Ciprofloxacin-Resistant Campylobacter spp. in Retail Chicken, Western Canada

Agnes Agunos, David Léger, Brent P. Avery, E. Jane Parmley, Anne Deckert, Carolee A. Carson, and Lucie Dutil,

During 2005–2010, the Canadian Integrated Program for Antimicrobial Resistance Surveillance identified an increased prevalence of ciprofloxacin (a fluoroquinolone) resistance among Campylobacter isolates from retail chicken in British Columbia (4%–17%) and Saskatchewan (6%–11%), Canada. Fluoroquinolones are critically important to human medicine and are not labeled for use in poultry in Canada.

H

Human campylobacteriosis, a notifiable disease in Canada, is the most common cause of bacterial enteric infections among persons in Canada; in 2005, the incidence rate of campylobacteriosis was 30.9 cases per 100,000 population (1). In chickens, Campylobacter spp. are not clinically relevant; however, the presence of these bacteria in poultry represents a potential threat to public health (2).

Ciprofloxacin, a fluoroquinolone antimicrobial drug, is indicated for the treatment of respiratory, urinary, skin, and bone/joint infections and gastroenteritis in adults (3). In 2008 in Canada, fluoroquinolones were the fourth most frequently dispensed class of antimicrobial drug (dispensed for oral use by retail pharmacists; www.phac-aspc.gc.ca/cipars-picra/2008/4-eng.php#Hum0). A study investigating antimicrobial drug use and resistance in 2 health units in Ontario found that ciprofloxacin was the antimicrobial drug most frequently used to treat human campylobacteriosis (4). Fluoroquinolones are considered “critically” or “very” important to human medicine by the World Health Organization (5) and the Veterinary Drugs Directorate (VDD), Health Canada (6). The veterinary fluoroquinolones enrofloxacin and danofloxacin are VDD Category I antimicrobial drugs labeled for use in companion animals and beef cattle, but they are not labeled for use in poultry. The VDD has established a policy recommending against the extra-label use of Category I antimicrobial drugs in food-producing animals (7); however, Canada does not have legislation restricting this extra-label use.

The Study

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), Public Health Agency of Canada, collects samples of fresh chicken, beef, and pork from retail outlets in British Columbia, Saskatchewan, Ontario, Québec, and Maritimes (New Brunswick, Nova Scotia, and Prince Edward Island) on a routine basis and cultures them for select bacteria. Retail food samples best reflect the level of consumer exposure to drug-resistant foodborne bacteria. Methods used for sample collection, culture, and antimicrobial drug-susceptibility testing are described in the CIPARS annual reports (www.phac-aspc.gc.ca/cipars-picra/2008/6-eng.php#Ant).

Up to and including 2010, Campylobacter spp. were isolated from retail chicken meat samples in the provinces of British Columbia (since 2007, 225 isolates/536 samples [42%]), Saskatchewan (since 2005, 276/884 [31%]), Ontario (since 2003, 845/2288 [37%]), Québec (since 2003, 683/2215 [31%]), and the Maritimes (since 2008, 117/444 [26%]) (Table). Temporal trends in ciprofloxacin resistance among Campylobacter spp. isolates are shown in the Figure. Since initiation of surveillance, prevalence of ciprofloxacin resistance has significantly increased in British Columbia and Saskatchewan. The highest recovery of ciprofloxacin-resistant Campylobacter spp. was in British Columbia in 2009 (28.6%, 22/77), when recovery of all Campylobacter spp. (52.7%, 77/146) was also highest.

