EMPIRICAL FIRST-LINE ANTIBIOTICOTHERAPY IN ADULT RURAL PATIENTS WITH ACUTE RESPIRATORY TRACT INFECTIONS

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Abstract: The objective of the study was the evaluation of the frequency of occurrence of acute respiratory infections among rural population from the Lublin Region, and verification of the appropriateness of the use of antibiotics in empirical first-line therapy of these diseases. The analysis covered medical records concerning 1,839 patients selected from 27 rural health centres within the period of one year (1 September 2005–31 August 2006). As many as 656 patient visits were recorded, the reasons for which were qualified by physicians as infections of the upper and lower airways. These disorders were diagnosed in 450 patients, which constituted 24.46% of the population examined. The following diagnoses were most frequently made: acute pharyngitis and tonsillitis (31.25% of the total number of diagnoses), acute upper respiratory infections of multiple and unspecified sites (22.25%), and common cold (21.64%). Antibiotics were used in empirical first-line therapy in as many as 82% of the total number of patients. The analysis showed that in the great majority of cases the use of antibiotics was inappropriate. If this situation persists, in the near future it will lead to an increase in the phenomenon of antibioticoresistance in Poland. In order to prevent this situation, it is necessary to carry out an extensive educational action concerning the hazardous effect of excessive use of antibiotics, both among physicians and the whole society.

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INTRODUCTION

In Poland, acute respiratory tract infections are among the most frequent causes of patients’ reporting to primary health care facilities [11]. However, there is a lack of precise data concerning the scale of this problem, and similarly, there is a lack of data pertaining to the correctness of the treatment applied in these diseases. The few reports published to-date usually concern the urban population [5]. It seems that the rural population, due to the exposure to changeable weather conditions in association with the occupation performed, is especially susceptible to the occurrence of acute respiratory infections.

The objective of the presented study was the evaluation of the frequency of occurrence of acute respiratory diseases among the rural population from the Lublin Region, and the verification of the appropriateness of the use of antibiotics in empirical first-line therapy of these diseases.

MATERIAL AND METHODS

The Lublin Region is a small province of an agricultural-industrial character, with a population of approximately 2,100,000. This region is one of the poorest areas in the European Union. Over 52% of the population are rural inhabitants, the majority of them working on rather small-
size production farms. There are 297 primary health care centres functioning in this area. One health centre covers with care approximately 3,500 rural inhabitants. The centres are open 5 days a week, the material for laboratory tests is taken once, or more rarely twice a week and sent to specialist laboratories. The distance to specialist health care facilities is from several to several dozen kilometres.

The analysis covered medical records of 1,839 patients from 27 rural health centres concerning the period of one year – 1 September 2005–31 August 2006. From among all the diagnoses, only newly diagnosed cases of acute respiratory tract infections were selected in patients who had no medical history of chronic respiratory diseases. A nosologic unit was considered as a unit de novo if at least one month had elapsed from the previous infection of the airways. Age and gender of patients were recorded, as well as the fact of prescribing or not prescribing an antibiotic by a physician during the first visit, as well as the type of antibiotic used. The diagnoses made by physicians were not subjected to verification. In order to enable the comparison of the treatment pattern applied with those recommended in the Recommendations 2003 Respiratory tract infections – etiology, diagnosis, treatment, and the ICD-10 classification (International Statistical Classification of Diseases and Health problems. Tenth Revision), the following nosologic units: acute pharyngitis and acute tonsillitis were handled as one group – acute pharyngitis and tonsillitis [15].

Statistical package Statistica 6.1 PL was applied, the relationships were examined with the use of chi-square test and analysis of variance (ANOVA).

RESULTS

The documentation concerning 1,839 patients contained the records of 656 visits, the reason for which was qualified by a physician as infection of the upper and lower airways. Respiratory infections were diagnosed in 450 patients, which constituted 24.46% of the population examined. In 306 patients (16.74%) one episode of respiratory tract infection occurred within one year, in 98 patients (5.32%) – two, in 31 patients (1.68%) – three episodes, whereas in 14 (0.76%) – four episodes of respiratory infection. In one patient, as many as five respiratory tract infections occurred within one year.

