ORIGINAL ARTICLE

Fluoroquinolone use in a rural practice

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Abstract

Introduction: Fluoroquinolones (FQs) are a commonly prescribed class of antibiotics in Canada. Evidence of a constellation of possible adverse events is developing. Central and peripheral nervous system abnormalities and collagen-related events (including aortic aneurysm/dissection, tendinopathy/rupture and retinal detachment) are associated with FQ exposure in large population-based aftermarket studies. In 2017, Health Canada warned about rare FQ-related persistent or disabling side effects. This study explores FQ use in a rural community.

Methods: Antibiotic prescriptions (including FQs) in the over 18 adult population (5416) were measured in the town of Sioux Lookout for 5 years, January 2013 to 31 December 2017.

Results: FQ prescriptions accounted for 16.0% of adult antibiotics, superseded by penicillins (21.1%) and macrolides (18.2%). Ciprofloxacin accounted for one half of FQ use (51.2%), followed by levofloxacin (36.7%) and norfloxacin (13.3%). FQs were commonly used for respiratory (33%) and urinary tract infections (18%).

Conclusion: Aftermarket evidence reports increased risk of 'disabling and persistent serious adverse events'(Health Canada) in patients using FQs. Appropriate clinical caution should be exercised in the prescribing of FQs. Common overuse seems to occur in the treatment of uncomplicated community-acquired pneumonia and cystitis, despite recommendations to use other antimicrobial agents as first-line treatments.

Keywords: Antibiotic, fluoroquinolone, rural

Résumé

Introduction: Les fluoroquinolones sont une classe d'antibiotiques souvent prescrite au Canada. Mais les données étayant une gamme d'événements indésirables possibles s'accumulent. Des anomalies du système nerveux central et périphérique, et des événements liés au collagène (dont anévrisme ou dissection de l'aorte, tendinopathie/rupture et décollement de la rétine) sont associés à l'exposition aux fluoroquinolones dans des études de pharmacovigilance d'envergure basées sur la population. En 2017, Santé Canada a émis une mise en garde au sujet des effets indésirables rares, persistants ou incapacitants liés aux fluoroquinolones. Cette étude se penche sur l'emploi de fluoroquinolones dans une communauté rurale.

Méthodologie: La prescription d'antibiotiques (y compris de fluoroquinolones) a été mesurée dans la ville de Sioux Lookout pendant 5 ans, soit de janvier 2013 au 31 décembre 2017 auprès de la population de 18 ans et plus (5416 personnes).

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Résultats: Les fluoroquinolones comptaient pour 16,0 % des antibiotiques prescrits aux adultes, elles étaient précédées des pénicillines (21,1 %) et des macrolides (18,2 %). La ciprofloxacine représentait la moitié de l'emploi de fluoroquinolones (51,2 %), suivie de la lévofloxacine (36,7 %) et de la norfloxacine (13,3 %). Les fluoroquinolones étaient fréquemment utilisées contre les infections respiratoires (33 %) et urinaires (18 %).
Conclusion: Les données de pharmacovigilance rapportent un risque accru « d'événements indésirables graves persistants et incapacitants » (Santé Canada) chez les patients sous fluoroquinolones. La prudence clinique appropriée est de mise lors de la prescription de fluoroquinolones. La pneumonie extra-hospitalière non compliquée et la cystite semblent être à l'origine de la surutilisation, malgré les recommandations d'utiliser d'autres antimicrobiens en première intention.

Mots-clés : Fluoroquinolones; antibiotiques; effets indésirables; rural

INTRODUCTION

Antibiotic stewardship is an important component of clinical practice.[1] Most antibiotics (90%) are prescribed in the community and patterns of use are recognised as a national and rural issue.[2,3] The (over) use of fluoroquinolones (FQs) is a common target for quality improvement discussions.[4-6]

Since the arrival of FQs in 1986, their perceived safety profile, excellent oral absorption, wide spectrum of activity and lack of established resistance have led to overprescribing.[7] They are the third most common adult antibiotic prescription in Canada; Newfoundland has the highest rate of FQ prescribing.[1,8] In 2017, FQ accounted for 12% of adult prescriptions in Northwest Ontario.[9]