Significant differences in prevalence between 2 periods were assessed by using χ² tests. The increased trend in British Columbia seems more abrupt, especially from 2008 to 2009, relative to Saskatchewan, where the increase is relatively more gradual. Combined data from 2009–2010 showed that 23% (34/147) of Campylobacter spp. isolates from British Columbia and 13% (11/84) of isolates from Saskatchewan were resistant to ciprofloxacin, compared with 6% (5/78, p = 0.002) and 6% (11/192, p = 0.04) of isolates resistant to ciprofloxacin in combined data before 2009 in British Columbia (2007–2008) and Saskatchewan (2005–2008), respectively. By comparison, in 2009–2010, the overall prevalence of ciprofloxacin-resistant Campylobacter spp. from retail chicken collected in Ontario, Québec, and the Maritimes has remained <3% (10/395), significantly lower (p<0.001) than the overall prevalence in British Columbia and Saskatchewan (19%, 45/231). The current prevalence of ciprofloxacin resistance in British Columbia and Saskatchewan is also higher than that reported by studies of antimicrobial
Ciprofloxacin resistance in *Campylobacter* spp. in Ontario (8) and Québec (9).

Several factors contributing to the emergence of ciprofloxacin resistance have been hypothesized and include antimicrobial drug use in broiler breeder and broiler chickens and importation of poultry products. Data for antimicrobial drug use in the poultry industry are not currently available. Fluoroquinolone use can select for ciprofloxacin resistance and result in the emergence and persistence of resistant *Campylobacter* spp. (10). Evidence indicates vertical transmission of fluoroquinolone-resistant *Campylobacter* spp. (11). Surveillance data from the United States showed the persistence of ciprofloxacin resistance, despite a 2005 ban on fluoroquinolone use in chickens (12). Ciprofloxacin resistance also persisted in broilers raised in Denmark after fluoroquinolone use decreased in 2006 (13). Current use of ciprofloxacin in US poultry is unknown. However, in Denmark, use in few broiler breeders has been reported (13). It is plausible that fluoroquinolone use in breeder and broiler chickens could explain the generation and maintenance of ciprofloxacin resistance.

Another antimicrobial drug-use practice might play a role in ciprofloxacin resistance. Tetracyclines are labeled for use in broiler chickens. Across the regions sampled by CIPARS, a high proportion (64%) of ciprofloxacin-resistant *Campylobacter* isolates were also resistant to tetracycline. Although the prevalence rates for ciprofloxacin and tetracycline resistance were quite different, the resistance trends in British Columbia and Saskatchewan were strikingly similar in shape. Tetracycline resistance was significantly associated with ciprofloxacin resistance in isolates from British Columbia and Saskatchewan (odds
Board of directors (6) are concerned with tetracycline resistance. Furthermore, the growth of antibiotic-resistant Campylobacter has increased by the emergence of resistance to ciprofloxacin, which is critically important for treatment of food-producing animals. More research is required to assess mechanisms responsible for the trends observed for tetracycline and ciprofloxacin resistance. Furthermore, genotyping of isolates from humans and chickens (retail and/or abattoir) from British Columbia and Saskatchewan is required to determine if strains are epidemiologically related.

Acknowledgments

This manuscript is dedicated to Lucie Dutil, a wonderful person and outstanding colleague. Dr Dutil passed away suddenly in August 2011 and is sadly missed by CIPARS and all who worked with her.

We would like to thank Danielle Daignault and the technical staff at the Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, Sainte-Hyacinthe, Québec; Nicol Janecko and all CIPARS retail field staff; J.T. McClure, Matt Saab, and Cynthia Mitchell at the University of Prince Edward Island; and Carol McClure and the Centre for Coastal Health in British Columbia. The authors would like to specially thank Rebecca Irwin for her critical review of the manuscript.

CIPARS is supported by the Public Health Agency of Canada, Health Canada, Agriculture and Agri-Food Canada, and the Canadian Food Inspection Agency.

Dr Agunos is a veterinarian/poultry specialist at the Laboratory for Foodborne Zoonoses of the Public Health Agency of Canada. She coordinates poultry farm-related antimicrobial use/resistance research and surveillance activities of CIPARS.

