Original Article

Antimicrobial resistance of *Escherichia coli* in Mexico: How serious is the problem?

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Abstract

Introduction: This study aimed to determine the resistance patterns of *Escherichia coli (E. coli)* in Mexico to several antibiotics and research some therapeutic options.

Methodology: Positive cultures for *E. coli* isolated from bronchial secretions, urine, central catheter, blood, and infected wounds in the Culiacan General Hospital, Sinaloa, Mexico from 30 June 2004 to 1 July 2007 were studied. Resistance against multiple antibiotics was measured and compared by gender and the hospital unit where the bacteria were isolated.

Results: In total, 1511 specimens were analyzed from men (45.4%) and women (54.5%), of which 251 were positive for *E. coli*. Antimicrobial resistance was highest in the neurosurgery service (58.4%). Samples included sputum (14.7%), bronchial secretions (17.9%), wounds (35.4%), urine/Foley catheter tip (35.5%), central catheter tips (5.6%), and blood cultures (7.2%). Resistance to ampicillin was highest at 91% followed by ciprofloxacin at 80.6%, trimethoprim-sulfamethoxazole at 70.2%, piperacillin/tazobactam at 14.4%, and imipenem at 6.8%.

Conclusions: Trimethoprim should not be recommended as an empiric option for *E. coli* infections and the benefit of quinolones is low. It is important to understand the resistance of the bacteria in each medical center, consider its frequency in each service within the same hospital, and *take* all *necessary measures* to ensure and create a clinical attitude of prevention.

Key words: *Escherichia coli*; antimicrobial resistance; hospital; patients

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Introduction

Antimicrobial resistance represents a major problem that threatens public health worldwide because it reduces the effectiveness of antibacterial treatment and increases morbidity, mortality, and costs for health-care assistance [1].

In Mexico, antimicrobial resistance has increased over the years [2]. We have previously participated in the SENTRY antimicrobial surveillance program. The substantial increase in bacterial resistance to various antimicrobial agents is allegedly due to uncontrolled use of antibiotics such as trimethoprim-sulfamethoxazole, ciprofloxacin, and ceftriaxone, among others [3]. In addition, many factors favor the emergence and spread of resistance, such as prolonged hospital stay, prior antibiotic therapy, advanced age, disease severity, use of invasive devices, and the use of antibiotics as feed additives for livestock growth promotion; however, the most important factor is likely excessive and inappropriate use of antibiotics [4,5,6].

The short and long-term consequences generated by bacterial resistance are severe. Reports have shown that 50-60% of the majority of nosocomial infections in some countries are caused by antibiotic-resistant bacteria.

Escherichia coli is a lactose fermenting facultative organism which has been studied because it is the most common bacteria that infects the urinary tract [12]. Treatment is usually empirical, mechanisms of resistance are varied, and resistance to multiple antibiotics is a problem [13]. Indeed there is

an increase in resistance worldwide [7,8]. In Latin America, *E. coli* is also responsible for a higher prevalence of bloodstream infections and pneumonia than in other regions, in addition to urinary tract infections [9]. In the Asia and Pacific regions, urinary tract infections by this micro-organism predominate with high reports of antimicrobial resistance [10].

Although the problem of antibiotic resistance is very high in Mexico, there are only local and isolated guidelines for the rational use of antibiotics in some states. At this time, we have no effective measure to control this growing problem.

Using biological samples collected from the Dr. Bernardo J. Gastelum Primary Care Hospital, Culiacan, Sinaloa, Mexico, our objective was to determine the frequency of bacterial resistance of *E. coli* to the most frequently used antibiotics. This information can be used to guide policy for the rational use of antibiotics by avoiding the empirical choice of wrong antibiotics, to create continuing education programs according to the needs and characteristics of resistance, and to underscore the need for ongoing monitoring of bacterial resistance.

Methodology

Retrospective, cross-sectional, and descriptive analyses of the microbiologic reports of positive cultures at the Dr. Bernardo J. Gastelum Primary Care Hospital in the period of 30 June 2004 to 1 July 2007 were conducted. Data from consecutive patients hospitalized within the internal medicine, general surgery, intensive care, and neurosurgery units of the hospital were included. The specimens cultured were from bronchial secretions, urine, central catheter, bloodstream, and infected wounds. Only data on *E. coli* positive cultures were analysed.

