SUSCEPTIBILITY OF STREPTOCOCCUS PNEUMONIAE TO FLUOROQUINOLONES AND MACROLIDES IN UPPER RESPIRATORY TRACT INFECTIONS

Yaroslav O. Mykhalko[1], Tetyana V. Duhovych[1], Pavlo P. Kish[2]

[1] SHEI "UZHHOROD NATIONAL UNIVERSITY", FACULTY OF POSTGRADUATE EDUCATION AND PRE-UNIVERSITY TRAINING, DEPARTMENT OF THERAPY AND FAMILY MEDICINE, UZHHOROD, UKRAINE

[2] SHEI "UZHHOROD NATIONAL UNIVERSITY", MEDICAL FACULTY, DEPARTMENT OF MICROBIOLOGY, VIROLOGY, IMMUNOLOGY WITH THE COURSE OF INFECTIOUS DISEASES, UZHHOROD, UKRAINE

ABSTRACT

Introduction: Streptococcal species are known as the most common cause of bacterial upper respiratory tract infections (URTI). Once bacterial infection is diagnosed it demands empirical antibiotic prescription. On the other hand antimicrobial resistance is a global burden in today's medicine. For that reason, knowing of antimicrobial susceptibility patterns in population is an important background for successful treatment of bacterial caused URTI.

The aim of this study was to analyze S. pneumoniae resistance and susceptibility patterns to fluoroquinolones and macrolides in URTI.

Materials and methods: The results of microbiological examination of 2,055 pharyngeal swabs taken from patients with bacterial caused tonsillitis, pharyngitis and laryngitis were analyzed. Antimicrobial susceptibility testing for levofloxacin, ofloxacin, gatifloxacin, erythromycin, clarithromycin, azithromycin was performed with the disk-diffusion method.

Results: The incidence of S. pneumoniae in the etiological structure of bacterial caused URTI was increasing from 22.47% of cases in 2011 to 36.48% in 2015. The susceptibility of this microorganism to ofloxacin, gatifloxacin and levofloxacin decreased from 96.25%, 100% and 95.00% in 2011 to 44.22%, 65.99% and 62.59% in 2015 respectively. The susceptibility of S. pneumoniae to erythromycin, azithromycin and clarithromycin also decreased from 30.00%, 63.75% and 41.25% in 2011 to 6.80%, 26.53%, 27.21 in 2015.

Conclusions: Among investigated antibiotics levofloxacin can be recommended for empiric therapy of URTI because of high pneumococci susceptibility to this drug.

KEY WORDS: Streptococcus pneumoniae, susceptibility, fluoroquinolones, macrolides.

Wiad Lek 2017, 70, 2, cz. I, 224-226

INTRODUCTION

Today, Streptococcus pneumoniae is considered as the most common cause of acute bacterial upper respiratory tract infections (URTI) [1, 2]. On the other hand, pneumococcal infection is one of the most dangerous due to high morbidity and mortality rates [3]. According to data, published by Ministry of Health of Ukraine, the incidence of pneumococcal infection among adults in 2007 and 2008 was 411 and 394 of 100 000 respectively. The highest incidence was reported in Kiev, Poltava and Ternopil regions [4]. Treatment of patients with pneumococcal infection is based on the use of antibiotics, mostly penicillins. However, since 1967 penicillin-resistant S. pneumoniae strains have been reported. In 1980s, the problem of antimicrobial resistance become be global. First multi-drug resistant pneumococcal strain was isolated in 1977 in South Africa. Since the mid-90s of last century resistance of this microorganism to lactam antibiotics, macrolides and fluoroquinolones began to grow steadily [5]. According to the European Antimicrobial Resistance Surveillance System, at the end of 2015 resistance of S. pneumoniae to penicillin varied in wide ranges from. In the majority of European countries resistance did not exceed 5 % but in the eastern part of the continent it was over 15%. Thus, in Slovakia pneumococcal resistance to penicillin was 18.5%, in Croatia – 19.0%, in Bulgaria – 22.9% and in Romania – 28.8% [6]. There are reports of high pneumococcal resistance to cotrimoxazole (66.7%), azithromycin (55.6%), erythromycin (16.7%), chloramphenicol (16.7%) and clindamycin (11.1%) [7]. Among the global trends of pneumococcal antibiotic resistance it is worth to mention about decreasing susceptibility to macrolides [8]. Thus, according to Torumkuney and coauthors, susceptibility of S. pneumoniae to these antimicrobial agents in South Korea was reported as 20% but in Thailand, Singapore and India ranged between 50%-60% [9]. There are also an increasing number of reports on strains resistant to glycopeptides, tetracyclines, sulfonamides, chloramphenicol and rifampin [10].

THE AIM

The aim of this study was to analyze S. pneumoniae resistance and susceptibility patterns to fluoroquinolones and macrolides in URTI.

