CIPROFLOXACIN RESISTANCE AMONG BACTERIAL ISOLATES IN A TEACHING HOSPITAL IN RIYADH SAUDI ARABIA 2001-2005

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ABSTRACT

Objective: To present trends of resistance to ciprofloxacin among common organisms isolated at King Khalid University Hospital (KKUH) between 2001-2005.

Methods: Ciprofloxacin susceptibility of all isolates of Gram negative and Gram positive organisms were retrospectively obtained during the period from 2001-2005 in KKUH. Data from intensive care unit (ICU) and non-ICU patients were separately analyzed.

Results: *Escherichia coli (E.coli*) resistance increased from 10% in 2001 to 22% in 2005. E*nterobacter cloacae* (*Ent.cloacae*) resistance decreased from 11-14% in 2003 -2004 to 7% as in 2001 and 2005. *Klebsiella pneumoniae (K.pneumoniae)* resistance fluctuated from 6% in 2002 and 2003, 13% in 2004 to 6% in 2005. *Pseudomonas aeruginosa (P.aeruginosa*) resistance ranged from 7% - 8% during this study period while that of *Acinetobacter* spp. ranged between 45% to 62% and *Staphylococcus aureus (S.aureus*) resistance doubled from 18% in 2001 to 39% in 2005. None of Streptococcus *pneumoniae (S.pneumoniae*) isolates showed resistance to ciprofloxacin. Isolates of *E .coli, Acinetobacter spp.* and *S.aureus* from non-ICU patients showed higher resistance to ciprofloxacin than isolates from ICU patients while *K.pneumoniae* and *P.aeruginosa* showed higher resistance from ICU patients than isolates from non-ICU patients.

Conclusion: Ciprofloxacin resistance among many Gram negative species and *S.aureus* is an increasing threat among many Gram negative species and *S.aureus* in our hospital in both ICU and non-ICU patients.

KEY WORDS: Ciprofloxacin resistance, *E.coli, K.pneumoniae, Ent.cloacae*, *P.aeruginosa, Acinetobacter spp, S.aureus, S.pneumoniae,* Intensive care unit, Misuse of antibiotics.

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INTRODUCTION

Ciprofloxacin is a potent broad spectrum fluoroquinolone antibacterial agent. Prior to its use resistance was rare.[1] 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.[2,3] A major point of medical concern is the recent emergence of ciprofloxacin resistance among *E.coli* and other *Enterobacteriacea*e.[1,4,5] Despite being a restricted antimicrobial agent in KKUH we have recently observed an increase in resistance to ciprofloxacin among many Gram negative and Gram positive bacteria in this hospital. In this study we aimed to highlight trends of resistance to ciprofloxacin among common organisms isolated in KKUH between 2001-2005.

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MATERIAL AND METHODS

This study was conducted at the microbiology laboratory at KKUH, Riyadh, Saudi Arabia. KKUH is a 700 bed hospital which provides a primary, secondary and tertiary health care and has five different ICUs. Ciprofloxacin susceptibility of all commonly isolated Gram negative organisms (*E. coli, K.pneumoniae , E. cloacae, P.mirabilis, P.aeruginosa , Acinetobacter* spp.) and Gram positive organisms (*S.aureus* and *S.pneumoniae*) were retrospectively obtained from a hospital computer system during the period from 2001-2005. Repeat isolates from the same patient were excluded. Data from ICU and non-ICU patients were then analyzed separately. Identification and susceptibility testing were carried out by the MicroScan Walk Away 96 system (Dade Behring Inc., West Sacramento, CA95691, USA). Intermediately susceptible strains were considered resistant.

RESULTS

Table-I depicts percentage resistance to ciprofloxacin of Gram negative and Gram positive isolates recovered from specimens at KKUH between 2001-2005. For *E.coli*, resistance increased from 10% in 2001 to 22% in 2005. Resistance of *E.cloacae* fluctuated from 11-14% in 2003- 2004 respectively, to 7% in 2005. That of *K.pneumoniae* changed from 6% in 2002 and 2003 to 13% in 2004 and reduced to 6% in 2005. *P.aeruginosa* resistance to ciprofloxacin showed gradual increase since 2001 (7%) till 2004 (10%) but decreased to 8% in 2005. A significant rise in resistance of *Acinetobacter* spp. was observed (45% in 2001 and 62% between 2003 and 2005). *S.aureus* (both oxacillin sensitive and resistant) resistance to ciprofloxacin doubled from 18% in 2001 to 39% in 2005. None of the *S.pneumoniae* isolates were resistant to ciprofloxacin during this five year study period. Table-II shows ciprofloxacin resistance from ICU and non-ICU patients. It demonstrates more numbers and higher resistance of *E.coli* and *Acinetobacter* spp. from non ICU patients compared to ICU patients. It also showed higher *K.pneumoniae* and *P.aeruginosa* resistance was among ICU patients compared to non–ICU Patients. *S.aureus* resistance was higher among ICU patients during 2002 and 2005 (78% and 51% respectively) compared to 2003 and 2004 (33 and 30% respectively). Most of the ciprofloxacin resistance from ICU was from adult patients during this study. However, there were considerable percentages of resistance to ciprofloxacin among *E.coli* strains from peadiatric ICU patients in 2002 17(41%).