Culture and identification of E. coli

The samples were cultured on blood agar and MacConkey agar and incubated for 24 hours at 37ºC. The macroscopic characteristics of the colonies were observed (shape, size, pigment production, smell) to be identified as *E. coli*. The analysis of antimicrobial susceptibility of strains was performed by the quantitative method of serial dilution according to the criteria of the Twelfth Informational Supplement of the National Committee for Clinical Laboratory Standards (NCCLS) [11]. The strains were inoculated in Mueller Hinton culture medium for broth tubes for subsequent inoculation on plates containing different established concentrations of the antibiotics studied: cefazolin (CEZ), ceftriaxone (CRO), ceftazidime (CAZ), imipenem (IMI), piperacillin/tazobactam (PTZ), amikacin (AMK), ciprofloxacin (CIP), trimethoprim-sulfamethoxazole (TMS), amoxicillin/clavulanic acid (AUG), and ampicillin (APC). The samples were then analyzed by the Sensititre Aris®2X system (TREK Diagnostic Systems, Inc., Cleveland, OH, USA) and observed for 18 hours to determine their antimicrobial susceptibility patterns.

Statistical analysis

Descriptive statistical analysis was performed and measures of central tendency and dispersion of the variables under study were obtained. We compared the frequencies of antimicrobial resistance among gender using the Chi-Square test, considering $\alpha < 0.05$ as statistically significant using the statistical program Stata (StataCorp LP, College Station, Texas, USA) Release 6.

Results

Of 1,511 patient samples tested, 251 were positive for *E. coli*. In 2004, there were 14 positive cultures for *E. coli*, 86 in 2005, 115 in 2006 and 36 in 2007. Samples were comprised of 37 from sputum and bronchial secretions (14.7%), 45 from wounds and bedsores (17.9%), 89 from urine/Foley catheter tips (35.5%), 14 from central catheter tips (5.6%), 18 from blood cultures (7.2%), and 48 from other sites. The samples came from internal medicine wards (n = 110; 43.8%), 81 from general surgery (32.2%), 39 from the intensive care unit (ICU) (15.5%), and 21 from the neurological care unit (8.4%).

Of the strains tested, we found a resistance for ciprofloxacin at 83.1%, piperacillin/tazobactam at 16.2%, and imipenem at 8.8% (Table 1). The frequency of resistance to ciprofloxacin and trimethoprim-sulfamethoxazole in samples from urine/Foley catheter tips was 77.6% and 73.5%; 90.4 and 85.7% in samples from wounds; 83.3% and 85.7% in samples from central catheters; and 94.12% and 43.75% from blood cultures, respectively (Table 1).

Gender differences were observed in resistance to ciprofloxacin with women at 80%, and men at 81% ($p < 0.05$).

An approximation of the frequency of antibiotic-resistant *E. coli* according to the service of the hospital where the samples were obtained is presented in Figure 1.

Table 1. Analysis of *E. coli* isolates from human sources resistant to antimicrobial agents by NCCLS disc diffusion methods

	Bronchial secretions	**Urine**	**Wounds**	**Central catheter**	**Bloodstream**	**TOTAL**
			n/N (%)			
CEZ	25/34 (73.5)	53/82 (64.6)	35/43 (81.3)	7/10 (70)	11/17 (64.7)	**131/186 (70.4)**
CRO	16/28 (57.1)	35/43 (81.3)	27/39 (69.2)	5/10 (50)	10/16 (62.5)	**93/136 (68.3)**
CAZ	18/31 (58)	41/77 (53.2)	23/35 (65.7)	4/9 (44.4)	6/13 (46.1)	**92/165 (55.7)**
IMI	4/32 (12.5)	2/33 (6)	1/42 (2.3)	1/12 (8.3)	4/16 (25)	**12/135 (8.8)**
PTZ	7/27 (25.9)	4/32 (12.5)	5/33 (15.1)	0/9 (0)	3/16 (18.7)	**19/117 (16.2)**
AMK	3/12 (25)	3/32 (9.3)	2/16 (12.5)	0/2 (0)	3/8 (37.5)	**11/70 (15.7)**
CIP	28/34 (82.3)	66/85 (77.6)	38/42 (90.4)	10/12 (83.3)	16/17 (94.1)	**158/190 (83.1)**
TMS	20/32 (62.5)	64/87 (73.5)	36/42 (85.7)	12/14 (85.7)	7/16 (43.7)	**139/191 (72.7)**
						)

