Revista Latinoamericana de MICROBIOLOGÍA
ALAM

Vol. 50, Nos. 3 y 4
July - September. 2008
October - December. 2008
pp. 72 - 78

ORIGINAL ARTICLE

Patterns of bacterial resistance in urinary isolates at a public health care center

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ABSTRACT. The objective of this paper was to evaluate the bacterial resistance to antibiotics in inpatients as well as in outpatients who have been diagnosed as having urinary tract infections (UTI), by analyzing the resistance profiles to different antibiotics related to *E. coli* and *Staphylococcus* sp. In this way, epidemiologic data was also added to the empirical prescription. We conducted our study on patients with UTI who attended a Public Health Care Center in Argentina. Data were collected by retrospective observational research from 2,800 adults, over a three-year period. Positive diagnoses were analyzed according to gender, and differences between outpatients and inpatients. The resistance of *E. coli* to nitrofurantoine (NIT) and gentamicin (GEN) in female outpatients was of 6 and 5% respectively, with these figures rising to 13 and 27% in inpatients. The resistance to trimethoprime-sulfamethoxazol (TMS) and norfloxacin (NOR) was higer in inpatients. The global resistance of *E. coli* and *Staphylococcus* sp. to NOR was approximately 55%, and the resistance to ampicillin (AMP) was greater than 70% in inpatients. Few previous studies have been undertaken in Argentina similar nature to this one. Therefore, the selection and prescription of an antimicrobial needs be evaluated in future with more complex parameters in order to obtain more accurate analysis of regional epidemiologic data, thus enabling better empirical therapies.

Key words: Epidemiology, bacterial resistance, antibiotics, public health, urinary tract infections.

RESUMEN. El objetivo de este trabajo fue comparar y evaluar la resistencia bacteriana a diferentes antibióticos en pacientes hospitalizados y ambulatorios con diagnóstico de infección en el tracto urinario (ITU). Se analizaron los perfiles de resistencia de *Escherichia coli* y *Staphylococcus* sp. a diferentes antibióticos y se aportaron datos epidemiológicos para la prescripción empírica de los mismos. Los datos corresponden a un estudio observacional retrospectivo, durante 3 años, de 2,800 adultos que fueron asistidos en un hospital público de Argentina con diagnóstico de IU. Los cultivos microbiológicos positivos fueron analizados según el sexo y si el pacientes era ambulatorio u hospitalizado. La resistencia de *E. coli* a nitrofurantoína (NIT) fue mayor al 6% y a gentamicina (GEN) fue de 5% en mujeres ambulatorias y del 13% y 27% respectivamente en hospitalizadas. La resistencia a trimetoprima-sulfametoxazol (TMS) y a norfloxacina (NOR) fue mayor en pacientes hospitalizados que ambulatorios. La resistencia global a *E. coli* y a *Staphylococcus* sp. por NOR fue cercana a 55%, y a ampicilina (AMP) mayor al 70% en internados. Existen pocos antecedentes en nuestro país de investigaciones epidemiológicas de este tipo. La selección y prescripción de los antimicrobianos debe ser evaluada en los más estrictos parámetros, con un análisis epidemiológico regional de datos para obtener mejores resultados en la terapia empírica.

Palabras clave: Epidemiología, resistencia bacteriana, antibióticos, salud pública, infecciones del tracto urinario.

INTRODUCTION

Hospital environments allow very aggressive germs to arise; these germs are easily transmitted from one patient to another, where the bacterial resistance becomes more relevant, leading to poor effectiveness in the conventional therapeutic resources.[1]

If we analyze the sepsis acquired in the community in relation to the in-hospital sepsis, the differences observed are mainly based on the sources of infection, the dominant germ and the sensitivity they have against the antimicrobials.[2]

Urine Infections (UTI) are a very important occurrence in medical appointments. They generally affect women, with the most frequently isolated germ being *Escherichia coli*. The infectious source of Staphylococcus *sp*. causing UTI in women is unknown. However, it has been shown that S. saprophyticus is widely spread in the ecosystem. Furthermore, rectal, vaginal, or urethral colonization with S. saprophyticus has been associated with UTI. This organism is second to coliforms as the most common cause of the acute urethral syndrome in women.[3] The frequency of *Staphylococcus aureus* increased over time, corresponding to an increase in the occurrence of methicillin-resistant *S. aureus* (MRSA).

