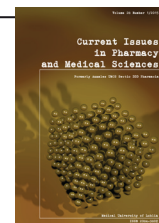


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A preliminary report on the susceptibility to aminoglycosides of *Escherichia coli* isolated from the community-acquired urinary tract infections in adults in south-east Poland

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ABSTRACT

World-wide, urinary tract infections (UTIs) are an important clinical problem. In such, the most frequently isolated uropathogen is *Escherichia coli*. In the treatment of uncomplicated UTIs, e.g. cystitis, the widely used antibiotics are nitrofurantoin, trimethoprim/sulfamethoxazole, fosfomycin trometamol or ciprofloxacin, while the treatment of pyelonephritis requires the usage of antibiotics with a broader spectrum of activity, such as cephalosporins of the 3rd and 4th generation, aminoglycosides or even carbapenems. The aim of this study was to assess the susceptibility to aminoglycosides (such as amikacin, gentamicin, netilmicin and tobramycin) of *E. coli* isolated from UTIs in adult community patients living in Lubelszczyzna. We found that all of the 86 strains of *E. coli* encountered were susceptible to amikacin. Moreover, the prevalence of susceptibility to tobramycin, gentamicin or netilmicin among the tested strains was found to be 89,5%, 90,7% or 94,2%, respectively. The data obtained in the present study shows the high susceptibility to aminoglycosides of *E. coli* isolated from the community-acquired UTIs in adults. These data, together with that derived from current literature, indicate that aminoglycosides, when employed in combination therapy with other antibiotics, may still be very useful group of antibacterial agents in the treatment of UTIs in Poland.

INTRODUCTION

Urinary tract infections (UTI) are a major clinical problem all over the world [1,6,10,14]. In this regard, nosocomial UTIs are the most prevalent healthcare-associated infections, but community-acquired UTIs occupy the second place after respiratory tract infections. The most common bacterial agent responsible for UTIs is *Escherichia coli* [7]. Colonization of the urethra by fecal microorganisms may lead to the their upward spread to the bladder or even kidney, causing cystitis or pyelonephritis, respectively. The virulence factors predisposing *E. coli* to induce UTIs are the surface adhesions (with the most important being *P fimbriae*), and the toxins, alpha-hemolysin (HlyA) or cytotoxic necrotizing factor 1 (CNF1) [2,3].

In the community, the most common type of UTI are uncomplicated infections such as cystitis. However, in actuality, these infections may become complicated, resulting in pyelonephritis or even the blood infections called 'urosepsis'

[4]. In the treatment of uncomplicated cystitis, the most often used antibiotics are nitrofurantoin, trimethoprim/sulfamethoxazole, fosfomycin trometamol or ciprofloxacin, while the treatment of pyelonephritis or urosepsis requires the usage of antibiotics with a broader spectrum of activity. Among these are cephalosporins of the 3rd and 4th generation, aminoglycosides or even carbapenems [4]. Aminoglycosides are the drugs that express the broadest spectrum of activity against Gram-positive and Gram-negative aerobic bacteria, including fermentative and non-fermentative Gram-negative rods [8].

The aim of this study was to assess the susceptibility to aminoglycosides such as amikacin, gentamicin, netilmicin and tobramycin, of the *E. coli* isolated from UTIs in adult patients living in Lubelszczyzna.

MATERIALS AND METHODS

Bacterial strains: A total of 86 *E. coli* strains were isolated from urine samples drawn from adult community patients living in Lubelszczyzna, with UTIs. These strains

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were confirmed microbiologically as significant bacteriuria. Routine bacteriological methods were then used for cultivation of the urine sample, while the evaluation of the species was done by using Vitek 2 Compact (bioMérieux). This study was approved by the local bioethics committee, number: KE-0254/75/2011.

Drug susceptibility: The evaluation of susceptibility to aminoglycosides such as amikacin, gentamicin, netilmicin and tobramycin, of the *E. coli* strains tested, was based on the disc diffusion method according to The European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines, version 5.0 [15]. On the basis of the obtained results, the strains were categorized into one of the following groups: susceptible, intermediate susceptible or resistant (Table 1).

Table 1. The zone diameter breakpoint of aminoglycosides for fermentative Gram-negative rods, according The European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines, version 5.0 [15]

Category of susceptibility	Antibiotic (zone diameter breakpoint in millimeters)			
	Amikacin	Gentamicin	Netilmicin	Tobramycin
Susceptible	≥18	≥17	≥15	≥17
Intermediate susceptible	15-17	14-16	12-14	14-16
Resistant	<15	<14	<12	<14

RESULTS

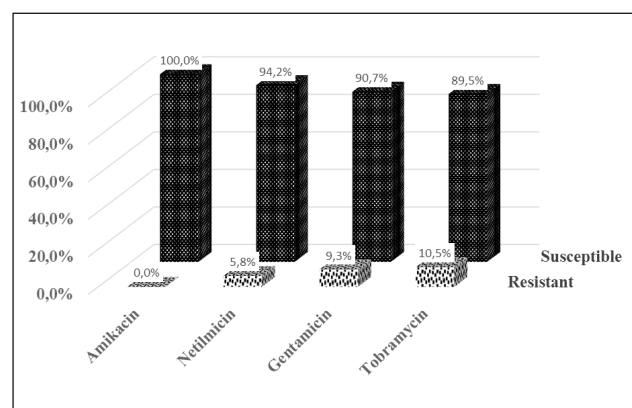


Figure 1. The susceptibility to aminoglycosides of *Escherichia coli* isolated from adults with urinary tract infections

Figure 1 shows data on susceptibility to aminoglycosides such as amikacin, gentamicin, netilmicin and tobramycin, of the 86 *E. coli* strains, as tested by the disc diffusion method. The work shows that all of the 86 strains were susceptible to amikacin. Among the tested strains, susceptibility to netilmicin was found in 81 (94.2%) isolates, that to gentamicin, in 78 (90.7%) isolates, and that to tobramycin, in 77 (89.5%) isolates. Moreover, the resistance rate was found to be 5.8-10.5%. Table 2 presents the drug resistance patterns to aminoglycosides of isolated *E. coli*. As evident in the tabled data, we found that one strain (1.2%) was resistant only to gentamicin, while to other aminoglycosides, the resistance patterns were detected as following: tobramycin and netilmicin – 1 (1.2%) strain, gentamicin and tobramycin – 3 (3.5%) strains, gentamicin with tobramycin and netilmicin – 4 (4.6%) strains.