CEZ = Cefazolin, CRO = Ceftriaxone, CAZ = Ceftazidime, IMI = Imipenem, PTZ = Piperacillin/tazobactam, AMK = Amikacin, CIP = Ciprofloxacin, TMS = Trimethoprim-sulfamethoxazole, AUG = Amoxicillin/clavulanic acid.
N = Total number of *E. coli* isolates tested according the type of specimen, n = Number of resistant *E. coli* isolates by type of specimen.

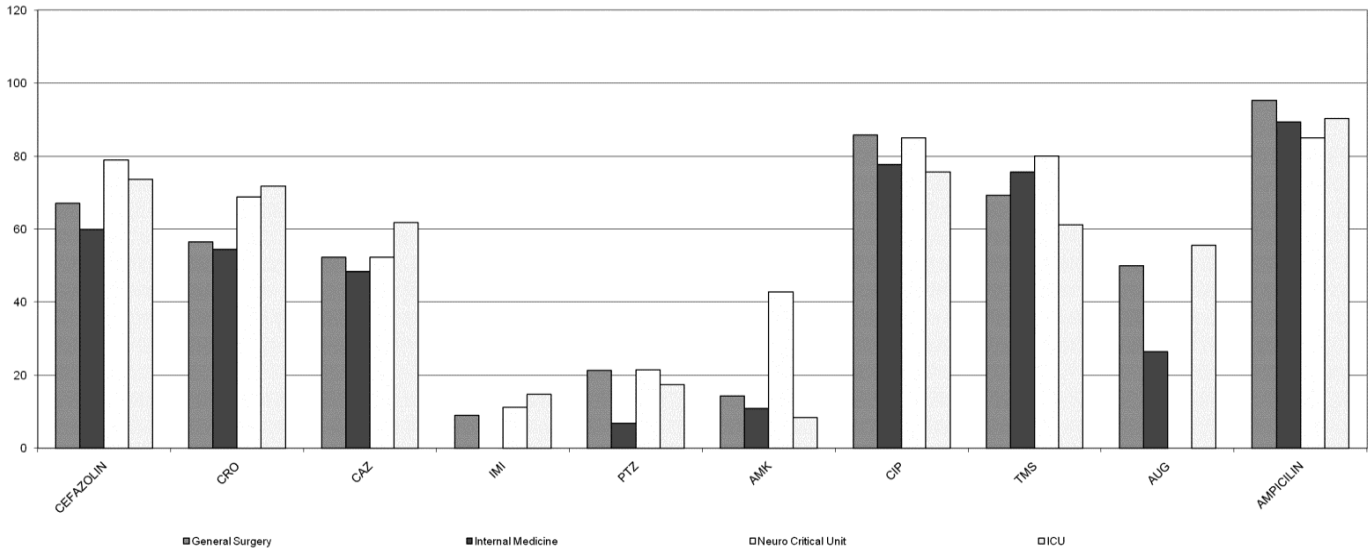
Discussion

Of the 251 *E. coli* isolates analyzed in our study, approximately half displayed resistance to one or more antimicrobials. These data are in agreement with diverse studies, suggesting that use of these drugs has been an important factor in the increase of antimicrobial-resistant *E. coli* [14].

Globally, antibiotic resistance susceptibility testing reports for *E. coli* range from 6.8% to 91% with an overall average of 52.9%. In Latin America, reported resistance to trimethoprim and sulfamethoxazole (TMS) is slightly more than 40% [15]. National reports within Mexico of resistance to TMS are less than 60% [16,17]; however, there are some reports in which ranges of resistance to TMS are higher at nearly 70% [18]. Our study shows an overall average resistance to TMS of slightly over 70%, which exceeds parameters reported in our country, and is even much higher than some of the reports in other parts of the world. The resistance of *E. coli* to TMS has been measured in many studies, and like the results that we obtained, the high percentage of resistance is something already well established. The use of this antibiotic in *E. coli* infections is not currently recommended as an empirical treatment option [19]. Other treatment options recommended, and commonly used against these bacteria, are fluoroquinolones. Overuse of these antibiotics has been a serious problem and the evidence on the resistance of *E. coli* against quinolones is high. Most of the series report a percentage of resistance to fluoroquinolones between 20-30% [13,14]. The average resistance to quinolones in our study was over 85%. This is an alarming finding that exceeds the resistance encountered in most previous reports [16,20,21]. These results should be taken with caution because they reflect the reality of our center only, but support the fact that resistance to these antibiotics is a reality and an emerging problem. The use of these antibiotics as an empiric choice for *E. coli* is ceasing to be a viable option [22].

