

In Vitro Activity of Gatifloxacin Against Respiratory Tract Pathogens from Hospitalized Patients Isolated in 108 Sites from the United States

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ABSTRACT

Background: Respiratory tract infections caused by *S. pneumoniae* (SPN), *H. influenzae* (HI) and *M. catarrhalis* (MC) are being treated more frequently with the newer respiratory fluoroquinolones due to increasing resistance to penicillin and macrolides. Because resistance trends in SPN, HI and MC are geographically specific, surveillance studies attempting to quantify overall national susceptibilities of both older and newer antimicrobial agents should include sufficient study sites to represent the entire U.S. The purpose of this study was to examine the activity of gatifloxacin and comparative agents to SPN, HI and MC in hospitalized patients throughout the U.S. in 1999/2000.

Methods: SPN, HI and MC from respiratory tract specimens were collected in 108 sites in 36 states across the U.S. from July 1999 to May 2000. MIC's to gatifloxacin and comparators were determined using E-test™ strips and interpreted following manufacturer's instructions and NCCLS guidelines as appropriate.

Results: MIC₉₀ (µg/ml)/%S are shown below

Antimicrobial	<i>S. pneumoniae</i> (4,750)	<i>H. influenzae</i> (2,799)	<i>M. catarrhalis</i> (948) ^a
Azithromycin ^b	256/71.3	12/88.3	0.5/98.5
Ceftriaxone	1/81.2	0.03/97.0	1/99.5
Ciprofloxacin	2/na	0.03/99.2	0.06/99.9
Gatifloxacin	0.38/99.4	0.03/99.7	0.06/100
Levofloxacin	1.5/98.7	0.06/99.8	0.06/100
Penicillin	2/59.0	>32/na	>32/5

^a Interpretation based on NCCLS breakpoints for *Staphylococcus* spp. ^b Based on AB Biodisk breakpoints.

Conclusions: Penicillin and macrolide resistance continues to grow in hospitalized patients with RTI. Among the agents examined, the fluoroquinolones, in particular gatifloxacin, were the most active compounds against SPN, HI and MC. Continued surveillance of both older and newer agents is warranted to monitor resistant phenotypes across the United States.

INTRODUCTION

Respiratory tract infections (RTI) are the most common infections requiring hospitalization and treatment. As resistance to penicillins, cephalosporins and macrolides rapidly increase from country to country and regionally within countries, the medical community is turning to newer and more effective fluoroquinolones, especially those with increased activity against both Gram-positive and Gram-

negative pathogens, to combat this growing therapeutic problem.

Gatifloxacin is an 8-methoxyfluoroquinolone with *in vitro* activity against a wide range of Gram-negative and Gram-positive microorganisms. The C-8-methoxy moiety contributes to enhanced activity and lower selection of resistant mutants of gram-positive bacteria and should exhibit activity over that of other fluoroquinolones. Gatifloxacin has shown to be effective against a wide variety of Gram-positive pathogens, especially *Streptococcus pneumoniae*, independent of penicillin and macrolide activity.

OBJECTIVE

This current surveillance study provides a comprehensive view of the activity of gatifloxacin and comparative antimicrobial agents against common respiratory pathogens from a broad range of geographically diverse centers within the United States.

MATERIALS & METHODS

- Isolates were collected between July 1999 and May 2000 from 108 study centers from 36 states within the continental United States.
- Each center was instructed to collect up to 100 pathogens of *Streptococcus pneumoniae* (50), *Haemophilus influenzae* (30), *Moraxella catarrhalis* (10) and other strains (10) associated with respiratory tract infections.
- Each isolate was identified and determined to be the causative agent of a recent respiratory infection using local laboratory criteria. Only one isolate per patient was accepted.
- Organism collection, transport, storage and antimicrobial susceptibility testing, as well as construction and management of a centralized database, was coordinated by International Health Management Associates, Inc. (IHMA, Rolling Meadows, IL).

ANTIMICROBIAL SUSCEPTIBILITY TESTING

- Gatifloxacin, levofloxacin, ciprofloxacin, azithromycin, ceftriaxone and penicillin minimum inhibitory concentrations (MICs) were determined using E-Test® strips (AB Biodisk, Solna, Sweden) according to the manufacturer's recommendations.
- Plates were inoculated with bacterial suspensions equivalent to a 0.5 McFarland standard and incubated at 35°C for 18-24 hours. *S. pneumoniae* and *H. influenzae* were incubated in the presence of 5% carbon dioxide.
- The antimicrobial breakpoints used for data analysis were those recommended by the NCCLS (M100-S11, 2001) for broth dilution susceptibility testing. Azithromycin breakpoints in CO₂ are Sen ≤4, Int = 8, Res ≥16 µg/ml (AB Biodisk). *Moraxella catarrhalis* breakpoints derived from *Staphylococcus* species.
- Control strains used were *S. pneumoniae* ATCC 49619, *E. coli* ATCC 25922; *S. aureus* ATCC 29213; and *H. influenzae* ATCC 49247. Test isolate results were accepted into the final analysis only if the quality control isolate MICs were within the acceptable range defined by NCCLS guidelines (M100-S11, 2001).

RESULTS

The results are contained in the following Figures and Tables.

Figure 1. Geographic Distribution of 108 Study Centers from 36 States.

