



Antibiotic Resistance in Travelers' diarrhea. A 13-year retrospective review in hospitalized patients in Lima, Peru.

Melissa Beraun Villa¹, Pita D¹, E. Luna¹, Hugo Siu^{1,3}, Luis Manuel Valdez^{1,2,3}.

¹British American Hospital. Lima, Perú. ²Universidad Peruana Cayetano Heredia, Lima, Perú. ³Geosentinel site co-directors.

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Introduction

Travelers' diarrhea (TD) is a common cause of illness in travelers. Antibiotic use is recommended as it modifies the course of disease in moderate to severe cases. Because of this, people traveling to high risk areas are advised to use antibiotic self-treatment for TD.¹

Currently the most commonly used drugs are fluoroquinolones, azithromycin and rifaximin as the resistance rates to trimethoprim-sulfamethoxazole (TMP-SMX) and tetracyclines have increased. Antibiotic resistance is increasing due to the widespread use and abuse of antimicrobial agents in tropical and subtropical countries.

According to Foodnet, Peru was the third top destination (after Mexico and India) where US patients get Travel-Associated Enteric Infections.²

As we need to know our local antibiotic resistance patterns in organisms causing TD, we did a retrospective study looking at the pathogens causing severe TD at our institution. We describe the frequency and change in antibiotic resistance over a period of 13 years.

Patients and Methods

We retrospectively reviewed the stool cultures of patients with TD hospitalized at the British American Hospital between January 2000 and December 2012. All those with positive stool cultures were included in the study. Charts were reviewed for demographic data.

Selective and differential media were used for detection of enteric pathogens. All suspicious colonies were identified by standard bacteriology procedures and/or serological testing for enteric pathogens.

Antibiotic susceptibility of bacterial pathogens was determined by the Kirby-Bauer disk diffusion technique. Isolates were tested for susceptibility to TMP/SMX, ampicillin, nalidixic acid, ciprofloxacin, erythromycin, ceftriaxone, tetracycline, amikacin, and chloramphenicol.

Data was analyzed using EPIINFO.

Table 1: Characteristics in Travelers hospitalized with Diarrhea

Variable	2000-June 2006 N (%)	July 2006-2012 N (%)	Total (%)
Subjects	56	51	107
Men	23 (41)	20 (39)	43 (40.2)
Age	37 ± 14	35 ± 11	36.3 ± 13.1
Country of Origin			
North America	20 (37)	21 (48)	41 (42.3)
Europe	23(43)	15 (35)	38 (39.2)
Latin America	8(15)	5 (12)	13 13.4)
Asia	3 (5)	2 (5)	5 (5.2)
Season			
Summer	22 (39)	15 (29)	37 (35)
Fall	13 (23)	17 (33)	30 (28)
Winter	11 (19)	13 (26)	24 (22)
Spring	10 (18)	6 (12)	16 (15)
Organism			
Diarrheogenic <i>E.coli</i>	29(44)	37 (56)	66 (61.7)
<i>Shigella</i>	14	7	21 (19.6)
<i>Salmonella</i>	13	2	15 (14)
<i>Vibrio parahemolyticus</i>	0	2	2 (1.9)
<i>Campylobacter</i>	0	1	1 (0.9)
<i>Plesiomonas</i>	0	1	1 (0.9)
<i>Aeromonas</i>	0	1	1 (0.9)

Table 2. Antibiotic Resistance organized by organism in two different time periods

Organism	Period	TMP/SMX N (%)	Ampicillin N (%)	Tetracycline N (%)	Nalidixic Acid N (%)	Ciprofloxacin N (%)
<i>E.coli</i>	2000-Jun2006	8 (28.6)	18 (64.3)	9 (32.1)	4 (14.3)	1 (3.6)
	Jul2006-2012	26 (70.3)	30 (81.1)	7 (18.9)	11 (30.6)	3 (8.3)
	Total	34 (52.3)	48 (73.8)	16 (24.6)	15 (23.4)	4 (6.3)
<i>Shigella</i>	2000-Jun2006	3 (23.1)	8 (61.5)	4 (30.8)	0	0
	Jul2006-2012	6 (85.7)	4 (57.1)	4 (57.1)	1 (14.3)	1 (14.3)
	Total	9 (45)	12 (60)	8 (60)	1 (5)	1 (5)
<i>Salmonella</i>	2000-Jun2006	5 (45.5)	8 (66.7)	3 (27.3)	2 (18.2)	0
	Jul2006-2012	1 (50)	1 (50)	1 (50)	0	0
	Total	6 (46.2)	9 (64.3)	4 (28.6)	2 (15.4)	0