We measured the resistance to other antibiotics and found some other relevant data. The rate of resistance to ceftriaxone was slightly less than 60%, and a little over 50% to ceftazidime; the bacteria displayed least resistance to imipenem. Our results are in agreement with those of many other studies in which imipenem was the antibiotic with the least

Figure 1. Frequency of antibiotic-resistant *E. coli* according to the origin service within the hospital of the samples



Y axis = Percentage of resistant isolates; X axis = Antibiotics.
ABBREVIATIONS: CEZ = Cefazolin, CRO = Ceftriaxone, CAZ = Ceftazidime, IMI = Imipenem, PTZ = Piperacillin / tazobactam, AMK = Amikacin, CIP= Ciprofloxacin, TMS = Trimethoprim-sulfamethoxazole, AUG = Amoxicillin / clavulanic acid, APC = Ampicillin

resistance reported. This observation should find some clinical applications [9,23,24].

Nitrofurantoin showed low resistance; this is something also consistent with many other reports. These findings are relevant because many authors recommend considering nitrofurantoin as an alternative empirical first choice in mild *E. coli* infections and imipenem as a therapeutic measure in severe infections [16,17,25].

Unlike many of the reports in which *E. coli* has been studied only in urinary tract infection, we describe the incidence of *E. coli* in wounds, respiratory and urinary tracts, the bloodstream, and in colonies from Foley and central catheters. Although the primary site of infection is the urinary tract, we found a considerable degree of *E. coli* infection in other sites. We also found that the site where the bacteria are isolated does not influence the range of antibiotic resistance. These facts suggest that these bacteria should be considered as potential causes for infections outside the urinary tract in hospitalized patients with mild or severe infections [26].

Some authors have mentioned a relationship between severity of infection by *E. coli* and gender of the patient [27]. We did not find any significant difference regarding gender.

Few data have been reported about the infection and prevalence of *E. coli* among the different services within the hospital. We classified the infection as from the area inside the hospital and measured the frequency of isolation of resistant *E. coli* from one service compared to another. There was a slightly higher rate of resistance in the neurological care unit. The clinical utility of this part of the investigation is to encourage early clinical monitoring in searching this pathogen in one service over another.

We also recognize that our study has some limitations. The first is the type of study design. The power of evidence generated by this model is weak, but does not diminish the importance of the results obtained. Another limitation is that it is difficult to extrapolate our results in the general population because they represent only the reality of our center; however, the number of patients included was relevant and even exceeds the total of many other studies. Furthermore, our results are similar in many aspects to those of other reports, reflecting a problem that is experienced not only in our center and our country, but in many places around the world.

Conclusion

Antibiotic options such as TMS used empirically in hospital infections caused by *E. coli* can no longer be recommended. The rate of resistance to quinolones is high and their use is declining significantly. Quinolones as an empirical first option for *E. coli*

infections might not be a reasonable choice. Other antibiotics should be considered, such as nitrofurantoin in mild infections and imipenem in severe infections. *E. coli* should be considered as a cause for infection not only in the urinary tract, but in other sites such as the respiratory tract and bloodstream. It is important to know the resistance of this bacterium in each center and to consider its frequency in each service within the same hospital. This information can be used to take the necessary measures to create a clinical attitude of prevention. The problem of antimicrobial resistance of *E. coli* is growing worldwide and there may be important differences in resistance patterns among developed and underdeveloped countries. Current treatment guidelines might not be useful in underdeveloped countries. Clinicians should raise awareness of this issue and take a new perspective on the use of antibiotics to try to prevent the emergence of bacterial resistance.

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