Acute pharyngitis and tonsillitis was diagnosed in 205 patients, which constituted 11.13% of the total number of respiratory diseases diagnosed. In 146 patients (22.25%) acute upper respiratory infection of multiple and unspecified sites was diagnosed, in 142 (21.64%) – a common cold, in 60 (9.14%) – acute bronchitis, in 56 (8.53%) – acute sinusitis, and in 24 (3.65%) acute laryngitis and tracheitis. The remaining diseases were rarely diagnosed: in 10 patients (1.52%) – pneumonia, in nine (1.37%) – otitis media, and in four patients (0.61%) – influenza.

While analysing all the cases of respiratory tract infections diagnosed it was noted that antibiotics were applied in empirical first-line therapy in 538 patients, which constituted 29.72% of all cases, followed by amoxicillin with clavulanic acid (13.72%), macrolides (11.89%), doxycycline (11.13%), second generation cephalosporins (6.4%), linkosamides (3.5%), first generation cephalosporins (2.7%), sulphonamethaxsole and trimetoprim TMP-SMX (1.68%). Other antibiotics were used sporadically: fusofungine in 1.06% of cases, and natural penicillin was applied in only one case.

Antibiotics were used in all cases of pneumonia and otitis media, in laryngitis and tonsillitis antibiotics were applied in 90.24% of patients, in acute bronchitis – in 90%, in acute upper respiratory infections of multiple and unspecified sites – 87.67%, in acute sinusitis – 87.75%, in acute laryngitis and tracheitis – 83.33%, in common cold – 57.25%, and in influenza – in 25% of patients.

Among 205 cases of acute pharyngitis and tonsillitis diagnosed, antibiotics were used in 90.24% of patients. The most frequently used antibiotic was amoxicillin (38.05%
Acute bronchitis was diagnosed in 60 patients. Antibiotic was used in 90% of patients with this diagnosis. The antibiotic most frequently prescribed was doxycycline (21.66%), followed by macrolides (20%), second generation cephalosporins (15%), and amoxicillin (11.66%). The remaining antibiotics were applied in single cases. Otitis media was diagnosed in nine patients. In all patients antibioticotherapy was applied. In the presented study, no statistically significant differences in the use of antibiotics were observed according to patients’ gender (p = 0.206). Antibiotics were administered to 84.68% of males and 80.65% of females aged 18-40, and to 85.11% of patients aged 41-60. Antibiotics were most rarely administered to patients aged over 60 (72.73% of cases).

**DISCUSSION**

Acute respiratory tract infections are one of the most frequent causes of patients’ reporting to primary health care physicians. According to the data by the National Ambulatory Care Survey in the USA, in 2002 acute pharyngitis constituted 1.1% of the total number of causes of patient visits to primary health care, and was among 20 of the most frequently made diagnoses [5]. Rural population, due to the specific character of everyday life and work in changeable weather conditions is especially exposed to the frequent occurrence of respiratory diseases. However, the number of these diseases may be reduced due to the lack of air pollution. According to various sources acute respiratory infections affect from 10-20% to several dozen percent of the population [5, 7]. This depends on many reasons, including weather conditions during a given time, viral epidemics, etc. The documentation analysed shows that acute respiratory infections occur in 24.46% of patients. It should be emphasized that during the period of the study no epidemics of viral diseases were noted in the area of the Lublin Region.

Clinical diagnosis of acute respiratory infection usually does not cause difficulties and in typical cases is based on the diagnosis of, among other things, fever, weakness, increased amount of sputum in the nasopharyngeal cavity, cough, and red throat. These symptoms, however, are not characteristic for individual nosologic units, and do not allow the determination of the microbe causing the infection, nor even to differentiate viral or bacterial etiology. Apart from clinical examination, medical history taking and own experience, bacteriological, viral and rapid streptococcal tests may be performed in order to confirm the diagnosis. The following is useful in order to detect bacterial etiology of the disease: Berg’s principle for foreseeing acute bacterial infection of the nasal and sinus mucosa, and Centor’s Scale in pharyngitis caused by type A beta-hemolytic streptococci [1, 4].

