

VILNIUS UNIVERSITY

AUŠRA BERŽANSKYTĖ

ANTIBIOTIC USE IN LITHUANIA, 2003 - 2008

**Summary of doctoral dissertation
Biomedical sciences, Public Health (10B)**

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The dissertation was carried out at Vilnius University and Ministry of Health of the Republic of Lithuania Institute of Hygiene in 2005-2009

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VILNIAUS UNIVERSITETAS

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**ANTIBIOTIKŲ VARTOJIMO YPATUMAI
2003 – 2008 M. LIETUVOJE**

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BACKGROUND

Antimicrobial resistance is mainly caused by inappropriate and abundant use of antibiotics. If not controlled it may condition the situation when many infections can be hardly cured just because of antimicrobial resistance. Nowadays bacteria that are already resistant to all available antibiotics have already emerged. Therefore it's important to understand, where the problem of unreasonable antibiotic use is the most relevant and what can be done to manage it. EU Council approved the recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC). WHO also declared control of antimicrobial resistance as the main priority in the area of infectious diseases and approved WHO Global strategy for containment of antimicrobial resistance in 2001.

In Lithuania the international incentives of projects/programmes are rather complicated to implement, as the problems are investigated just in sporadic studies.

To enlighten the most relevant problematic areas in antibiotic use, where the decisions should be made, the different levels were analysed in this study: the self-medication with antibiotics of the population, ambulatory and also hospital antibiotic use. The prevalence of self-medication and perception of inhabitants about antibiotics were investigated applying requirements of multicenter study carried out in 19 European states, disclosing the extent of the problem in each country. Analysis of ambulatory antibiotic use revealed the frequencies of antibiotic prescribing and spectrum of antibacterials, also their changes after intervention. Hospital antibiotic use was examined in nursing hospitals, estimating the general antibiotic consumption and possible influencing factors in those institutions.

THE AIM – to evaluate antibiotic use and influencing factors in different groups of Lithuanian population, ambulatory and hospital care.

OBJECTIVES

1. To define the prevalence of self-medication and determinant factors among adults.
2. To ascertain the population's privity and perception about antibiotics.
3. To estimate the actual proportion of inhabitants, who store antibiotics at home, spectrum of stored antibiotics by review of home medicine cabinets.

4. In ambulatory care to evaluate frequency of antibiotic prescribing, spectrum of prescribed antibiotics, used diagnostic tests to substantiate diagnosis of infectious disease and also the spectrum and frequency of diseases which were treated with antibacterials.
5. To define influence of intervention in ambulatory care in management of one infection (acute pharyngitis/tonsillitis).
6. To estimate consumed antibiotics' quantity and their spectrum in nursing hospitals.
7. To identify the factors that may influence antibiotic consumption in nursing hospitals.

SCIENTIFIC NOVELTY

The comprehensive investigation on antibiotic use in different population groups, also in ambulatory and hospital care was carried out in this work. That enabled to identify the most problematic areas, where the urgent solutions are needed.

For the first time the self-medication among urban and rural inhabitants was traversed separately, their perception about antibiotics was enlightened by thorough face-to-face interviews, the antibiotic amount and spectrum were evaluated through review the home medicine cabinets.

The situation in ambulatory care was analysed after changes have been made in health care system, particularly in primary health care. Although in general the most antibiotics are used in ambulatory care and very often irrational (according antibiotic prescribing for the infections that are viral most often), the differences were noted between various clinics. The changes in antibiotic prescribing after intervention were compared in two clinics, which were selected from the situation analysis as with the highest initial antibiotic prescribing (HAP clinic) and with the lowest antibiotic prescribing (LAP clinic).

The antibiotic consumption in hospitals is low considering general antibiotic consumption in the population, but it exerts high pressure, as antibiotics are used in isolated territory (institution) for limited number of persons. The irrational use might be prevalent here as well; however there is no systematic knowledge about that in Lithuania. Moreover the situation in nursing hospitals, the institutions which provide primary health care, about antibiotic use was completely unknown; therefore it was

investigated in this study. The antibiotic consumption was estimated with daily defined doses (DDD) and examining possible influencing factors.

The results might be used (some of them are already used) for carrying out the measures of the Lithuanian Programme 2008-2014 on prevention of spread of micro organisms resistant to antimicrobials to improve antibiotic use and management.

THE DEFENSIVE STATEMENTS

- The wrong perception about antibiotics is characteristic to Lithuanian population, as there is lack of privity, while traditions of self-medication and also habits to apply the previous experience, when doctor prescribed antibiotics, are entrenched.
- As the ambulatory care covers the most of the population, the most antibiotics are consumed in this level. However often they are prescribed irrationally for non-bacterial infections just on the basis of clinical symptoms. The antibiotic prescribing for one of the most frequent infection acute pharyngitis / tonsillitis might be improved by implementation of rapid antigen detection tests (RADT).
- The extent of antibiotic consumption in nursing hospitals is low, but it is uncontrolled.

LITERATURE REVIEW

The literature review covered different most relevant references from Lithuania and foreign countries. The increasing antibiotic consumption, growing price of health care globally during last decades was revealed as world problem. The antibiotic use, influencing factors between different countries was compared. The association of abundant and inappropriate antibiotic use with spread of antimicrobial resistance was proved in various studies. Different experiences of antibiotic use management were analysed. The ways of antibiotic prescribing improvement were discussed.

MATERIALS AND METHODS

Self-medication with antibiotics in Lithuanian population

Methodology of multicenter European study „Self-Medication with Antibiotics and Resistance Levels in Europe“ (SAR project) was applied in this study.

The prevalence of self-medication was determined from respondents' answers about used antibacterials (how many and what), gained with prescription or without. The people's perception about antibiotics was evaluated from face-to-face interviews. The actual amount and spectrum of antibiotics stored at home were determined by review of home medicine cabinets.

The respondents were included to actual self-medication group, if they used antibiotics without prescription during last 12 months. The respondents were included to intended self-medication group, if they would use antibiotics in case they see the need.

The study was carried out in two stages:

- 1) The extent of antibiotic use and prevalence of self-medication were determined in **the first stage**.
- 2) People's perception about antibiotics, their behaviour in case they are sick were enlightened, home medicine cabinets were evaluated in the **second stage of the study**.

To describe situation in urban and rural area one Lithuanian town (Klaipėda) and one region (Rietavas) were randomly selected for **the first stage**. The sample size needed was 400. According to the experience of other studies done in Lithuania the response rate was expected not more than 30%. Therefore the questionnaires were sent by mail to 3000 randomly selected adult inhabitants, with reminder after one month. Response rate was 25.4 % (753). After checking the data, 746 questionnaires were left for analysis. To assess possible bias due to low response rates, "adjusted" prevalence rates were also estimated. The "continuum of the resistance model", based on the assumption that late respondents most resemble non-respondents, was applied. Late respondents in our study were those who replied after reminder. The adjusted prevalence was considered similar to the prevalence of earlier respondents when it fell in the 95% confidence intervals (CI) of the prevalence of earlier respondents. The prevalence of late respondents (24.5 %) was a bit higher than the earlier (21.7%), but it fell into their CI - 95% CI: 18.7-24.9%. Therefore the low response rate didn't bias the result.

The extended investigation was carried out in **the second stage** of the study, performing face-to-face interviews at respondents' home. The interviewees were selected from the first stage according to their agreement to participate in the second stage. Similar in size self-medication (exposed) and reference groups were formed by:

1) The participants, who used antibiotics without prescription, were included into exposed group.

2) The participants, that didn't use antibiotics or used them with prescription were included into reference group.

For the general analysis 103 interviews were examined. For comparison of exposed and reference group 48 interviews of each group were analysed, as seven respondents couldn't recall if they have used antibiotics with or without prescription.

The standardized questionnaires from SAR project were used for both stages: general questionnaire of situation review for the first stage and in-depth interviews in the second stage.

In **the first stage** the questions covered the general information (age, gender, education, occupation), also if respondent had any chronic disease, and data about antibiotic use (what, with or without prescription, their storage at home).

In **the second stage** the interviewees were asked about their understanding what antibiotic was, its good and bad effects, and their behaviour when they get sick mostly with different acute respiratory diseases, possible ways to get antibiotic without prescription, etc.

Antibiotic use in ambulatory sector

Antibiotic use in ambulatory sector was assessed by antibacterials prescribing retrospectively from the records in patients' cards and prospectively analysing the change of prescribing after intervention. The study was carried out in two stages:

1) **The first stage** – retrospective prevalence study, which aimed to describe the situation of antibiotic prescribing in ambulatory care in 2004.

2) **The second stage** – prospective intervention study, which aimed to assess the changes in prescribing antibiotics for the treatment of acute pharyngitis/tonsillitis (APh/T).

Intervention consisted of:

- 1) Implementation of rapid antigen detection test (RADT - Quidel - Quickvue dipstick);
- 2) Preintervention education of general practitioners (GP) of diagnostics and appropriate treatment, including antibiotic prescribing, for upper

respiratory tract infections, particularly for APh/T, also of the use of RADT and interpretation of its results;

3) The recommendations of antibiotic prescribing for APh/T.

1) RADT (strep test) for detection of Group A haemolytic streptococcus (GABHS) was given to GPs for free, they were trained to take swab from the tonsils correctly and interpret the results. To avoid mistaken result RADT shouldn't be done, if the patient used antibiotics during the last two weeks. To evaluate RADT characteristics microbiological tests (as „gold standard“) should be carried out to every patient to whom RADT was done.

2) The course for GPs were held in Denmark and Lithuania, were theoretical knowledge was given and practical experience was shared by Danish and Lithuanian professionals. The RADT was presented and GPs tried it themselves. The RADT results' interpretation was discussed.

3) Optimal treatment scheme recommended by clinical microbiologists, based on guidelines and experience of good practise in other countries but GPs were free to choose any for each individual case.

For **the first stage** seven out-patient clinics were selected randomly from all primary care institutions in Lithuania. The sample size needed was not less 968 adults and children. The nested sampling of patients' cards was applied in each clinic, taking not less than 210 cards. The patients who consulted GP in 2004 were enrolled into the sample - in general 1289 children, and 1767 adults.