MATERIALS AND METHODS

This study included data of bacteriological examination of 2,055 pharyngeal swabs taken from patients treated in Uzhhorod outpatient facilities during 2011-2015 due to bacterial caused tonsillitis, pharyngitis and laryngitis. Isolation and cultivation of pathogens were performed according to standard methods in the Uzhhorod central clinical hospital microbiology laboratory. Antimicrobial susceptibility testing was performed by the disk-diffusion method. The following disks with antibiotics were used: levofloxacin (5 mg), ofloxacin (5 mg), gatifloxacin (5 mg), erythromycin (15 mg), clarithromycin (15 mg), azithromycin (15 mg). All the statistical inferences were carried out using Statistica® software.

RESULTS AND DISCUSSION

Among all identified in the study pathogens S. pneumoniae was found as the most common cause of acute bacterial URTI. Besides, the incidence of this microorganism was growing year by year. Thus, in 2011 S. pneumoniae was isolated in 22.47% of cases, and in 2015 – in 36.48% (table. I).

Also an increasing frequency of Str. pyogenes caused infections (from 13.48% in 2011 to 19.11% in 2015) was found. However, reducing levels of S. aureus, Str. agalactiae and Candida spp. (from 34.55%, 19.94% and 8.99% in 2011 to 22.83%, 14.39% and 5.46% in 2015 respectively) was noticed.

Analysis of S. pneumoniae antimicrobial susceptibility to fluoroquinolones during the studied period showed a statistically significant decrease in the susceptibility of this pathogen to studied antibiotics. Thus, the susceptibility to ofloxacin decreased almost by half (from 96.25% in 2011 to 44.22% in 2015, $p<0.001$). Susceptibility to gatifloxacin and levofloxacin also decreased, although not so significantly (from 100% and 95.00% in 2011 to 65.99% and 62.59% in 2015 respectively, $p<0.001$). These changes of antimicrobial susceptibility were at the background of increasing resistance (table. II).

In particular, antimicrobial resistance of S. pneumoniae to ofloxacin rised from 3.75% in 2011 to 30.61% in 2015 ($p<0.001$), to levofloxacin – from 5.00% to 19.05% ($p=0.003$) and to gatifloxacin from 0.00% to 17.01% ($p<0.001$).

It should also be noted a steady increase frequency of intermediate resistant strains occurrence. So, in 2011 there were no detected cases of intermediate antibiotic resistance to studied fluoroquinolones, but in 2015 this values were 17.01%, 25.17% and 18.37% to gatifloxacin, ofloxacin and levofloxacin, respectively. This increment in percentage of pneumococcal strains with intermediate resistance to tested fluoroquinolones was statistically significant ($p<0.05$).

Analysis of S. pneumoniae susceptibility patterns to macrolides showed that susceptibility to erythromycin significantly decreased almost in 4.5 times (from 30.00% in 2011 to 6.80% in 2015, $p<0.001$). Susceptibility of this microorganism to azithromycin also significantly decreased (from 63.7552% to 26.53%, $p<0.001$). A decreasing susceptibility trend to clarithromycin (from 41.25% to 27.21%, $p=0.053$) was also found. In contrast, statistically significant increasing in frequency of pneumococci strains resistant to erythromycin (from 46.25% to 77.55%, $p<0.001$), clarithromycin (from 35.00% to 49.66%, $p=0.037$) and azithromycin (from 31.25% to 48.98%, $p=0.012$) took place (table. III).

Researching the peculiarities of intermediate resistance patterns showed its decreasing for erythromycin (from 23.75% to 15.65%, $p>0.05$), and statistically significant increasing to azithromycin (from 5.00% to 24.49%, $p<0.001$), however intermediate resistance to clarithromycin remained at almost the same level (23.75% in 2011 and 23.13% in 2015, $p>0.05$) during the studied period.

CONCLUSIONS

According to received results, S. pneumoniae is one of the most common causative agent of acute bacterial URTI. The frequency of this pathogen is constantly rising. Among investigated fluoroquinolones levofloxacin can be recommended for empiric therapy because of high susceptibility of pneumococci to this drug. Despite good susceptibility and resistance patterns to gatifloxacin, a relatively high frequency of described serious side effects, particularly cardiovascular, restricts its use as a drug of choice. Low susceptibility of S. pneumoniae to studied macrolides combined with

Table I. The structure of pathogens in acute bacterial URTI (%).

Pathogen \ Year	2011, n=356	2012, n=419	2013, n=436	2014, n=441	2015, n=403
S. pneumoniae	22,47	20,29	32,11	33,79	36,48
Str. pyogenes	13,48	20,29	19,04	23,13	19,11
S. aureus	34,55	35,80	23,17	19,05	22,83
Str. agalactiae	19,94	15,99	17,89	17,69	14,39
Candida species	8,99	6,21	7,80	4,99	5,46

n – number of tested isolates

Table II. S. pneumoniae resistance and susceptibility patterns to fluoroquinolones (n, %).