Own studies show that while making a definite diagnosis, family physicians were mainly guided by complaints reported by a patient, clinical examination and own
experience. Only in several patients bacteriological tests were performed. None of the patients was referred for a viral test, nor a rapid streptococcal test, also none of the patients was referred for specialist consultation. The above-quoted results are consistent with other observations made in Poland. In urban centres physicians also sporadically perform diagnostic tests [5, 6].

Since 1995, efforts have been undertaken by the Forum on Advancement of Infection Diseases Management – FAIDM consisting of experts from East-European countries, which established the patterns of antibioticotherapy adjusted to the conditions in individual countries. These patterns, on assumption, have no character, canons, nor rigours, but are only the recommendations for undertaking rational procedures. The result of efforts by Polish experts was the development of ‘Recommendations ’97 for treatment of upper respiratory infections’. These guidelines were up-dated in 2003 [15]. While making the diagnosis physicians used the ICD-10 scale which served reporting purposes. However, there are great discrepancies concerning nomenclature between ICD-10 classification and the classification of respiratory diseases used in the recommendations developed. The ICD classification does not consider new achievements of knowledge pertaining to the etiology and pathogenesis of diseases. Due to the lack of, or not using bacteriological tests for verification, the physicians having no diagnostic certainty overused the diagnosis – acute upper respiratory infections of multiple and unspecified sites. In the presented study, such a diagnosis was made in as many as 22.25% of cases. This percentage is three times higher than that noted in Polish studies concerning urban areas, where the percentage of uncertain diagnoses was 7.8% [5, 6]. Not performing verification tests results also from the considerable distance between primary health care units and specialist laboratories, as well as from the fact that the material for testing is taken generally only once a week, which would require another visit by a patient to a PHC unit. Difficulties with making the correct diagnosis may also result from the fact that, in Polish conditions, patients report to primary health unit early, immediately after the occurrence of the first symptoms, e.g. fever, before the manifestation of the whole clinical image. In many European countries, schemes have been developed for patient self-treatment, recommending the taking of specified drugs at individual phases of the disease. A visit to a physician is recommended only in the case of lack of the effects of to-date treatment. In patients reporting to a physician there usually occurs a more unequivocal image of the disease, which considerably facilitates making a correct diagnosis.

For many years, in many countries, including Poland there has been a discussion devoted to the appropriateness of the use of antibiotics in acute respiratory infections. Increasingly more often the necessity is considered of adopting the tactic of watchful waiting, and the application of antibiotics only in cases in which no considerable improvement is observed despite treatment, or when there occurs a deterioration of the state of health. The effectiveness of individual groups of antibiotics in infections with bacterial etiology is also considered [15]. Modern rational antibioticotherapy is based on the application of so-called standards or patterns of treatment. In the USA, these patterns have the character of legal canons, because their non-observance exposes the physician to legal responsibility. In other countries, e.g. in the United Kingdom and Sweden, the use of antibioticotherapy patterns is restricted by financial rigors – the lack of their observance and application of an antibiotic which is more expensive than within the scheme may result in the lack of cost reimbursement for the purchase, and therefore the physician may be liable for the financial responsibility. In the countries where there are no unequivocal antibioticotherapy patterns, e.g. in France and other Mediterranean countries, there is a rapid increase in the phenomenon of antibioticoresistance [9, 13].