For **the second stage** two out-patient clinics were selected: one with initially (in 2004) high antibiotic prescribing (HAP clinic) and one with initially low antibiotic prescribing (LAP clinic). Control (reference) group was formed from the first stage - all APh/T cases (463) in medical records of patients, who have visited GP at those clinics in 2004, were enrolled into the sample. Intervention group was formed of all APh/T cases (318) from prospectively included patients, who have visited GP in 2006, till the needed sample size (300) was reached. Sample size was calculated from the nomogram according to the results from previous studies, where antibiotics were prescribed approximately for 60-80% of APh/T cases. The decrease of antibiotic prescribing was expected about 10%. Sample size needed was not less 80 in each group. Expecting possible exclusions 150 cases were enrolled from each clinic.

Data were recorded into case report form according to the variables needed: general data (birth date, gender), diagnosis, performed diagnostic tests, prescribed antibiotic, respiratory complication (complication was registered, if in 14 days after primary diagnosis patient applied with more serious respiratory tract complaints, symptoms), recurrent events (recurrence was registered, if in 4 weeks after the last antibiotic dose patient applied again for streptococcal APh/T).

The economical impact was estimated by reimbursement prices of State Patient Fund for antibiotics exclusively for the patients up to 18 years old, as in Lithuania antibiotics (with very few exceptions) are reimbursed just for children.

Antibiotic use in nursing hospitals

The antibiotic use in the hospitals was evaluated by consumption data – the purchased antibacterials during one year, calculating number of DDD per 100 bed–days.

The study was carried out in two stages:

- 1) The amount and spectrum of consumed antibacterials, also possible influencing factors were evaluated in **the first stage** of the study.
- 2) Discussions with focus groups were organized in **the second stage** to get in-depth view of health care professionals' attitude towards antibiotic prescribing and influencing factors.

All nursing hospitals were invited to participate in the study in **the first stage**. Two questionnaires were sent by fax to 50 nursing hospitals: 1) the first - about purchased antibiotics in 2007; 2) the second - about possible influencing factors. The first questionnaire was gained from 48 hospitals (response rate 96%), the second – from 44 hospitals (response rate 88%).

Focus groups in **the second stage** were organised inviting the staff of nursing hospitals for open conversation. They discussed their routine work concerning antibiotic prescribing, using or not using guidelines, prescribing procedures, performing microbiological cultures, administration approach to this subject, obvious problems, ways to improve the system, etc. Conversations were recorded to voice recorder and analysed later.

DDD was calculated with ABC calculator (ABC Calc), recommended by WHO. The data about name of product, grams per unit dose, number unit doses per package, number

of packages, and hospital bed-days per year were entered. ABC Calc transformed those data to DDD number per 100 bed-days. Antibiotic consumption was estimated for each hospital separately, from what mean antibiotic consumption in Lithuanian nursing hospitals was assessed. Consumption was evaluated also in separate antibacterials groups according to anatomical therapeutic chemical (ATC) classification.

To compare possible influencing factors the hospitals were divided into groups according

- hospital bed number: small ≤ 30 beds; average 31-50 beds; big ≥ 51 beds;
- antibiotic consumption: 1st gr. – less than mean consumption and 2nd gr. – more than mean consumption.

If there was no statistical significant difference between the groups, general proportions were presented.

The ideas discussed in focus groups conversations were transcribed, summarised and given as approach, explaining more profound the results from the questionnaires of the first stage. Content analysis was applied working up the discussion material in several steps: multiple listening/reading of discussions; search of semantically close answers and keywords; summarising by forming categories, subcategories; interpretation.

Statistical methods

Data analysis was carried out with SPSS for Windows 13.0 and Winpepi statistical packages.

The frequencies are given with 95% confidence level. The differences were accepted as statistically significant, when $P \leq 0.05$, with 95% confidence level. P value was calculated with χ^2 test for categorical data with nominal distribution. If expected values were less than 5, Fisher exact test was applied.

The total effect of the analysed factors in self-medication study was evaluated by logistic regression, where the dependant variable was binary response – used antibiotics with prescription or without it (didn't use antibiotics at all or used just with prescription), independent variables were all sociodemographic variables and storage of antibiotics at home. Nagelkerke R^2 criterion (determination coefficient), classification table were

applied to evaluate correspondence of the expected values to observed ones. The significance of coefficient β was assessed with Wald test. The best model was selected by stepwise backward regression, when $P \leq 0.05$. The factors' influence was estimated by odds ratio (OR) with 95% CI.

In the study of ambulatory antibiotic use children's and adults' data were analysed separately. Logistic regression was applied to find out the main possible factors, that could effect antibiotic prescribing: dependant variable – antibiotic was prescribed to the patient or not; independent variables – out-patient clinic, diagnostic tests, their results, the group of patient's age. For more clear interpretation the results were presented as proportions of cases that were treated with antibiotics for each factor separately. The difference of the cost of one mean APh/T case between intervention and control groups was identified by ratio, estimating statistical significance with Mann-Whitney test.

ROC curve and RADT parameters were processed with NCSS and PASS statistical package. CI of RADT parameters were calculated applying Newcombe-Wilson method without continuity correction. ROC curve was evaluated by following criteria:

- area under curve (AUC): 0.90-1.0 – excellent test, 0.80-0.90 – good test, 0.70-0.80 – fair, 0.60-0.70 – poor, 0.50-0.60 –fail
- likelihood ratio (LR): positive LR^+ - good, if more than 2.0, negative LR^- - good, if less than 0.5.

Continuous variable number of DDD per 100 bed-days in all categories (hospital groups, antibiotic groups, etc.) was presented as mean, as the normal distribution was determined with Cholmogorov-Smirnov test. The differences of DDD between different hospitals groups according to their size were estimated with ANOVA procedure, calculating P value with F test.

RESULTS

1. Self-medication with antibiotics in population.

The respondents were similar in both stages, also in self-medication and reference groups. The mean age was 60 years, there were more men than women (65.1% and 34.9% respectively), a bit more from urban than from rural area (54.0% and 46.0% respectively). The higher technical education prevailed in both stages in general, but

among elder respondents (≥ 65 years) education was mostly primary (33.6%). Male and female proportion in each education group didn't differ. According to the occupation the most of the respondents were retired and representatives of skilled occupation group.

About one third of respondents pointed out as being sick at least with one chronic disease: 39.5 % total – 37.5 % in exposed group, 35.4 % in control group.

Antibiotic use

During the last 12 months before the study was carried out almost 40% of respondents pointed out the use of antibiotics, females more than males (Table 1).

Table 1. Antibiotic use by gender

	Total		Males		Females		χ^2	df	P value
	(n = 746)		(n = 476)		(n = 255)				
	N	%	N	%	n	%			
Antibiotic use during last 12 months	298	39.9	174	36.6	121	47.5	8.191	1	0.004
Antibiotic use with prescription	218	29.2	138	29.0	78	30.6	0.203	1	0.652
Self-medication with antibiotics	164	22.0	85	17.9	78	30.6	15.533	1	0.0001
Intended self-medication with antibiotics	308	41.3	198	41.6	106	41.6	0.000	1	0.994

The actual self-medication prevailed in more than one fifth of respondents – 22.0% (95% CI: 19.1-25.1%), more females than males. Intended self-medication discloses the attitude of inhabitants towards antibiotic use even more accurately, as reflects the possible behaviour if being sick. Here the prevalence of intended self-medication was higher than actual – 41.3% (95% CI: 37.8-44.9%) with no differences between genders. Also there were respondents, who used antibiotics in both ways – with and without prescription.

Risk factors of self-medication with antibiotics

Logistic regression of risk factors revealed that from all sociodemographic factors the main influencing factor was gender. The females self-medicated with antibiotics more often than males OR=1.94 (95% CI: 1.32-2.87). The rural inhabitants also pointed out self-medication more often than urban, but that was not statistically significant. However the most meaningful factor determining self-medication was storage of antibiotics at OR=5.11 (95% CI: 3.47-7.52).

The latter risk factor was also very strong for intended self-medication. The respondents who had antibiotics in home medicine cabinets admitted more often to self-medicate than those who didn't store antibiotics OR=1.98 (95% CI: 1.35-2.65).

From all sociodemographic factors the younger age and the lower education influenced the intended self-medication most of all. Taking the eldest group as reference OR of respondents up to 46 years was 3.73 (95% CI: 2.12-6.56), up to 65 years OR=3.21 (95% CI: 1.87-5.52). Taking reference the high education OR of the respondents having primary education was 2.30 (95% CI: 1.34-3.94).

Symptoms or diseases treated with antibiotics

Antibiotics were prescribed mostly to treat lower respiratory tract infections (bronchitis 24.6%, pneumonia 16.8%), urogenital infections, tonsillitis. Self-medication was noted most frequently to treat tonsillitis / sore throat (17.3 %), bronchitis / cough (13.8%) and upper respiratory tract infections (13.8%), also rather often urogenital symptoms (11.8%) (Figure 1).

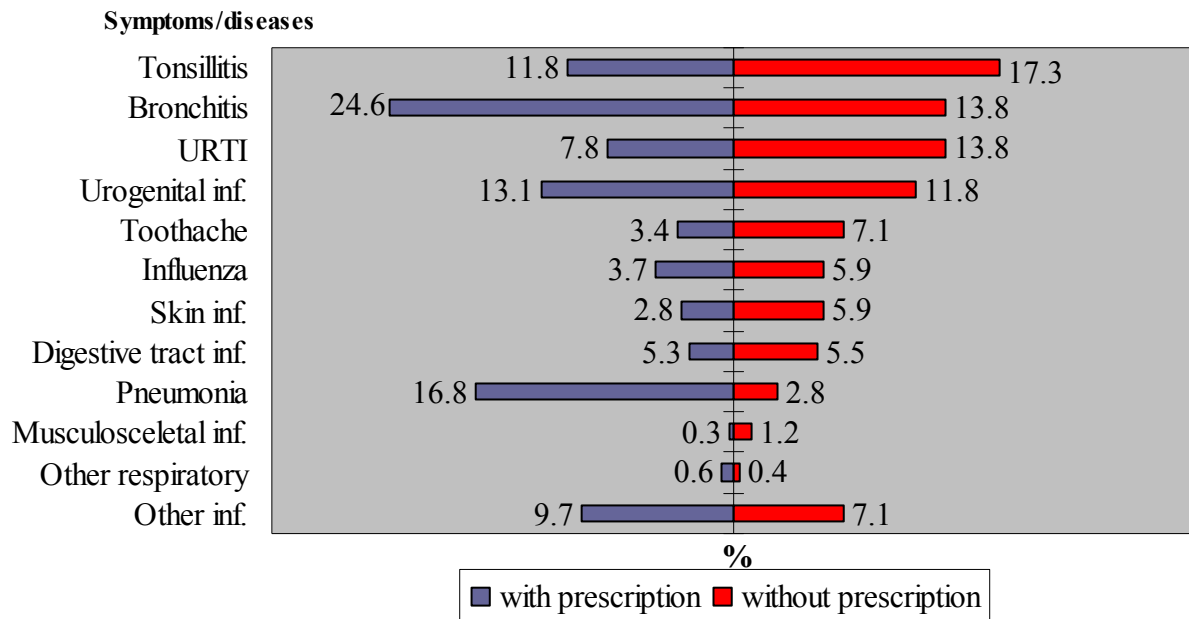


Figure 1. Antibiotics used for different symptoms/diseases

The intended self-medication was chosen mostly for respiratory tract infections. Many respondents pointed out viral infections as influenza, runny nose/cold, etc. (Figure 2).

