Ciprofloxacin Use Under a Reserved Drug and Stepdown Promotion Program

Luciana Frighetto, Shelagh M. Martinusen, Fatima Mamdani and Peter J. Jewesson

ABSTRACT

This study retrospectively evaluated the use of parenteral ciprofloxacin (PC) under the influence of a reserved antimicrobial drug program and an intravenous-oral stepdown program.

During the first three months following its formulary introduction, 92 PC treatment courses were initiated. Fifty of these treatment courses in 49 adults were randomly selected for study. The hematology service accounted for 50% of the courses reviewed. The balance were initiated in the intensive care unit (16%), and six other services (34%). PC was used for the treatment of febrile neutropenia (50%), respiratory tract infections (20%), gram-negative sepsis (10%), and five other indications. Initial use of the intravenous formulation was considered appropriate in 92% of courses. Stepdown therapy occurred in 17 (34%) of treatment courses. Of the 26 patients considered candidates for oral therapy, seven patients (27%) were eligible for earlier stepdown and nine patients (35%) did not receive oral drug. According to our criteria, unnecessary use of the intravenous route occurred in 20% of PC treatment days. Mean total cost (acquisition plus delivery) of therapy per course was $668. This cost was higher in the hematology service (mean $990) than any other service (p = 0.0015). When stepdown therapy was employed the mean daily cost of therapy was $43.63 vs. $55.61 when the oral dosage form was not used (p = 0.04). Parenteral drug costs totalling $6245 were avoided by subsequent use of the oral dosage form. If full compliance with stepdown criteria had occurred, an estimated total savings of $10,769 could have been realized.

Key Words: *Ciprofloxacin, Utilization Review*

RÉSUMÉ

Cette étude consistait en une évaluation rétrospective de l'administration parentérale de la ciprofloxacine (CP), dans le cadre d'un programme d'antibiothérapie réservée et d'un programme de conversion d'antibiothérapie de la voie intraveineuse à la voie orale.

Au cours des trois premiers mois où la CP a été ajoutée au formulaire, 92 traitements par cet antibiotique ont été administrés. Cinquante de ces traitements ont été administrés à 49 adultes, et ont été sélectionnés au hasard pour les fins de l'études. De ce nombre, 50 % ont été administrés par le département d'hématologie; l'autre 50 % l'ont été par les soins intensifs (16 %) et par d'autres départements (34 %). La CP a été utilisée pour le traitement de la neutropénie fébrile (50 %), des infections des voies respiratoires (20 %), des septicémies à germes gram-négatifs (10 %) et dans cinq autres affections. Le traitement initial par voie intraveineuse était considéré pertinent dans 92 % des cas. Dix-sept traitements (34 %)ont été l'objet d'une conversion à la voie orale. Des 26 patients considérés aptes au traitement par voie orale, sept (27 %) auraient pu passer à la voie orale plus tôt et neuf (35 %) n'ont reçu aucun traitement per os. Selon nos critères d'évaluation, le recours non nécessaire à la voie intraveineuse est survenu dans 20 % des jours de traitement à la CP. Le coût moyen (achat + administration) d'un traitement était de 668 $, et il était plus élevé pour le département d'hématologie (moyenne : 990 $) que pour tout autre département (p = 0,0015). Lorsqu'on passait au traitement par voie orale, le coût moyen d'un traitement par jour était de 43,63 $ comparativement à 55,61 $ pour le traitement par voie parentérale (p = 0,04). Par suite de l'administration orale d'antibiotiques, l'on a pu réaliser des économies de 6 245 $ en antibiotiques parentéraux. Si le programme de conversion voie i.v.-voie orale avait été pleinement utilisé, on estime qu'on aurait pu épargner 10 769 $ au total.

Mots clés : *ciprofloxacine, revue d'utilisation.*

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INTRODUCTION

Antibiotics continue to account for a major portion of Canadian drug expenditures.[1] In 1991, 159 of the 744 (21%) patented medicines offered for sale in Canada were systemic anti-infectives. These agents accounted for $307 million in revenue from sales, second only to the 87 patented cardiac drugs ($325 million) available.