Pathogen / Year	Gatifloxacin,%			Ofloxacin, %			Levofloxacin, %		
	R	S	I	R	S	I	R	S	I
2011, n=80	0,00	100,00	0,00	3,75	96,25	0,00	5,00	95,00	0,00
2012, n=85	3,53	94,12	2,35	3,53	96,47	0,00	3,53	96,47	0,00
2013, n=140	3,57	92,86	3,57	3,57	90,71	5,71	4,29	92,14	3,57
2014, n=149	8,72	81,88	9,40	8,72	81,88	9,40	18,12	75,17	6,71
2015, n=147	17,01*	65,99*	17,01*	30,61*	44,22*	25,17*	19,05*	62,59*	18,37*

R – resistant;
S – sensitive;
I – intermediate;
n – number of isolates;
** - the difference is statistically significant when comparing data between 2011 and 2015 ($p<0.05$).*

Table III. S. pneumoniae resistance and susceptibility patterns to macrolides (n, %)

Pathogen / Year	Erythromycin, %			Azithromycin, %			Clarithromycin, %		
	R	S	I	R	S	I	R	S	I
2011, n=80	46,25	30,00	23,75	31,25	63,75	5,00	35,00	41,25	23,75
2012, n=85	20,00	62,35	17,65	28,24	71,76	0,00	34,12	54,12	11,76
2013, n=140	35,71	44,29	20,00	32,14	47,14	20,71	49,29	27,14	23,57
2014, n=149	43,62	33,56	22,82	52,35	36,91	10,74	38,93	40,27	20,81
2015, n=147	77,55*	6,80*	15,65	48,98	26,53*	24,49*	49,66*	27,21	23,13

R – resistant;
S – sensitive;
I – intermediate;
n – number of isolates;
** - the difference is statistically significant when comparing data between 2011 and 2015 ($p<0.05$).*

quite high level of intermediate resistant strains does not allow to recommend these antibiotics as a first-line drugs in URTI treatment unless maximal therapeutic doses can be used.

REFERENCES

1. А. Є. Абатуров, О. М. Герасименко, Особенности антибактериальной терапии респираторных инфекций у детей. Здоровье ребёнка. 2014. 5 (65). 61–65.
2. С.М. Пухлик, Адекватная терапия острого тонзилита. Журнал вушних і горлових хвороб. 2016. 3. 122.
3. Козлов Р.С. Антимикробная резистентность Streptococcus pneumoniae в России: результаты проспек тивного многоцентрового исследования (фаза А проекта ПеГАС I), КМАХ. 2002. 3, Т. 4. 267–277
4. Ю. И. Фещенко, А. Я. Дзюбик, Рациональная антибиотикотерапия больных с инфекциями нижних дыхательных путей. Український пульмонологічний журнал. 2009. 4. 5–8
5. TI. Welte, A. Torres, A. Nathwani, Clinical and economic burden of community-acquired pneumonia among adults in Europe. Thorax. 2012. Vol. 67(1). 71-9
6. Surveillance Atlas of Infectious Diseases. Available from: URL: http://atlas.ecdc.europa.eu/public/index.aspx?Instance=GeneralAtlas
7. P. Krishnan, P. Rajendran, A. P. Sambandan [et al.], Evaluation of coamoxiclav and other antibiotics against S. pneumonia and H. influenae from paediatric cases of acute respiratory infections. J Indian Med Assoc. 2011. Vol. 109 (4). 241–2, 244.
8. S. G. Jenkins, D. J. Farrell, Increase in pneumococcus macrolide resistance, United States. Emerg. Infect. Dis. 2009. Vol. 15 (8). 1260–1264.
9. D. Torumkuney, R. Chaiwarith, W. Reechaipichitkul [et al.], Results from the Survey of Antibiotic Resistance (SOAR) 2012-14 in Thailand, India, South Korea and Singapore. Antimicrob. Chemother. 2016. Vol. 71. 13–19.
10. J. D. Fuller, D. E. Low, A review of Streptococcus pneumoniae infection treatment failures associated with fluoroquinolones resistance. Clin. In fect. Dis. 2005. Vol. 41. 118–121.

ADDRESS FOR CORRESPONDENCE:
Yaroslav Mykhalko.
Mynaiska str., 71, Uzhhorod, Ukraine.
tel: +380312664694
e-mail.: yaroslavik@gmail.com

Nadesłano: 20.03.2017
Zaakceptowano: 20.04.2017

TOM LXX, 2017, Nr 2 część I

cena 30 zł
(w tym VAT)

Wiadomości Lekarskie

ISSN 0043-5147

Czasopismo Polskiego Towarzystwa Lekarskiego

Rok założenia 1928

CZASOPISMO INDEKSOWANE W PUBMED/MEDLINE, EBSCO, INDEX COPERNICUS oraz MNiSW (11 pkt), SCOPUS
I POLSKIEJ BIBLIOGRAFII LEKARSKIEJ