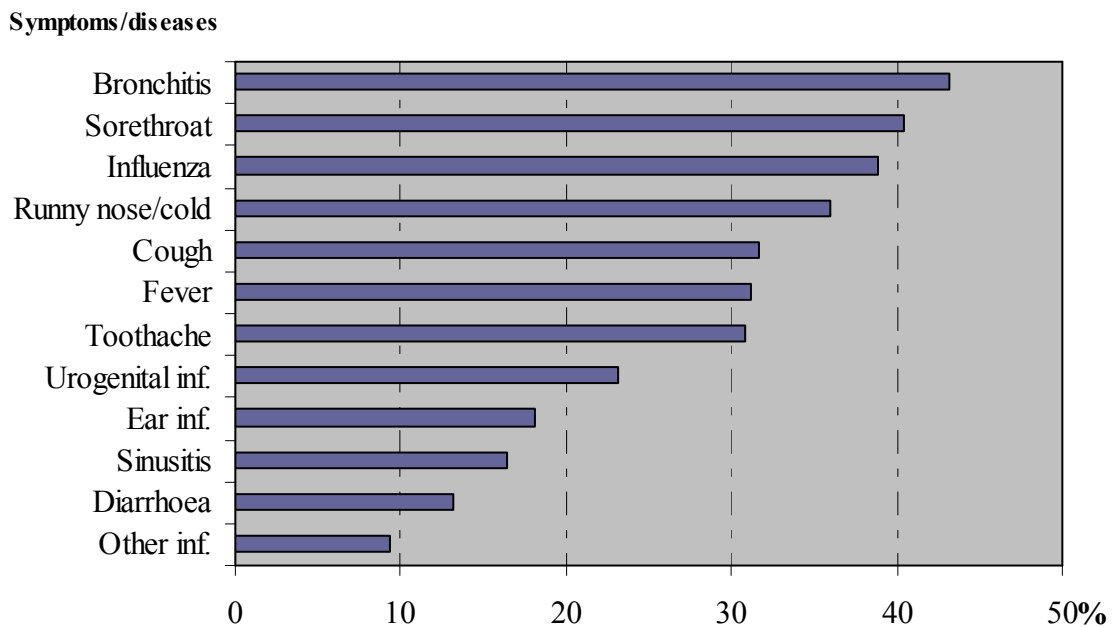


Figure 2. Intended self-medication with antibiotics for different symptoms/diseases

Perception about antibiotics

Due to interview method it was possible to figure out in-depth if people know antibiotics, what they know, what positive and negative effects they consider. Contradictions in people's understanding and behaviour were found in this stage.

In the first stage 87.3% respondents defined antibiotics correctly, telling right name of this group of medication. In the second stage 93.2% interviewees gave exact examples of antibacterials. However it's not seldom case that people consider antibiotic as panacea for many diseases. Giving choices of possible antibacterials functions (right and wrong) almost half of respondents (46.6%) pointed out the function to kill bacteria, but there were opinions, that antibiotics cure infections, kill viruses, have anti-inflammatory, antipyretic or anti-analgesic effect (Figure 3.). This perception was general and didn't differ statistically significantly between exposed and reference group.

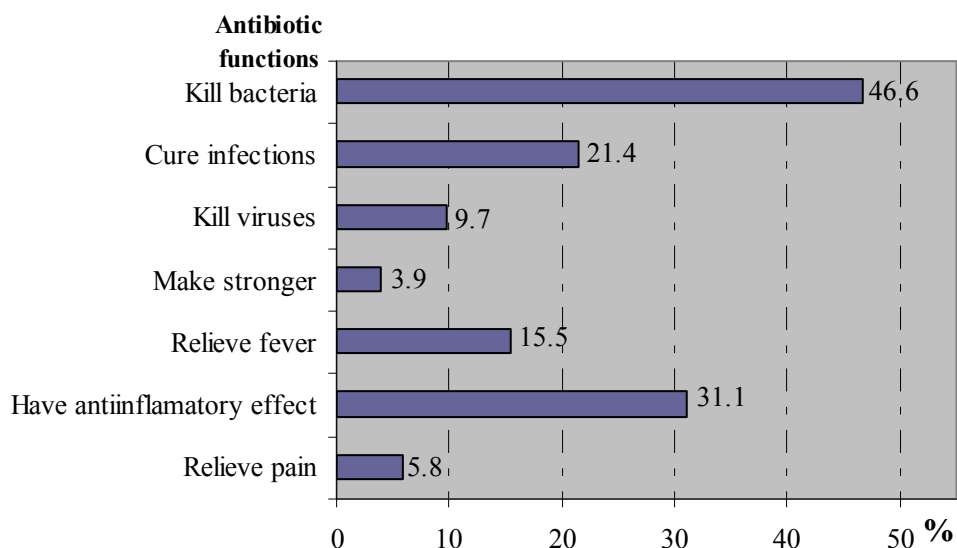


Figure 3. The responses to the questions „what is antibiotic and what does it do?”

Sometimes it was clear, that interviewees couldn't discern bacterium and virus. Some respondents called them microbes in general. Consequently they couldn't understand disparities of bacterial and viral infection, also their treatment principles.

More than half of respondents (62.1%) knew the harm of antibiotics; those proportions were similar in both groups. Allergic reactions were mentioned as the main side effects, and they were pointed out by 26.2% of all respondents. Antibiotics' ability

to kill „good“ bacteria was indicated by 20.3%, to cause adverse events – by 16.5%, to develop resistance – by 13.6% of interviewees.

Many respondents (72.8% in exposed group, 80.6% in reference group) preferred not to take antibiotics at all, but in case of sickness they would accept doctor's recommendations on antibiotic need. Contrary to expectations there was no statistically significant difference between analysed groups. Three respondents (all from exposed group) confessed pressing doctor if he didn't prescribe antibiotics, when the patient thought he needed them.

However the self-medication's advantages were noted during interviews. The participants considered it more convenient, quicker way to gain medication, not disturbing the doctor, although it is possible to choose the wrong drug, or it may cause side effects.

The high prevalence of self-medication determined in the first stage and contrary frequent opinion of no wish to use antibiotics in the second stage could be conditioned by insufficient knowledge and even more – its application in practice. Most likely the people don't consider analysed matter as relevant problem, and don't think they lack information. However the results show that there is inadequate understanding in the society about differences between bacterial and viral infections and antibiotic effect.

Respondents' behaviour when they are sick

Analysis of responses to different questions about the behaviour what people do when they get sick with different diseases/symptoms showed the tendency to take antibiotics when the symptoms get more serious. The respondents preferred home remedies (herbal teas, honey, hot water bottle, vitamins, etc.) and non-prescription medicine (nasal drops, syrup for cough, antipyretics, analgesics, etc) for easy symptoms/diseases (cold, cough, fever). If more symptoms were added or more serious disease was considered, some of respondents pointed out taking antibiotics without doctor's consultation, more in exposed than reference group.

It seems, that the procedure (laws) to gain antibiotics is not completely clear to people. It was found in the first stage that over-the-counter acquisition in community pharmacies was the most common (86.0%) source of antibiotics for self-medication. This was followed by leftovers (23.2%) and from friends or family (6.1%). Sometimes

people reported several of aforesaid sources of obtaining one antibiotic. The same sources were mentioned during interviews (77.1%; 4.2%, 16.7% for mentioned sources respectively).

Different view was found, when the interviewees in the second stage were asked about opportunity to gain antibiotics without prescription and availability of each source. In general the participants thought that it was easy to get antibiotics without prescription. That was noted by 79.2% in exposed group and 45.8% in reference group (P=0.001). Discussing each source separately the left-overs as possible easy way were mentioned much more frequent and by both groups (50-85%).

Evaluation of home medicine cabinets

Review of home medicine cabinets showed that more than half (55.9%) from 93 interviewees, who had and agreed to show home medicine cabinets, had at least one antibiotic at home. That could witness about not completed treatment course or having gained larger amount of medicine. Usually the pharmacies sell them in standard packages and the return of left-overs is not organised. Doctors prescribing antibiotics have difficulties to apply exactly the package to the treatment course.

The actual storage of antibiotics (more than 50%) was found in home medicine cabinets. That exceeded twice the one that was indicated by respondents themselves in the first stage (23.5%). Also during interview larger proportion of participants (41.9%) pointed out gaining antibiotics without prescription. One might guess that those numbers might be exaggerated due to recall bias, as there were medications gained long ago. On the other hand, this index might be accepted as cumulative one.

Comparing exposed and reference group, statistically significant difference was found in storage of antibiotics gained without prescription. According to the interviewees' statement 60.0% of them in exposed group had at least one antibiotic gained without prescription, while 20.9% indicated that in reference group ($\chi^2=17.374$, df=3, P=0.001).

The spectrum of antibiotics at home corresponded the one that was found in the first stage questionnaires. Beta-lactam antibacterials, penicillins were the most frequent (Figure 4).

