Effect of Utilization Policies for Fluoroquinolones: A Pilot Study in Nova Scotia Hospitals

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ABSTRACT

Background: Antimicrobial resistance results in increased morbidity, mortality, and costs to the health care system. Evidence suggests an association between the use of antimicrobials in hospitals and the development of antimicrobial resistance. Fluoroquinolones constitute one group of antimicrobials that are effective against a variety of bacterial infections, yet they may be subject to misuse. Many hospitals in Nova Scotia have implemented policies to improve antimicrobial prescribing, but the impact of these policies on utilization is unknown.

Objectives: To evaluate the use of fluoroquinolones in Nova Scotia hospitals using the World Health Organization's Anatomical Therapeutic Chemical classification system with defined daily doses (ATC/DDD) and to examine the influence of hospital policies for utilization of fluoroquinolones in community-acquired pneumonia.

Methods: During the study period (April 1, 1997, to March 31, 2003), fluoroquinolones were administered at 31 of the 37 hospitals in Nova Scotia's 9 district health authorities. Hospital administrative data, hospital characteristics, and pharmaceutical purchasing data related to use of these drugs were aggregated using the ATC/DDD methodology for the fiscal years 1997/1998 to 2002/2003. District pharmacy directors were surveyed to obtain information about district and individual hospital antibiotic policies. Descriptive statistics were calculated, and univariable regression and multilevel analyses were performed.

Results: Mean overall fluoroquinolone use increased over the study period, from 47.2 DDD/1000 bed-days per year in fiscal year 1997/1998 to 163.8 DDD/1000 bed-days per year in fiscal year 2002/2003 ($p < 0.001$). Multilevel analysis showed that utilization policies aimed at appropriate prescribing did not affect the use of fluoroquinolones.

Conclusion: This study revealed that drug purchasing, hospital administrative, and diagnostic data could be combined to compare the utilization of fluoroquinolones among different hospitals and district health authorities. Utilization policies had little effect on the amount, type, or route of fluoroquinolone use.

Key words: drug utilization, antimicrobials, fluoroquinolones, policies

RÉSUMÉ

Contexte : La résistance aux antimicrobiens se traduit par une hausse de la morbidité, de la mortalité et des coûts pour le système de santé. Des données suggèrent un lien entre l'utilisation des antimicrobiens dans les hôpitaux et l'apparition de résistance antimicrobienne. Les fluoroquinolones, qui sont un groupe d'antimicrobiens efficaces contre une variété d'infections bactériennes, peuvent pourtant être mal utilisées. De nombreux hôpitaux en Nouvelle-Écosse ont donc mis de l'avant des politiques visant à améliorer la prescription des antimicrobiens, mais on ignore quelle est leur incidence sur l'emploi de ces derniers.

Objectifs : Évaluer l'utilisation des fluoroquinolones dans les hôpitaux de la Nouvelle-Écosse, à l'aide du système de classification anatomique, thérapeutique et chimique (ATC) et des doses journalières définies (DDD) de l'Organisation mondiale de la Santé, et analyser l'influence des politiques des hôpitaux sur l'utilisation des fluoroquinolones dans le traitement des pneumonies extrahospitalières.

Méthodes : Au cours de la période de l'étude (du 1er avril 1997 au 31 mars 2003), des fluoroquinolones ont été administrées dans 31 des 37 hôpitaux des 9 régies régionales de la santé de la Nouvelle-Écosse. Des données sur les caractéristiques démographiques, les diagnostics et l'achat des médicaments concernant l'utilisation des fluoroquinolones dans ces hôpitaux ont été groupées à l'aide de la méthode ATC/DDD pour les exercices financiers de 1997–1998 à 2002–2003. Les directeurs de pharmacie des régies ont répondu à un sondage pour obtenir des renseignements sur les politiques d'utilisation des antibiotiques des régies et de chaque hôpital. Des statistiques descriptives ont été compilées, et des analyses de régression à variable simple et de modélisation hiérarchique ont été effectuées.

Résultats : L'utilisation moyenne globale de fluoroquinolones a augmenté pendant la période de l'étude, passant de 47,2 DDD/1000 jours-lits par année pour l'exercice financier de 1997–1998 à 163,8 DDD/1000 jours-lits pour l'exercice financier de 2002–2003 ($p < 0,001$). L'analyse hiérarchique a montré que les politiques d'utilisation visant une meilleure prescription des fluoroquinolones n'ont pas eu d'effet sur leur utilisation.