The beginning of the treatment is mostly empirical and various factors must be considered when choosing the antimicrobial. However, the microorganism susceptibility related to the particular Health Care Center's geographical location

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First version received: December 21, 2007; first version revised: April 03, 2008 and April 14, 2008; second version received: May 26, 2008; second version revised: July 11, 2008 and August 28, 2008; third version received: September 9, 2008; Accepted: December 16, 2008.

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where diagnosis took place is very important, as many differences are observed when analyzing infections in outpatients compared to those infections in inpatients.[4] Within this context, a patient being catheterized is more exposed to infections caused by multi-resistant germs. Antimicrobial resistance among intensive care unit pathogens is generally increasing, probably due to individual antimicrobial use patterns. When new medical practices and alternative antimicrobials are introduced, changes in the dominant microbial etiologies may emerge prompting novel empiric selections.

In inpatient, a number of factors has been considerate to choose the antimicrobial therapy, including the severity of patient illness, predisposition to nosocomial infections, cross-transmission of pathogens characteristic of critical care areas within the hospital, compromised membrane and skin barriers following the use of invasive devices, extended length of hospital stay, and the widespread use of prophylactic and therapeutic anti-infective agents.[5]

Furthermore, a prudent antibiotic policy must take into account not only the dominant microorganisms of each clinical presentation but also the epidemiologic knowledge of the pathogens as well as their sensitivity in infections affecting each hospital or non-hospital community.[6]

The epidemiological record as a tool is indispensable in order to improve the quality when assisting patients.[7-9] An epidemiological assessment of its infection and the resistance through research about its prevention and hygiene measures, allows us to determine resistance and infection rates for the different medical services of each institution. Knowledge about the coverage and residence of these infections will enable the assessment of probable advantages and drawbacks in the use of antibiotics. Better information about the use of drugs at each institution as well as the dominant germs related to the types of infections will make the empirical treatments more adequate and will help in reducing the production of multi-resistant bacteria.

The objective of this paper was to evaluate the bacterial resistance to antibiotics in inpatients as well as in outpatients with urine infection. The resistance profiles to different antibiotics of *E. coli* and *Staphylococcus* sp. were collected over a 3-year period in order to add epidemiologic data to the empirical prescription of antibiotics in UTI.

MATERIALS AND METHODS

Retrospective observational research was done on 2,800 adult patients who attended a Public Health Care Center in Argentina. A microbiological diagnosis for the UTI was requested over a 3- years period of time.

The samples were cultivated in CLDE medium (Cysteine-lactose electrolit deficient agar-Britania) and were considered positive when greater than or equal to 10^5 u.f.c/ml of urine, unique isolation or in two samples with associated isolation. Althought, as equal to was relationate with presence of leucocytes in urine.

Positive diagnoses were evaluated according to gender, and also considering the differences between outpatients and inpatients. Two types of microorganisms were selected in *E. coli* and *Staphylococcus* sp., which were then isolated for microbiological culture.

Data about resistance in relation to the studied microorganisms were gathered by the specialized Microbiology Diagnosis Laboratory of the institution, using the Diffusion Method according to recommendations made by CLSI (Clinical Laboratory Standards Institute).

The antimicrobials compared in this represented research different groups: Quinolones (norfloxacin-NOR), β Lactamic (ampicillin- AMP, cephalotine-CEF), Aminoglucosid (gentamicin-GEN), Trimethoprime-sulfamethoxazol (TMS) and Nitrofurans (nitrofurantoine-NIT).

