EFFECT OF ANTIBIOTIC ORDER FORM GUIDING RATIONAL USE OF EXPENSIVE DRUGS ON COST CONTAINMENT

Sayomporn Sirinavin[1], Patcharin Suvanakoot[2], Boonmee Sathapatayavongs[3], Kamthorn Malatham[3]

Department of Pediatrics[1]; Hospital Central Pharmacy[2]; and Department of Medicine[3], Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Abstract. New injectable antimicrobial agents are generally costly and broad-spectrum. Overusage results in unnecessary economic loss and multi-drug resistant organisms. Effective strategies for decreasing costs without compromising patient care are required. This study aimed to evaluate the economic impact of a system using an antimicrobial order form to assist rational usage of expensive antimicrobial agents. The study was performed during 1988-1996 at a 900-bed, tertiary-care, medical school hospital in Bangkok. The target drugs were 3 costly, broad-spectrum antibacterial drugs, namely imipenem, vancomycin, and injectable ciprofloxacin. The restriction of these 3 drugs was started in 1992 and was extended to netilmicin and ceftazidime in 1995. A filled antimicrobial order form (AOF) was required by pharmacists before dispensing the drugs. The AOF guided the physicians to give explicit information about anatomic diagnosis, etiologic diagnosis, and suspected antimicrobial resistance patterns of the organisms. It also contained information about indications of the restricted drugs. The filled forms were audited daily during working days by the chairman of The Hospital Antibiotic Committee. Feedback was given to the prescribers by infectious disease specialists at least twice a week. The strategy was endorsed by the executive committee of the hospital. Impact of AOF without endorsement, audit and feedback, was evaluated in 1996. The expenditures of the drugs were adjusted to the average admitted patient-days per fiscal year of the study period.

The system with endorsement was well accepted and could be maintained for 4 years. The adjusted expenditures per year of the 3 restricted antibiotics were 1.41-1.87 million baht less (22-29%) in 1992-1994 than the pre-intervention year 1991. The cost reduction of imipenem and injectable ciprofloxacin could also be maintained for 1995 but not vancomycin for which use increased. The costs of these 3 restricted drugs increased very sharply (69%) in 1996 when there was loss of endorsement and capacity to perform auditing and feed back by infectious disease specialists. The system did not work with ceftazidime which was commonly used for febrile neutropenia and nosocomial infections.

INTRODUCTION

Antimicrobial agents account for the largest expense of all drugs used in hospitals (Col and O'Connor, 1987; O'Brien, 1997). Rapidly increasing costs of treatment of infectious diseases and problems from antimicrobial-resistant microbes are substantially caused by inappropriate usage of antimicrobial drugs (O'Brien et al, 1987; Goldmann and Huskins, 1997). It is suggested that the use of high-cost, specialized antimicrobial agents should be a privilege of infectious disease consultants and others trained in their use, just as a performance of invasive procedures are limited to those who are

qualified (Kunin, 1985). There have been a number of attempts to reduce the problems (Counts, 1977; John and Fishman, 19/4; Kunin, 1981; Marr et al, 1988; Quintiliani et al, 1991; Soumerai et al, 1989). Requirement of consultations with an infectious disease specialist before drug prescription had a positive effect in decreasing cost and antimicrobial resistance (Kunin et al, 1973; McGowan and Finland, 1974; Moleski and Andriole, 1986; Recco et al, 1979; Seligman, 1981). But, it is not always possible, and can cause delay of treatment in places where infectious disease specialists are scarce. A need to implement ongoing monitoring of antimicrobial use and physician prescribing habits has led to development of several antimicrobial order forms (AOF) of different structure and methods of intervention (Kowalsky et al, 1982; Echols and Kowalsky, 1984; Durbin et al, 1981; Aswapokee et al, 1992; Avorn et al, 1988; Soumerai

Correspondence: Sayomporn Sirinavin, Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Rama 6 Road, Bangkok 10400, Thailand.

et al, 1993; Lipsy *et al,* 1993). Almost all of them aimed at improving dosing intervals and duration of therapy. There has been controversy over the value of the AOF as a method of cost containment and quality assurance (Quintiliani *et al,* 1991).

This article describes our 5-year experience with a system of using AOF, guiding the rational use of expensive broad-spectrum antibacterial agents, and the economic impact in a medical school hospital in Bangkok.