Awareness of serious adverse effects associated with FQ use has grown.[5] Large population-based studies describe increased incidences of aortic dissection, tendon ruptures and retinal detachment.[10-15] While these adverse events appear widely divergent, a proposed common denominator by FQ is the disruption of fibroblast enzymes responsible for collagen cross-linking in structures reliant upon collagen type 1 fibres (retina, tendons and major vessels).[16-18]

In 2017, Health Canada warned of an association with permanent peripheral neuropathy, seizures and Achilles tendon rupture.[12] In 2018, the American Federal Drug Agency added aortic rupture, mental health and hypoglycaemic coma to its warning.[19-21] One focus of overuse has been in uncomplicated urinary tract infections. Surprisingly, in Canada in 2014, 46% of uncomplicated urinary tract infections were treated with ciprofloxacin[22] despite recommendations for its limited use as a second-line agent.[22] Little is known about the use of FQs in rural Canada. This study will examine their use in a rural setting in Northern Ontario.

METHODS

Antibiotic prescribing was calculated in the 18 + years population in the town of Sioux Lookout, Ontario, over a 5-year period, January 2013 to 31 December 2017. Prescriptions were tabulated as individual episodes (a patient who received two concurrent antibiotics was counted as two prescriptions) using Anatomic Therapeutic Classification 9ATC) coding for antibacterial drugs.[23] Since the inception of the electronic medical records (EMR) in 2013, family physicians almost universally prescribed electronically. A review of the OSCAR electronic health records (EMR) at the Hugh Allen Clinic (the primary clinic for the group of MDs in this study) included clinic visits (13,829), hospital outpatient and emergency department electronic prescriptions for the practice population; it excluded handwritten scripts and specialist prescriptions. Only adult population data were used as FQs are rarely prescribed in the paediatric population due to concerns around cartilage development.[24]

The study was approved by the Sioux Lookout Meno Ya Win Health Centre Research Review and Ethics Committee.

RESULTS

There were 4563 outpatient antibiotic prescriptions from 2013 to 2017 for the adult practice population of 5416 adults (2760 females), an average of 843 prescriptions per 1000 persons. These were prescribed to 2275 unique patients [Table 1].

Table 1: Adult antibiotic prescribing rate for Sioux Lookout, NW Ontario and Canada			
	Sioux Lookout	Northwest Ontario	Ontario
Antibiotic prescriptions per 1000 adults	843	687	697
FQ use, % of all	15.7	12	12

FQ: Fluoroquinolone

Table 2: Adult antibiotic prescriptions by class 1 January 2013-31 December 2017 Sioux Lookout	
Antibiotic	Number of adult 18+prescriptions (%)
Macrolides	975 (21.0)
Penicillins	825 (18.1)
Fluoroquinolones	718 (15.7)
Cephalosporins	588 (12.9)
TMP/SMX	566 (12.4)
Tetracyclines	309 (6.8)
Nitrofurantoin	313 (6.9)
Metronidazole	239 (5.2)
Others	30 (0.7)
Total	4563 (100)

Table 3: Diagnoses associated with fluoroquinolone use in Sioux Lookout, 2013-2017*	
Diagnosis	Percentage of FQ scripts
Respiratory	33
Genitourinary	20
Uncomplicated UTI	18
SSTI	9
Gastrointestinal	9
Travel prophylaxis	8
ENT	4

*Derived from a random sample of 25% (180) of all 718 FQ prescriptions.
FQ: Fluoroquinolone, UTI: Urinary tract infection, ENT: Ear, nose and throat, SSTI: Skin and soft tissue infection

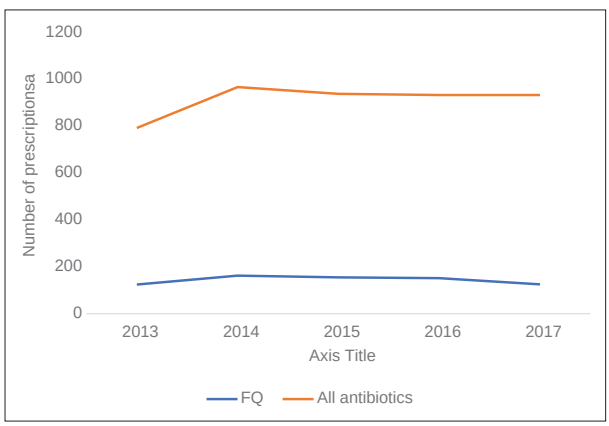

Figure 1: Number of adult antibiotic and fluoroquinolone prescriptions in Sioux Lookout, 2013–2017.