Conclusion : Cette étude a révélé que les données sur l'achat des médicaments, les caractéristiques démographiques et les diagnostics pouvaient être combinées pour comparer l'utilisation des fluoroquinolones dans divers hôpitaux et régies régionales de la santé. Les politiques sur l'utilisation des antimicrobiens ont eu très peu d'effet sur la quantité et le type de fluoroquinolones utilisées ou leur voie d'administration.

Mots clés : utilisation des médicaments, antimicrobiens, fluoroquinolones, politiques

[Traduction par l'éditeur]

INTRODUCTION

Infections with antimicrobial-resistant bacteria result in increased patient morbidity and mortality, and extra costs to the health care system.[1,2] There is mounting evidence to suggest an association between antimicrobial use in hospitals and antimicrobial resistance.[1-4] Fluoroquinolones are useful in the treatment of a variety of infections. Unfortunately, these drugs are sometimes used inappropriately, and these uses may contribute to increasing bacterial resistance and drug expenditures.[5,6] Many hospitals have implemented policies and programs to limit and monitor inappropriate use. The effect of such policies on fluoroquinolone use across the province of Nova Scotia, Canada, is unknown.

In Nova Scotia, district health authorities (DHAs) are responsible for providing care in acute care facilities and for monitoring and evaluating the use of medications prescribed, including antimicrobial agents. However, monitoring systems may not be well established, and even when they are present, data collection and analysis methods may differ across the province. Furthermore, no system exists to routinely and systematically collect and compare data at the district or provincial level.

Since the 1970s, European and Nordic countries have employed the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification system with defined daily doses (DDDs) as a standardized method to compare antimicrobial utilization within and between countries.[7-11] The ATC/DDD system is managed by the WHO Collaborating Centre for Drug Statistics Methodology, with expert advice from the corresponding WHO International Working Group. The working group comprises members from different professional backgrounds, who represent the 6 WHO global regions. The DDD is the assumed average maintenance dose for the main indication of a particular drug.[12] The actual dose for individual patients may differ according to individual characteristics. Drug consumption data presented as DDDs provide a rough estimate of consumption and yield a fixed unit of measure, independent of price and formulation, which allows researchers to assess and compare trends among population groups and countries.[13]

The objectives of this study were to evaluate the use of fluoroquinolones in Nova Scotia hospitals using the ATC/DDD classification system and to examine the influence of utilization policies on the use of all fluoroquinolones (i.e., throughout the hospital) and of respiratory fluoroquinolones (levofloxacin, moxifloxacin, and gatifloxacin), especially in relation to community-acquired pneumonia.

METHODS

Ethics approval for this study was granted by the Health Sciences Human Research Ethics Board of Dalhousie University in January 2004.

Setting

Nova Scotia, a province on the east coast of Canada, has about 908 000 inhabitants, with roughly one-third living in or near the capital city, Halifax.[14] The province's health care system is organized into 9 DHAs, each of which is responsible for the delivery and administration of health care services to the population in a specific geographic area. The cost of all hospital services and in-hospital drugs is covered under the Canadian medicare system. There are 37 hospitals in Nova Scotia, of which 31 administered fluoroquinolones over the study period of April 1, 1997, to March 31, 2003. Given the low use of fluoroquinolones for children, the province's only free-standing pediatric hospital was not included in this study (i.e., was excluded from the analysis entirely). At the time of the study, the only participating facility that offered infectious disease consultation services was the tertiary care centre located in Halifax and was included in all analyses.