Differences between means were assessed using relative values and ANOVA followed by the Student-Newman-Keuls test for multiple comparisons. A p value < 0.05 was considered statistically significant.

RESULTS

Positive urine culture analyses (674) of *E. coli* (outpatient 446 and inpatient 98) and *Staphylococcus* sp. (outpatient 85 and inpatient 45) performed between 2003 – 2005 on outpatients and inpatients of both sexes are shown in Figure 1. The genus *Staphylococcus* sp. corre-

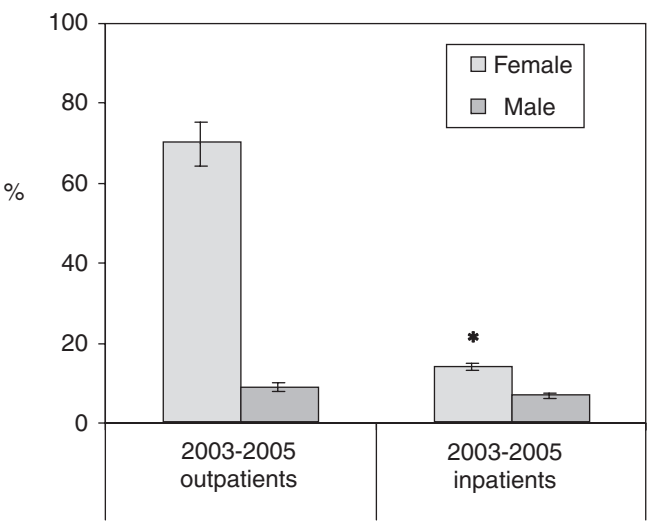

Figure 1. *Total resistance to antibiotics of* E. coli *and* Staphylococcus *sp. isolated from urine cultures in outpatients (n = 531) and inpatients (n = 143) over a three-year period. * p value < 0.05 outpatients vs. inpatients*

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sponded to 20% of *S. aureus* with predominance in inpatients. *Staphylococcus coagulase* negative was prevalent in out patient (data not show). If we analyze the results as per microbial species, the isolations of *E. coli* were found to represent 85% in female outpatients and 62% in male outpatients, with the corresponding percentages for *Staphylococcus* sp. being 74 and 46% respectively.

The data for the resistance of *E. coli* to TMS, NOR, GEN, NIT, AMP and CEF, obtained according to the characteristics of type of patient (outpatients n = 446 or inpatients n = 98) and gender are depicted in Table 1. In the isolates of *E. coli* in outpatients and inpatients, the resistance to NIT was lower than 22%. The resistance to GEN was 5.667% in female outpatients in contrast with 28.667% in female inpatients. When the resistance to TMS was evaluated in female outpatients and in patients, 35.667 and 47.667% tested positive respectively (Table 1), with these figures being 26.0 and 41.333 % for NOR.

The isolations of *E. coli* in male patients presented a resistance to GEN of 23.667% in outpatients and 37.333% in inpatients (Table 1). As son *Staphylococcus* sp., a low resistance to NIT (< 4%) was observed in both these types of patients, with this increasing to 55.333 and 70.0% in the resistance to GEN in female and male inpatients, respectively. There was also a remarkably high resistance to NOR in male outpatients (78.0%) (Table 2).

The global results are depicted in Figures 2 and 3, in which there is no gender differentiation. These reveal a low resistance of *E. coli* to NIT, both in outpatients and in inpatients, of close to 10% and an even lower one to *Staphylococcus* sp. (approximately 3%). Also, there is a resis-

Table 1. Female and male isolates with indicated resistance to *E. coli* (n = 544).