The educational actions concerning the hazardous effect of excessive use of antibiotics undertaken, which cover both the physicians and patients, have led to a considerable reduction in the use of antibiotics in acute respiratory infections [16]. New studies confirm that viruses are responsible for the majority of respiratory diseases, and the use of antibiotics in these diseases is not advantageous, but only leads to an increase in the phenomenon of antibioticotherapy. Within the framework of the Alexander Project, in Poland, the etiopathogenesis of individual respiratory tract diseases and resistance of bacterial strains to the antibiotics used is being constantly monitored. In Poland, Streplococcus aureus, Hemophilus influenzae, Moraxella cataralis, and less often Streptococcus pyogenes, Staphylococcus aureus, Mycoplasma pneumoniae, Pseudomonas aeruginosa, and anaerobic bacteria are responsible for the majority of diseases of bacterial etiology. At present in Poland, a high resistance of Streptococcus pneumoniae to penicillins, tetracycline, cotrimoxasol, macrolides, and increasingly more often to second generation cephalosporins, is noted. High percentage of Hemphilus influenzae strain is resistant to betalactams and cotrimoxasol. Staphylococcus aureus, the role of which as an etiologic factor, is frequently overestimated and characterised by high resistance to betalactams [11, 15]. These data indicate that the phenomenon of drug resistance is rapidly increasing and suggest the necessity for great caution while using these drugs.

In the presented study, antibiotics were used in 82% of diagnosed cases of upper respiratory infections. This is considerably more than in Sweden, where physicians apply antibiotics in only 54% of respiratory infections, and slightly less than in Turkey, where antibiotics are used in 92% of cases [12, 18]. In addition, the data from the urban centres in Poland show a smaller scale of the use of antibiotics in these diseases, reaching 61% [5, 6]. Many causes contribute to a large number of antibiotics applied. One of them is the uncertainty concerning the correctness of the diagnosis made. Due to uncertainty, the physicians, in the majority of such diseases, suspect a bacterial etiology.
Rapid streptococcal tests may be useful while making a diagnosis. The introduction in France of rapid streptococcal tests with cost reimbursement by insurance agencies led to a considerable decrease in the number of antibiotics applied [9]. A large number of antibiotics used may also result from fear of severe complications, which are the consequence of diseases with streptococcal etiology. Another reason is the lack of comprehensive knowledge concerning the etiology and pathogenesis of acute respiratory tract infections. Practical guidelines developed by Polish scientists do not reach those who are the most interested, i.e. primary health care physicians. The large number of antibiotics used is also due to strong pressure from patients accustomed to taking antibiotics, who expect a quick recovery. During the time of high unemployment, the pressure on the part of patients is especially high. Also, pharmaceutical companies may contribute to this situation by inclining physicians to use their products. Moreover, physicians are guided by the fear that the lack of quick relief would result in patients’ transferring to a competitive health unit. Poland is experiencing a transitional period, especially proprietary changes in primary health care, due to which the competition in the market of medical services is especially great. Another reason for an excessive prescribing of antibiotics is that PHC physicians are overloaded with work, and have little time to explain precisely to their patients the reasons for not using an antibiotic. Resigning from the practice of ‘watchful waiting’ and instantly prescribing an antibiotic considerably reduces the number of patient visits to a medical practice. In addition, according to Polish legal regulations, even inappropriate prescribing of an antibiotic does not threaten physicians with any responsibility, while not applying antibioticotherapy, even when consistent with the recommendations, exposes them to full occupational or even penal responsibility in the case of the occurrence of any complications.

The antibiotics most frequently used by rural physicians were amoxicillin, amoxicillin with clavulanic acid, macrolides, and doxycycline. These data are close to the observations made in Polish urban centres [5, 6]. Rural physicians more frequently prescribed doxycycline, while less often second generation cephalosporins. A relatively large part of the antibiotics used were ineffective, with respect to which a high drug resistance of microbes was observed. This confirms the fact that there is a lack of comprehensive knowledge among physicians, and that they are unfamiliar with the existing recommendations.