MATERIALS AND METHODS

Setting

Ramathibodi Hospital is a 900-bed medical school hospital in Bangkok. Admission rates during 1988-1996 were 21,254 - 26,361 admissions per year or 188,659 - 213,851 admitted patient-days per year. The hospital pharmacy has been equipped with a computerized system since 1987, from which pharmacy gross utilization data of dispensed drugs can be obtained. Restriction of antimicrobial usage had never been done in this hospital before, physcians had been able to order any antibacterial drugs according to their own judgement. Infectious disease consultations depended on requests. Almost all prescription forms for in-patients were filled by residents.

Methods

Target drugs : The Hospital Antibiotic Committee was first appointed in August 1991. Annual gross utilization data of antimicrobial usage during 1988-1991 was reviewed. It was found that there was very rapid increase in costs of antimicrobial usage (Sirinavin *et al,* 1992) . It was also noticed that the new, expensive, broad-spectrum antimicrobial agents had rapidly increased popularity without real indications. The committee therefore decided to start restriction of the 3 most expensive broad-spectrum antibacterial drugs by using AOF in 1992. They were imipenem (4,176 baht or US$ 167 per patient-day), vancomycin (3,200 baht or US$ 128 per patients-day), and injectable ciprofloxacin (1,200 baht or US$ 48 per patient-day).

It was found later that netilmicin was unexpectedly largely used in the Department of Surgery, most commonly in place of gentamicin while its cost per adult-day was 20 times more than gentamicin and 3-4 times more than amikacin. In-

termittent education was provided with short-period effectiveness. It was also found that ceftazidime accounted for the highest expense of all injectable drugs while it was in most place used as "broad-spectrum antimicrobial agents". Restriction was then extended to netilmicin and ceftazidime since January 1995.

The intervention : A special AOF was designed and aimed at guiding physicians towards rational selection of antibacterial agents (Appendix). It was aimed to encourage the prescribers to review basic clinical and laboratory information, *ie* anatomic diagnosis, etiologic diagnosis, and antimicrobial susceptibility, before making a decision to use a restricted drug. The format included patient identification, age, underlying disease, site of infection, suspected or known causative bacteria, hospital or community based acquisition of this infection, microbial investigation, and reasons for using the drug. Brief educational information about indications for the drugs appeared right after the name of each restricted drug listed in the AOF. It was recommended that imipenem, vancomycin, and ciprofloxacin should be used for infections caused by multi-drug-resistant bacteria where there was no other choice. The suggested indication for netilmicin was for infection by bacteria which were resistant to gentamicin and amikacin while an aminoglycoside was needed. The indication for ceftazidime was loosely presented as infection which a third-generation cephalosporin was indicated and *Pseudomonas aeruginosa* was a suspected or known cause.

The AOFs were available at the nursing counters of all patient wards. The filled AOFs were required by the pharmacists for dispensing the restricted drugs. The AOFs were collected and sent to the office of the Hospital Antibiotic Committee every day. They were daily audited during working days by the chairman of the Hospital Antibiotic Committee who was also the chairman of Hospital Infection Control Committee and an infectious disease specialist. They were then distributed to each of the 3 (1-pediatric, 2-adult) infectious disease specialists. The filled forms were reviewed at least twice weekly and consultation given if the indication appeared inappropriate. The data collected from the filled AOFs were also used to identify areas where other educational interventions might be of benefit. The strategy was endorsed by the executive committee of the hospital. All new residents, medical students and related personnel were orien-

tated about this implementation before starting to work in the hospital.

It took a few months before the requirement for AOF in prescription of the restricted drugs was fully effective. The full program started in January 1992, from then no restricted antimicrobial drugs would be dispensed from the pharmacy without receipt of the AOF.

The executive team changed in mid 1995, or approximately the beginning of the fiscal year 1996, which affected the hospital and departmental policy about drug usage and related management. There was no orientation to the newcomers about the policy and system, and no endorsement from the related administrators. In addition, one of the three responsible infectious disease physicians left for further training. Though the requirement for AOF was continued, the reviewing process of the AOF was performed irregularly due to the work load of the two infectious disease specialists, and hardly any review was performed in 1996.