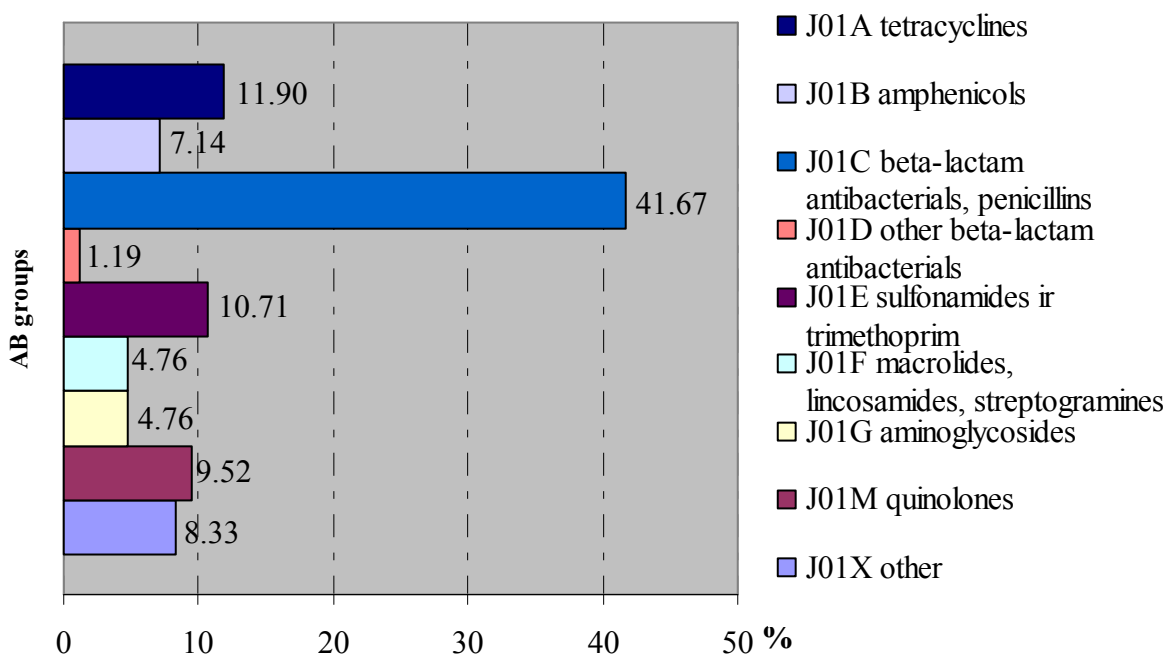


Figure 4. Antibiotic groups found in home medicine cabinets (% from all antibiotics)

2. Ambulatory antibiotic use

The first stage – situation analysis

From 3056 reviewed patients' cards there were 42.2% of children and 57.8% of adults. The age had normal distribution with mean age 9 years of children and 41 years of adults.

Antibiotic prescribing

Antibacterials were prescribed for 58.3% (95% CI 55.6 – 61.0) of children and 33.3% (95% CI 31.2 – 35.6) of adults most often to treat lower respiratory infections (in pneumonia case more than 90%). However even infections that are viral most often, were treated with antibiotics: upper respiratory tract infections - more than 40%, pharyngitis - about 50%, tonsillitis - more than 80%.

The most frequent antibiotics that were prescribed in out-patient clinics were J01C group beta-lactam antibacterials, penicillins (more than 60%), among which broad spectrum penicillins aminopenicillins were the most common (40.4% for children, 51.6% for adults). Macrolides also were administered not seldom (22.7% for children, 6.3% for adults) and tetracyclines was not rare case for adults (11.3%).

Use of diagnostic tests

At least one diagnostic test was performed for 24% of cases diagnosing infectious disease. General blood test and urine test were carried out most often. The antibacterials were prescribed without any diagnostic test for 75.1% of children and 58.5% of adults. Most likely it's usual that clinical diagnosis is determined and antibiotics are administered just on the basis of clinical symptoms.

The second stage – intervention study

The cases of acute pharyngitis / tonsillitis were included into the study – in total 781 (583 children and 198 adults). In both control and intervention groups there were about three fourths of children's cases.

Diagnostic tests

According to microbiological tests in intervention group the prevalence of APh/T, caused by group A beta-haemolytic streptococcus (GABHS), was found in 37.7% of all cultured cases in total: 43.5% in children, 23.9% in adults.

After implementation of RADT increase in use of other diagnostic tests was noted. At least one diagnostic test (with exception of microbiological culture (MC) and RADT) to prove clinical diagnosis was carried out for 22.0% of all cases in control group and 29.9% in intervention group ($P=0.012$). GB test was performed 1.34 times ($P=0.028$), ESR – 5.89 times ($P=0.0001$) more often, CRP test (not used before intervention at all) was started to use. Chest X-ray was done in later days of the disease or if lower respiratory tract diseases suspected.

RADT for GABHS differential diagnostics was carried out for 86.79%, microbiological culture - for 75.16% of all APh/T cases in intervention group. Bacterial APh/T was diagnosed to 42.3% of cases. The most frequent isolated pathogen from all the positive swabs (101) was GABHS – 94 cases (93.07%). Only in 5 cases (4.95%) group B haemolytic streptococcus and in 2 cases (1.98%) group C haemolytic streptococcus were isolated. RADT was negative in those cases. All isolated GABHS were sensitive to penicillin, while 3(2.97%) strains resistant to erythromycin were detected.

Treatment

Total antibiotic prescribing rate hasn't changed statistically significantly, as opposite changes in prescribing in both clinics were found - it decreased 1.57 times (95% CI 1.28-1.94; $X^2=22.02$, $df=1$, $P=0.0001$) in HAP clinic, but increased 1.23 times (95% CI 1.00-1.52; $X^2=4.11$, $df=1$, $P=0.044$) in LAP clinic (Figure 5).

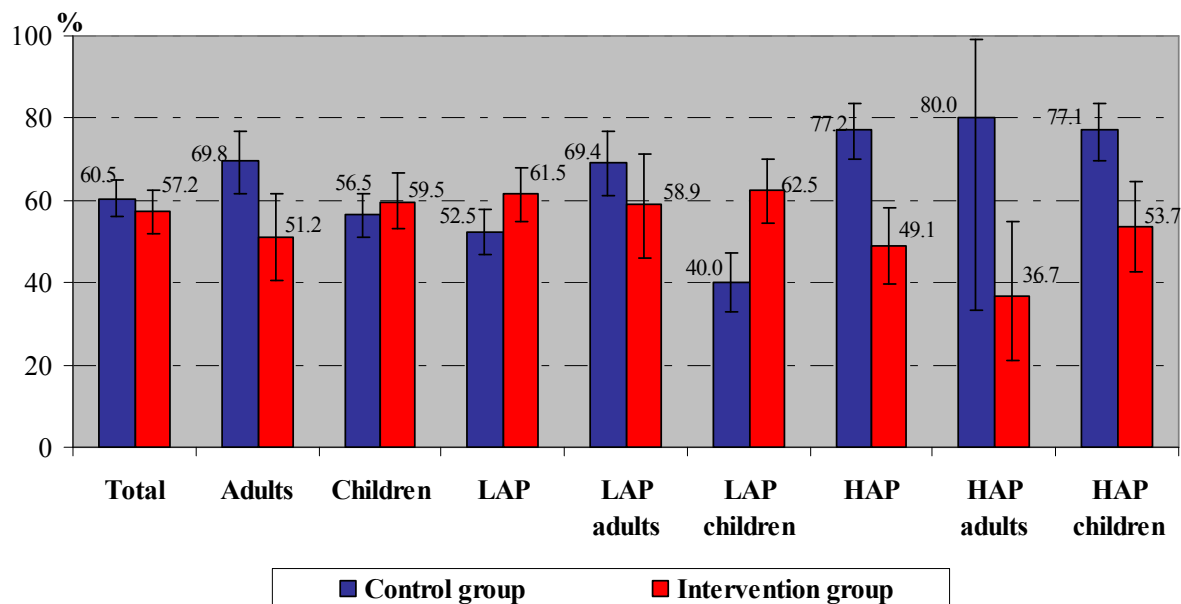


Figure 5. Proportions of cases treated with antibiotics

The analysis of antibiotic prescribing in various age groups revealed decrease in adult group 1.36 times (95% CI 1.08-1.72; $X^2=7.87$, $df=1$, $P=0.005$), in young children group (up to 6 years) 1.20 times. (95% CI 0.94-1.53; $X^2=2.28$, $df=1$, $P=0.132$), but for children 6-18 years it even increased 1.36 times (95% CI 1.00-1.80; $X^2=4.80$, $df=1$, $P=0.031$).

Positive RADT result necessitated 2.3 ($p=0.0001$) times more frequent antibiotic prescribing than its negative result. However antibiotics were administered to 40.4% cases also when RADT was negative.

The major changes occurred in pattern of prescribed antibiotics (Figure 6). Penicillin was prescribed 5 times, clarythromycin and cefadroxil 2 times more often, while broad spectrum penicillins, also amoxicillin and amoxicillin with clavulanic acid decreased (respectively 2 and 5 times respectively).

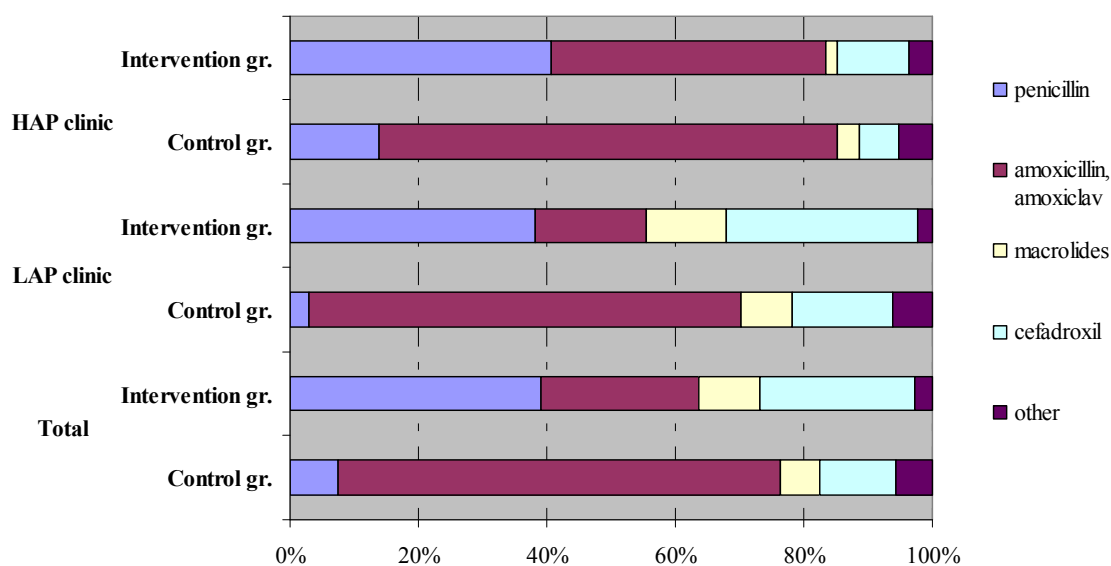


Figure 6. Prescribed antibiotics in both groups and both clinics

Treatment outcomes and expenses

Proportions of respiratory complications and recurrences decreased respectively 2.06 times (95% CI 1.02-4.16; $X^2=4.314$, $df=1$, $P=0.038$) and 3.78 times (95% CI 1.31-10.86; $X^2=7.15$, $df=1$, $P=0.014$).