The great majority of cases of acute pharyngitis and tonsillitis have a viral etiology. The symptoms which suggest this cover: conjunctivitis, cough, runny nose and diarrhoea. Pharyngitis and tonsillitis caused by group A beta-hemolitic streptococcus is responsible for 15-30% of the cases of pharyngitis in children, and approximately 10% in adults [2, 3, 7, 11]. In the presented study, pharyngitis and tonsillitis was diagnosed in 31.25% patients. Current guidelines by the Alliance Working for Antibiotic Resistance Education (AWARE) recommend the performance of rapid streptococcal test in each patient suspected of streptococcal etiology, and antibioticotherapy only in the case of positive test results [3]. In Sweden, rapid streptococcal tests are performed in over 57% of patients [18]. The recommendations based on confirmed data by the American College of Physicians recommend the performance by physicians of the evaluation of the risk of streptococcal pharyngitis, based on the designed clinical scales [4]. According to all recommendations, both Polish and international, in non-streptococcal pharyngitis and tonsillitis the administration of antibiotics is not recommended. In the treatment of streptococcal pharyngitis and tonsillitis, penicillin still remain first-line antibiotics. According to Polish recommendations, alternative drugs are second generation cephalosporins, and in frequent relapses, amoxicillin with clavulanic acid, while in the case of allergy to beta-lactams – macrolides. The recommendations by AWARE allow the following as an alternative treatment: amoxicillin, macrolides, cephalosporins and clindamycin [1, 3, 15]. The use of antibiotics in streptococcal pharyngitis and tonsillitis is aimed primarily at prevention of complications, such as: rheumatic fever, nephritis, etc. These complications considerably more rarely occur in the adult population. In the presented study, despite a smaller probability of streptococcal etiology of the disease and a smaller probability of the occurrence of serious complications, an antibiotic was used in 90.24% of patients. The majority of antibiotics applied were consistent with Polish or international recommendations. Only in one case a basic drug was applied – natural penicillin. Penicillins still remain the basic drugs applied by physicians in Sweden (44% of the antibiotics used), in Norway (32%), and in Finland (17%) [5, 16, 18]. The unwillingness to apply penicillins in Poland, also confirmed by other studies, most probably results from fear of the occurrence of complications associated with its use, the duration of therapy, which exceeds twice the duration of treatment with other antibiotics [5, 6]. In many cases, physicians applied doxycycline – a drug which is ineffective in acute pharyngitis and tonsillitis.

According to both Polish and international recommendations, the use of antibiotics for the common cold is not recommended. In this disease, only nursing procedures should be applied, and antipyretic drugs and analgesic administered, which is well documented in systematic literature reviews [3, 15]. The presented study shows that physicians from the rural areas of the Lublin Region, in as many as 57.25% of cases, inappropriately prescribed antibiotics to patients, several times more often than physicians from urban centres [5].

In the new recommendations concerning acute sinusitis the term ‘rhinosinusitis’ is used instead of sinusitis, which is more adequate to the etiology of the disease, and always begins with viral rhinitis and ends up with bacterial infection. It is considered that almost all cases of acute bacterial sinusitis regress without the administration of antibiotics.
Therefore, the use of antibiotics should be reserved for cases with moderate symptoms without improvement within 10 days or deteriorating after 5-7 days, and for cases with severe symptoms. In the case of necessity to apply an antibiotic, the first-line drugs should be: amoxicillin, amoxicillin with clavulanic acid or second generation cephalosporins. In the case of allergy to betalactams, the administration of trimetoprim and sulfametaxasol, macrolides and clindamycin is recommended [1, 14, 15]. In the presented study, in 87.5% of cases, an antibiotic was prescribed already during the first visit. The following antibiotics recommended in the guidelines were applied as first-line drugs: in 25% of cases – amoxicillin, in 17.85% of cases – amoxicillin with clavulanic acid, and in 8.92% of cases – second generation cephalosporins. In the remaining cases, antibiotics inconsistent with the recommendations were used: macrolides (10.7%), and lincosamides (8.9%), which are recommended only in the cases of allergy to betalactams. In 10.7% of patients, doxycycline was used – a drug ineffective in sinusitis.

Acute bronchitis is an inflammatory state of the bronchial mucosa causing cough with coughing up. The diagnosis is based on clinical symptoms, and no verification test is available. Clinical features of sputum, e.g. its colour, are not useful in the differentiation of bacterial or viral etiology of the disease. More than 90% of cases of uncomplicated acute bronchitis is of non-bacterial etiology. Therefore, in acute bronchitis antibiotics are usually not recommended. In acute bronchitis for a period of 7-10 days in the first phase of treatment procedure antipyretic drugs, analgesics, anti-inflammatory drugs, drugs decreasing oedema and antitussive drugs should be used. In the second phase of treatment, mucolytics and mucokinetics, expectorants or physical therapy may be applied. As late as with the lack of improvement: purulent secretion, persistent fever and typical bronchogenous changes in chest RTG, the administration of betalactams is recommended. In the case of suspicion of atypical pneumonia (persistent dry cough, subfebrile body temperature, atypical changes in the chest RTG image), the administration of a macrolide is recommended [3, 8, 15].