Data Sources

The data for this study were obtained from 4 sources. The first type of data was purchasing data, expressed as drug volume and expenditures and obtained from the Provincial Drug Distribution Program. This program operates through the Capital District Health Authority in Halifax and since 1997 has been responsible for negotiation of contracts for all pharmaceuticals and provision of the drugs to all hospitals in the province. The fluoroquinolone antimicrobials investigated in this study (and their respective DDDs) were ciprofloxacin (oral 1 g, parenteral 0.5 g), gatifloxacin (oral and parenteral 0.4 g), levofloxacin (oral and parenteral 0.25 g), moxifloxacin (oral and parenteral 0.4 g), norfloxacin (oral 0.8 g), and ofloxacin (oral and parenteral 0.4 g). These are the "assumed average maintenance doses per day for a drug used for its main indication in adults", as published by the WHO.[12] Data on trovafloxacin were also available for this study, but this medication had minimal use within the province during the study period and has since been removed from the Canadian market, so no results for this drug are presented here. The second type of data was hospital data (the name of the hospital, the DHA in which it was located, and the number of acute care beds); this information was obtained from the NS Department of Health. The third type of data was the number of admissions to hospital for community-acquired pneumonia, which was retrieved from the Canadian Institute of Health Information discharge database (accessed through the NS Department of Health). The fourth type of data was information about hospital policies on antimicrobial use and therapeutic pathways, which was collected by a survey mailed to the director of pharmacy of each DHA. The survey contained questions on restriction policies, therapeutic pathways for 2 specific conditions, and step-down programs from IV to oral administration. The survey questionnaire was pilot-tested with drug

information and drug utilization evaluation pharmacists for clarity and readability. In addition, the survey was reviewed and discussed at an infectious diseases research-in-progress seminar hosted by the Capital District Health Authority, which was attended by microbiologists, infectious disease physicians, and pharmacists. The survey was revised on the basis of input from both groups.

Data Analysis

All hospitals that had purchased the fluoroquinolones investigated in this study and that had admitted patients with community-acquired pneumonia were included in the study. All statistical analyses were restricted to hospitals with at least 10 acute care beds (to reduce statistical bias). Provincial drug purchasing data were aggregated using the WHO ATC/DDD classification system (2003 edition) for the fiscal years 1997/1998 to 2002/2003. Raw data were coded and computed using a standard spreadsheet program (Office 97 Excel, Microsoft, Redmond, Washington). Drugs were classified and volume data were transformed to ATC/DDD values. Values for utilization of fluoroquinolones were expressed as number of DDDs per 1000 (acute care) bed-days per year and number of DDDs per 100 cases of community-acquired pneumonia with admission to hospital per year.

Use of fluoroquinolones was determined for each hospital, and the results were also aggregated for each of the 9 DHAs in the province. Hospital size was categorized according to the number of acute care beds: small = 10–15 beds, medium = 16–100 beds, and large = more than 100 beds. Each hospital-size category contained approximately the same number of hospital-year observations. Annual periods were related to fiscal years (i.e., from April 1 to March 31).

Survey data from the director of pharmacy in each DHA were used to determine whether or not a given hospital had antimicrobial policies and care pathways for fluoroquinolones. It was assumed that policies applied across each district, but respondents were asked to complete multiple surveys if one or more hospitals within their respective districts had policies that differed from the district policies. These data were incorporated into a dichotomous variable indicating whether or not a hospital had a policy. Hospitals were also coded according to the presence of more than one utilization policy or no utilization policies. Because the survey was administered during the last year of the study period, data for only the 2002/2003 year were used to examine the impact of hospital pharmacy policies (number and type) on fluoroquinolone use. Student t tests were performed to determine statistical differences in fluoroquinolone use between hospitals with and without antimicrobial policies and therapeutic pathways. Trends in the use of specific fluoroquinolones and percentage of ciprofloxacin use relative to respiratory fluoroquinolone use over time were examined in a post hoc analysis.

The results were aggregated and combined, using a standard statistical software package (STATA, version 7, STATA Corporation, College Station, Texas), to produce simple descriptive statistics of fluoroquinolone use. Data are reported as means and 95% confidence intervals. The relationship among the 3 predictor variables (DHA, year, and hospital size) and DDD values was assessed. A regression approach that accounted for clustered data was employed because hospital-year data were clustered within years. Regressions were estimated using a generalized estimating equation and employing a log correlation structure between study years. Because of the limited sample size, only unadjusted associations were examined, and the statistical level of significance was $\alpha = 0.05$.