At Vancouver Hospital and Health Sciences Centre (VHHSC), drug costs are increasing at a rate of approximately 7% per annum. The total drug budget in 1991/92 was $10.5 million; 31% of these costs were aassociated with anti-infective drugs. To minimize unnecessary drug expenditures, we have successfully implemented a number of cost containment programs.[2-12] These programs have been developed in accordance with Health andWelfare guidelines[13] and have resulted in a cost avoidance of well over one million dollars in drug and drug administration expenditures. Our Reserved Antimicrobial Drug (RAD) Program and our Parenteral-Oral (IV-PO) Stepdown Program have been particularly useful to assist us with the introduction of new antimicrobial agents and to promote the cost effective use of oral dosage forms. These programs have been described in detail elsewhere.[7,12]

The ultimate role of parenteral ciprofloxacin in the Canadian hospital setting will be largely determined by the manner in which this drug is introduced to the prescribing body. Improper application of this drug (e.g., empiric treatment of community-acquired pneumonia) will lead to economic and therapeutic problems which will seriously affect the usefulness of this drug. The Society of Infectious Diseases Pharmacists recommends judicious use of parenteral ciprofloxacin.[14] Cautious hospital introduction of this formulation should help ensure a high level of appropriate use. Promotion of IV-PO stepdown therapy can facilitate dramatic cost reductions associated with drug acquisition and delivery expenditures. Early patient discharge may also be facilitated.

We have had considerable experience with parenteral ciprofloxacin as an emergency release drug prior to its release on the market.[15] To our knowledge there are no reports in the literature regarding Canadian hospital experience with this agent prior to or following its general release. The objectives of this study were to: 1) characterize the utilization of parenteral ciprofloxacin as a previous emergency release drug in our hospital; 2) introduce parenteral ciprofloxacin onto the formulary and evaluate service, patient, and treatment course characteristics under a RAD Program; and 3) determine whether an IV-PO Stepdown Program can be used to promote early conversion to the oral dosage form of ciprofloxacin.

METHODS

This study was an open, unblinded, retrospective evaluation of ciprofloxacin use at a 1000-bed tertiary, acute care, teaching hospital. Parenteral ciprofloxacin was added to the hospital formulary as a reserved agent under an existing RAD Program and the oral dosage form was promoted concurrently under an IV-PO Stepdown Program. Parenteral and oral ciprofloxacin drug supplies were supplied by the hospital during the study period.

All dispensing records of parenteral ciprofloxacin while an emergency release drug in 1991 were reviewed to characterize its utilization. The review was followed by a three-month study period (May-July 1992), in which all patients admitted to (VHHSC) with an infectious diagnosis and prescribed parenteral ciprofloxacin were identified via a screen of computerized pharmacy records. Using a computer random number generator, a random selection of 50 parenteral ciprofloxacin treatment courses were identified for a detailed treatment course evaluation.

The health records of these selected patients were subsequently reviewed by three investigators (LF, SM, FM) to identify those patients who were prescribed the study drug. Those patients who did not actually receive at least one dose of parenteral ciprofloxacin during the study period were excluded from review.

As this study was considered part of a hospital-approved cost containment program and did not require treatment arm randomization nor deviation from normal hospital care practice, informed patient consent was not required.

Formal approval for both the addition of parenteral ciprofloxacin to the formulary and implementation of the intervention was obtained through the Antibiotic Utilization Subcommittee, the Drugs and Therapeutics Committee and the Medical Advisory Committee. Parenteral ciprofloxacin was introduced to the formulary as a Reserved Antimicrobial Drug (RAD) on the first day of the study period. As a RAD, parenteral ciprofloxacin could be prescribed only for approved indications and each treatment course was monitored closely by a pharmacist. A pharmacy newsletter was distributed to all prescribers to inform them of the formulary addition. The purpose of this publication was to review ciprofloxacin properties, identify the hospital-approved indications for parenteral ciprofloxacin, and to promote the oral formulation. Oral ciprofloxacin remained on formulary during the study period as an unrestricted drug.