	Outpatients Resistant (%)		Inpatients Resistant (%)	
Antimicrobial agent	Female (n = 404)	Male (n = 42)	Female (n = 72)	Male (n = 26)
TMS	35.7 ± 3.2	31.0 ± 12.1	47.7 ± 5.9*	58.0 ± 14.1
NOR	26.0 ± 5.0	55.3 ± 23.2	41.3 ± 6.5*	76.0 ± 21.9
GEN	5.7 ± 4.0	23.7 ± 6.4	28.7 ± 9.0	37.3 ± 7.4
NIT	5.7 ± 1.5	13.3 ± 3.2	13.4 ± 5.7*	21.3 ± 11.9
AMP	59.0 ± 8.2	88.0 ± 10.4	81.7 ± 9.1*	81.7 ± 3.8*
CEF	19.3 ± 9.9	38.7 ± 18.5	35.3 ± 10.6	58.0 ± 14.1

* p value < 0.05 outpatients *vs.* inpatients

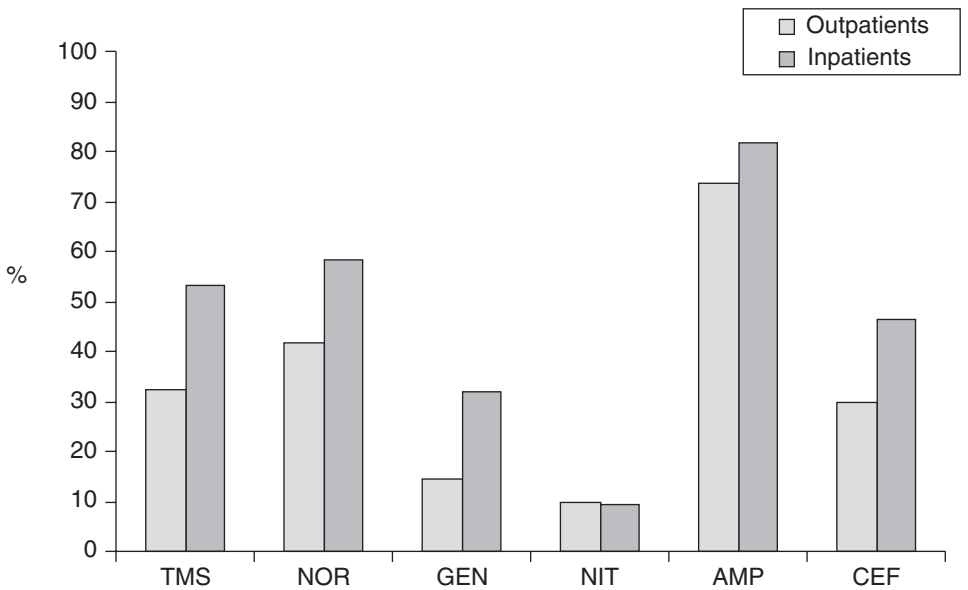

Figure 2. *Global resistance of* E. coli *isolated from urine cultures in outpatients (n = 446) and inpatients (n = 98).*

tance of *Staphylococcus* sp. to TMS. The global resistance to NOR was about 55%, and the resistance to AMP was higher than 70% in inpatients for both studied microorganisms. The average resistance of *Staphylococcus* sp. to GEN and CEF was 44 and 48.7% respectively and there was a low resistance of this bacterium to NIT whereas there was a high one to AMP.

In Figure 4, we can observe the tendency of the antibiotic resistance found in the isolates of *E. coli* in females outpatients (A) and inpatients (B) during 2003, 2004 and 2005 and global resistance outpatients *vs* inpatients (C). A tendency for a reduction in the resistance in female outpatients, took place except for NOR and GEN. There was a more remarkable increase in the resistance to TMS and NOR in male outpatients. A reduction in the resistance to CEF was observed in male outpatients.

The resistance of *E. coli* in female inpatients, to NOR tended to decrease. It is important to highlight the relevant sensitivity of NIT in both male and female patients.

There was a more remarkable increase in the global resistance to TMS and NOR in females inpatients (Figure 4C).

An analysis of *Staphylococcus* sp. covering the same period of time, shows a variable resistance to TMS y NIT being observed in outpatients, and a tendency for a reduction in the resistance to AMP, CEF Y GEN in out and inpatients of both sexes. We can observe that in inpatients there was a tendency for the resistance to NOR to be reduced (data not show).