Analysis

The hospital central pharmacy obtained the dispensing data of antibacterial drugs by fiscal year using a dBase computer program. The costs of antimicrobial agents slightly changed during the study period and a fixed average cost was used in analysis. Comparisons of antibiotic usage between years are presented as costs in Thai baht, and amounts as prescribed daily doses (PDD). Approximately 25 Thai baht were equivalent to one US dollar during the study period. A PDD is a modification of the defined daily dose (DDD) which is the average maintenance dose for the main indication of a particular drug used for an adult (Col and O'Connor, 1987). The PDD units used in this report were developed by the National Committee for Development of Guidelines for Antibiotic Usage in Thailand, 1992. Information about admission rates were obtained from the hospital medical statistics. The yearly expenditures of antibiotics were adjusted to baht per 200,000 patient-days which was derived from the round up of an average number (200,665) of admitted patient-days per year during the study period.

RESULTS

With endorsement from the executive committee and good cooperation of ward nurses and hospi-

tal pharmacists, there was no physician resistance to this method. It was found that injectable antibacterial drugs accounted for about 70 % (66-75 %) of the total yearly costs of antibacterial drugs dispensed from the hospital pharmacy during the study period. Fig 1 shows the adjusted costs and amounts of injectable antibacterial agents dispensed from the hospital pharmacy during fiscal years 1988 to 1996. The adjusted costs increased from 14 million baht in 1988 to 29 and 36 million baht in 1995 and 1996. It was found that while the costs of antibacterial drug usage increased very rapidly (Fig 1a), there were only slight changes in prescribed daily doses of antibacterial drugs (Fig 1b). This was also reflected by findings of rapid increase in calculated costs per daily dose, especially during 1988-1991. The cost increased at a much slower rate after implementation of AOF for expensive drugs in 1992-1995 (Fig 1c). There was a sharp rise of the total cost, and cost per PDD in 1996.

There were 3 -10 filled AOFs each day. Figs 2 and 3 demonstrate the effect of the AOF system on expenditure of the restricted drugs. There was a substantial decrease in the 3 restricted antibiotic expenditures during the 3 years following the institution of the AOF system. The reduction in the total cost was 29% in the first year and about the same percentage (25 and 22%) in the second and third years, compared to the baseline cost in 1991 (Fig 3). The yearly expenditures of the 3 restricted antibiotics were 1.41-1.87 million baht less in 1992-1994 than the pre-intervention year 1991 (Fig 2). The effects on imipenem and injectable cipro- floxacin were also maintained during 1995 but not for vancomycin. Rapid increase of vancomycin expenditure in 1995 was probably related to increased problems of methicillin-resistant staphylococci and ampicillin-and-gentamicin-resistant enterococci. In 1996, total drug cost for the three restricted drugs increased 69%; from 6.6 million baht in 1995 to 11.6 million baht in 1996.