The institution variable was nested within the DHA variable, and a standard univariable regression analysis was therefore not appropriate (because of violation of independence of observations). Thus, a multilevel linear model was constructed to account for the natural hierarchical structure of the data. The use of a multilevel linear model is often suggested when data are nested naturally, as in this study.[15,16]

RESULTS

Over the 6-year study period, a total of 31 hospitals administered fluoroquinolones, and there were 169 hospital–year observations. Because hospitals with fewer than 10 acute care beds were excluded, data from only 27 hospitals (with 149 hospital–year observations) were examined in the final analysis.

Total Fluoroquinolone Use

Mean total fluoroquinolone use per district increased by more than 3 times over the 6 years, from 47.2 DDDs/1000 bed-days per year in 1997/1998 to 163.8 DDDs/1000 bed-days per year in 2002/2003 ($p < 0.001$) (Table 1). Oral administration as a percentage of total fluoroquinolone use descreased over the study period, from 89% in 1997/1998 to 78% in 2002/2003. The mean extent of use varied among the DHAs, from 78.9 DDDs/1000 bed-days per year in DHA A to 138.7 DDDs/1000 bed-days per year in DHA E. The utilization of fluoroquinolones did not differ statistically between small and medium-sized hospitals ($p = 0.31$) or between small and large facilities ($p = 0.94$); medium-sized and large hospitals were not compared directly.

Ciprofloxacin

Total annual ciprofloxacin use was highest over the period 2000/2001 to 2002/2003, relative to 1997/1998 and 1998/1999. The use of this drug in the final year of the study was 70.5% greater than use in the first year (52.5 DDDs/1000 bed-days in 2002/2003 versus 30.8 DDDs/1000 bed-days in

Table 1. Use of Fluoroquinolones in 31 Hospitals in Nova Scotia, 1997/1998 to 2002/2003

Drug	Fiscal Year; Drug Use (Mean DDDs/1000 bed-days per year and 95% CI)					
	1997/1998	**1998/1999**	**1999/2000**	**2000/2001**	**2001/2002**	**2002/2003**
Ciprofloxacin	30.8 (19.8–41.8)	29.4 (20.5–38.5)	38.4 (26.3–50.4)	46.8 (32.0–61.6)*	51.0 (39.1–63.0)*	52.5 (40.1–64.9)*
Levofloxacin	0.2 (0.0–0.5)	14.1 (4.7–23.5)	61.7 (39.9–83.6)*	79.9 (56.3–103.5)*	104.4 (71.8–137.1)*	94.1 (62.7–125.5)*
Gatifloxacin	0	0	0	0	0.7 (0.0–1.5)	11.5 (2.9–20.1)*
Moxifloxacin	0	0	0	0.4 (0.0–1.1)	2.0 (0.0–4.8)	2.8 (0.0–6.6)
Norfloxacin	14.4 (8.3–20.6)	12.0 (6.4–17.6)	6.2 (3.8–8.5)*	1.9 (0.0–4.0)*	2.4 (0.0–5.5)*	1.9 (0.0–4.3)
Ofloxacin	1.8 (0.0–4.0)	0.9 (0.1–1.6)	1.3 (0.0–2.9)	0.5 (0.0–1.3)	1.6 (0.1–3.2)	0.9 (0.0–2.3)
Total	47.2 (33.1–61.4)	56.5 (38.7–74.2)	107.6 (76.4–138.8)*	129.6 (97.7–161.4)*	162.2 (123.5–200.8)*	163.8 (124.3–203.3)*

CI = confidence interval, DDD = defined daily dose.
*Statistically significant difference from 1997/1998 value ($p \leq 0.05$).

1997/1998) (Table 1). Oral use of this drug increased by 40.3% over the study peroid, whereas IV use increased by 290% (data not shown). The percentage of total use that involved oral administration declined from 90.5% in 1997/1998 to 76.0% in 2002/2003. The ratio of IV to oral use in 2002/2003 was 0.325.

Ciprofloxacin use varied greatly among the districts (Figure 1), with district I in particular having higher use; however, this variation was not statistically significant. District I did not employ any restrictions on the use of ciprofloxacin (Table 2). The percentage of total use of this drug that involved oral administration also differed greatly among districts, ranging from 58.7% to 95.1%.

Norfloxacin and Ofloxacin

Norfloxacin use decreased by 86.8% over the study period ($p < 0.001$) (Table 1). Use of ofloxacin was limited, and no trends were evident (Table 1).