Table 2. The drug resistance patterns to aminoglycosides of *Escherichia coli* isolated from adults with urinary tract infections

Drug resistance patterns	GM+TOB+NET	GM+TOB	TOB+NET	GM
Resistance strains	4 (4,6%)	3 (3,5%)	1 (1,2%)	1 (1,2%)

Legend: GM – gentamicin, TOB – tobramycin, NET – netilmicin

DISCUSSION

Aminoglycosides inhibit bacterial protein synthesis by binding with the 30S ribosomal subunit. They are active only against aerobic bacterias, as the transport across the cytoplasmic membrane is an oxygen-dependent process. However, they express a bactericidal effect against a broad spectrum of microorganisms, such as Gram-positive and Gram-negative, including fermentative and non-fermentative Gram-negative rods [8]. Aminoglycosides are commonly used in the combination with other antibiotics (broad spectrum beta-lactams or fluoroquinolones), as doing so promotes their penetration through the bacterial cell wall and also reduces the appearance of common aminoglycoside side effects [8]. As the result of their antibacterial activity, these antibiotics are the one of the drugs recommended for the treatment of acute pyelonephritis or urosepsis [4,8]. According to European Recommendations, this group of antibacterial agents should be administered as a consolidated 24 hours dose in combination with oral fluoroquinolones, including ciprofloxacin or oral beta-lactams. However, the application of aminoglycosides may be limited by the appearance of resistant strains. Yet, aminoglycosides usage, in combination with other antibiotics, but not in monotherapy, can be regarded as an important factor limiting the emergence of resistance [4,8].

E. coli seems to be still the most important uropathogen, especially in community-acquired infections. Indeed, 60-95% of all UTIs in the community were reported to be caused by this bacterial species [1,10]. The data obtained in the present study shows the high susceptibility of *E. coli* isolated from adult patients with community-acquired UTIs. With regard to treatment, susceptibility to gentamicin, netilmicin and tobramycin has been found in about 90% or more of the strains, while to tobramycin, susceptibility was detected in all of the isolates tested. These data are in agreement with those from the literature [13]. Data by Sorlozano *et al.* [14] present the susceptibility of *E. coli* involved in community-acquired and nosocomial UTIs in Spain during a 7-year period (2006-2013). Accordingly, there were also no significant differences in the susceptibility patterns between the community and hospital isolates for amikacin, gentamicin and tobramycin. In the report, the highest susceptibility was found in case of amikacin (97.3%-99.5%), with annual resistance rates < 5%. A retrospective analysis of Ironmonger *et al.* [7] reveals that gentamicin susceptibility of *E. coli* isolates from urine samples of patients from the community and from hospitals, for the period 2010-2013, in the United Kingdom, was high, with the resistance rate being 5-7% for the community isolates. Huang *et al.* [6] also studied the antimicrobial susceptibility pattern among *E. coli* isolates from UTIs, including community-acquired infections in Taiwan, in 2012. They also found the highest sensitivity to

amikacin (> 99%), while a lower susceptibility was seen to gentamicin (63.5%). However, Jafri *et al.* [9], in performing a study on antibiotic resistance of *E. coli* isolates drawn from urine samples in hospitalized patients in 2014, in Pakistan, found extremely high resistance rates to aminoglycosides (for amikacin - 55%, and for gentamicin – 70%). In contrast, Soleimani *et al.* [13] found high sensitivity to amikacin (93.8%) and netilmicin (91.3%) and somewhat lower sensitivity to gentamicin (77.5%) and tobramycin (75.4%) among *E. coli* isolates obtained from samples obtained in an Iranian hospital. Several mechanisms of aminoglycoside resistance have been described, however, that which is of major importance from the clinical and epidemiological viewpoints, is the resistant bacteria's ability to produce aminoglycoside modifying enzymes. These enzymes are divided into the three classes: aminoglycoside acetyltransferases (AACs), aminoglycoside phosphotransferases (APHs) and aminoglycoside nucleotidyltransferases (ANTs), also known as adenyltransferases [8,12,13]. The clinical significance of this phenomenon results in differences in the drug resistance patterns of the strains to aminoglycosides, as an end effect of the different spectrum of activity of the produced enzymes against each of the aminoglycosides. The total effect of the individual enzymic activity can lead to the cross-resistance of microorganisms to this group of antibiotics. In the presented studies, the isolated *E. coli* usually expressed a resistance to three aminoglycosides: gentamicin, tobramycin and netilmicin. This is probably the result of producing by the encountered strains, aminoglycosides acetyltransferases type AAC(3'')-II or AAC(3'')-IV [8,11-13].

CONCLUSION

The data presented in this paper, together with that derived from the literature, indicate that aminoglycosides, with their high activity against uropathogenic *E. coli*, when used in combination therapy with other antibiotics, may still be a very useful group of antibacterial agents in the treatment of UTI's in several countries, including Poland.

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