Under the RAD Program, prescribers in areas outside of the Hematology Service were required to complete a RAD request form concurrent with their prescription for parenteral ciprofloxacin. Hematology

has been excluded from the RAD program as all antibiotics are prescribed as part of a standard protocol and do not require individual treatment course justification.

Parenteral ciprofloxacin was recommended for the empiric or directed therapy of bacterial infections in which the patient was intolerant or incapable of absorbing the oral dosage form. Prophylactic use of parenteral ciprofloxacin was not considered an acceptable indication. Since oral ciprofloxacin had been a formulary drug for more than two years at this hospital and prescribers were considered generally familiar with the attributes of this antibacterial agent, specific infectious indications (e.g., *Pseudomonas aeruginosa* bacteremia) for the parenteral formulation of ciprofloxacin were not specified on the RAD request form. Prescribers were required to complete a RAD form on initiation of therapy. Failure to complete this form resulted in the dispensing of a 24-hour drug supply with notification that a completed form was required before further supplies would be dispensed. All treatment courses were reviewed by a pharmacist within 24 hours of initiation and at least every three days thereafter to determine appropriateness of therapy. These pharmacists interacted with prescribers during patient ward rounds and via both personal and telephone communication to provide information regarding the appropriate use of this drug and to assist in optimizing therapy for each patient. Drug monitoring data (demographic, drug regimen, microbiology, and progress) were recorded daily by the pharmacist using a standard patient monitoring form.

Parenteral ciprofloxacin was added to the existing IV-PO Stepdown Program on the same day as the formulary addition. Within three days of initiation of a parenteral ciprofloxacin treatment course, a reminder ("chart talker") was placed on the front cover of the patient's health record.[12] A reminder was sent by the pharmacy department every three days during parenteral therapy. Clinical pharmacists also promoted oral therapy through their interactions with physicians.

Using a computerized database (dBaseIV®, Borland), information regarding patient demographics (including modified Apache II score [16]), drug therapy characteristics, relevant microbiological data, treatment course appropriateness and outcome, cost, and adverse drug reactions were collected for each treatment course. Health records, pharmacist drug monitoring records, and RAD request forms were reviewed by three (LF, SM, FM) investigators. These data were subsequently reviewed in collaboration with the senior investigator (PJ) and assessments of appropriateness of therapy, clinical and microbiological outcomes, and verification of data were accomplished for each treatment course.

Empiric therapy was defined as the initiation of therapy in the absence of pathogen identification. *Directed therapy* implied knowledge of pathogen identity (in the presence or absence of susceptibility information). Parenteral ciprofloxacin was considered to be *primary therapy* when prescribed as a part of the initial regimen to treat infection. *Augmentation therapy* implied addition of ciprofloxacin to a pre-existing regimen while *replacement therapy* inferred discontinuation of initial therapy and initiation of parenteral ciprofloxacin. Any pathogens identified were classified as being responsible for the infection for which ciprofloxacin was initiated *(causative pathogens),* responsible for a subsequent *superinfection* or *colonizers* according to previously used definitions.[17]

Treatment courses were evaluated for clinical and microbiological outcome when initiated for acceptable indications and maintained for a minimum of three days.[8] Acceptable indications included the treatment of known (directed therapy) or suspected (empiric therapy) infections involving susceptible aerobic pathogens cultured from any anatomic site excluding the central nervous system. Treatment courses initiated for infections in which the pathogens were initially resistant to the study drug were not evaluated for outcome. Patients who died from causes not judged to be related to infection were also excluded from outcome evaluation. Gram positive aerobes are not routinely tested for ciprofloxacin susceptibility at this institution.

