

Clinical use of rifampicin during routine reporting of rifampicin susceptibilities: a lesson in selective reporting of antimicrobial susceptibility data

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Increased use of rifampicin for in-patients was noted after the laboratory began reporting rifampicin susceptibilities routinely for all Gram-positive bacterial isolates. The appropriateness of rifampicin use was evaluated by chart review for in-patients administered rifampicin during two time periods, before and during routine rifampicin susceptibility reporting, respectively. While rifampicin susceptibility was reported routinely, four patients were subjected to potentially harmful misuse of rifampicin. These findings reconfirm the necessity of interdepartmental consultation and extensive staff education whenever a modification of antimicrobial susceptibility profile reporting is contemplated. Furthermore, they underscore the role of the clinical microbiology laboratory in guiding antimicrobial therapy through limited reporting of susceptibility data.

Introduction

The physician's choice of an antimicrobial agent is determined not only by clinical data, but is also influenced by factors such as education and experience, exposure to pharmaceutical literature, pharmacy controls, and laboratory antimicrobial susceptibility reporting formats. We describe the unexpected result of a change in laboratory reporting format, when rifampicin was added to the routine Gram-positive susceptibility testing panel without accompanying pharmacy controls or medical staff education. The subsequent increase in the use of rifampicin within our in-patient population argues strongly against such isolated changes, and reconfirms the necessity of coordinated efforts among the microbiology laboratory, infectious disease clinicians, and pharmacy.

Materials and methods

Chronology

The clinical microbiology laboratory of the North Carolina Baptist Hospital uses 96-well microtitre plates incorporating custom panels of antimicrobials for non-fastidious Gram-positive organisms, with antibiotics in twofold

dilutions spanning relevant breakpoints, which are inoculated, incubated, and read in accordance with NCCLS guidelines. In July 1994, the clinical microbiology laboratory initiated routine testing and reporting of rifampicin, without pharmacy or infectious disease staff consultation, because pharmacy data had revealed rifampicin to be the most commonly prescribed in-patient antibiotic not routinely tested in our laboratory. The concentration range of rifampicin tested was 0.06–2.0 mg/L.

In October 1994, a pharmacist alerted us to a case where rifampicin had been chosen as the sole agent to treat a staphylococcal wound infection. Based on this case finding, and pharmacy data documenting a significantly increased use of rifampicin since late July, routine reporting of rifampicin susceptibility was discontinued.

Chart review and data analysis

Chart histories for all in-patients receiving rifampicin during two months of 1994 (August and September), when rifampicin susceptibility data were being routinely reported for Gram-positive isolates (49 patients), were reviewed by a physician (C. H. S.). For comparison, chart histories for all in-patients receiving rifampicin during the same two calendar months of the previous year (1993),

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when rifampicin susceptibility data were not reported (23 patients), were also reviewed.

Results

The number of patients receiving rifampicin from January 1993 to July 1996 is shown graphically in the Figure. The average number of in-patients administered rifampicin during the three months of routine susceptibility reporting was significantly higher than the average for the 19 months before routine reporting (Student's *t*-test, $P < 0.01$), and significantly higher than the average for the 21 months after discontinuation of reporting (Student's *t*-test, $P < 0.01$).

Each patient case was classified into one of 13 categories, arranged according to degree of appropriateness, as summarized in Table I. Four cases of potentially harmful employment of rifampicin were identified during the two months in 1994 that rifampicin susceptibility was reported; none were identified in the previous year. The difference was, however, not statistically significant (Fisher's exact test, $P = 0.29$). Rifampicin was administered as single agent therapy for methicillin-resistant *Staphylococcus aureus* (MRSA) in two patients, who had infections involving an amputation stump and abdominal wound, respectively. Rifampicin was administered as functionally single agent antibacterial therapy (because of resistance of the MRSA isolate to the co-administered antibiotic, ciprofloxacin) in two other patients, who had nosocomial pneumonia and chronic osteomyelitis, respectively. Rifampicin was prescribed immediately after

receipt of a susceptibility report showing the isolate to be susceptible in three of the four cases; in the last case (osteomyelitis), no new culture had been obtained but rifampicin MICs had been specially requested on a previous culture isolate.

Discussion

Rifampicin is a unique antimicrobial agent in that its spectrum of utility appears to span infections caused by bacteria, mycobacteria, and fungi.¹⁻⁶ Therefore, clinicians see it employed against a wide variety of pathogens and are encountering the drug in patient situations ranging from the in-patient bone marrow transplant unit to out-patients with chronic osteomyelitis or mycobacterial disease. Rifampicin is, however, generally contraindicated as single agent therapy for bacterial infections, because of the risk of acquired resistance.

Routine reporting of rifampicin MIC data for Gram-positive isolates was initiated autonomously by the laboratory based upon (1) pharmacy data showing rifampicin to be the most commonly prescribed in-patient antibiotic for which testing was not routinely done, and (2) faith that physicians would prescribe it in combination with another appropriate antimicrobial agent when such multiagent therapy was clinically indicated.

