

Lack of Emergence of Fluoroquinolone (FQ) resistance and gyrA Mutations in *S. pneumoniae* (SP) Despite Increased FQ Use

R Melano², SN Patel³, A McGeer^{1,3*}, KA Green¹, DR Pillai², SM Poutanen^{1,3}, DE Low^{1,2,3},

Canadian Bacterial Surveillance Network (CBSN)

1Mount Sinai Hospital, Toronto, Canada, 2Ontario Public Health Laboratory, Toronto, Canada, 3University of Toronto, Toronto, Canada

Background: Use of FQ has been associated with increasing FQ resistance in *S. pneumoniae*. Because respiratory FQs (levofloxacin (Levo) and moxifloxacin (Moxi)) are first line therapy for serious respiratory infections, increasing FQ resistance (FQR) in SP is a concern. Levo targets parC, and Moxi targets gyrA, which may permit differentiation of degree of selective pressure. We examined FQ use, and changes in the prevalence of FQR and QRDR mutations in Canadian isolates of SP.

Methods: CBSN is a Canadian collaborative network of microbiology laboratories that has performed surveillance for antibiotic resistance in SP since 1988. Antimicrobial resistance is performed in a central lab to CLSI standards. We sequenced QRDR regions of all FQR isolates and a stratified sample of FQ susceptible isolates. Population FQ use was obtained from IMS Canada.

Results: From 1995-2007, FQ use increased from 53-97 Rx/1000pop/yr; Levo use from 0-10 Rx/1000pop/yr, and Moxi use from 0-17 Rx/1000pop/yr. 31081 isolates were available for testing. Levo R rates increased from 0 in 1993 to 1.8% in 2002 then remained stable until 2008 (1.6% in 2008). Moxi R rates increased to 0.6% in 2004, then stabilized (0.7% in 2008). The prevalence of parC only mutations has not increased significantly in the last decade (see Table). The prevalence of isolates with both parC and gyrA mutations increased until 2002, but has decreased in 2008. . The first gyrA only mutant was detected in 2000; the prevalence of gyrA only mutants since then has increased, but remains very low (7/2044, 0.34% in 2007).

Year	Rates of mutations in QRDR regions			
	N	parC only	parC&gyrA	gyrA only
1997	1409	1.72	0.40	0
1998	1426	1.89	0.21	0
1999	2086	1.52	0.28	0
2000	2191	1.46	0.64	0.14
2001	2240	1.74	0.85	0.04
2002	2504	1.11	1.55	0.04
2003	2419	0.83	0.87	0.12
2004	2548	0.63	1.35	0.12
2005	2662	1.05	1.24	0.08
2006	2224	1.88	1.27	0.39
2007	2044	1.03	0.68	0.34

Conclusion: Despite increasing use of respiratory FQs, FQR in pneumococci is very low and not increasing in Canada. The prevalence of isolates with parC mutations is decreasing. Isolates with mutations in gyrA alone remain extremely rare, suggesting that Moxi exerts minimal selective pressure for resistance.