FQs accounted for 15.7% (718/4,563) of adult antibiotic prescriptions and were the third most commonly prescribed class of antibiotic, after macrolides and penicillins [Table 2], [Figure 1].

Half of all Sioux Lookout FQ prescriptions were for ciprofloxacin (51.2%), followed by levofloxacin (35.5%) and norfloxacin (13.6%). The most common indication was respiratory, followed by genitourinary infection [Table 3].

DISCUSSION

Antibiotic and FQ use in this primary care practice in Sioux Lookout remained stable during the 5-year study period, with FQs the third most prescribed antibiotic class in the adult population. This is similar to Canada-wide adult prescribing patterns, where ciprofloxacin followed amoxicillin and azithromycin in frequency. [1]

The rate of antibiotic prescribing per 1000 persons was higher with an average annual adult prescription rate of 842 prescriptions compared to provincial and regional rates (697, 687 respectively). We also prescribed more FQs than the regional proportion of adult antibiotic prescriptions (15.7% vs. 12.0%).[9]

FQs are not recommended for the treatment of community-acquired pneumonia in healthy adults nor for uncomplicated urinary tract infections, but accounted for an estimated 33% and 18% of our FQ use, respectively, leaving substantial room for improvement.[24,25]

A 2017 survey of the antibiotic-prescribing habits of 202 Canadian primary care providers documented an urban-rural difference: rural physicians were less likely to prescribe an FQ as a first-line therapy for uncomplicated cystitis than urban providers (10% vs. 50%), perhaps due to concern regarding patient costs.[5] FQ overuse increases resistance; in 2015, *Escherichia coli* isolates were resistant to ciprofloxacin in Ontario and the Sioux Lookout Meno Ya Win Health Centre at 20% and 16%, respectively.[26,27]

Risk can be individualised to specific adverse events, including athletes (Achilles tendon rupture) and patients with

common regional risk factors: diabetic retinopathy (retinal detachment) and patients with hypertension (aortic rupture).

The U. S. Food and Drug Administration boxed warnings have shown to have minimal effect on prescribing.[28,29] Health Canada warns of 'disabling and persistent serious adverse events'.[12] This study focussed on the specific prescribing pattern for a single rural practice; it is hoped that circulation of the results within the practice and presentation at local educational grand rounds will effect change in prescribing and influence discussions of side effects with patients.

A regional initiative by the Northern Health Authority in northern BC is developing a community-based antibiotic stewardship program; it includes the involvement of a clinical pharmacist, the development of approved practical order sets and clinical pathway tools for clinicians and provision of a patient-specific pharmacy support.[30]

Limitations

The occurrence of serious FQ side effects was not feasible in such a small population and limited study period. Only primary care prescribing was analysed, excluding the antibiotic choices of the two community general surgeons.

CONCLUSION

This study demonstrates a greater than expected rate of antibiotic prescribing and FQ use in a rural primary care practice in Northwest Ontario. Appropriate clinical caution should be exercised in the prescribing of FQs, particularly avoidance in the treatment of uncomplicated cystitis.

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Conflicts of interest: There are no conflicts of interest.

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The SRPC would like to express our support for all of those responding to COVID-19 committed to providing safe and quality care to patients across Canada.
Join the RuralMed and or Rural Anesthesia Listservs. A lot of useful, detailed COVID-19 information has come from these email lists and has proven to be a great resource.
A working group with representatives from all the provinces and territories with isolated fly-in communities has been formed to share concerns and offer advice. We will keep you posted on further initiatives.

Together we can work towards keeping everyone connected, safe, and up to date.
Visit the SRPC.CA home page to find links to these pages.
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