Taking into account expenses to treat respiratory complications and recurrent events, the price increased 1.08 times due to intervention, but it was not statistically significant (Table 2). In that aspect HAP clinic again demonstrated expected decrease 1.6 times ($P=0.0001$).

Table 2. Mean cost to treat one APH/T case including expenses to treat respiratory complications and recurrent events

	Cost (Lt) (mean)		Mann-Whitney test	P value
	Control group	Intervention group		
Total	9.80	10.55	36748.50	0.640
LAP clinic	7.91	12.01	10920.50	0.001
HAP clinic	12.16	7.78	4091.50	0.0001

Characteristics of RADT

Characteristics of used in study RADT (Quidel - Quickvue dipstick) were estimated: sensitivity 72.34% (95% PI 62.56-80.37%), specificity 92.30% (95% PI

86.75-95.65%), positive prognostic value 86.08% (95% PI 76.76-92.04%), negative prognostic value 83.54% (95% PI 76.98-88.52%). ROC curve showed high sensitivity with high specificity (Figure 7). The area under curve (0.82 (95% CI 0.76-0.88)), positive and negative likelihood ratios (respectively 9.40 (95% CI 5.26-16.82) and 0.30 (95% CI 0.22-0.42)) confirmed good result. Positive likelihood ratio 9.4 would predicate, that for every 1 healthy subject that test as GABHS positive, 9.4 sick with APh/T patients will test as GABHS positive. Negative likelihood ratio 0.3 would confirm, that that for every 3 sick with APh/T patients that test as GABHS negative, 10 healthy subjects will test as GABHS negative.

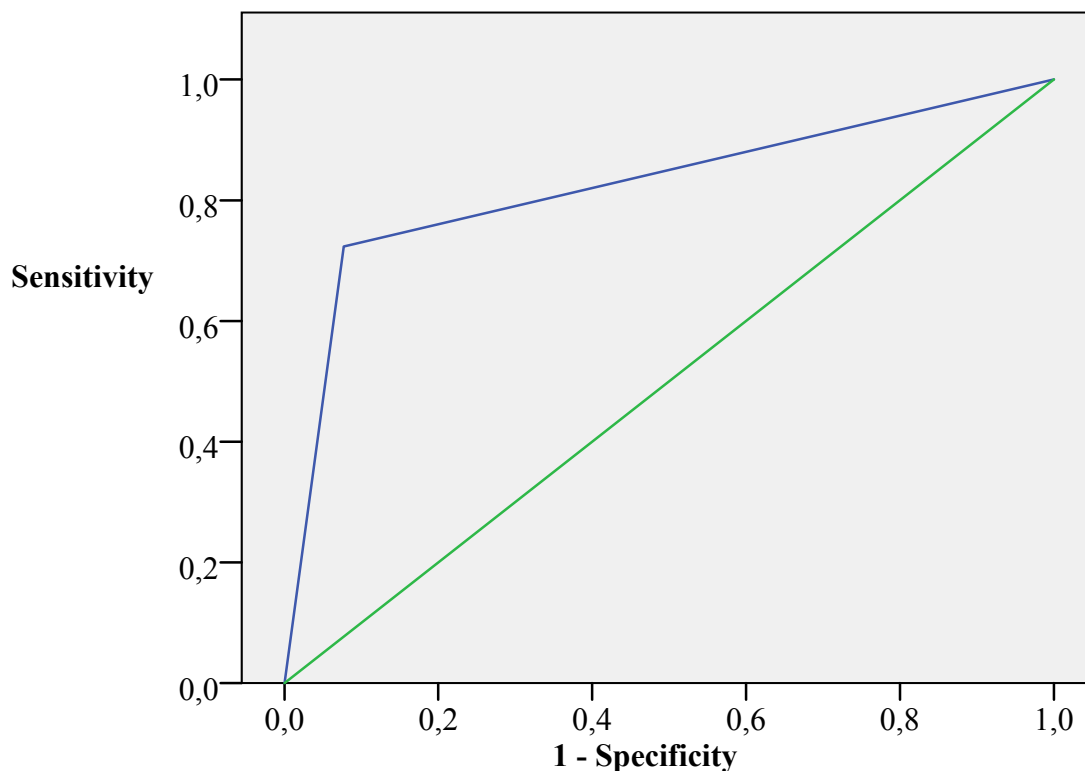


Figure 7. ROC curve

3. Antibiotic use in the nursing hospitals

The size of 48 nursing hospitals that have participated in the study varied from 10 to 286 beds: mean 55, median 36, and the most common (mode) were hospitals with 30 beds. Small hospitals (18) consisted 37.5%, average (16) – 33.3%, large (14) – 29.2% of all nursing hospitals. More than 100 beds were in 10% of the hospitals.

The first stage – general analysis of antibiotic use in nursing hospitals

Antibiotic use

Nursing hospitals consume antibiotics in average 10.68 (95 % CI 8.51-12.84) DDD per 100 bed-days (Table 3). Wide variation was determined between the institutions. Antibiotic consumption varied from 0.8 to 26.6 DDD per 100 bed-days in 2007, two hospitals indicated about having not purchased any antibiotics. Antibiotic consumption was a bit lower in larger hospitals, but this difference was not statistically significant (F=0.250, P=0.780).

Table 3. Antibiotic consumption (DDD per 100 bed-days) in Lithuanian nursing hospitals

Hospitals	Mean of antibiotic consumption	Standard deviation	Coefficient of variations (%)	Sample range
Total (n=44)	10.68	7.3	68.4	26.6
Small hospitals (n=15)	11.69	7.3	62.4	22.4
Average hospitals (n=15)	10.47	7.9	75.5	24.9
Large hospitals (n=14)	9.81	6.4	65.2	25.8

According to antibiotic consumption 23 hospitals attributed to the 1st group – consuming less than average (<10.68 DDD per 100 bed-days), 21 hospital- to the 2nd group – consuming more than average (>10.68 DDD per 100 bed-days).

Pattern of consumed antibiotics

The most common antibiotics, gained by nursing hospitals, were antibacterials of group J01C (beta-lactam antibacterials, penicillins) (Figure 8). Also antibacterials of group J01A (tetracyclines) and J01G (aminoglycosides) were rather usual. Antibiotics of other groups were purchased pretty seldom, antibacterials of group J01B (amphenicols) were not listed at all. Analysis of group J01C showed, that broad spectrum penicillins were consumed the most (69%), while narrow spectrum penicillins, such as penicillin, accounted for just 29%.

The pattern of consumed antibiotics was similar in hospitals of different size (small, average, large), also in two groups according antibiotic consumption.

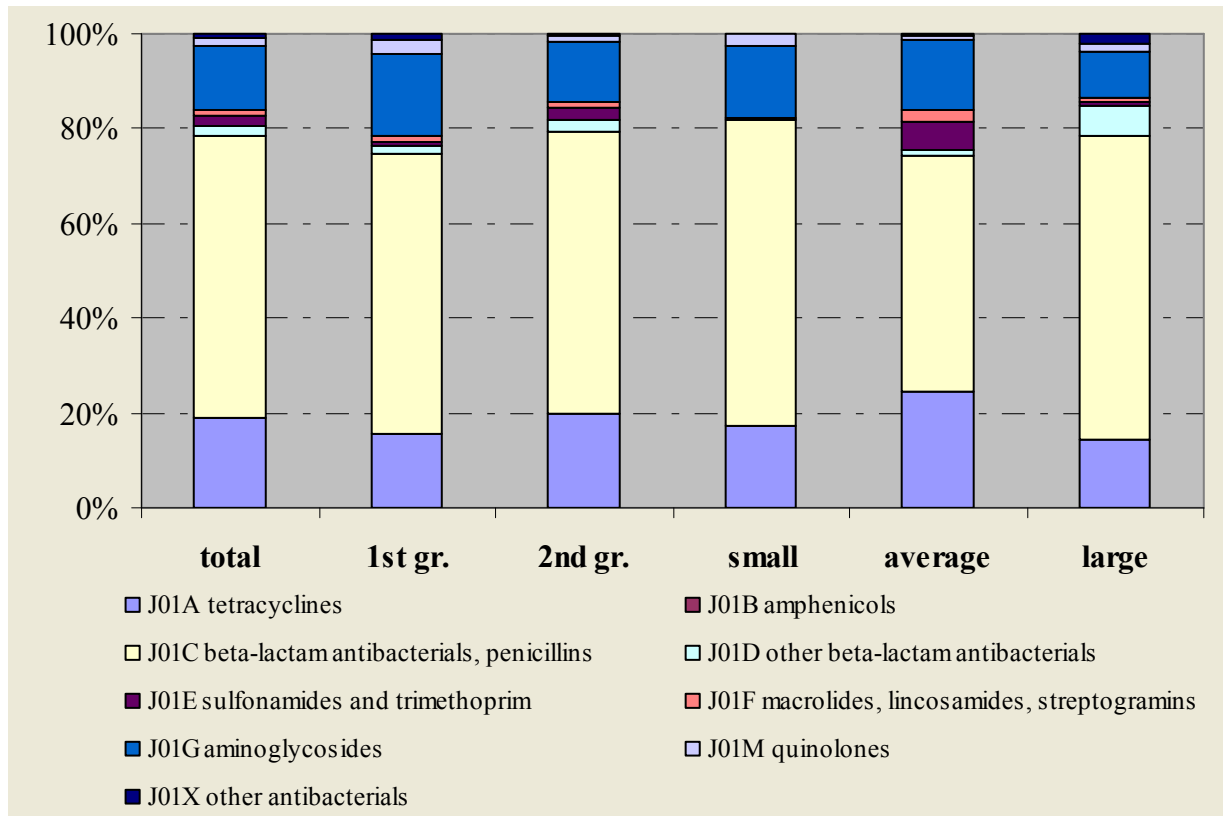


Figure 8. DDD per 100 bed-days in antibiotic groups in all nursing hospitals and in separate groups according hospital size and antibiotic consumption

Influencing factors of antibiotic consumption

On the basis of the information gained from the hospitals it was assessed that some guidelines were used just in one fourth of institutions (Table 4). The procedure of antibiotic prescribing was approved just in one of participated hospitals.