Clinical response to empiric and directed treatment courses was classified as cure, improvement, failure, or relapse. Where parenteral ciprofloxacin was followed by oral ciprofloxacin (i.e., sequential or stepdown therapy) for a combined duration of at least 72 hours, the overall treatment course was evaluated. *Cure* was defined as resolution of clinical signs and symptoms (including elevated temperature and white blood cell count) with no evidence of infection at the time ciprofloxacin treatment was discontinued and without evidence of relapse during the seven-day immediate follow-up period in hospital. If discharge occurred prior to the seven-day follow-up period and there was no readmission, cure was assumed. *Improvement* was defined as a significant reduction in clinical signs and symptoms with incomplete resolution of clinical evidence of infection at the time of treatment course discontinuation. *Failure* was defined as no apparent clinical and microbiological response to therapy. *Relapse* was defined as recurrence of similar signs and symptoms with the same pathogens

isolated following discontinuation of the drug. Re-isolation of the same pathogens within five days of discontinuing the study drug was considered *early relapse*. Isolation of these pathogens after this period was considered *late relapse*.

To be evaluated for microbiological outcome, treatment courses required microbiological evidence of infection obtained prior to the initiation of therapy. Microbiological response was categorized as eradication, persistence, eradication with recurrence of pathogens, superinfection, or new organism colonization. *Eradication* was defined as negative follow-up cultures. Where follow-up specimens were not obtained within 48 hours of study drug discontinuation, eradication of baseline pathogens was assumed if a clinical cure or improvement response was determined. *Persistence* was defined as elimination of recurrence of the same pathogens from same site(s). *Eradication* with recurrence was defined as negative repeat cultures with subsequent positive cultures within five days (early recurrence) or 30 days (late recurrence) of treatment course discontinuation. *Superinfection* was defined as the appearance of a new infecting pathogen in cultures obtained after 48 hours of therapy associated with the development of fever or other clinical evidence of infection. New organism *colonization* was defined as the appearance of any potentially pathogenic organisms obtained at least 48 hours after commencement of therapy but without signs or symptoms of infection.

All treatment courses were evaluated for overall appropriateness according to a pre-established categorization scheme.[18] In addition, the appropriateness of the parenteral route of administration on the initial day of therapy was assessed. Parenteral therapy was considered *initially inappropriate* if the infection was judged to be of mild to moderate severity and the patient received either at least one regularly scheduled oral drug for a minimum of 24 hours or oral nutritional feeds. Each treatment course was also assessed to determine whether parenteral to oral ciprofloxacin stepdown was feasible and, if so, how efficiently this process occurred. A patient was further classified as a *stepdown candidate* if the patient was receiving parenteral ciprofloxacin, continued to need the drug, and was both clinically stable and able to tolerate the oral dosage form with no evidence of impaired oral absorption. If stepdown did occur, but it was judged that the conversion could have been initiated earlier, the number of unnecessary parenteral therapy days was recorded. Drug costs associated with parenteral to oral ciprofloxacin stepdown and lost savings due to delayed use of the oral dosage form was also determined for each treatment course.

All treatment courses were assessed for evidence of adverse drug reactions. Events which were considered possibly or probably related to ciprofloxacin were recorded. Laboratory indices (i.e., chemistry, hematology, liver function tests) which altered by at least 20% during therapy were also recorded.

The acquisition and delivery costs associated with various parenteral and oral ciprofloxacin regimens were determined. These costs were then recorded for each treatment course and assessed using previously determined methods.[8,12,17] Drug preparation costs (reconstitution of drug, IV set hardware, nursing, and pharmacy personnel) at the time of the study were calculated to be $4.32 per dose.

The sample size was limited by the resources available. Fifty treatment courses were considered adequate to permit characterization of the initial role of parenteral ciprofloxacin in this hospital. Where appropriate, data were stratified by medical service. Comparisons of continuous variables were undertaken using ANOVA, while categorical variables were tested using the Chi-square statistic and Fisher's exact test. Significance was set at $p < 0.05$.