DISCUSSION

Ciprofloxacin resistance among *E.coli, P.aeruginosa, Acinetobacter* spp and *S.aureus* appears to be increasing in our hospital. This could be due to increasing consumption of

Table-I: Percentage resistance to ciprofloxacin of gram negative and gram positive bacterial species isolated at KKUH from 2001-2005.

Organisms	year *2001* *Tn [NR (%)]*	*2002* *Tn [NR (%)]*	*2003* *Tn [NR (%)]*	*2004* *Tn [NR (%)]*	*2005* *Tn [NR (%)]*
E. coli Gram negative	1191[119(10)]	1812[236(13)]	1937[329(17)]	1927[366(19)]	1759 [387 (22)]
K.pneumoniae	600[30 (5)]	624[37 (6)]	640[38(6)]	576 [75 (13)]	576 [40 (6)]
Ent. cloacea	136 [10 (7)]	152 [12 (8)]	140 [15 (11)]	154 [22 (14)]	148 [10 (7)]
P. mirabilis	132 [8(6)]	135[8 (6)]	118[9 (8)]	99[8 (8)]	81[8 (10)]
P. aeruginosa	760 [53(7)]	709 [57 (8)]	758 [68 (9)]	623 [62(10)]	571[46(8)]
Acinetobacter spp.	229 [103(45)]	159 [52 (33)]	181 [112(62)]	160[77(48)]	180[112 (62)]
Gram positive					
S. aureus	NA*	99 [178 (18)]	1024[399(39)]	900[324 (36)]	742[289 (39)]
S. pneumoniae	NA*	84 [0(0)]	90 [0 (0)]	80 [0 (0)]	28 [0 (0)]

NA*: not available. Tn: total number NR: number resistant

Table-II: Percentage resistance to ciprofloxacin of organisms isolated from ICU and non-ICU patients, 2002-2005*

Organisms	Year							
	2002		2003		2004		2005	
	ICU n (%)	Non-ICU n (%)	ICU n (%)	Non-ICU n (%)	ICU n (%)	Non-ICU n (%)	ICU n (%)	Non-ICU n (%)
E.coli	55(23)	181(77)	60(18)	269(82)	25(7)	341(93)	42(11)	345(89)
K.pneumoniae	27(73)	10(27)	28(74)	10(26)	49(65)	26(35)	20(50)	20(50
Ent.cloacae	10(83)	2(17)	13(87)	2(13)	0(0)	22(100)	0(0)	10(100)
P. aeruginosa	38(67)	19(33)	44(65)	24(35)	48(77)	14(23)	36(78)	10(22)
P.mirabilis	0(0)	8(100)	0(0)	9(100)	0(0)	8(100)	0(0)	8(100)
Acinetobacter spp.	33(63)	19(27)	48(43)	64(57)	44(57)	33(43)	44(39)	68(61)
S.aureus	139(78)	39(22)	133(33)	266(67)	98(30)	226(70)	98(51)	141(49)

* 2001 data not available

ciprofloxacin and other fluoroquinolones.[5] Al-Lawati et al estimated a ciprofloxacin consumption equivalent to 33 days per 100 hospital discharges in Oman.[6] Increasing ciprofloxacin consumption particularly in ICU leads to selection of resistant mutants among nosocomial pathogens since fluoroquinolones are particularly greater selectors of resistance among aminoglycosides, carbapenems, or other â-lactams and these resistant strains can more easily spread than strains resistant to other drugs.[7] Our results showed increasing trend of resistance of *E.coli*, and *Acinetobacter* spp as well as *S.aureus* to ciprofloxacin .These results are comparable with studies from United States, France, Germany, Italy , Spain, Canada and Taiwan.[5,7-10] A disturbing trend is development of cross resistance to other fluoroquinolones which are introduced into hospital use.[5] In this study, a point of particular importance is that *Acinetobacter* spp. is becoming a common pathogen isolated from non-ICUs. These organisms showed higher resistance to ciprofloxacin in both ICU and non-ICU patients. There was also cross resistance of these isolates to other agents including: cefepime, carbapenem, piperacillin-tazobactam and aminoglycosides. The importance of these facts could be more clear if linked to the cases in previous studies.[7] The percentage of *P.aeruginosa* resistance in ICU setting increased from 67% in 2002 to 78% in 2005, which is more than the 30% reported by Villegas et al.[11] An interesting finding is that there was considerable ciprofloxacin resistance in *E.coli* among paediatric ICU patients although ciprofloxacin is rarely used in children. This could be explained by acquisition of resistant strains in the gastrointestinal tract via the food chain without exposure to the antibiotic as reported before.[5] Furthermore, introduction of quinolones in veterinary medicine in Saudi Arabia has been associated with increase in *E.coli* resistance in poultry clinical isolates.[3] Prevalence of fluoroquinolone resistance among *S.pneumoniae* was reported to be between 2.6-7% particularly among elderly patients reflecting increased ciprofloxacin use in this age group particularly to treat respiratory infections.[9,12] Our *S.pneumoniae* isolates showed no ciprofloxacin resistance, this may be due to the use of penicillin, third generation cephalosporins and vancomycin for the treatment of pneumococcal infections in our hospital. Ciprofloxacin resistance among our *S.aureus* isolates (approximately 33%) is comparable to that reported in 2000-2002 from United States 51%, Canada 24.1%, Italy 58.6%, Germany 26.1% and France 40.5% respectively.[8] Cohen et al reported strains of methicillin resistant *S.aureus* minimum inhibitory concentration 128µg/ml to ciprofloxacin, this indicates that ciprofloxacin is becoming less effective for treatment of infections caused by this organism.[13] This resistance may be due to more than one resistance mechanisms present in a single strain of *S. aureus* as reported by Kaatz et al. This can be selected at high frequency.[14]