The expenditures of netilmicin usage decreased by half from 0.7 million baht in 1994 to 0.3 million baht in 1995 and then increased to 0.5 million baht in 1996. But, the system had no effect on decreasing ceftazidime expenditure. Expenditure of ceftazidime continued increasing from 3.9 million baht in 1994 to 4.6 million baht in 1995 and 5.1 million baht in 1996.
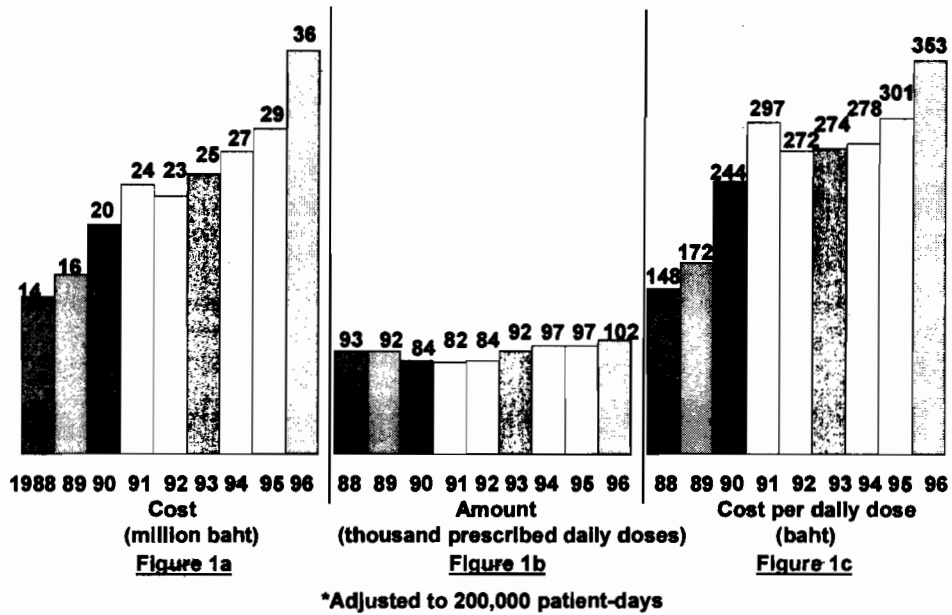
Fig 1– Comparison of total costs*, prescribed daily doses*, and cost per prescribed daily dose of injectable antibacterial drugs, 1988-1996.
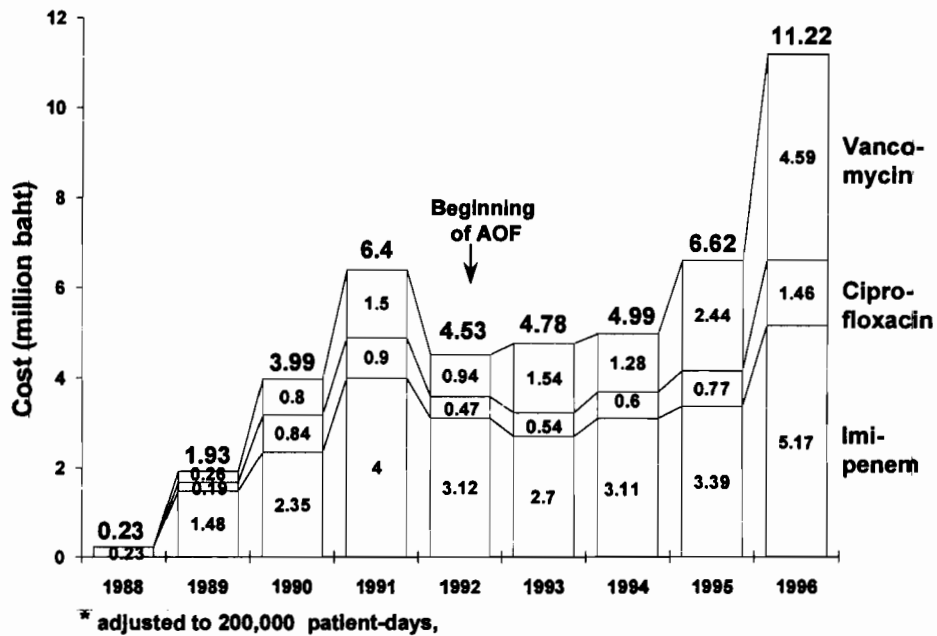

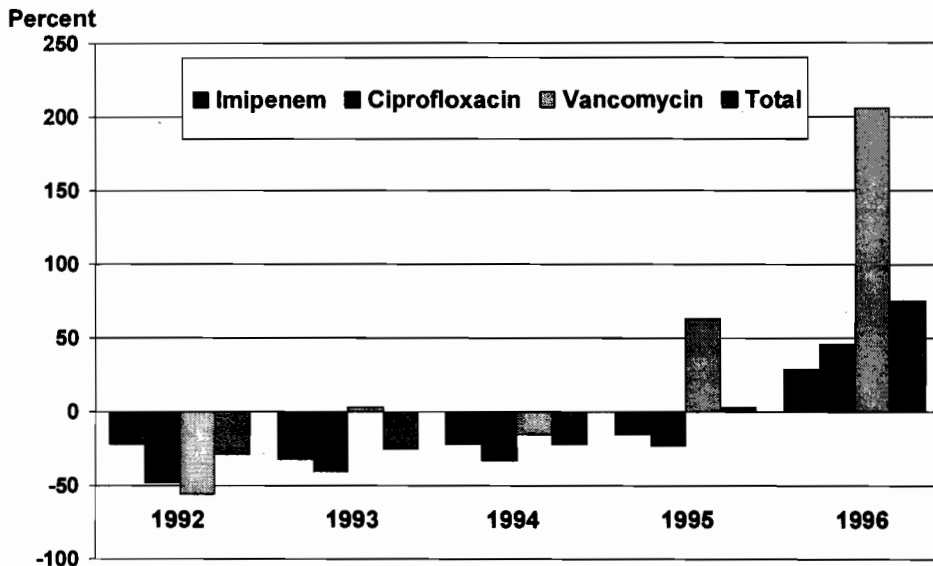Fig 2– Adjusted costs of restricted antibacterial drugs*.

Percent

Fig 3– Changes of costs of restricted antibacterial drugs in percentages of the cost in pre-intervention year 1991.

