IN VITRO CIPROFLOXACIN RESISTANCE PATTERNS OF GRAM-POSITIVE BACTERIA ISOLATED FROM CLINICAL SPECIMENS IN A TEACHING HOSPITAL IN SAUDI ARABIA

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Background: Over the last few decades the ever-increasing level of bacterial resistance to antimicrobials has been a cause of worldwide concern. Fluoroquinolones, particularly ciprofloxacin has been used indiscriminately for both gram-positive and gram-negative bacterial infections. The increased use of ciprofloxacin has led to a progressive loss of bacterial susceptibility to this antibiotic. Therefore it is necessary to have update knowledge of resistance pattern of bacteria to this antibiotic so that alternate appropriate antibiotics can be used for ciprofloxacin-resistant bacterial infections. **Objective:** To evaluate the trends of ciprofloxacin resistance pattern in commonly isolated gram-positive bacteria over time in a Saudi Arabian teaching hospital. **Methods:** A retrospective analysis was carried out for ciprofloxacin susceptibility patterns of 5534 isolates of gram-positive bacteria isolated from clinical specimens submitted to microbiology laboratories at King Fahd Hospital of the University (KFHU), Al-Khobar, Saudi Arabia during the period from January 2002 to August 2005. **Results:** Increase in ciprofloxacin resistance rates with some fluctuations, among these isolates, were observed. For *Staphylococcus aureus*, it varied from 4.62, 1.83, 7.01 and 3.98%, methicillin resistant *Staphylococcus aureus* (MRSA) 97.92, 97.75, 87.01 and 88.26%, *Streptococcus pyogenes* 5.35, 4.47, 14.44 and 3.53% during the years 2002, 2003, 2004 and 2005 respectively. Cirprofloxacin resistance during the years 2002, 2004 and 2005 for other isolates was as follows: *Streptococcus pneumoniae*, 30.23, 23.02 and 26.47%; enterococcus group D, 43.05, 20.68 and 57.03% and non-enterococcus group D, 62.96, 76.92 and 87.50% respectively. **Conclusion:** Ciprofloxacin resistance in gram-positive bacterial clinical isolates particularly *Staphylococcus aureus*, methicillin resistant *Staphylococcus aureus* (MRSA) enterococcus group D, and non-enterococcus group D, has greatly increased and ciprofloxacin no more remains the drug of choice for these infections.

Keywords: Ciprofloxacin, Antibiotic resistance, Staphylococci, Streptococcus pyogenes, Streptococcus pneumoniae, Enterococci

INTRODUCTION

Over the last few decades the ever-increasing level of bacterial resistance to antimicrobials has been a cause of worldwide concern. This situation is aggravated by over the counter availability, indiscriminate and inappropriate use of antimicrobial agents.[1] Although it is well recognised that the increased use of ciprofloxacin has led to a progressive loss of susceptibility.[2,3] Since its introduction in the treatment of a broad range of clinical conditions such as the treatment of urinary tract infections and upper respiratory tract infections and as a prophylaxis of neutropenic patients as well as its use in veterinary medicine, resistant strains started to emerge much earlier.[4–6] A major point of medical concern is the emergence of ciprofloxacin resistance among gram-positive cocci like *S. aureus* and enterococci.[7,8]

Surveillance studies are one of the main tools for tackling the problem of antimicrobial resistance, as they enable resistance patterns to be monitored and allow early detection of any potential resistance trends.[1] In this study we aimed to highlight trends of resistance to ciprofloxacin among *S. aureus*, MRSA, *S. pyogenes*, *S. pneumoniae*, enterococcus group D, and non-enterococcus group D, isolated in KFHU during the period from January 2002 to August 2005.

MATERIALS AND METHODS

A retrospective analysis was carried out for ciprofloxacin susceptibility patterns of gram-positive bacteria commonly isolated from clinical specimens submitted to microbiology laboratories at King Fahd Hospital of the University (KFHU), Alkhobar, Saudi Arabia. Data of total of 5534 of gram positive organisms [*Staphylococcus aureu*s (n=2145), methicillin-resistant *Staphylococcus aureu*s (n=1918), *Streptococcus pyogenes* (n=595), *Streptococcus pneumoniae* (n=297), Enterococcus group D (n=515) and non-enterococcus group D (n=64)] was obtained from a hospital computer system during the period from January 2002 to August 2005. The bacterial isolates, except *S. pneumoniae,* were identified and their susceptibility testing was carried out by using the MicroScan Walk Away 96 system (Dade Behring Inc., West Sacramento, CA95691, USA). Identification and susceptibility testing of *S. pneumoniae* isolates was carried out by standard manual methods.

Intermediately susceptible strains were considered resistant.