DISCUSSION

The selection and prescription of an antimicrobial must be evaluated with more complex parameters whereby an

Table 2. Female and male isolates with indicated resistance to *Staphylococcus* sp. (n = 130).

	Outpatients Resistant (%)		Inpatients Resistant (%)	
Antimicrobial agent	Female (n = 67)	Male (n = 18)	Female (n = 24)	Male (n = 21)
TMS	16.3 ± 13.9	23.0 ± 17.0	24.7 ± 14.4	14.0 ± 10.4
NOR	28.0 ± 13.0	78.0 ± 23.1	63.7 ± 21.2	57.0 ± 20.4
GEN	13.3 ± 9.9	39.7 ± 31.8	55.3 ± 9.2*	70.0 ± 26.5
NIT	3.3 ± 5.8	3.0 ± 5.2	1.0 ± 0.0	2.7 ± 4.6
AMP	41.0 ± 16.7	68.0 ± 27.8	66.7 ± 16.5	76.7 ± 25.2
CEF	23.3 ± 9.5	51.3 ± 23.2	58.3 ± 14.1*	61.6 ± 14.4

* p value < 0.05 outpatients *vs.* inpatients

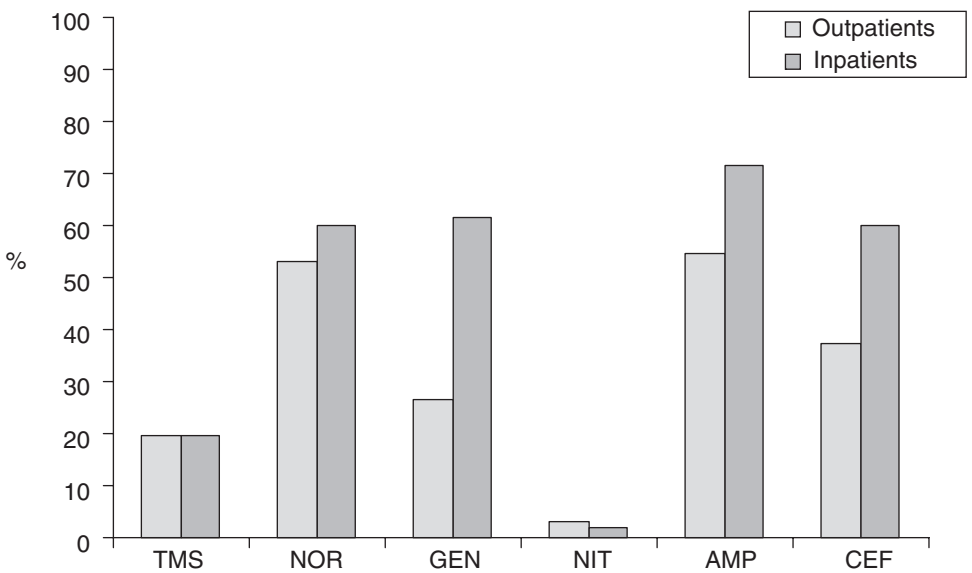

Figure 3. *Global resistance of* Staphylococcus *sp. isolated from urine cultures in outpatients (n = 85) and inpatients (n = 45).*

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accurate analysis of regional epidemiologic data can produce better results of the empirical therapies. In the case of UTI, it is indispensable to assess whether it is actually a UTI or a bacterial contamination, in both outpatients and inpatients. In this research, outpatients presented a higher number of urine infections, with women being the most affected and *E. coli* the bacterium most frequently isolated.