RESULTS

The medical services utilizing parenteral ciprofloxacin as an emergency release drug in 1991 (i.e., pre-study) are presented in Figure 1. The hematology service was responsible for the largest number of courses initiated during this period. During the first three months following formulary introduction in mid-1992, 92 parenteral ciprofloxacin treatment courses were initiated. During this period, the hematology service accounted for one-half of the 50 randomly selected courses reviewed. The balance were initiated in the intensive care unit (16%) and six other services (34%) (Figure 1). A difference in service distribution

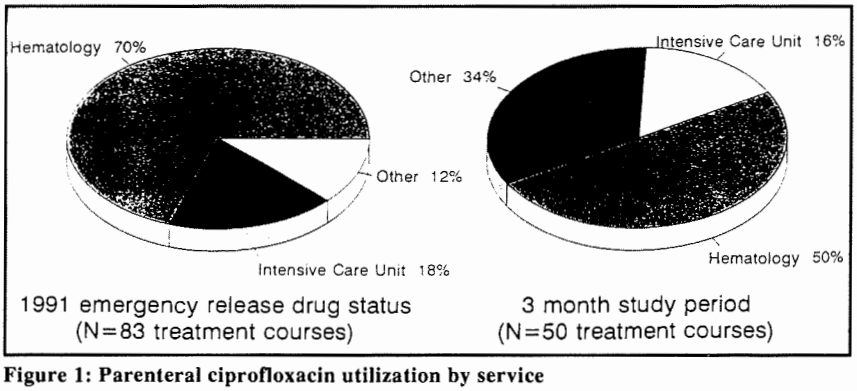

Figure 1: Parenteral ciprofloxacin utilization by service

between 1991 and the study period in 1992 was identified (p = 0.009).

Patient demographics according to service are shown in Table I. Patients were similar according to sex, weight, and baseline renal function. Renal impairment was common at the time of initiation of therapy. Hematology patients tended to be younger (p=0.004), and intensive care unit patients scored a higher mean Apache rating than other services (p=0.009).

The general rationale for initiating parenteral ciprofloxacin therapy according to service is shown in Table II. There was a difference in the distribution of indication types across services (p=0.0008). Empiric treatment courses were common (40 courses; 80% of total) with only four (10%) of these 40 courses resulting in subsequent microbiological confirmation of causative pathogens. Microbiological support for therapy was observed in only 28% of all treatment courses. No cases of prophylaxis were observed. Sixty-seven percent (24 of 36) of all empiric courses were initiated by the hematology service. Parenteral ciprofloxacin was used for the treatment of febrile neutropenia in approximately half of courses (47%) while lower respiratory tract infections (19%), gram-negative sepsis (9%), and five other indications accounted for the balance of use. Parenteral ciprofloxacin was initiated as primary therapy in 52% of treatment courses, augmentation therapy in 14%, and replacement therapy in 34% of cases. Ciprofloxacin monotherapy was observed in only 22% of treatment courses. Combination was very common in the hematology (25 treatment courses (100%)), the ICU (75%) settings, and less common (47%) in the balance of the hospital. When combination therapy was used (78% of treatment courses), the antibiotics included vancomycin (59% by treatment courses), imipenem (33%), ceftazidime (33%), metronidazole (18%), aminoglycosides (14%), and others (18%).

Microbiological data associated with parenteral ciprofloxacin treatment courses are identified in Table III. Only 29 causative pathogens were identified, and gram positive and negative bacteria were equally represented.

Thirty-eight (76%) treatment courses were considered evaluable for clinical outcome. Clinical cure was observed in 22 (58%) of the evaluable treatment courses, and improvement was seen in five (13%) of evaluable cases. Failure was identified in seven (18%), and relapse occurred in four (11%) treatment courses. Failure and relapse were more common in the hematology group (39%) and the intensive care unit (43%) than the balance of hospital (8%). There were no late relapses identified. Of the seven clinical failures, one case had microbiological eradication; one case was microbiologically unevaluable; two cases had negative baseline cultures; and there were three cases with superinfections noted. Of the four cases of relapse, one case was microbiologically confirmed while the remaining three cases had negative baseline cultures.

Microbiological outcome was evaluable in 21 (42%) treatment courses. Eradication was identified in 12 (57%) of these. No pathogen persistence was observed while early recurrence occurred in two (10%), and superinfection in six (29%) of the treatment courses (Table III). Colonization was noted in one (5%) of the evaluable courses.