Respiratory Fluoroquinolones

Gatifloxacin and moxifloxacin did not come onto the market until after the year 2000; as such, these drugs were not used at all in the early years of the study period, and their use was low after 2000. Therefore, these agents were combined with levofloxacin for evaluating the use of fluoroquinolones for community-acquired pneumonia over the entire study period. Together, these 3 medications are known as the "respiratory fluoroquinolones". Use of these drugs increased significantly over the study period ($p < 0.001$) (Table 1). In 1997/1998, respiratory fluoroquinolones represented 0.65% of the combined total of respiratory fluoroquinolones and ciprofloxacin. This proportion increased to 67.4% in

2002/2003. In 2002/2003, the ratio of IV to oral use was 0.2. Variations in relative use existed among the DHAs, with districts A and I using more ciprofloxacin than respiratory fluoroquinolones (Figure 1).

Use of Respiratory Fluoroquinolones in Relation to Community-Acquired Pneumonia

The use of respiratory fluoroquinolones was also assessed with the WHO ATC/DDD methodology in relation to cases of community-acquired pneumonia in which the patients were admitted to hospital. Over the study period, mean use of respiratory fluoroquinolones increased from 3.4 to 1747.5 DDDs/100 cases of community-acquired pneumonia with hospital admission per year (Figure 2). From 1997/1998 to 2001/2002, mean use of levofloxacin increased from 3.4 to 1730.0 DDDs/100 cases of community-acquired pneumonia per year, but fell to 1593.8 DDDs/100 cases of community-acquired pneumonia per year in 2002/2003. Mean levofloxacin use varied among DHAs over the study period, ranging from 445.9 (DHA A) to 1506.5 (DHA H) DDDs/100 cases of community-acquired pneumonia with hospital admission per year. However, statistical tests of comparisons between DHA A and each of the other DHAs indicated no significant differences.

Effect of Utilization Policies

All of the 9 surveys that were mailed (one to each DHA) were returned, for a 100% response rate. The types of policies in place and how they were enforced and audited varied widely among the 9 DHAs (Table 2). Combining the survey results with the fluoroquinolone utilization data provided additional insights into drug utilization policies in Nova Scotia. Student *t*

Table 2. Policies Related to Fluoroquinolone Use in 9 District Health Authorities in Nova Scotia

District	Policy Restricting Use For Ciprofloxacin	For Respiratory Fluoroquinolones*	Audits	Policy for IV/PO Step-down	Pathway CAP	AECOPD
A	IV: yes; pharmacist follow-up PO: no	No	Every 2 years, but only for ciprofloxacin IV	Yes: chart reminder	Yes	No
B	IV: nonformulary†	No	Performed in 1999, for levofloxacin	No	No	No
C	IV: consult only PO: no	Allowed for treatment of CAP only	3 times in year preceding survey year (2003)	Yes: pharmacist mandated, automatic switch	Yes	Yes
D	No	No	No	Not for fluoroquinolones	No	No
E	No‡	No	"Limited audits"	Yes, but for levofloxacin and gatifloxacin only: pharmacist mandated, automatic switch	No	No
F	IV and PO: restricted drug request form	Allowed for treatment of CAP only	Performed in May 2000, for fluoroquinolones on formulary	No	No	No
G	No	No	No	Yes: chart reminder	Yes	No
H	No; guidelines in place but not enforced	No	Annual	Yes: pharmacist recommendation	Yes	No
I	No	No	No	Yes, but for ciprofloxacin only	Yes	No

AECOPD = acute exacerbation of chronic obstructive pulmonary disease, CAP = community-acquired pneumonia,
IV = intravenous administration, PO = oral administration.
*Defined as levofloxacin, gatifloxacin, and moxifloxacin.
†Will obtain upon request.
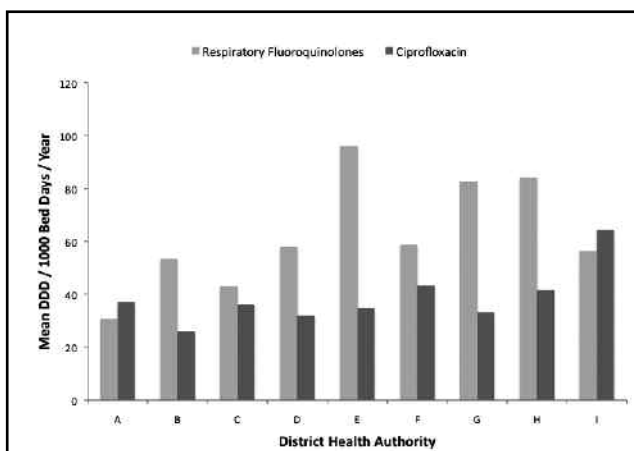‡No restrictions because of a lack of staff to provide monitoring.