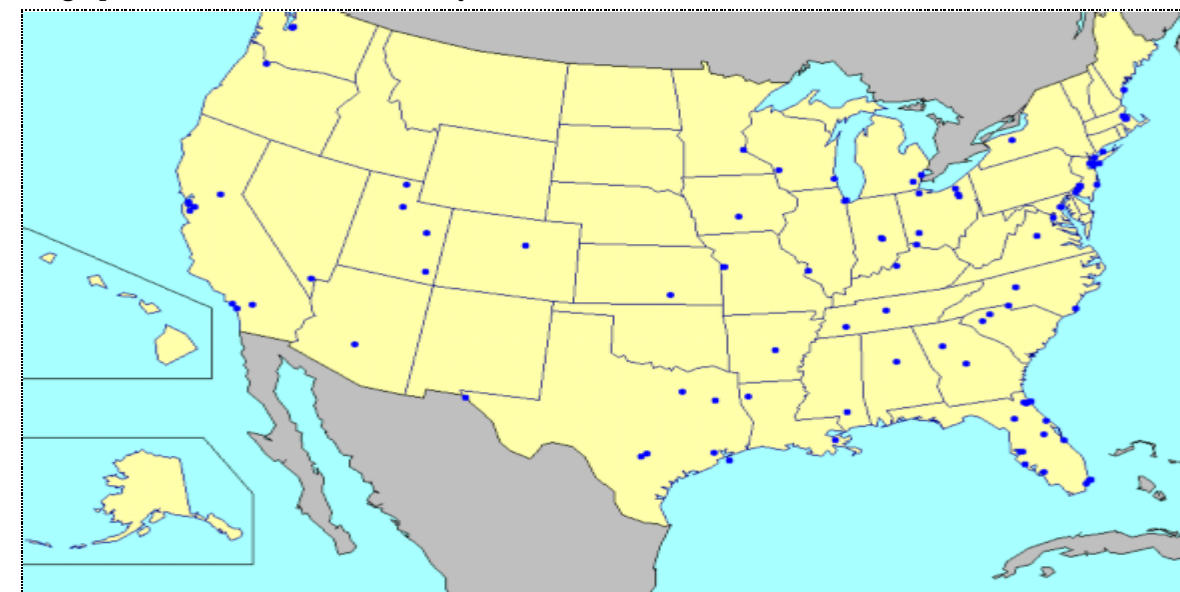


Table 1. CDC Regional Distribution of Investigator Sites and Isolates Collected.

CDC Region	No. of Sites	No. of Isolates
East North Central	16	1366
East South Central	5	376
Mid-Atlantic	14	1068
Mountain	8	606
New England	7	594
Pacific	11	824
South Atlantic	27	1981
West North Central	7	605
West South Central	13	1079

Table 2. In Vitro Activity (MIC µg/ml) of Gatifloxacin against Respiratory Isolates from 108 centers in 36 States from the United States.

Organism (n)	Antimicrobial	% S ^a	% I ^a	% R ^a	MIC ₅₀	MIC ₉₀	Range
<i>Streptococcus pneumoniae</i> (n=4751)	Azithromycin	68.5	2.8	28.7	1.5	256	<0.016->256
	Ceftriaxone	99.7	0.0	0.3	0.032	1	0.003->32
	Ciprofloxacin	na	na	na	1	2	0.008->32
	Gatifloxacin	99.5	0.1	0.4	0.25	0.38	0.016->32
	Levofloxacin	98.7	0.7	0.6	1	1.5	0.016->32
	Penicillin	61.2	0.0	38.8	0.047	2	0.002->256
<i>Haemophilus influenzae</i> (n=2800)	Azithromycin	20.1	39.2	40.7	4	12	<0.016->256
	Ceftriaxone	97.2	0.0	2.8	0.008	0.023	0.002->256
	Ciprofloxacin	99.4	0.3	0.3	0.016	0.032	0.002->32
	Gatifloxacin	99.8	0.1	0.1	0.016	0.032	0.002-32
	Levofloxacin	99.8	0.1	0.1	0.023	0.047	0.002->32
	Penicillin	1.2	0.0	98.8	1	>32	0.004->256
<i>Moraxella catarrhalis</i> (n=948) ^b	Azithromycin	98.5	0.4	1.1	0.125	0.5	<0.016->256
	Ceftriaxone	99.5	0.1	0.4	0.25	1	0.002->32
	Ciprofloxacin	99.9	0.0	0.1	0.047	0.064	0.002-4
	Gatifloxacin	100.0	0.0	0.0	0.032	0.064	0.002-0.38
	Levofloxacin	100.0	0.0	0.0	0.047	0.064	0.002-2
	Penicillin	5.1	0.0	94.9	32	>32	<0.016->32

^a NCCLS breakpoints (M100-S11, 2001) were used to determine the percents susceptible (%S), intermediate (%I) and resistant (%R).

^b *Staphylococcus* spp breakpoints were used for all antimicrobial agents against *Moraxella catarrhalis*.

^c na = Not available. NCCLS breakpoints are not available for ciprofloxacin and *S. pneumoniae*.

CONCLUSIONS

- Penicillin and macrolide resistance continues to grow in hospitalized patients with RTI.
- Among the agents examined, the fluoroquinolones, in particular gatifloxacin, were the most active compounds against *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*.
- Gatifloxacin activity (MIC₉₀) against *S. pneumoniae* was 4 fold greater than levofloxacin and ciprofloxacin.
- Continued surveillance of both older and newer agents is warranted to monitor resistant phenotypes across the United States.

REFERENCES

- National Committee for Clinical Laboratory Standards. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*. Villanova, PA, USA: NCCLS, 1997: approved standard M7-A4.
- National Committee for Clinical Laboratory Standards. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*. Villanova, PA, USA: NCCLS, 2000: approved standard M100-S10.

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