Table 4. The influencing factors of antibiotic consumption

Influencing factors of antibiotic consumption	Hospitals (n=48)	
	n	%
Procedure of antibiotic prescribing	1	2.1
Applied guidelines for antibiotic use for prevention	8	16.7
Applied guidelines for antibiotic use for treatment	12	25.0
Registration of consumed antibiotics	28	58.3
The data on antibiotic use are discussed	29	60.4
in morning staff meetings	19	65.5
treatment board	12	41.4
administration	10	34.5
Microbiological cultures are done	27	56.3
Lectures on antibiotic topic are held	20	41.7

Antibiotics usually are prescribed just by doctors' decision (36 hospitals (75%)). One fourth (12) of the hospitals use broad spectrum antibiotics, such as carbapenems. The antibacterials of this group are allowed to be administered by doctor himself in 4 nursing hospitals. The rest institutions noted, that such decision should be agreed with chief of the department, hospital administration or microbiologist.

The control how staff keeps to guidelines for antibiotic use is performed in less than half of the nursing hospitals (7), the ones that mentioned some of guidelines are used in their institutions (15). This control is done by chief of the department or deputy director for medical affairs, sometimes by audit group of the hospital.

Antibiotic committee doesn't exist in any of the hospitals, infection control is present in 8 (16.7%) nursing hospitals.

The registration of antibiotic consumption is performed in less than half of the hospitals, and those data are discussed in morning staff meetings most often. This is kind of proof that some attention to antibiotic consumption affairs is given.

Microbiological cultures are performed just by more than half of nursing hospitals (56.3%). 1st group hospitals make them less - 11 (47.8%), 2nd group more – 14 (70.0%),

however this difference was not statistically significant. If needed microbiologist consults in 8 (16.7%) nursing hospitals.

Antibiotics most usually are purchased according to their price (70.8%) and staff wishes (66.7%). Two nursing hospitals mentioned approved drug list.

Theoretical knowledge on antibiotic use is gained during lectures, what is not seldom event. They are held and given by pharmacy companies in one third of the nursing hospitals. It was found that pharmacy companies are twice more active organising lectures in the 2nd group (higher consumption) hospitals than in the 1st group (respectively 83.3% and 37.5% from all the hospitals, which noted that lectures were held in their institutions). However due to the small numbers of hospitals in separate groups it was not statistically significant.

The lecturers from the universities are five times more common in the 1st group than in the 2nd group – respectively 7 hospitals (87.5% of all hospitals where lectures are given) and 2 hospitals (16.7%), $P=0,005$.

The second stage - discussions with focus groups

1. Category – antibiotic use.

1.1. Subcategory – antibiotic consumption (amount).

Conversation with the staff proved low antibiotic use in nursing hospitals. Diverse patients are hospitalised here and antibiotics are administered to very few of them.

1.2. Subcategory – the pattern of used antibiotics at the hospitals

The same groups of antibacterials were mentioned in discussions as found in questionnaires. The most usual was penicillin group. Penicillin was mentioned as available and used often. If special care and other antibiotics are needed, patients are sent to the hospitals of higher level. Only antibacterials, that are purchased by hospital, are prescribed. Some of hospitals have approved drug list.

1.3. Subcategory – registration of antibiotics.

The registration is not systematic. Some hospitals use electronic database and know the amount, others can calculate if required, what requires additional efforts. According to the doctor's reasoning sometimes if it is needed the patient is suggested to buy himself another more expensive antibiotics. That is not registered, but such cases are exclusively seldom and shouldn't distort the general consumption much.

2. Category – antibiotic prescribing procedure

2.1. Subcategory – doctor’s decision to administer antibiotic.

Antibiotics are prescribed by doctor’s decision, most often empirically. In larger hospitals there is some procedure, when the consultation with chief of department is needed in more severe cases. In small regional hospitals everything is left for doctor’s responsibility. There if more complicated cases occur, consulting council of doctors is organised with the help from out-patient clinic staff, as there are very few physicians working in nursing hospital in the regions. The criteria to prescribe antibiotic varied among different professionals – some of them would administer antibacterial after several days if fever doesn’t relieve, others would wait for additional symptoms of bacterial infection (worsening status, suppuration, etc.).

2.2. Subcategory – procedure of antibiotic prescribing at the hospitals.

Guidelines for antibiotic use are used in larger hospitals. Sometimes they are established locally as procedures, algorithms. However in regional or smaller hospitals the staff prefers not to change any routine, leaving all decisions to the doctor, his knowledge.

2.3. Subcategory – control of antibiotic prescribing and how staff keeps to guidelines.

In larger hospitals sometimes patients’ cards are reviewed. According to the statement of discussions’ participants usually antibiotic prescribing is substantiated. However in regional or smaller hospitals the staff doesn’t see the benefit neither of such control, nor of analysis.

2.4. Subcategory – tests to substantiate antibiotic prescribing.

Microbiological cultures are done just in solitary instances. The most usual case is to administer empirically antibiotics that are available in the hospital. If the treatment is not effective, corrections are made after. Some health care professionals would like to have possibility to perform microbiological cultures and have results to find the best treatment, while other don’t see such necessity.

3. Category – influence of exterior factors.

3.1. Subcategory – influence of pharmacy companies.

Due to low consumption of antibiotics in nursing hospitals pharmacy companies are not interested in advertising, presenting them in such institutions.

3.2. Subcategory – teaching effect.

The need of knowledge and teaching on antibiotic matter was not expressed much; other topics more relevant to nursing hospitals were more desired. The participants would prefer higher level course or conference, than the lectures in nursing hospitals. The lectures inside the hospitals are held in large nursing hospitals, where despite exterior lecturers the staff itself makes reports on chosen topic.

4. Category – Suggestions for management and situation improvement.

Almost all participants expressed wish to have national guidelines or algorithms.

POSSIBLE WAYS TO SOLVE THE PROBLEM

Lithuania has joined *European antimicrobial resistance surveillance system* just in 2006. The map of such laboratories covers all the country, but the data until now are very limited, not displaying real situation. It's rather hard to estimate in time, but those summarized data are the first ones, though just of one category (blood cultures from the hospitals). Such information is very important in separate institutions. Nursing hospitals due to long-term hospitalization might be a reservoir of resistant strains, but that data are not available.

The sites of high risk were disclosed in this integrated study - the self-medication of the population, antibiotic prescribing in out-patient clinics, also the absence of the stewardship of antibiotic use in nursing hospitals.

Therefore the very important task is to evaluate and monitor the resistance spread and antibiotic use in society level. Some sporadic studies don't show high levels of resistance, though prevalence of antibiotic use especially in primary health care is high. The data of resistance overall in Lithuania and particularly in specific institution would be very useful and motivate the staff. Due to known reasons such information in our country is not liked to be publicized, therefore it's hard to imagine the reality. Thus it's hard to take measures on national level – neither corrections, nor prevention if the problem is not that serious. The situation might worsen in the future radically, if not learning from the mistakes of other countries.

Lithuania has already joined European surveillance of antimicrobial consumption (ESAC) that stated the main priorities for the countries: the rational antibiotic use, control of antibiotic sales, educational programmes.

The studies show surprising result of more rational prescribing which is reached by teaching health care professionals, who work already many years. Besides that privity of general population is very important point. According to the experience of other states the national campaigns are very effective enlightening this matter to people, as just the implementation of new technologies and laws don't give complete result. Education of society is very strong tool, particularly applying to focus groups as young people, who haven't developed their approach and are more flexible. The example is European Antibiotic Awareness Day 2008, which was a European health initiative in close collaboration with the World Health Organization, as well as many other relevant representative stakeholder groups such as health professionals and scientists. The lectures on this occasion were given in unusual manner at the schools of two Lithuanian cities – Vilnius and Kaunas. That was accepted with great enthusiasm by children and teachers. This nice initiative organised by European Centre for Disease Prevention and Control met approval in different countries and it was decided to commemorate this day every year on 18th of November.

Therefore it's very important for decision makers to understand that antimicrobial resistance is relevant problem and if just few countries take care, the result will be scarce. The development of correct population approach, education of health care professionals, implementation of diagnostic tools, antibiotic sales' control, guidelines for diagnostics and treatment, improvement of antibiotic prescribing procedures – all those items would promote rational antibiotic use.

CONCLUSIONS

1. The prevalence of self-medication with antibiotics among adults in Lithuania is high (22%). Antibiotics without prescription were used more by females than males (OR=1.94) and by respondents, who stored antibiotics in their home medicine cabinets (OR=5.11).
2. People's perception about antibiotics is rather contradictory, what may condition wrong use of those drugs. Correct function of antibiotics – kill bacteria – was indicated by 46.6% of respondents; however 31.1% thought, that they had anti-inflammatory effect, 15.5% – antipyretic effect, 9.7% – killed viruses, 5.8% – had

- analgesic effect. More than half of respondents (62.1%) knew about the harm caused by antibiotics.
3. Antibiotics were found in more than 50% of 93 reviewed home medicine cabinets. According to the interviewees' statement 60.0% of them in exposed group had at least one antibiotic gained without prescription, while 20.9% indicated that in reference group. Most common were beta-lactam antibacterials, penicillins.
 4. High antibiotic prescribing in ambulatory care is still present: to children 56.7%, to adults 33.3%. Penicillins, especially the subgroup aminopenicilins (broad spectrum penicillins) are administered most often; also macrolides are not seldom, tetracyclines – for adults. Diagnostic tests are done not often – at least one test (general blood test, urine test, CRP, microbiological culture, etc.) was performed just to 24.9% of children and 41.5% of adults, who were administered antibacterial treatment. Antibiotics are prescribed often to treat upper respiratory infection and tonsillitis: respectively 48.9% and 82.6% for children and 41.8% and 88.1% for adults.
 5. After implementation rapid antigen test (RADT) and teaching the total antibiotic prescribing reduced in initially high antibiotic prescribing clinic 1.6 times, what caused fewer expenses to the State Patient Fund for the treatment of acute pharyngitis/tonsillitis. Antibiotic prescribing depended on the RADT result – when it was positive, antibiotics were administered 2.3 times more often than when it was negative. The pattern of used antibiotics has changed – prescribing of penicillin (narrow spectrum antibacterial) increased 5 times, amoxicillin (broad spectrum antibacterial) decreased 2 times. Expedience of treatment with penicillin was proved – GABHS was sensitive to penicillin in all cases.
 6. The consumption of antibiotics is not high in nursing hospitals (10.68 DDD per 100 bed-days), ranging from not consuming antibiotics at all to 26.6 DDD per 100 bed-days. The most common group was found J01C – beta-lactam antibacterials, penicillins, with broad spectrum penicillins as the largest proportion (69%). J01A (tetracyclines) and J01G (aminoglycosides) groups were also not seldom.
 7. Antibiotic prescribing procedures are rare, guidelines used seldom; microbiological cultures are done sporadically in nursing hospitals.

