proper antibiotic prescribing to the top of the agenda at many hospitals.

There have been a number of attempts to reduce inappropriate utilization of antibiotics, particularly in the inpatient setting. Initially, these efforts were motivated primarily by concern about the emergence of resistant organisms. Early programs restricted use of specific antibiotics, requiring the permission of an infectious disease consultant before they could be prescribed. Such policies did indeed control the utilization patterns of the controlled drugs, with positive effects demonstrated on the patterns of antibiotic resistance; cost was decreased as well.

In addition to the earlier restrictive approaches, more recent studies have investigated the impact of less obtrusive methods of control, including the requirement of consultation with an infectious disease specialist, with the ultimate prescribing decision left in the hands of the ordering physician. Both restriction and required consultation have been shown to reduce antibiotic costs sharply by decreasing the prescribing of these medications. However, if such interventions are withdrawn, their positive effects have been found to decay rapidly, a phenomenon seen in other settings as well. Antibiotic use audits followed by feedback of their prescribing records to phy-
Physicians, either alone or in combination with group discussions, have uncertain efficacy. Repetitive, ongoing feedback of individual physician antibiotic use patterns, measured against explicit criteria or group norms, is a promising approach that has worked well in ambulatory settings but has not as yet been adequately studied in the inpatient setting.

Several earlier attempts at improving the accuracy of inpatient antibiotic use have contained inherent limitations that the present study was designed to overcome. First, the requirement of approval by a hospital-based infectious disease consultant necessitates that such expertise be readily available around the clock every day of the year, something that is possible in many teaching hospitals but impractical in the vast majority of hospitals without adequate subspecialty backup. Second, the requirement of involving a subspecialist to confer on antibiotic use decisions is not a cost-free one; either an actual consultation will occur, with its attendant cost in time and dollars, or an informal telephone consultation may occur, still requiring the expenditure of time by both the referring and consulting physician. To the extent that such consultations sometimes become pro forma and the utilization in question is nearly always approved, the utility of this approach diminishes greatly.

Third, there are important educational issues surrounding the requirement in the teaching hospital setting that physicians seek guidance or permission every time that a particular medication is used. Literature from research on education, as well as common sense, indicates that “decisions” that are made in this way are less useful learning experiences than are actions taken after the physician has considered all possible options on his or her own. On a broader scale, at a time when hospitals are increasingly concerned about reducing suboptimal clinical decision making on a variety of fronts, the strategy of needing to ask permission for each decision becomes impractical as a generalizable approach. For all of these reasons, we attempted to devise a method for reducing specific incorrect antibiotic prescribing practices through an educational intervention that would be of low cost and capable of replication in a variety of settings. The problem of dosing schedules incompatible with available pharmacokinetic literature was chosen as the first area of intervention.

Our earlier work demonstrated that it is possible to reduce improper prescribing of several medications (including antibiotics) in ambulatory patients through “academic detailing” by medical school-based clinical pharmacists sent to physicians’ offices to educate them about current therapeutic principles. Similar work was done by Schaffner et al, using physician educators, with comparable results. Both interventions were tested through randomized controlled trials, and both have been subjected to follow-up analyses, which demonstrated that these efforts can save more dollars than they consume. However, despite the favorable benefit-cost ratio that resulted from this earlier work, in the present study we attempted to learn whether an even more inexpensive intervention might be useful in improving selected antibiotic prescribing decisions in the hospital setting. The findings of such a study, if positive, could then be replicated widely with very modest costs. The approach described below was also selected as a step toward computer-based on-line ordering of all therapies and tests, which will probably become routine in most American hospitals within a decade. The educational strategy described, although paper based, will be readily adaptable to such technology as it becomes more widely available.

Fig 1.—Excerpt from educational materials on clindamycin kinetics. Literature emphasized rational therapy first, cost secondarily. Graph shows that at 600 mg every eight hours, trough levels in serum never drop below minimum inhibitory concentration for virtually all clinically relevant anaerobes.

METHODS

A review was conducted of the current and recent trends in antibiotic prescribing at the Beth Israel Hospital in Boston to select suboptimal antibiotic prescribing practices whose correction would result in more rational clinical care and reduction of unnecessary expenditures. One area that emerged was the use of dosing schedules inconsistent with available pharmacokinetic data. For several potential target practices, a literature review was conducted to be certain that therapeutic recommendations could be based on well-documented studies justifying the changes proposed.

Three commonly used parenteral antibiotics were selected as targets for dose interval recommendations: clindamycin, cefazolin sodium, and metronidazole hydrochloride. Each of these drugs has a relatively long serum half-life after intravenous bolus administration: about three hours for clindamycin, 1.8 hours for cefazolin, and seven hours for metronidazole. However, prevalent patterns of use often do not take such pharmacokinetic considerations into account. For each drug, we recommended a dose interval of every eight hours. Favorable clinical experience has been reported with the use of eight-hour dosing with each of the targeted antibiotics. For clindamycin, based on reported clinical experience using eight-hour dosing and in vivo susceptibility data, we concluded that a dose of 600 mg every eight hours was appropriate for essentially all adult patients, except...
those with severe renal impairment. We found no justification in the literature for higher doses.