Most cases of UTI in the hospital setting are initially treated empirically based on the frequency of potential pathogens, local antimicrobial resistance rates and illness severity. The use of inappropriate empirical therapy to be able a predictor of mortality in patients who had bacteriemia originating from a urinary tract source. Catheter-associated urinary tract infections (CAUTIs) are cause of nosocomial infections. Additionally, the frequency distribution of pathogens causing CAUTIs might differ from of pathogens isolated from patients without catheters. The incidence of UTI caused by MRSA is increasing because patients are more frequently fitted with various urinary stents and catheters as endourology progresses technologically.[10] The resistance of these uropathogens to commonly prescribe antibiotics is clinically essential and would be helpful in improving the efficacy of empirical treatment. The use of the antibacterial agents has been reduced as much as possible, because the prolonged and uncontrolled use of antibacterial agents, especially third-generation cephalosporins, will induce the emergence of antimicrobial-resistant bacteria such as MRSA.[11]

In Argentina, TMS is the most common drug chosen for the treatment of non-complex urine infections, being effective against 85% of the urine pathogens occurring in this type of infection (*in vitro*) and having an even better clinical response thanks to the drug kinetic.[12,13] In our present study, we have observed that the community analyzed presented values of resistance of *E. coli* to TMS of between 35 and 60% in female and male outpatients respectively (p value < 0.05).

The second most frequent drug chosen for the treatment of non-complex urine infections is NOR. All data shown in this paper demonstrate a high resistance of *E. coli* to this antibiotic in inpatients. Similar results on the resistance of *E. coli* to fluorquinolones have also been found by other authors.[12] Moreover, some research has demonstrated that, in Argentina, NOR is used as an alternative drug, -between 3 or 4 times more than TMS, with the second most used drug being Cephalexin. In various research studies, 50% of antimicrobials have been demonstrated to be inadequately used.[13]

The use of Cephalosporin 1st. generation, cephalexin on cephadroxil is not recommended if the resistance rates of *E. coli* are higher than 20%.[13] In particular, Cephalexin should be only prescribed after proven sensitivity to