In the presented study, acute bronchitis was diagnosed in 60 patients. Only in 10% of patients antibiotics were not administered, and according to the recommendations other forms of treatment were applied. In 90% of cases an antibiotic was administered, most often doxycycline (21.67%). Polish studies conducted in urban centres showed a similar scale of the use of antibiotics; however, the following antibiotics were prescribed more frequently: second generation cephalosporins, amoxicillin with clavulanic acid and macrolides [5].

In Recommendations 2003, a European strategy of non-hospital antibioticotherapy of pneumonia is in effect, which consists in an attempt of clinical differentiation between pneumonia with typical etiology, in which a betalactams should be used, and pneumonia of atypical etiology, where macrolides are recommended [15]. Such a strategy is completely different from North American recommendations, according to which it is not possible to clinically and radiologically differentiate between typical and atypical pneumonia; therefore, non-hospital infections are approached as being milder, thus probably of atypical etiology, and should be treated with macrolides [3, 17]. According to Polish authors, based on Spanish recommendations (Baquero and Garau), the decision to use a betalactams is always most important, and should be the first because it allows the prevention of development of purulent complications (lung abscess and thoracic empyema). It seems, however, that the use of both betalactams and macrolides is the correct decision [15]. In all diagnosed cases of pneumonia, second generation cephalosporins and macrolides were used.

Due to the small number of cases it is difficult to analyse otitis media and influenza. According to the Recommendations 2003, in otitis media the strategy of ‘watchful waiting’ may be adopted, and only when no improvement is observed amoxicillin, amoxicillin with clavulanic acid or second generation cephalosporins should be prescribed [15]. In the patients examined, an antibiotic was prescribed as early as during the first visit. In four cases of influenza, adequate procedure was applied in three patients.

A high percentage of diagnoses of acute upper respiratory infections of multiple and unspecified sites is noteworthy (22.25%). This results from safeguarding the approach of physicians who do not possess diagnostic tools and are not willing and not capable of making a more precise diagnosis of the disease. It appears that within this diagnosis there are many cases of diseases of viral etiology, which do not require antibiotics. Nevertheless, in the patients examined, antibiotics were not used only in 12.33% of cases, while it was administered to the remaining 87.6% of patients.

The scale of the use of antibiotics according to patient gender and age was also subject to analysis. No statistically significant differences were noted in the use of antibiotics according to patients’ gender. However, a smaller scale of the use of antibiotics was observed in the age group over 60, compared to those aged 18-40 and 41-60. This is probably due to the smaller intensity of pathological symptoms in the oldest age group, and a lesser urgency for obtaining instant effects of treatment.

**SUMMING UP**

An excessive use of antibiotics in acute respiratory tract infections results from conservative procedures of physicians, uncertainty concerning the diagnosis made, lack of availability or unfamiliarity with recommendations, patient expectations, pressure on the part of pharmaceutical companies, and overloading primary health care physicians with work. If this situation persists, in the near future it will lead to an increase in the phenomenon of drug resistance in Poland. The following actions should be undertaken in order to prevent this situation:
• to conduct soon a wide media action in Poland (radio, press, television, education at schools) informing patients about hazardous effect of overusing antibiotics in acute respiratory infections;
• making available as soon as possible for primary health care physicians the guidelines concerning procedures in these diseases (the guidelines should be sent to all practices, and also included in a generally available internet page);
• the implementation as soon as possible of logistic and financial solutions which would facilitate the diagnosing of respiratory diseases (rapid streptococcal tests) and prevent the excessive use of antibiotics.

REFERENCES