RESULTS

Ciprofloxacin resistance of gram positive isolates recovered from specimens at KFHU during the period from January 2002 to August 2005 is given in Table-1. Among these isolates fluctuations in resistance trend were observed. For *S. aureus,* it varied from 4.62, 1.83, 7.01 and 3.98%; MRSA, 97.92, 97.75, 87.01 and 88.26%; *Streptococcus pyogenes,* 5.35, 4.47, 14.44, 3.53% during the years 2002, 2003, 2004 and 2005 respectively. For *S. pneumoniae*, enterococcus group D and non-enterococcus group D, sufficient data was not available for the year 2003. Cirprofloxacin resistance during the years 2002, 2004 and 2005 for these isolates was as follows: *S. pneumoniae*, 30.23, 23.02 and 26.47%; enterococcus group D, 43.05, 20.68 and 57.03% and non-enterococcus group D, 62.96, 76.92 and 87.50% respectively.

DISCUSSION

Ciprofloxacin being a broad spectrum antibacterial agent, resistance emerged soon after its clinical use both in gram-positive and gram negative infections.[4–7] Widely varying percentages of ciprofloxacin resistance have been reported in particular bacterial species with a global trend of increasing resistance.[9] Fluctuations in resistance trend were observed in gram-positive isolates during this study period. This may be due to the lesser and variable use of ciprofloxacin against gram-positive infections as compared to gram-negative infections. One important fact is that about 50% of *S. aureus* isolates were MRSA. *S. aureus* particularly MRSA rapidly develop resistance to ciprofloxacin.[1] In this study resistance in *S. aureus* is on the increase but is not very high unlike another report[10] showing that ciprofloxacin can still be used for empirical therapy in *S. aureus* infections in our setup. Resistance in MRSA is already very high approaching 100% in some studies[10,11] indicating that it can no more be used in infections caused by this organism. In another study from Saudi Arabia, the highest resistance rate of 39% was reported[12] but that was cumulative resistance in methicillin sensitive *S. aureus* and MRSA; resistance for the later was not reported separately.

Increasing resistance in *S. pyogenes* is worth to be mentioned with a highest rate (14.44%) in year 2004. This is closer to another study from Japan reporting 10.4% of the isolates as intermediately resistant.[13] This high resistance may be due to the use of ciprofloxacin in ear, nose and throat infections. A very high ciprofloxacin resistance (up to 35%) in *S. pneumoniae*, is of major concern as this is in contrast to other studies from Saudi Arabia where very low (2.6%)[14] or no resistance was reported[12].This difference could be due to different ciprofloxacin prescribing practices or the use of penicillin, third generation cephalosporins and vancomycin for the treatment of pneumococcal infections rather than ciprofloxacin. However higher resistance rates are reported in other healthcare settings.[10] High resistance rate like earlier reports[8,15] among enterococcus group D or non-enterococcus group D indicates that ciprofloxacin is no longer suitable to treat infections caused by these organisms.

CONCLUSION

It is obvious from present study that due to high ciprofloxacin resistance in gram-positive cocci, particularly *Staphylococcus aureus*, methicillin resistant *Staphylococcus aureus* (MRSA) enterococcus group D, and non-enterococcus group D, it no more remains drug of choice for treatment of infections by these pathogens. During the time period lapsed after this study, ciprofloxacin resistance must have increased further. It is essential that those concerned be alerted to the possibility of a trend towards further increased resistance to ciprofloxacin, so that the judicious use of ciprofloxacin and its alternatives can be considered particularly in areas of high fluoroquinolone resistance rates.[16]

Table-1: Ciprofloxacin resistance pattern in Staphylococci, enterococci, *Streptococcus pyogenes*, and *Streptococcus pneumoniae* isolated from clinical specimens (n=10,089) during the years 2002–2005

	YEARS									
	2002		2003		2004		2005		2002-2005	
Organisms	TN* (NR)**	NR%	TN (NR)	NR %	TN (NR)	NR %	TN (NR)	NR %	TN (NR)	NR %
S. aureus	324 (15)	4.62	653 (12)	1.83	741 (52)	7.01	427 (17)	3.98	2145 (96)	4.47
MRSA	433 (424)	97.92	579 (566)	97.75	693 (603)	87.01	213 (188)	88.26	1918 (1781)	92.85
S. pyogenes	56 (3)	5.35	246 (11)	4.47	180 (26)	14.44	113 (4)	3.53	595 (44)	7.39
S. pneumoniae	43 (13)	30.23	NA	NA	152 (35)	23.02	102 (27)	26.47	297 (75)	25.25
Enterococcus D	216 (93)	43.05	NA	NA	29 (6)	20.68	270 (154)	57.03	515 (253)	49.12
Non-enterococcus D	27 (17)	62.96	NA	NA	13 (10)	76.92	24 (21)	87.5	64 (48)	49.12

Key: MRSA: Methcilline Resistant *Staphylococcus aureus*; *TN: Total Number, **NR: Number Resistant, *NA: Not Available

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