Figure 1. Use of respiratory fluoroquinolones and ciprofloxacin in 9 district health authorities in Nova Scotia (identifed by letters). The differences in usage among the districts was not statistically significant. DDD = defined daily dose.
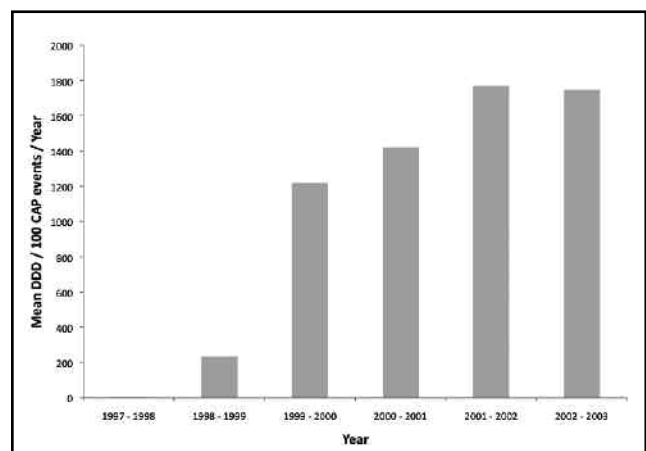

Figure 2. Use of all respiratory fluoroquinolones combined (levofloxacin, moxifloxacin, and gatifloxacin) by fiscal year, relative to cases of community-acquired pneumonia in which patients were admitted to hospital ("CAP events"). Use increased significantly over the study period ($p < 0.01$) but levelled off in the last 2 years. DDD = defined daily dose.

tests comparing drug utilization rates between hospitals with no utilization policies and those with more than one policy revealed no statistically significant differences in the use of ciprofloxacin ($p = 0.20$) or levofloxacin ($p = 0.38$).

The relation between the number of antimicrobial policies and fluoroquinolone use was explored for ciprofloxacin and respiratory fluoroquinolones (expressed in terms of both DDDs per 1000 bed-days per year and DDDs per 100 cases of community-acquired pneumonia with hospital admisison per year). Multilevel analysis revealed that fluoroquinolone use did not differ significantly between districts with more than one utilization policy and those with no policies.

Multilevel modelling analyses were then performed to estimate the variance of fluoroquinolone use across DHAs and the hospital–DHA interaction. This methodology was used to account for the hierarchical structure of the data set and to explore the variance (dispersion among measures) of 2 drug utilization variables, each represented by a different denominator (fluoroquinolone DDDs by hospital bed-days and by cases of community-acquired pneumonia with hospital admission). This analysis demonstrated that, except in the case of ciprofloxacin, the variability in fluoroquinolone utilization rates could not be explained simply by the DHA to which the hospital belonged. For ciprofloxacin use (expressed as DDDs per 1000 bed-days per year), the DHA did represent a small component of the variability. In other words, much of the variation in fluoroquinolone use occurred at the hospital level rather than the district level, and variation in drug utilization rates was not attributable to a clustering effect of hospitals. This also suggests that adherence to DHA pharmacy policies might have varied among hospitals within a given DHA.

DISCUSSION

Total annual use of all fluoroquinolones increased significantly over the study period. This corroborates other antimicrobial utilization studies, which showed an overall decrease in consumption of antimicrobials but an increase in fluoroquinolone use in Canada from 1995 to 1998.[17,18] The total fluoroquinolone use reported here (mean of 163.8 DDDs/1000 bed-days for 2002/2003) was similar to that reported for 42 hospitals in the United States (mean of 150 DDDs/1000 bed-days for 2003).[19] There is evidence to suggest that increased bacterial resistance is correlated with increased use of antimicrobials.[1-4] According to the Canadian Bacterial Surveillance Network, resistance to fluoroquinolones is increasing in Canada. Between 1993 and 1998, resistance of *Streptococcus pneumoniae* to fluoroquinolones increased from 1.5% to 2.9%, which coincided with an increase in the number of prescriptions for ciprofloxacin during the same period.[20] Rates of resistance to fluoroquinolones are still low; however, as the use of these agents increases, resistance is expected to increase as well.