The typical initial parenteral ciprofloxacin regimen prescribed was 400mg Q12H (58%) for a mean

Table I. Patient demographics according to service.

	Mean (SD)			
	Hematology	Intensive Care Unit	Balance	P Value
Treatment Courses[1]	25	8	17	–
Male (%)	28	14	18	0.219
Age (yr)	44 (17)	59 (18)	61 (17)	0.004
Weight (kg)	75 (16)	68 (31)	69 (15)	0.478
Serum Creatinine (mmol/L)	110 (47)	184 (175)	132 (78)	0.132
Apache II score	11 (5)	17 (6)	9 (5)	0.009
Duration of hospital stay (days)	42 (19)	28 (28)	20 (38)	0.067

1. One patient received two courses of parenteral ciprofloxacin during the study period.

Table II. General indication for parenteral ciprofloxacin according to service.

	No. of Patients (% by Service)			
	Hematology	Intensive Care Unit	Balance	Total
General Indication[1]				
Empiric	24 (96)	2 (25)	10 (59)	36 (72)
Directed	0 (0)	5 (63)	5 (29)	10 (20)
Empiric—Directed	1 (4)	1 (12)	2 (12)	4 (8)
Prophylactic	0 (0)	0 (0)	0 (0)	0 (0)

[1] p=0.0008

Table III: Microbiological data

	n (%)
Causative Pathogens	29 (100)
Gram positive	12 (41)
Staphylococcus	9 (31)
Enterococci	2 (7)
Streptococcus	1 (3)
Gram negative	16 (55)
Xanthomonas maltophilia	4 (14)
Enterobacter cloacae	3 (10)
Escherichia Coli	2 (7)
Acinetobacter calcoaceticus	2 (7)
Hafnia alvei	2 (7)
Others*	3 (10)
Anaerobic	1 (4)
Bacteroides	1 (4)
Superinfections	15 (100)
Gram positive	9 (60)
Staphylococcus epidermidis	5 (33)
Clostridium difficile	2 (13)
Other (*S. aureus, Strep. viridans*)	2 (13)
Gram negative**	3 (20)
Yeast	3 (20)
Candida	3 (20)
Colonizers	1 (100)
Gram positive	0 (0)
Gram negative	0 (0)
Yeast	1 (100)

* others include *H. influenza, Klebsiella pneumoniae,* and *Serratia marcescens*

** *Acinetobacter calcoaceticus* (1), *Escherichia coli* (1), *Alcaligenes xylosoxidans* (1)

duration of 13 days (range 1-50 days). Hematology treatment courses were longer (mean 18 days) than those initiated by other services (mean 8 days) (p=.0019). There was no significant difference in the initial daily regimen prescribed across services.

Initial use of the intravenous formulation of ciprofloxacin was considered appropriate in 46 (92%) of the courses reviewed. According to our criteria, unnecessary initial use of the intravenous route occurred in 20% of parenteral ciprofloxacin treatment days. Parenteral to oral stepdown therapy occurred in 17 (34%) treatment courses. There was no difference in incidence of stepdown between services. Of the 26 patients (52% of total) considered candidates for stepdown to oral ciprofloxacin therapy, seven patients (27%) were eligible for earlier stepdown than they actually experienced, and nine patients (35%) did not receive oral ciprofloxacin. No cases of premature stepdown were identified.

Employing the treatment course evaluation criteria, 37 (74%) of the reviewed courses were considered to be appropriate overall. In eight (16%) cases, an alternative agent(s) was considered appropriate and in the remaining five (10%) treatment courses, the dosage regimen was considered incorrect for the clinical indication.

Patient tolerance to ciprofloxacin was good. One patient experienced a possible drug fever which resolved upon discontinuation of drug. No patients experienced changes in laboratory indices which could be attributed to the drug.

