

HIGH RATES OF FLUOROQUINOLONE-RESISTANT CAMPYLOBACTER IN PORTUGAL - NEED FOR SURVEILLANCE

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Introduction

Gastrointestinal infections caused by *Campylobacter* spp. can manifest as self-limited gastroenteritis or more severe diarrhoea. They can also cause secondary complications, such as reactive arthritis and Guillian-Barré syndrome. Recent publications have indicated that *Campylobacter* is a leading cause of food-borne diseases in many countries in Europe, clearly surpassing former frontrunners, such as non-typhoidal *Salmonella* [1,2]. Furthermore, recent studies from Europe have reported a worrying rise in resistance to fluoroquinolones among *Campylobacter* strains [2,3]. However, few data on *Campylobacter* are available from Portugal. A report from 2003 singled out Portugal as the only country among 18 European states that had no existing surveillance system for *Campylobacter* infections in 2000 [4]. A PubMed search in February 2008, using the terms *Campylobacter* and Portugal, retrieved just seven publications. Only one of these reported results collected on the national level, but it was published in 1992 [5]. Official notification reports in Portugal do not include many food-borne diseases; among the bacterial infections, only cholera, salmonellosis, shigellosis and botulism are reported [6]. Furthermore, stool cultures for *Campylobacter* are not routinely performed in all Portuguese laboratories.

However, it is important to bear in mind that food-borne infections in Portugal have a broader European dimension, given the large tourism industry. In 2006 alone, 22.5 million people entered Portugal, 50% of them tourists [7], a high number comparing to the national population of around 10.5 million. In fact, part of the recent, although scarce, data on *Campylobacter* and resistance patterns in Portugal comes from studies done in north European countries on tourists who had been infected during their visit abroad [8]. A study of English tourists visiting European countries showed that those returning from Portugal had the highest risk (odds ratio: 22.4) of acquiring fluoroquinolone-resistant *Campylobacter* infection [9].

Study objectives

We set out to collect data on fluoroquinolone resistance in Portugal. First, several hospital laboratories were contacted to see if stool cultures for *Campylobacter* spp. were performed and isolates stored. Five laboratories were identified and invited to participate, by providing stored isolates from 2003-2005 and/or strains isolated recently during 2006 and 2007. Only one sample per patient was included.

Methods

A total of 123 samples from five laboratories were available for sensitivity testing (Hospital Universitaria de Santa Maria, Lisbon, n=68; Hospital Distrital das Caldas, Caldas da Rainha, n=5; Centro Hospitalar de Coimbra, Coimbra, n=20; Hospital de Dona Estefânia, Lisbon, n=19; and Hospital Santa Maria da Feira, Santa Maria da Feira, n=11). The activity of three antimicrobial drugs, ciprofloxacin, moxifloxacin and gatifloxacin, was tested using E-test® strips. A suspension of a 48-hour-old culture in 0.9% NaCl was adjusted to McFarland standard 1.0 and streaked on Muller-Hinton agar supplemented with 5% sheep blood. After 48 hours of incubation at 37°C under microaerophilic conditions, the results were read. As no specific breakpoints for *Campylobacter* were available from the Clinical Laboratory Standards Institute (CLSI) during the study period, we used the CLSI breakpoints commonly used in other studies on *Enterobacteriaceae* (for ciprofloxacin and gatifloxacin) and *Streptococcus pneumoniae* (for

moxifloxacin) [10].

Results

A total of 123 *Campylobacter* spp. were tested, of which 15 were isolated in 2003, nine in 2004, 32 in 2005, 37 in 2006 and 30 in 2007. Eighty-five isolates (69.1%) were obtained from children younger than 14 years old. Fifty-seven (46.3%) were isolated from October to March, and 66 (53.7%) from April to September. Although complete data on the patients' origin was not available we may assume the samples were taken from Portuguese citizens. Of the 123 *Campylobacter* isolates from stool cultures, 110 were *Campylobacter jejuni* and 13 were *C. coli*. A total of 99 (80.5%) *Campylobacter* isolates were found to be resistant to ciprofloxacin (Table).

TABLE 1

Fluoroquinolone-resistance in *Campylobacter* spp. isolates from five laboratories in Portugal, 2003-2007 (n=1

	Sensitive (S)	Intermediate (I)	Resistant (R)	Resistant to >32µg
Ciprofloxacin	23 (18.7%)	1 (0.8%)	99 (80.5%)	86 (69.9%)
Moxifloxacin	30 (24.4%)	30 (24.4%)	63 (51.2%)	44 (35.8%)
Gatifloxacin	41 (33.3%)	24 (19.5%)	58 (47.2%)	47 (38.2%)

Breakpoints: ciprofloxacin and moxifloxacin: S ≤ 1µg/mL, 1µg/mL < I < 4µg/mL, R ≥ 4µg/mL; gatifloxacin: S ≤ 2µg/mL, 2µg/mL < I < 8µg/mL, R ≥ 8µg/mL

Conclusion

This study provides some data on the current situation of fluoroquinolone resistance in Portugal. Even though five laboratories collaborated, the small sample size poses limitations to the study and the data may not be entirely representative. On the other hand, the majority of isolates were obtained from children and outpatients, and many were taken during seasons when people do not usually travel. Thus the results are very likely to reflect the real actual situation of antimicrobial resistance among *Campylobacter* strains circulating in Portugal.

With these limitations in mind, the results of our small study suggest that Portugal may have one of the highest quinolone resistance rates in Europe, comparable only with results previously reported from Spain [11]. Although antimicrobial treatment of *Campylobacter* gastroenteritis is not generally indicated, it may be necessary in some cases. One example are HIV-infected patients that often present with more severe bacterial gastroenteritis which is frequently caused by non-typhoidal *Salmonella*, but *Campylobacter* spp. are also well known to produce a protracted illness in these patients. In some countries, including Portugal, antibiotics are largely overused in treating patients with diarrhoea. In adults, the choice for empirical treatment is frequently a quinolone, to ensure that the most common and most important enteric pathogens are covered, including *Escherichia coli*, *Salmonella*, *Shigella* and *Campylobacter*. The results from our study suggest that empirical quinolone therapy alone may not be an option anymore for the treatment of more severe gastroenteritis in Portugal, when *Campylobacter* is the cause [12].

Our study also highlights the importance of implementing an adequate and up-to-date notification system of *Campylobacter* infections. We believe that the Portuguese authorities could encourage hospital laboratories to include the detection of *Campylobacter* in the analysis of all stool cultures. Furthermore, the existing notification system could be adjusted, following the guidance of the European Commission decision 2000/96/EC [13], which recommends the surveillance of campylobacteriosis. Given the structure of the national health services in Portugal, it could also be helpful if the notification was not the sole responsibility of the attending physicians, but laboratories would also be included in the notification process. In fact, all these changes would allow the provision of more reliable and better-quality data to the European Centre for Disease Prevention and Control.

Ethical approval

Ethical approval was obtained from the Faculdade de Medicina de Lisboa.

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