A format was needed that would bring the relevant educational messages to the attention of the physician each time a prescribing decision was made. To accomplish this, we designed a new parenteral antibiotic order form. Consensus was developed among representatives of the various clinical services, nursing, pharmacy, and administrative and hospital policy was changed so that any parenteral antibiotic had to be ordered on the specially prepared form. Educational sessions were held with house officers, nurses, unit secretaries, and others throughout the hospital to make them aware of this change in policy and the need for it. The form was pilot tested in part of the hospital initially and implemented hospitalwide two months later. Messages were supplemented with appropriate written and poster material (Fig 1). For cefazolin, printed "unadvertised" was placed in every patient chart in the hospital, mailed out to all physicians, and posted in new display cases in all patient-care areas several months in advance of the implementation of the new order form. For clindamycin, the written materials were disseminated concurrently with the hospitalwide implementation of the order form. In the initial weeks after adoption of the form, orders written on old order forms were filled by the pharmacy, but followed by a page to the appropriate house officer restating the new policy. Within a month, compliance with use of the new form exceeded 95%.

An important principle underlying the new form was that it would not require additional paperwork and would not restrict physician prerogative in any area, but instead would rely on the assumption that a physician given appropriate data and reminders would generally prescribe in the approved manner through freedom of choice. This approach was reflected in several ways in the resulting structured order form. The page was divided into four sections, one each for penicillins, aminoglycosides, cephalosporins, and other antibiotics. In each section, the names of one or more drugs of choice were printed, requiring the physician merely to check a box to order them. To order other drugs, the name of the antibiotic had to be written in by the ordering physician. For each drug, frequency of dosage was similarly translated into uniform columns to be checked (eg, q4h [every four hours], q6h, q8h, etc), rather than requiring the physician to specify the number of hours between doses. A final column labeled "q-h" was left blank so that physicians could fill in any idiosyncratic dosage interval they chose, even if it deviated from recommended standards. The educational messages themselves were printed in a box next to the appropriate drug box.

For clindamycin, cefazolin, and metronidazole, the "q4h" and "q6h" boxes that would have to be checked to order the pharmacokinetically incorrect dosing schedule were shaded in gray, to remind physicians that such a choice was not in keeping with recommended policy. Occasional aberrant orders were followed up by pharmacists who reinforced the educational messages.

A few data on the effect of the recommendations it contained had been developed with the support of the hospital's infectious disease division, working in collaboration with the Harvard Medical School Drug Information Program, Boston. Literature references supporting the recommendations were placed in a special plastic section inserted into each patient chart in the hospital. This information could also be obtained by accessing the drug information option on the hospital pharmacy computer system known as "Drugman," or by telephoning the pharmacy for further information.

For statistical analysis, special programming was written for use with a pharmacy-based computer system that made it possible to track, on a daily basis, which medications had been prescribed at specified dosage intervals on each service throughout the hospital, as well as to yield information on total grams prescribed. This information was aggregated for 39 separate four-week periods for a period beginning two years before introduction of the structured order form, through a year after its inception. Interrupted time-series analysis was used to study changes in prescribing that occurred at the time the program was introduced. Segmented regression models were fit that assessed whether the regression in trend or levels of inappropriate prescribing for each target drug at the point of intervention.

The monthly outcome for the dosage interval measures were calculated as the hospital-wide percentage of all days of therapy (for each drug) that were prescribed at intervals more frequent than every eight hours. Because of a significant compression in the variation around the regression line after the start of the intervention, we performed a logit transformation of these monthly values before calculating regression coefficients and SEs. Two-sided t tests were used to estimate the statistical significance of estimated changes in levels or trends. Statistically nonsignificant effect coefficients (P>.05) were dropped in a step-down manner. The regression lines fit the data well, as evidenced by R2 statistics of .86 to .95 for the time-series models. Costs to the pharmacy for all study drugs were also measured for the entire study period.

RESULTS
Compliance With Form

Use of the new form increased steadily during the first month after its introduction. Within two months and continuing to the present, virtually all parenteral antibiotic orders are written on the new form, although periodic protests are voiced by isolated physicians.

Figures 2 through 4 demonstrate the changes observed in dosing of clindamycin, cefazolin, and metronidazole, respectively. For clindamycin, the percentage of patient-days at the excessively high dose frequency had been stable at approximately 90% in the 22 periods before the educational intervention. The sudden, negative change in slope coincident with initiation of the program (P=.001; Fig 2) strongly suggests a cause-and-effect relationship between education and the hospitalwide improvement in use of this antibiotic. By three fiscal periods after full-scale implementation of the form and distribution of the
Printed materials, excessive dosing of clindamycin was reduced to approximately 3% of patient-days.

Similarly, too-frequent cefazolin dosing averaged 60% in the preintervention period, with no significant downward trend. Following widespread distribution of the educational materials alone (which, in the case of cefazolin, preceded the order form by five periods), there was only a modest downward trend ($P < .001$) in excessive cefazolin dosing. A further reduction, which essentially eliminated incorrect dosage schedules, followed introduction of the order form (Fig 3).