References

1. Public Health Agency of Canada. Canadian Notifiable Disease Surveillance System national report: 2005–2008 [cited 2013 Apr 29]. http://publications.gc.ca/collections/collection_2012/aspc-phae/HPI40-75-2012-eng.pdf
2. Zhang Q. Campylobacteriosis. In: Saif YM, Fadly AM, Glisson JR, McDougald LR, Nolan LK, Swayne DE, editors. Diseases of food-producing animals. 12th ed. Ames (IA): Blackwell Publishing; 2008. p. 675–89.
3. Dryden MS, Gabb RJ, Wright SK. Empirical treatment of severe acute community-acquired gastroenteritis with ciprofloxacin. Clin Infect Dis. 1996;22:1019–25. http://dx.doi.org/10.1093/clinids/22.6.1019
4. Deckert AE, Reid-Smith RJ, Tamblyn SE, Morrell L, Seliske P, Jamieson FB, Irwin R, Dewey CE, Boerlin P, McEwen SA. Antimicrobial resistance and antimicrobial use associated with laboratory-confirmed cases of Campylobacter in two health units in Ontario. Can J Infect Dis Med Microbiol. 2013; 24:e16-21.
5. Food and Agriculture Organization of the United Nations/World Health Organization/World Organisation for Animal Health. Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials; 2007 Nov 26–30; Rome, Italy [cited 2011 Jun 10]. http://www.who.int/foodborne_disease/resources/Report_CIA_Meeting.pdf
6. Health Canada. Categorization of antimicrobial drugs based on importance in human medicine [cited 2011 Jun 10]. http://www.hc-sc.gc.ca/dhp-msp/vet/antimicro/amr_ram_hum-med-rev-eng.php
7. Health Canada. Policy on extra-label drug use (ELDU) in food producing animals [cited 2011 Aug 2]. http://www.hc-sc.gc.ca/dhp-msp/vet/label-etiquet/pol_eldu-under-eng.php
8. Deckert A, Valdivieso-Garcia A, Reid-Smith R, Tamblyn S, Seliske P, Irwin R, et al. Prevalence and antimicrobial resistance in Campylobacter spp. isolated from retail chicken in two health units in Ontario. J Food Prot. 2010;73:1317–24.

9. Lévesque S, Frost E, Arbeit RD, Michaud S. Multilocus sequence typing of Campylobacter jejuni isolates from humans, chickens, raw milk, and environmental water in Quebec, Canada. J Clin Microbiol. 2008;46:3404–11. http://dx.doi.org/10.1128/JCM.00042-08

10. McDermott PF, Bodeis SM, English LL, White DG, Walker RD, Zhao S, et al. Ciprofloxacin resistance in Campylobacter jejuni evolves rapidly in chickens treated with fluoroquinolones. J Infect Dis. 2002;185:837–40. http://dx.doi.org/10.1086/339195

11. Idris U, Lu J, Maier M, Sanchez S, Hofacre CL, Harmon BG, et al. Dissemination of fluoroquinolone-resistant Campylobacter spp. within an integrated commercial poultry production system. Appl Environ Microbiol. 2006;72:3441–7. http://dx.doi.org/10.1128/AEM.72.5.3441-3447.2006

12. United States Food and Drug Administration. 2008 retail meat report: National Antimicrobial Resistance Monitoring System [cited 2011 Jun 13]. http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/UCM237111.pdf

13. Danish Integrated Antimicrobial Resistance Monitoring and Research Programme. DANMAP 2009–use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark [cited 2011 Jun 13]. http://www.danmap.org/pdfFiles/Danmap_2009.pdf

14. Ge B, McDermott PF, White DG, Meng J. Role of efflux pumps and topoisomerase mutations in fluoroquinolone resistance in Campylobacter jejuni and Campylobacter coli. Antimicrob Agents Chemother. 2005;49:3347–54. http://dx.doi.org/10.1128/AAC.49.8.3347-3354.2005

15. Foreign Affairs and International Trade Canada. Report of the Minister of Foreign Affairs respecting operations under the Export and Import Permits Act for the year 2010 [cited 2013 Apr 29]. http://www.international.gc.ca/controls-controles/report-rapports/report-rapport-2010.aspx?view=d

Address for correspondence: Agnes Agunos, Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, 160 Research Lane, Unit 103, Guelph, Ontario N1G 5B2, Canada; email: agnes.agunos@phac-aspc.gc.ca