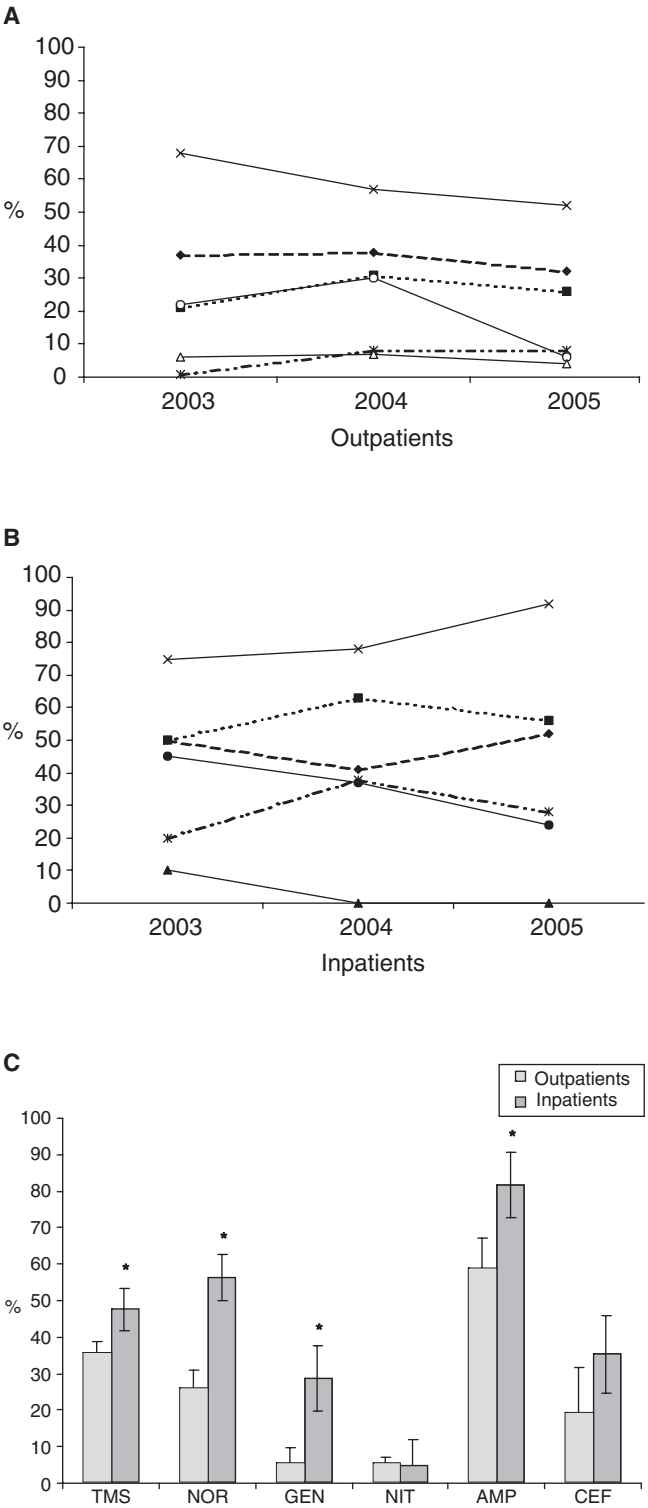

Figure 4. *The tendency of antibiotic resistance to TMS (◆), NOR (■), NIT(▲), AMP (×), GEN (*) and CEF (●) found in the isolates to* E. coli *in females outpatients (A) and inpatients (B) during 2003, 2004 and 2005. (C) Global resistance outpatients* vs *inpatients 2003-2005 (* p value < 0.05).*

this drug and on the basis of documented resistance to TMS and NOR. In the present study, we observed resistance indicators of 58% to TMS and 76% to NOR in male inpatients for the strains of *E. coli*. We must also consider that the use of alternative drugs may cause pressure on the germs' resistance, thus having an impact on future morbidity.

Lopardo et al presented results of the resistance of outpatients' *E. coli*, to NIT and GEN of 5 and 4% respectively.[13] In the current work, we observed resistance of *E. coli* to these antibiotics of 6 and 5%.

When evaluating UTI in male patients, we could observe a greater resistance of *E. coli* to both NOR and TMS. However, NIT was an exception, but its use is not recommended due to the low concentration that it reaches in tissues, and also because of the risk of prostitis, pyelonefritis and hidden pyelonefritis, which are quite frequent among male patients.[14-18]

We were able to determine the global resistance (in both sexes) of *E. coli* and *Staphylococcus* sp. to NOR - approximately 55%, and also show that the resistance to AMP was greater than 70% in inpatients. These values could be related to the use of high generation betalactamic antibiotics and new quinolones in the treatment of infectious pathologies associated to other illnesses in inpatients.

The values of resistance of *E. coli* to NIT are low in male as well as in female inpatients. These results may be conditioned by the little or no use made of nitrofurans in this type of patient due to the low concentrations found of this antibiotic in tissues and fluids, with the exception of urinary tract.

The variation profile over these three years has changed, with the most important impact being on inpatients and on NOR, GEN, AMP and CEF antibiotics.[19-21]

Few previous studies, have been undertaken in Argentina of a similar nature to this one, despite the fact that they are very important in any institution in order to plan the rational use of antibiotics and avoid the appearance of resistant strains as much as possible.

The results presented in this report confirm that bacterial resistance continues to be a great problem in the health care center. We postulate that the results obtained in this study could be generalized for other center that have the same epidemiological characteristics as ours. However, distinct local conditions such as local population, antimicrobial use and local infection control policies could result in differences in the etiology and susceptibility profile of bacterial pathogens.

Therefore, programs for the vigilance of anti-microbial resistance in all health care institutions should be implemented so that an assessment can be carried out of the modification of local resistance patterns and the selection of microorganisms in relation to the antimicrobials used, since microorganisms are considered to have the capacity to modify the susceptibility of a drug according to the exposed causes.

ACKNOWLEDGMENTS

MG Paraje is a career member of CONICET.

The authors want to thank the Ministerio de Salud Pública de Córdoba.

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