RECOMMENDATIONS

Seeking correct attitude of population and good traditions to antibiotic use interventions should start from the general public of Lithuania. Public health bureaus of municipalities should organize the overall education of general population on the topic of antibiotic use, giving the most priority to children, spreading information in the schools. The serious consequences of inappropriate antibiotic use, prevention of infectious diseases should be enlightened clearly.

State Medicines Control Agency of Lithuania should organize return of the left-overs to the pharmacies, disseminating this information to society.

The measures of the Programme 2008-2014 on prevention of spread of micro organisms resistant to antimicrobials were delayed due to financial obstacles. To improve antibiotic prescribing they are of high need to be executed urgently now. First and foremost the programmes of medical education on the antibiotic therapy topic should be estimated, and corrected if needed. The dissemination of modern knowledge about appropriate antibiotic use could be facilitated by universities, organising courses for the specialists, working in out-patient clinics, nursing hospitals. Those courses could be obligatory for the needed hours to maintain licence.

The standards of treatment are very essential in improvement of antibiotic prescribing. The guidelines on diagnostics and treatment of upper respiratory tract infections are extremely important to primary health care specialists. Group of experts for the problems of antimicrobial resistance should initiate establishment and expertise of such guidelines.

RADT implementation in primary health care as reimbursed diagnostic tool is recommended. Having completed the teaching and approved clear guidelines that could give positive results.

The requirement to substantiate prescribing of each antibacterial should be validated in national level by Ministry of Health. If RADT is not available to be done, microbiological cultures according guidelines should be promoted to substantiate or correct antibiotic prescribing.

ACKNOWLEDGEMENTS

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„Ekspres testų įtaka tonzilofaringitų gydymui“ (*Impact of express tests to the treatment of tonsillopharyngitis*) mokslinėje praktinėje konferencijoje „Kur esame ir kur einame? Infekcijų valdymo modeliai ir naujos technologijos“, 2008 m. spalio, Vilnius.

(Conference „Where are we and where do we go? Models of infection management and new technologies“, Vilnius, October, 2008)

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2003 project "Epidemiological analysis of needs in health services, activity of hospitals and questioning of inhabitants of Vilnius region

Projects in Institute of Hygiene 2003-2004 multinational survey on self-medication with antibiotics in Europe (Lithuanian part).
2004 study „Influence of adolescents' self-being and life events to health disorders and unhealthy behaviour“ by Hygiene Institute and National Institute of Warsaw.
2005 study „Influence of diagnostic tests to antibiotic usage“
2008-2009 study „Evaluation of antibiotic consumption and influencing factors in general and nursing hospitals“

Giving lectures of epidemiology and introduction of biostatistics for undergraduate students of Faculty of Medicine.

ANTIBIOTIKŲ VARTOJIMO YPATUMAI 2003-2008 M. LIETUVOJE

Disertacijos reziumė

DARBO AKTUALUMAS

Pagrindinė mikrobu atsparumo antibiotikams priežastis – neteisingas ir gausus jų vartojimas. Ne tik medicinoje, bet ir veterinarijoje bei žemės ūkyje nekontroliuojamas vartojimas gali gražinti mus į laikmetį iki antibiotikų (prieš penicilino atradimą), kai daugelį infekcijų vargiai būtų galima pagydyti tiesiog dėl mikrobu atsparumo. Jau dabar yra bakterijų, kurios atsparios visiems turimiems antibiotikams. Todėl svarbu suprasti, kur ši problema yra aktualiausia, kas ją sąlygoja ir ką galima padaryti siekiant ją suvaldyti. Pasaulyje daug dirbama racionalaus antibiotikų vartojimo srityje, kai kurios šalys galėtų būti pavyzdys, tačiau bendri rezultatai dar nėra patenkinami, o kai kur ir itin prasti.

Siekiant išsiaiškinti problemiškesnias antibiotikų vartojimo sritis, kur būtini sprendimai, šiame darbe sujungti keli lygmenys: gyventojų savigyda antibiotikais, antibiotikų vartojimas ambulatorinėje ir stacionarinėje grandyse. Gyventojų savigydos antibiotikais paplitimas ir žmonių suvokimas apie antibakterinius vaistus vertinti atsižvelgiant į 19 Europos šalių atlikto daugiacentrio tyrimo metodologijos reikalavimus – pagal vieno miesto ir vieno rajono rezultatus parodant galimą iki tol nenagrinėtos problemos mastą šalyje. Ambulatorinėje grandyje siekta įvertinti antibakterinių vaistų paskyrimų dažnį ir spektrą bei jų pokyčius atlikus intervenciją. Slaugos ligoninėse nustatytas bendrasis antibiotikų suvartojimas, siejant su galimai tam įtakos turinčiais veiksniais.

TIKSLAS

Įvertinti antibiotikų vartojimo ypatumus ir tam įtakos turinčius veiksnius įvairiose Lietuvos gyventojų grupėse, ambulatorinėje ir stacionarinėje grandyse.

UŽDAVINIAI

1. Nustatyti suaugusių gyventojų savigydos antibiotikais paplitimą ir jį sąlygojančius veiksnius.
2. Išsiaiškinti gyventojų informuotumą ir supratimą apie antibiotikus.

3. Nustatyti faktinį gyventojų, kurie turi namuose antibiotikų, skaičių ir antibiotikų spektrą, įvertinant namų vaistinėlių turinį.
4. Ambulatorinėje grandyje nustatyti antibiotikų skyrimo dažnį, spektrą, naudojamus diagnostinius metodus infekcinei diagnozei pagrįsti ir susirgimų, kuriems skirtas antibakterinis gydymas, pobūdį bei dažnį.
5. Nustatyti intervencijos įtaką antibiotikų skyrimui remiantis vienos indikacijos (ūminio faringito / tonzilito) pavyzdžiu pirminės sveikatos priežiūros įstaigose.
6. Išsiaiškinti slaugos ligoninėse suvartojamų antibiotikų kiekį ir spektrą.
7. Nustatyti antibiotikų vartojimui įtakos turinčius veiksnius slaugos ligoninėse.

MOKSLINIS NAUJUMAS

Šiame darbe kompleksiskai ištirtas antibiotikų vartojimas įvairiose gyventojų grupėse, ambulatorinėje ir stacionarinėje grandyse. Tai pirmą kartą leido nustatyti problemiškausias sritis, kur reikalingi neatidėliotini sprendimai.

Pirmą kartą nagrinėta miesto ir kaimo gyventojų savigyda antibiotikais. Remiantis išsamiais asmeniniais interviu išsiaiškintas respondentų supratimas apie antibiotikus, įvertintas namų vaistinėlose turimų antibiotikų kiekis ir spektras, o tai yra tiesioginis savigydos veiksnys.

Ambulatorinėje grandyje analizuota situacija, įvykus sveikatos sistemos restruktūrizacijai. Nors pirminiame sveikatos priežiūros lygyje antibiotikų vartojimas yra didžiausias ir dažnai neracionalus (pagal antibiotikų skyrimą susirgimams, kurie dažniausiai yra virusinės etiologijos, gydyti), pastebėta skirtumų tarp įstaigų. Pasirinkus didelio ir mažo pradinio antibiotikų skyrimo PSPĮ, palyginti antibiotikų skyrimo pokyčiai, panaudojus intervenciją, akcentuoti visuomenės sveikatos aspektai.

Ligoninėse suvartojamų antibiotikų kiekis, sudarydamas mažą bendrojo populiacijos suvartojimo dalį, pasižymi dideliu intensyvumu (aukšti suvartojimo rodikliai, nes vaistai skiriami ribotoje teritorijoje (įstaigoje) nedideliame kontingentui). Be to, čia taip pat paplitęs neracionalus jų vartojimas. Tačiau apie tai Lietuvoje nėra sisteminių žinių. Aprašyta iki šiol visiškai nežinoma padėtis slaugos ligoninėse, kurios teikia pirminės sveikatos priežiūros paslaugas. Pirmą kartą Lietuvoje įvertintas antibiotikų suvartojimas skaičiuojant VPD. Išnagrinėtas įtakos turinčių veiksnių poveikis antibiotikų vartojimui.

Darbo rezultatus galima panaudoti (dalis jau naudojama) vykdant Antimikrobiniams preparatams atsparių mikroorganizmų plitimo prevencijos 2008–2014 m. programoje numatytas priemones, optimizuojant antibiotikų vartojimą ir valdymą.

GINAMIEJI TEIGINIAI

Lietuvos gyventojams būdingas klaidingas supratimas apie antibiotikus, kadangi stinga informacijos apie šiuos vaistus, įsigalėjusios tradicijos patiems gydytis vaistais, taip pat išpročiai remtis buvusiu patirtimi, kai gydytojas skyrė antibiotikų.

Kadangi ambulatorinė grandis aptarnauja didžiausią populiacijos dalį, joje ir antibiotikų vartojama daugiausia, tuo pačiu jų gausiai neteisingai skiriama nebakterinės kilmės infekcijoms gydyti, kai remiamasi vien klinikiniais požymiais. Vienos iš dažniausių infekcijų – ūminio faringito / tonzilito gydymas būtų veiksmingesnis, jei optimizuojant antibiotikų skyrimą būtų atliekami greitieji A grupės beta hemolizinio streptokoko testai.

Slaugos ligoninėse suvartojama antibiotikų nedaug, bet tai nėra kontroliuojama.

DISERTACIJOS STRUKTŪRA IR APIMTYS

Darbą sudaro struktūrinės dalys, 19 lentelių, 20 paveikslų.

Įvadiniame skyriuje bendrais bruožais aprašoma tiriamoji problema, darbo aktualumas, darbo tikslai ir uždaviniai, mokslinis naujumas, suformuluoti ginamieji teiginiai.