Norfloxacin was the one fluoroquinolone for which utilization decreased over the study period. Use of this drug was higher in small and medium-sized hospitals than in large hospitals. This may be because norfloxacin was removed from the formulary of one of the large hospitals in the province in November 1996 (just before the beginning of the study period). The reason for removal was primarily to "streamline" the use of antibiotics in the institution. Streamlining is a process that many hospitals use to simplify therapeutic choices and to contain costs.[21,22]

The lack of statistically significant differences in fluoroquinolone use related to the presence or absence of at least one utilization policy may have been due to the small number of observations and the relatively short period of the study. As well, the presence of a drug utilization policy does not necessarily mean that it is enforced. One of the biggest problems with utilization policies that rely on completion of forms by the physician is the resources required for pharmacy auditing and follow-up. One survey respondent commented that the DHA had never implemented antimicrobial utilization policies because there were insufficient staff to monitor adherence. Insufficient staffing, especially in rural areas, is an issue facing many hospital pharmacies in Nova Scotia, one that can impede optimization of use of antimicrobials through utilization policies. In a previous study, a US hospital pharmacy implemented an interventional program to improve antibiotic use.[23] The program consisted of a pharmacist's personal intervention and an educational component, and it decreased ciprofloxacin use by 43%. Another study examined an intervention that involved completion of restriction forms, which were audited daily, with prescribers receiving feedback from infectious disease specialists twice a week.[24] Over a 4-year period with the program in place (from 1992 to 1995), expenditures for ciprofloxacin decreased, but in 1996, costs increased sharply (by 69%) when the capacity to audit the forms and provide feedback was withdrawn. Ongoing education and follow-up are necessary to successfully operate restriction policies.

The advantages of stepping down from IV to oral therapy include lower cost, less administration time by nursing staff, decreased length of stay, and decreased potential for adverse events associated with IV therapy.[25-31] One possible reason for the trend of decreasing oral usage may be the decline in hospital length of stay. Patients are typically switched to oral therapy just before discharge, and oral therapy continues on an outpatient basis; however, outpatient therapy was not included in this study. Another reason may be that patients who were admitted later in the study period were sicker, and their care was more complex, than patients admitted earlier in the study period.

Switching patients from IV to oral medications also has economic advantages. In 2002/2003, the ratio of IV to oral use of ciprofloxacin was 0.325, and NS provincial expenditures for

ciprofloxacin were approximately $860 000. Lowering the IV–oral ratio to 0.25 would represent a cost avoidance of approximately $330 000. Similarly, if the ratio of IV to oral use of respiratory fluoroquinolones was decreased from 0.2, its reported level in 2002/2003, to 0.15, approximately $180 000 in cost avoidance could be realized.

If one assumes that each case of community-acquired pneumonia should be treated with 1 DDD of moxifloxacin or gatifloxacin and 2 DDDs of levofloxacin (the DDD of levofloxacin is 0.25 g [250 mg], which is half the usual dose of 500 mg once daily used in Canada to treat community-acquired pneumonia at the time of the study), the rate of use in facilities was high and increased over time.[32] This suggests that respiratory fluoroquinolones were used to treat infections other than community-acquired pneumonia, which may be inappropriate. Zhanel and others[33] reported that resistance to penicillin and macrolides increased over time in the Maritime provinces of Canada (i.e., Nova Scotia, New Brunswick, and Prince Edward Island), whereas fluoroquinolone resistance declined between 1997 and 1998 and then stabilized. The Canadian Bacterial Surveillance Network has reported stabilization of penicillin resistance in the Atlantic provinces (i.e., Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador), but a decrease in high-level resistance and an increase in macrolide resistance from 1997 to 2001.[34] A study of susceptibility results for invasive pneumococcal isolates collected in 2002 and 2003,[35] at the end of the current study period, demonstrated rates of resistance to macrolides, penicillin, and fluoroquinolones similar to those of the study by Zhanel and others.[33] This suggests that resistance rates did not go up in the last year of our study. However, even if resistance rates increased and the increasing use of fluoroquinolones was justified on the basis of macrolide and ß-lactam resistance, this would not explain why fluoroquinolone usage was greater than would be accounted for by all cases of community-acquired pneumonia in which hospital admission was required. The use of levofloxacin fell in the last year of the study, while the combined use of respiratory fluoroquinolones remained the same. One factor may be the reporting of *Streptococcus pneumoniae* resistance to levofloxacin in the literature,[33,36] which may have led prescribers to switch to the newer respiratory fluoroquinolones. In support of this supposition, 3 of the DHAs changed the respiratory fluoroquinolone on their pneumonia pathways from levofloxacin to either moxifloxacin or gatifloxacin during the last year of the study.