We observed a prominent increase in the use of rifampicin for in-patients coincident with routine rifampicin susceptibility reporting, and a slow but sustained decline after reporting was terminated. Although rifampicin use depends upon the number of in-patients with infectious

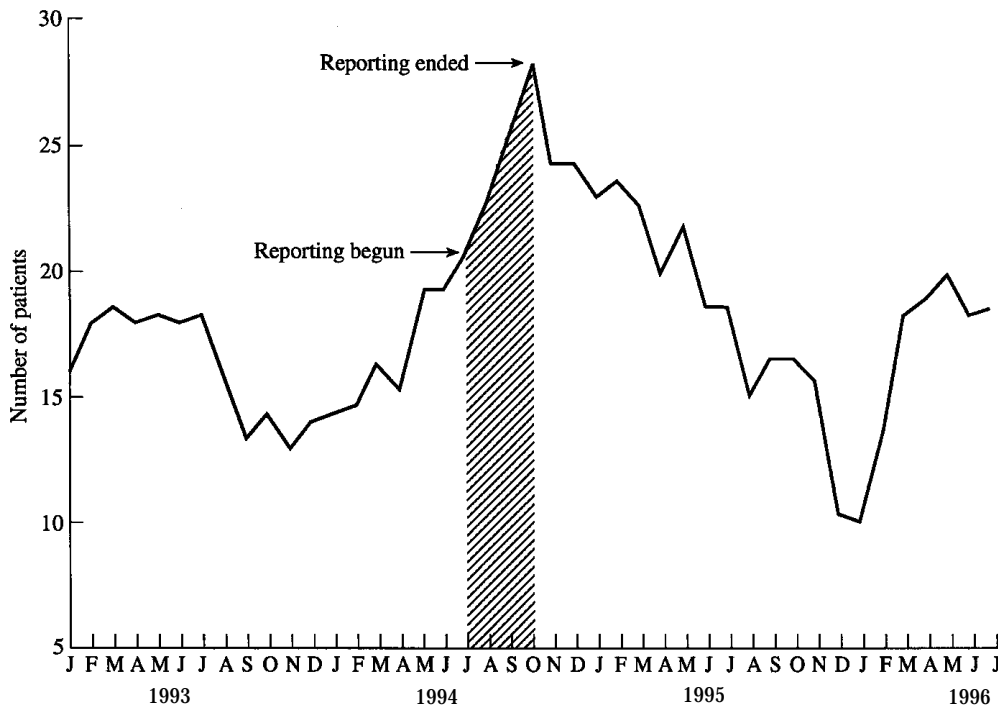


Figure. Number of in-patients administered rifampicin, running three-month average, January 1993–July 1996.

Rifampicin susceptibility reporting and use

Table. Rifampicin use before (1993) and during (1994) routine rifampicin susceptibility reporting for Gram-positive bacterial isolates, number of cases in each category

Category	Rifampicin susceptibility reporting	
	not reported (1993, <i>n</i> = 23)	reported (1994, <i>n</i> = 49)
Indicated	3 (13%)	11 (22%)
Potentially beneficial	17 (74%)	27 (55%)
Unnecessary	3 (13%)	7 (14%)
Potentially harmful	0 (0%)	4 (8%)
Indicated		
mycobacteria	3	11
Potentially beneficial		
orthopaedic implant	4	7
osteomyelitis	1	2
central nervous system implant	2	2
endovascular infection	7	6
miscellaneous antibacterial	2	5
known aspergillus infection	1	3
possible aspergillus infection	0	2
Unnecessary		
fungal infection, non-aspergillus	0	3
empirical antibacterial	1	1
uncomplicated MRSA infection	2	3
Potentially harmful		
single agent	0	2
miscombination	0	2

processes clinically deemed eligible for rifampicin therapy, only while routine susceptibility was reported did rifampicin use rise to a level significantly higher than fluctuations observed during the previous 19 months or the subsequent 21 months.

Given the small number of patients in each clinical category, the increased total number of patients administered rifampicin might none the less be attributed to a chance increase in the hospital in-patient census of so-affected individuals. We have no reason to suspect that susceptibility data reporting prompted clearly indicated, standard application of rifampicin. Routine reporting was, however, associated with four instances of potentially harmful misuse as single agent antistaphylococcal therapy, all within a two-month span. The power of suggestion, embodied in the presence of rifampicin MIC data on the antimicrobial susceptibility report, may have directly prompted at least three of these four cases of rifampicin misuse.

Clinicians often regard the susceptibility report as a menu of potential therapies. The availability of oral rifampicin formulations is familiar to clinicians in the context of antimycobacterial therapy, and makes the drug particularly attractive for the treatment of in-patients

whose discharge from the hospital is expected in the near future.

The contemporary role of the clinical microbiology laboratory encompasses more than merely providing pathogen identification and antimicrobial susceptibility data. The susceptibility report is a powerful clinical guide to the choice of antimicrobial therapy in terms of its format as well as the actual MIC data values presented. Presence of an antimicrobial agent on this report not only constitutes free advertising, but implies hospital pharmacy approval and suggests efficacy in the therapy of the patient's specific pathogen and site of infection.

The NCCLS recommends selective reporting of certain drug or organism test results,⁷ which in the case of anti-staphylococcal therapy includes rifampicin among those agents whose MIC should be reported only in certain clinical situations. Clinical microbiology laboratory directors are more than guarantors of accurate microbiologic data; they are increasingly responsible for guiding antimicrobial therapy by this selective presentation of these data. Changes to the report format and content should be made with great caution, and only after thorough consultation with pharmacy and clinical colleagues.

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