DISCUSSION

It was found in this study that implementation of a system using AOF, guiding rational selection of expensive broad-spectrum antibacterial drugs, had an impact on large cost-savings. This AOF system did not prohibit physicians' prescription, therefore it did not cause delay or limitation of drug use when the drug was indicated and did not compromise patient care. A system using this AOF was useful as self-guide for rational selection of antibacterial drugs. It was also valuable in drug utilization auditing with performance feedback, identifying potential problems in antimicrobial prescribing practices, and providing a continuous monitoring device for evaluation and documentation of antimicrobial use. It helped infectious disease consultants to effectively control the drug usage in their limited availability.

The system did not work with ceftazidime, which was most commonly used in patients with hematological malignancy as well as first-line treatment for suspected nosocomial infections. Since antimicrobial usage is strongly linked to the emergence of resistant pathogens, an increase in infections caused by methicillin-resistant staphylo- cocci would be expected to result in increased use of vancomycin in 1995.

This system integrated several aspects of the previous recommendation for successful controlling antibiotic costs in the hospitals (Counts, 1977; Kunin, 1981; Marr *et al*, 1988; Quintiliani *et al*, 1991, John and Fishman, 1997; Avorn *et al*, 1988; Soumerai *et al*, 1989), including restricition of costly drugs, education, required infectious disease physician consultation, audit and feed-back, utilization review. Although it has been proved that requirement of consultations with an antibiotic utilization expert is very effective in controlling antibiotic utilization, they are not always available which can cause delay of patient care (McGowan and Finland, 1974; Moleski and Andriole, 1986; Recco *et al*, 1979; Kunin *et al*, 1973; Seligman, 1981). The structural approach in this AOF guides the physician to rational selection of the drugs through clinical diagnosis, etiologic diagnosis, and susceptibillity patterns. This first system should help physicians to more appropriate selection of antibiotics. Education and endorsement are also important. It was easier to recommend them to use netilmicin, vancomycin, imipenem, ciprofloxacin for infections caused by multi-drug-resistant bacteria. But, it was much more difficult to educate the physicians about the setting of *Pseudomonas aeruginosa* infection for which ceftazidime was indicated. Immediate audit and feed-back is very

important part of a system using antibiotic order forms for drug selection. In 1996 there was a sharp increase in costs of restricted drugs when auditing and feed-back stopped. The finding in this study agrees with the previous finding that the form alone is insufficient to ensure rational use of the restricted drugs (Aswapokee *et al*, 1992), it required auditing and feed-back by those who were trained to use the drugs well.

These restricted drugs were indicated mostly for infections with multi-drug-resistant organisms which occurred in a hospital. Increased hospital infection with these organisms would increase demand for the drugs. In contrary, these filled AOFs helped infectious disease consultants in controlling source cases and keep informed with the problems.

A utilization review can be obtained from the filled AOF, which give information for improvement of the system. Enforcing restriction policy can be difficult, particularly in hospitals that have rotating house staff. Good orientation of the new comers, together with audit and feed-back make the system successful.

It appeared that a successful AOF system for rational drug selection should include clear indication for the drug usage, endorsement from involved administrators, audit and feedback process. It was learned from this study that the reasons for failure of this AOF in controlling costs included: poorly specified indications for the drug usage, no endorsement, uncontrolled drug resistance problems, and absence of auditing and feedback.

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APPENDIX

Restricted Antibiotic Order Form

Name .... Age .... Ward .... HN ....

Underlying diseases   1 ....

2 ....

Place of acquisition of this infection   [   ] Hospital

[   ] community

Site of infection   [   ]   sepsis   [   ] gastrointestinal tract

[   ]   bacteremia   [   ] urinary tract

[   ]   lung

[   ]   others, specify...........................

Predicted / known causative organism

1 ....

2 ....

Microbiology tests: Gram stain [   ]

Culture - [   ] Not done

[   ] Done- Result pending [   ]

Result known   [   ]

as ....

Drugs	Reasons for use
[ ] Ceftazidime	[ ] For *Ps. aeruginosa* infection, or else cefotaxime when a cephalosporin is indicated
[ ] Netilmicin	[ ] For gentamicin and amikacin resistant bacteria.
[ ] Ciprofloxacin	[ ] For multi-drug resistant Gram-negative bacilli and *Ps. aeruginosa* infection
[ ] Vancomycin	[ ] For infection with methicillin-resistant *S. aureus*
[ ] Imipenem	[ ] For infection with Gram-negative bacteria resistant to all drugs except imipenem

Other reasons for prescription of the restricted drug...

Prescriber ....   Date ....