In conclusion, ciprofloxacin resistance is a growing threat among many Gram negative species as well as *S.aureus* in our hospital in both ICU and non-ICU patients. The increasing and promiscuous use of this agent is an important risk factor. The best approach to control the growing resistance is to control the use of ciprofloxacin and other fluoroquinolones use coupled with adherence to infection control measures to prevent spread of such resistant strains among patients. Surveillance of resistance pattern of prevalent strains and reduction of antibiotic consumption are essential for hospital prescribing policy and use of antibiotics.

REFERENCES

1. Barry AL, Fuchs PC, Pfaller MA, Allen SD, Gerlach EH. Prevalence of fluoroqinolone-resistant bacterial isolates in four medical centers during the first quarter of 1990. Eur J Clin Microbiol Infect Dis 1990;9:906-8.
2. Chaslus- Dancla E, Martel JL, Carlier C, Lafont JP, Courvalin P. Emergence of aminoglycoside 3- N-acetyltransferase IV in *Escherichia coli* and *Salmonella typhimurium* isolated from animals in France. Antimicrob Agents Chemother 1986;29:239-43.
3. Bazile- Pham- Khac S, Truong QC, Lafont JP, Gutmann L, Zhou XY, Osman M, et al. Resistance to fluoroquinolones in *Escherichia coli* isolated from poultry. Antimicrob Agents Chemother 1996;40:1504-7.
4. Pena C, Albareda JM, Pallares R, Pujol M, Tubau F, Ariza J. Relationship between quinolone use and emergence of ciprofloxacin – resistant *Escherichia coli* in bloodstream infections. Antimicrob Agents Chemother 1995;39:520-4.
5. Livermore DM, James D, Reacher M, Catriona G, Nichola T, Stephens P, et al. Trends in fluoroquinolone (ciprofloxacin) resistance in *Enterobacteriaceae* from bacteremias, England and Wales, 1990-1999. Emerg Infect Dis 2002;8:473-8.
6. Al- Lawati AM, Crouch ND, Elhag KM. Antibiotic consumption and development of resistance among Gram- negative bacilli in intensive care units in Oman. Annals Saudi Med 2000;20:324-7.
7. Karlowsky JA, Draghi DC, Jones ME, Thornsberry C, Friedland IR, Sahm DF. Surveillance for antimicrobial susceptibility among clinical isolates of *Pseudomonas aeruginosa* and *Acinetobacter baunannii* from hospitalized patients in the United States, 1998 to 2001. Antimocrob Agents Chemother 2003;47:1681-8.
8. Jones ME, Draghi DC, Thornsberry C, Karlowsky JA, Sahm DF, Wenzel RP. Emerging resistance among bacterial pathogens in the intensive care unit- a European and North American Surveillance study (2000-2002). Annals Clin Microbiol and Antimicrob 2004;3:1-11.
9. Campa AG, Balsalobre L, Ardanuy C, Fenoll A, Perez-Trallero E, Linares J. The Spanish Pneumococcal Infection Study Network G03/103. Fluoroquinolone resistance in penicillin-resistant *Streptococcus pneumoniae* clones, Spain. Emerg Infect Dis 2004;10:1751-9.
10. Jean SS, Teng LJ, Hsueh PR, Ho SW, Luh KT. Antimicrobial susceptibilities among clinical isolates of extended- spectrum cephalosporin-resistant Gram – negative bacteria in a Taiwanese University Hospital. J Antimicrob Chemother 2002;49: 69-76.
11. Villegas MV, Quinn JP. An update on antibiotic-resistant Gram – negative bacteria. Infect Med 2004;21:595-9.
12. Linares J, de la Campa AG, Pallares R. Fluroquinolone resistance in *Streptococcus pneumoniae*. N Eng J Med 1999;341:1546-7.
13. Cohen MA, Huband MD, Gage JW, Yoder SL, Roland GE, Gracheck SJ. In-vitro activity of clinafloxacin, trovafloxacin, and ciprofloxacin. J Antimicrob Chemother 1997;40:205-11.
14. Kaatz GW, Seo SM. Mechanisms of fluoroquinolone resistance in genetically related strains of *Staphylococcus aureus*. Antimicrob Agents Chemother 1997;41:2733-7.