Mean total cost of therapy per course which includes acquisition plus delivery (reconstitution materials, pharmacy, and nursing time) costs was $688 (($IV $649 (range $37-$2277); PO $54 (range $6-$165)). This cost was higher in the hematology service (mean $990) than other services (mean $310; p=0.015). When parenteral to oral stepdown therapy was employed, the mean daily cost of therapy was $43.63 (range $13.76-$69.84) compared to $55.61 (range $20.82-$74.64) when parenteral therapy alone was used (p=.04). Lost potential savings due to delayed or lack of stepdown was calculated for each course and the mean lost savings per treatment course was $90.48. Parenteral drug costs totalling $6245 were avoided by the subsequent use of the oral dosage form in the patients reviewed. If full compliance with stepdown criteria had occurred, an estimated total savings of $10,769 could have been realized over these 50 treatment courses.

DISCUSSION

This study has characterized the initial role of parenteral ciprofloxacin in our hospital. Not unexpectedly, the major use of this agent was in the critical care areas. Although the hematology and intensive care services account for most of its use, prescribing of parenteral ciprofloxacin in other areas actually doubled following formulary introduction. Ongoing monitoring of utilization patterns will be necessary to determine whether this trend continues.

Therapeutic indications for use of parenteral ciprofloxacin were diverse. As observed with other antibacterials, most treatment courses were initiated empirically. Where causative pathogens were identified, an equal distribution of gram negative and gram positive organisms were

documented. Parenteral ciprofloxacin was commonly combined with other agents. This drug often acted as a substitute for an aminoglycoside and was combined with a beta lactam and/or aminoglycoside for the treatment of febrile neutropenia in hematology patients. Superinfections were relatively common while colonization without evidence of infection was not typically observed. The rate of clinical cure or improvement was lower than that previously published.[19,20] This is likely due to the high severity of illness of the patients receiving this drug (as supported by high Apache II scores) and the relatively high incidence of empiric therapy for which a causative pathogen could not be identified. In this latter scenario, it is quite possible that the infection for which ciprofloxacin was empirically initiated was not due to pathogens which were susceptible to this drug. Consequently, response would appear to be poor. As observed in previous studies, the microbiological response rate was poorer than the clinical response rate.[8,17]

In this study, the appropriateness of the indication for parenteral ciprofloxacin use was superior to that observed in previous studies involving non-reserved antibacterials.[18] The appropriateness of use of the parenteral route was also high. We concur with the recommendations of the Society of Infectious Diseases Pharmacists[14] that ciprofloxacin monotherapy is inappropriate for the treatment of febrile neutropenia. We do not agree that ciprofloxacin "...offers no advantages over other currently used and proven regimens...".[14] Patients with beta lactam allergies who cannot tolerate cephalosporins and those with impaired renal function in whom aminoglycosides should be avoided are candidates for parenteral ciprofloxacin. Parenteral ciprofloxacin is less expensive than ceftazidime, is administered twice rather than three times daily, and, thus, may be economically preferable to ceftazidime.

The results of this uncontrolled study, though useful, should be interpreted with caution. We did not employ a control group to assess the characteristics of drug use in the absence of our program. Consequently, we do not know how well the concept of stepdown would have been received without our efforts to promote the oral dosage form. In our calculation of cost savings, we examined only those courses involving parenteral-to-oral ciprofloxacin stepdown. We cannot extrapolate our results to include other potential scenarios such as a stepdown to co-trimoxazole or other oral antibiotics. Finally, we relied on the accuracy and completeness of the health record as our primary source of data. It is possible that inaccuracies in this database would lead to erroneous interpretations on our part.

The economic benefit of stepdown from parenteral to oral therapy has also been reported by others.[21-24] In addition to the quantifiable costs (i.e., acquisition, preparation, and delivery) associated with parenteral drug therapy, there are also "hidden costs" which need to be considered.[24] The parenteral route can result in greater possibility of dose-related side effects and immediate allergic reactions, phlebitis, possible line-related infection, injection of solution precipitate or air and the need for hospitalization. These can generally be avoided with the oral route, although possibly at the cost of reduced bioavailability and slower onset of action.[25]

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