Literatūros apžvalgoje aprašomi pagrindiniai antibiotikų vartojimo aspektai įvairiose šalyse, išskiriant ambulatorinę ir stacionarinę grandis, aptariant gyventojų savigydos antibiotikais problemas. Aprašyta kai kurių ligų diagnostika ir gydymas antibiotikais, skirtumai įvairiose šalyse. Aptarti tyrimų duomenys Lietuvoje.

Tyrimo metodologija pateikiama kiekvienai daliai atskirai: gyventojų savigydos antibiotikais tyrimas, antibiotikų vartojimas ambulatorinėje grandyje bei antibiotikų vartojimas slaugos ligoninėse. Aprašytas duomenų statistinis apdorojimas.

Tyrimų rezultatai pateikiami tekste, lentelėse, paveiksluose.

Rezultatų aptarime gauti tyrimų rezultatai lyginami su kitų autorių duomenimis, svarstomi darbo privalumai ir trūkumai.

Išvadose ir rekomendacijose apibendrinami tyrimų rezultatai, pateikiami galimi problemų sprendimo būdai.

Disertacija baigiama literatūros sąrašu, kuriame yra 199 bibliografiniai šaltiniai ir 7 priedai.

Atlikus darbą ir išanalizavus rezultatus, padarytos šios IŠVADOS:

1. Lietuvoje nustatyta didelė (22 proc.) suaugusių gyventojų savigyda antibiotikais. Be gydytojo recepto šių vaistų daugiau vartojo moterys nei vyrai ($\check{S}S = 1,94$) ir respondentai, kurie turėjo namie antibiotikų ($\check{S}S = 5,11$).
2. Gyventojų supratimas apie antibiotikus gana prieštaringas, tai gali sąlygoti ir netinkamą šių vaistų vartojimą. 46,6 proc. respondentų teisingai teigė, jog antibiotikai sunaikina bakterijas, tačiau 31,1 proc. apklaustų asmenų manė, jog šie vaistai turi priešuždegiminį poveikį, 15,5 proc. – mažina karščiavimą, 9,7 proc. – sunaikina virusus, 5,8 proc. – mažina skausmą. Daugiau nei pusė respondentų (62,1 proc.) žinojo apie antibiotikų žalą.
3. Iš 93 patikrintų namų vaistinėlių daugiau nei 50 proc. buvo antibiotikų, iš jų bent vieną antibiotiką be recepto įsigijo 60,0 proc. savigydos grupės ir 20,9 proc. kontrolinės grupės respondentų. Daugiausia tai buvo beta laktaminių antibiotikų, penicilinų grupės preparatai.
4. Ambulatorinėje grandyje gana daug skiriama antibakterinių vaistų: vaikams – 56,7 proc., suaugusiems asmenims – 33,3 proc. Dažniausiai buvo skiriami penicilinai, o iš jų daugiausia plataus veikimo spektro aminopenicilinų, nemažai buvo makrolidų, suaugusiesiems – tetraciklinų. Diagnostiniai tyrimai atlikti tik nedidelei ligonių daliai – bent vienas diagnostinis tyrimas (kraujo, ENG, šlapimo, CRB, mikrobiologinis pasėlis ar kt.) darytas tik 24,9 proc. vaikų ir 41,5 proc. suaugusių asmenų, kuriems buvo paskirtas antibakterinis gydymas. Dažnai antibakteriniai vaistai yra išrašomi ūminei viršutinių kvėpavimo takų infekcijai ir tonzilitams gydyti: atitinkamai 48,9 proc. ir 82,6 proc. vaikų bei 41,8 proc. ir 88,1 proc. suaugusių asmenų.
5. Įdiegus greitąjį A grupės beta hemolizinio streptokoko antígeno nustatymo testą (GAST) ir atlikus mokymus, bendrasis antibiotikų skyrimo dažnumas pradinio didelio vartojimo PSPĮ sumažėjo 1,6 karto, dėl to sumažėjo ir Valstybinės ligonių kasos išlaidos ŪF/T gydyti. Antibiotikų skyrimas priklausė nuo GAST rezultato –

esant teigiamam rezultatui, antibiotikais buvo gydoma 2,3 karto daugiau, negu esant neigiamam. Pakito skirtų antibiotikų struktūra – 5 kartus padaugėjo siauro veikimo spektro penicilino, 2 kartus sumažėjo plataus veikimo spektro amoksicilino. Įrodytas gydymo penicilinu tikslingumas – visais atvejais AGBHS buvo jautrūs penicilinui.

6. Slaugos ligoninėse antibiotikų suvartojimas nėra didelis (10,68 VPD 100 lovadienių), varijuoja nuo visai neskiriančių iki 26,6 VPD 100 lovadienių. Dažniausiai vartojama J01C – beta laktaminių antibiotikų, penicilinų grupės antibiotikų, iš jų daugiausia (69 proc.) plataus veikimo spektro penicilinų, kiek mažiau skiriama J01A (tetraciklinų) ir J01G (aminoglikozidų) grupės antibakterinių vaistų.
7. Slaugos ligoninės retai turi antibiotikų skyrimo taisykles (tvarką) ar remiasi rekomendacijomis, retai atlieka mikrobiologinius tyrimus.

REKOMENDACIJOS

Būtina formuoti teisingą gyventojų požiūrį į antibiotikus ir geras vartojimo tradicijas. Savivaldybių visuomenės sveikatos biurams siūloma organizuoti visuotinę sistemingą gyventojų švietimą antibiotikų vartojimo klausimais, prioritetą teikti vaikams ir skleisti informaciją mokyklose. Šiuo aspektu svarbu viešinti sunkias neteisingo vartojimo pasekmes, infekcijų prevencijos svarbą.

VVKT rekomenduojama organizuoti vaistų likučių priėmimą vaistinėse ir šią žinią skleisti visuomenėje.

Optimizuojant antibiotikų skyrimą, reikia neatidėliotinai vykdyti Antimikrobiniam preparatams atsparių mikroorganizmų plitimo prevencijos 2008–2014 m. programoje numatytas, bet dėl finansinių kliūčių neįgyvendintas priemones. Pirmiausia būtina įvertinti ir, reikalui esant, pakoreguoti medikų rengimo programas antibiotikoterapijos požiūriu. Platinti naujausias žinias apie racionalų antibiotikų vartojimą gali ir universitetai, organizuodami ambulatorinės grandies, slaugos ligoninių specialistų mokymus, privalomai įtraukiant į renkamų valandų skaičių teisingo gydymo antibiotikais kursą.

Antibiotikų skyrimo optimizavimui taip pat neabejotinos reikšmės turi gydymo standartai. Pirminiame sveikatos priežiūros lygyje dirbantiems specialistams būtinos viršutinių kvėpavimo takų infekcijų diagnostikos ir gydymo rekomendacijos. Ekspertų

grupė, sudaryta antimikrobinio atsparumo klausimams spręsti, turėtų inicijuoti tokių rekomendacijų rengimą ir ekspertizę.

Rekomenduojama įdiegti GAST, kaip kompensuojamą diagnostikos priemonę. Atlikus mokymus ir parengus detalias rekomendacijas tai duotų laukiamų rezultatų pirminiame asmens sveikatos priežiūros lygyje.

SAM įsakymu siūloma priimti reikalavimą asmens sveikatos istorijose nurodyti kiekvieno antibakterinio vaisto paskyrimo pagrįstumą.

Jei nėra galimybės atlikti greituosius diagnostinius tyrimus, PSPĮ skatinti atlikti mikrobiologinius pasėlius, numatytus rekomendacijose, ir pagal gautus rezultatus pagrįsti ar koreguoti antibiotikų skyrimą.

PADĖKA

Finansinė parama atskiriems tyrimams gauta iš Europos komisijos Visuomenės sveikatos valdybos DG SANCO, taip pat Danijos bei Norvegijos Sveikatos ministerijų „*Task Force on Communicable Disease Control in the Baltic Sea Region*“ projekto rėmuose. Geranorišką pagalbą suteikė pirminės sveikatos priežiūros įstaigų ir BPG centrų, o taip pat slaugos ligoninių vadovai bei gydytojai.

CURRICULUM VITAE

- Vardas, Pavardė: Aušra Beržanskytė
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1986-92 m. Vilniaus Universiteto medicinos fakultetas, specialybė - higiena ir epidemiologija. Gydytojo higienisto diplomas.
- Podiplominis mokymas:
- 1992-1994 m. Epidemiologijos rezidentūra Vilniaus Universitete. Gydytojo epidemiologo profesinės kvalifikacijos pažymėjimas.
- 1997-2009 m. Kursai Šiaurės šalių visuomenės sveikatos mokykloje (Goteburge, Švedijoje). Visuomenės sveikatos magistro diplomas 2003 m.
- nuo 2005 m. Vilniaus Universiteto medicinos fakulteto Visuomenės sveikatos instituto doktorantė
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- Nuo 2002 m. Jaunesnioji mokslo darbuotoja Lietuvos SAM Higienos institute
- Patirtis (ir dalyvavimas projektuose bei programose):
- 1995 m. Studentų apskaitos programos tarp Vilniaus ir Viskonsino (Medisonas, JAV) universitetų analizė ir įvertinimas.
- 1995-98 m. valstybinis ECOSLIT projektas, kur buvo išnagrinėta geocheminių faktorių įtaka sergamumui virškinamojo trakto vėžiu.
- 2003 m. projektas „Epidemiologinė Vilniaus m. ir apskrities gyventojų sveikatos priežiūros paslaugų poreikio analizė, stacionarų veiklos analizė, bei gyventojų apklausa“
- Higienos institute vykdyti projektai:
- 2003-2004 m. tarptautinis Europos šalių tyrimas dėl savigydos antibiotikais Lietuvoje.
- 2004 m. Higienos instituto ir Varšuvos Nacionalinio Higienos instituto tyrimas „Paauglių savijautos ir gyvenimo įvykių įtaka sveikatos sutrikimams ir nesveikai elgsenai“.
- 2005 m. „Diagnostinių testų įtaka antibakterinių vaistų vartojimui“.
- 2008-2009 m. „Antibiotikų suvartojimo ypatumai Lietuvos bendrojo pobūdžio ir slaugos ligoninėse bei suvartojimą įtakojantys veiksniai“.
- Dėstymas - epidemiologijos ir biostatistikos pagrindų užsiėmimai studentams Socialinės medicinos skyriuje.