Many factors, such as patient acuity, number of intensive care beds, and patient demographic characteristics, can confound differences in utilization rates of antimicrobials across different facilities; therefore, comparisons between hospitals and districts should be used only as a guide. There was a nonsignificant trend for small hospitals to have higher use of

fluoroquinolones than large hospitals, which suggests overuse of these drugs by some facilities.

Data on patient acuity and outcomes after the use of specific agents were not available for this particular study. Furthermore, information on hospital infection control policies and their implementation was not collected. This study was also limited by the relatively small number of hospitals and districts and the short time frame over which policies might have been introduced and implemented. Although the statistical power to detect a difference in the use of fluoroquinolones between hospitals with no utilization policies and those with more than one policy was low (post hoc power = 0.2434), it is important to note that the geographic region of the study had only a limited number of institutions. Therefore, this pilot study was restricted in the number of institutions available for analysis. Future studies could include additional hospitals outside of Nova Scotia. The year in which policies were instated was requested, but this information was not provided in all cases. Two of the policies were implemented sometime in 1999 and another in 2000. One limitation to interpreting the influence of utilization policies on actual fluoroquinolone use is the assumption that each hospital within a DHA followed the district's policies as reported by the survey respondent; however, adherence to policies was not verified in this study, nor were changing policies over time examined. The DDDs for some fluoroquinolones (levofloxacin, ciprofloxacin) are lower than the dosages commonly used for certain infections in Nova Scotia, which might have led to an overestimation of use. Nevertheless, this methodology does provide a way of comparing drug utilization among DHAs and hospitals and provides guidance to improving their use.

By comparing drug utilization data from different locations, it is often possible to detect substantial differences requiring further evaluation, and such evaluation may lead to the identification and promotion of best practices, often called benchmarking. Such comparisons will be accurate as long as the data are collected in a uniform way. The ATC/DDD methodology recommended by WHO and the European Drug Utilization Research Group (see http://www.eurodurg.com) allows these comparisons.[13] Bhavnani and others[37] used the WHO ATC/DDD methodology to compare use of fluoroquinolones and found an insufficient number of hospitals that could provide data on actual antimicrobial use. They concluded that surrogate markers such as expenditures would suffice until more hospitals are able to provide running totals for drug use on a patient-by-patient basis. The current study has shown that the WHO ATC/DDD methodology applied to purchasing data offers a simple and effective method of comparing use between hospitals, in attempts to develop best practices. Additionally, this study had the advantage of investigating all NS hospitals that used fluoroquinolones and thus represented

true (or "real") utilization patterns in the province. This represents valuable information for policy-makers, pharmacists, and clinicians.

CONCLUSIONS

This study demonstrated application of the WHO ATC/DDD methodology to compare drug utilization between hospitals and health districts. This tool should be applied more widely to detect trends or signals in utilization patterns that could be investigated in more formal drug use management programs and thereby to improve the appropriate utilization of antimicrobials. In this study, fluoroquinolone use increased significantly over time. These data will provide a useful baseline for examination of future use and its association with antimicrobial susceptibility patterns in Nova Scotia. Although limitations in study design prevented demonstration of statistically significant differences in utilization rates between hospitals with and without utilization policies, further studies of the effectiveness of these strategies are warranted. Lack of resources for education and follow-up may prevent hospitals from gaining full benefit from policy interventions.

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