Figure 4 presents the time-series data for metronidazole dosages. Because of less frequent use of this antibiotic, metronidazole data were aggregated over 12-week rather than four-week periods to increase stability of the time-series. Excessive (every six hours) metronidazole therapy schedules also dropped precipitously from 75% of patient-days in the preintervention period to approximately 6% after the start of the intervention ($P < .01$). The similarity and sudden changes in utilization trends for all three drugs reinforce the conclusion that the combined program of educational communications, printed materials, and the order form were highly effective in altering antibiotic use patterns.

**Economic Consequences**

Projection of data on utilization of clindamycin for the preceding two fiscal years, when compared with actual utilization data for the fiscal year following introduction of the form, indicates that $44,500 in savings was realized annually as a result of changes in ingredient costs relating to use of this drug alone. For cefazolin and metronidazole, the ingredient cost savings were $9400 and $5400, respectively. In addition to these ingredient costs, staff time and supply costs are saved when an every-six-hour medication is changed to an every-eight-hour medication. One published report by Tanner estimated such noningredient costs at $7 per dose. This figure may be high, as actual costs at the Beth Israel Hospital are approximately $2 per dose. A hospital similar in size to the Beth Israel Hospital (460 beds) that incurred ingredient and labor costs close to the figures cited would have saved an additional $60,000 in such costs for the 8500 unnecessary doses that no longer were administered, bringing total savings to $119,300 annually through changes brought about by the form in the use of these three drugs alone. At our institution, actual savings from this category amounted to $17,000 owing to preexisting economies of administration of intravenous antibiotics, bringing form-related savings for these three drugs to $76,300 annually. In comparison, costs for producing the form were quite modest. Its development and updating can be accomplished by medical staff as part of ongoing activities of a Pharmacy and Therapeutics Committee. Printing costs at our institution were about $0.10 per multiple-copy, perforated form. In part because of introduction of this approach, total antibiotic expenditures at the hospital actually declined by 4% in the year after introduction of the form.

**COMMENT**

Until recent changes in reimbursement, there was little motivation to reinvestigate the scientific basis of various antibiotic dosing schedules, even though these medications have been the most costly at most hospitals; clindamycin alone, at the time this study began, accounted for more than $400,000 in patient charges annually at our institution. Propelled by the need of the hospital to reduce unnecessary costs, and funded by an agency that shared some of the same motivations, we found it relatively easy to document the pharmacokinetic issues that underlay the recommendations we developed and that have been available in the literature for many years. In part as a result of this experience, this practice is now becoming standard in several other institutions. It is likely that other previously neglected clinical topics will be investigated in this way as similar groups throughout the country are provided with the support and motivation to improve the precision and efficiency of therapeutic interventions.

The data presented above suggest that transformation of the ordering process for parenteral antibiotics into one that involves education and guidance, but not restriction, can effectively eliminate improper dosing intervals and reduce expenditures considerably, without the need for additional surveillance of prescribing practices by subspecialists. At negligible cost, new changes in recommended hospital policy can be reflected in changes in the messages and references that are incorporated into the ordering process. These messages are far more likely to be read and acted on than is information provided through an often-ignored pharmacy bulletin or hospital newsletter. By contrast, enforcing behavior by regulation can control physicians' actions, but it may not educate.

This approach can be broadened beyond dosage interval issues to drug choice decisions when these are fairly straightforward (eg, "The aminoglycoside of choice in this hospital is gentamicin unless infection with *Pseudomonas aeruginosa* is suspected."). A form can also concisely remind physicians at the moment of prescribing of acceptable criteria for use of specific antibiotics (eg, vancomycin hydrochloride, ciprofloxacin) as developed by the Pharmacy and Therapeutics Committee and infectious disease consultants. However, for more complex situations, a paper-based form would need to be replaced by interactive software, a development that has already begun in some institutions. As computer terminals are increasingly used in the order-entry process, the opportunity presents itself to provide concurrent feedback to the physician concerning therapeutic choices. A more sophisticated version of such software would integrate information from other domains of a hospital's information system as well, eg, scanning culture and sensitivity results and renal function tests for feedback to the physician at the time an antibiotic order is entered or updated. Of course, this will work only for situations in which "optimal practice" is well defined, but such instances comprise a nontrivial proportion of clinical decisions.

With increasing use of the computer in routine hospital
care, this approach could provide the groundwork for a practitioner-specific form of individualized "tutorials" relevant to specific resource utilization decisions. If clinical decisions are appropriate (ie, in keeping with decision rules adopted by the hospital medical staff and based on the best available scientific literature), the computer could be used merely as a passive order entry device. However, should an order appear to be beyond the limits of plausible decisions as established by the staff of a given institution, the computer could then be used to ask additional questions, provide information, and present alternative strategies to the physician. In many cases, one would expect that the physician, presented with additional data from the literature, along with the collective advice of peers, would choose to act in a way consistent with such recommendations. However, it is our position that the ultimate discretion must remain in the hands of the ordering physician, who after all maintains final responsibility for the welfare of the patient.

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