Results

During the study period 352 travelers were hospitalized because of TD. Of the 242 who had a stool culture done, 107 (44.2%) had a positive stool culture. The median age was 36.3 years (range: 18-72, SD 13.1). Most travelers were from North America (42%) and Europe (39%). More than one third of cases (35.5%) occurred during the summer months. The most common pathogen isolated was diarrheogenic *E.coli* (66 cases, 61.7%), followed by *Shigella* (21 cases, 19.6%) and *Salmonella* (15 cases, 14%). Among the *Shigella* isolates, 5 were *S. flexneri*, 4 *S. sonnei*, 1 *S. boydii* and 11 were not typified. There were 2 cases of *Vibrio parahemolyticus* and one case each of *Aeromonas*, *Plesiomonas shigelloides* and *Campylobacter*. As our microbiology laboratory capability improved after 2007, all cases of *Vibrio parahemolyticus*, *Aeromonas*, *Plesiomonas shigelloides* and *Campylobacter* were found after that year (Table 1).

In diarrheogenic *E.coli* resistance to trimethoprim-sulfamethoxazole (TMP-SMX), ampicillin, nalidixic acid (NA), and tetracycline was common (52.3%, 69.2%, 23.4%, 24.6% respectively). There were only 4 (6.3%) cases of documented ciprofloxacin resistance. Among *Shigella*, 60% of strains were resistant to ampicillin, and 45% to TMP-SMX. Quinolone resistance was seen only in one case (5%). In *Salmonella* resistance to ampicillin was seen in 57% and to TMP-SMX and chloramphenicol in 46.2% of isolates. Only 2 cases (15.4%) were resistant to NA, and no cases resistant to ciprofloxacin. All isolates were susceptible to third-generation cephalosporins.

Among all the isolates, 12 of 18 cases resistant to NA and 4 of 5 cases resistant to ciprofloxacin occurred over the last 6 years. For *E. coli* and *Shigella*, there is a clear trend that shows an increase in resistance against most antibiotics when the two time periods are compared. In the case of TMP/SMX the difference was statistically significant ($p < 0.01$).

Discussion

Our results show that TD requiring hospitalization is a disease that affects young travelers, with a majority of patients coming from developed countries and that antibiotic resistance is gradually increasing.

The most common pathogen causing TD in our patients was diarrheogenic *E. coli*, followed by *Shigella* and *Salmonella*. The fact that our patients were hospitalized probably explains why we saw a higher frequency of *Salmonella* and *Shigella* than what is reported in the literature. A review on the global etiology of TD mentions that in Latin America 81% of the episodes of TD were caused by diarrheogenic *E.coli*, followed by *Shigella* (6.6%), *Salmonella* (4.4%) and *Campylobacter* (2.5%).³ We had only one case of *Campylobacter* infection, which was susceptible to quinolones. A 10 year surveillance study done in three different geographic areas of Peru showed that fluoroquinolone resistance is increasing in isolates from native Peruvians.⁴ In Lima and Cusco (an important tourist destination) more than 80% of isolates were resistant. Quinolone resistant *Campylobacter* has been isolated from poultry in Peruvian shanty towns and live birds sold in Peruvian markets. Quinolones are known to be used as antibiotics in some food animals in Peru⁴

Our study has several limitations, the fact that it was retrospective and some information could not be found in the medical records as well as our limited laboratory capability during the first time period may have affected our results. In addition our population included patients whose TD was severe enough to require hospitalization, a group not considered in most studies on TD. Ciprofloxacin may still be adequate for empirically treating travelers' diarrhea as long as *Campylobacter* is not suspected. However, quinolone resistance is beginning to emerge in diarrheogenic *E.coli* and *Shigella*. Surveillance studies in travelers are critical to determine when ciprofloxacin will be no longer a drug of choice for empiric treatment in travelers visiting Peru.

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