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EVALUATION OF THE EFFICIENCY OF HOSPITAL ANTIBIOTIC POLICY APPLIED IN DR JAN BIZIEL UNIVERSITY HOSPITAL NO 2 IN BYDGOSZCZ IN 2009-2013

Jan Biziel University Hospital No 2 in Bydgoszcz

ABSTRACT

The Hospital Infection Control Team (HICT) of Dr Jan Biziel University Hospital No 2 in Bydgoszcz developed and implemented the principles of a rational antibiotic therapy in 2008. A behavior algorithm has worked since 01.10.2008. Implementation of the principles of a rational antibiotic therapy was part of the hospital antibiotic policy.

THE AIM OF THE STUDY is to evaluate either introductory principles of the rational antibiotic therapy, after five-year experience lived up to expectations in the range specified by the authors.

MATERIAL AND METHODS. Hospital microbiological maps, comparisons of antibiotic cost, specification of microbiological tests made before and after introduction of the principles of a rational antibiotic therapy have been analyzed. Annual antibiotic consumption has been counted according to the defined daily dose (DDD) index created by the WHO.

RESULTS. After 6 years of implementation of the rational antibiotic therapy principles, the decrease in number of isolated strains which are resistant to *Klebsiella pneumoniae* ESBL and *Acinetobacter baumanii* (resistant to carbapenems) has been indicated. The number of the *Pseudomonas aeruginosa* isolates has increased approximately three times, and the number of resistant isolates to carbapenem has grown six times. The cost of antibiotics has been gradually decreased in 2012 in order to represent 9,66 % of all drug budget (without drug programs). Detailed analysis of antibiotic consumption has showed that after the implementation of rational antibiotic therapy principles the consumption of meropenem has increased twice in comparison to the all drugs. The number of microbiological tests grew from 0,20 to 0,29 per one patient, which means material to microbiological tests has been taken from every third patient. Annual DDD index calculated on 100 person-days has been reduced from 59,552 in 2007 to 39,90 in 2009, and it is 47,88 in 2013. The principles of rational antibiotic therapy in comparison with the other elements of antibiotic policy in hospital have caused positive changes in antibiotic ordinance.

CONCLUSIONS.

1. It is required to adhere to the principles of a rational antibiotic therapy by medical staff mainly on the administrative restriction of access to antibiotics.
2. Monitoring changes in drug resistance of hospital flora is an essential element of the principles of a rational antibiotic therapy modification.

Key words: *antibiotic usage, hospital antibiotic policy*

INTRODUCTION

The consequence of implementing a quality management system ISO 9001:2008 (QMS) by the Hospital Infection Control Team (HICT) was to develop principles of a rational antibiotic therapy. HICT has collected data of commonly used antibiotics from a particular hospital department and a hospital pharmacy prior to their introduction. Analysis has showed that some of them were abused. Approximately 80% of the antibiotic budget was assigned for the purchase of only three drugs: amoxicillin with inhibitor, cefuroxime and ciprofloxacin all of which are intravenous. It has been found out by the analysis of a hospital microbiological

map that hospital flora has not changed for some years and consisted of similar phenotypic pathogens with similar antibiotic resistance. Strains of Klebsiella pneumoniae, Acinetobacter baumannii and Staphylococcus aureus dominated. This stagnation could have been a consequence of antibiotics overuse and threatened the selection of drug-resistant bacteria which had been not observed. It has been found out that the number of microbiological diagnostic tests did not equal to the real needs. In this context it was evident that antibiotics were often used empirically. The pharmacy data has showed that the lack of a coherent antibiotic policy in hospital complicated the conduct of tender procedures. Analysis of antibiotic costs in drug annual budget has showed that the budget was too high and ranged from 15 to 27%. Based on these findings, HICT has identified the following priorities for the rational antibiotic therapy:

1. Administrative access restriction to antibiotics as a preventive action against appearance of pathogens resistant to antibiotics in the hospital microbial flora.
2. Adaptation of microbiological diagnostics to the actual needs in the context of targeted antibiotic therapy.
3. Limitation of indications for empiric antibiotic therapy.
4. Simplification of antibiotic purchase procedures during tenders.
5. Cost reduction of the in antibiotic treatment.

The aim of the study is to evaluate either introductory principles of the rational antibiotic therapy, after five-year experience lived up to expectations in the range specified by the authors.

MATERIAL AND METHODS

The study included the hospital records from the years 2001-2013 which contains:

1. Hospital microbiological maps (2007-2013). Particular attention was given to the phenotype of isolated bacterial strains, especially in the context of their drug resistance. The number of carried out tests and antibiograms clinically indicated. The result interpretation of drug resistance was in accordance to recommendations of the European Committee on Antimicrobial Susceptibility Testing.
2. Comparison of pharmacy cost of antibiotics (2001-2013). We have analyzed annual cost of antibiotics compared with the budget of all the medicines, and the cost of individual antibiotics.
3. It has been recorded that usage of antibiotics in the Units divided into groups of antibiotics after implementation of the principles of the rational antibiotic therapy (2008-2013). Their cost share and basis of usage.

The principles of the rational antibiotic therapy have been worked out according to the following assumptions.

The antibiotics have been divided into four groups according to their therapeutic effect and their accessibility:

Group I - prophylactic antibiotic therapy is used if there are no markers of infection, risk factors are present or surgery is planned. Unrestricted access.

Group II - empirical antibiotic therapy is used as monotherapy or combination therapy if it is clinically indicated: serious condition a patient, manifestation of an infection, a toxic septic state. Unrestricted access.

Group III - the first-line antibiotic therapy is used if a patient's clinical condition requires the inclusion of an antibiotic due to the current markers of infection (clinical, local, etc). Unrestricted access.

Group IV - restricted antibiotic therapy can be used after obtaining a Director's written consent. *Antibiotic order execution* will take place after applying justification in cause: it is required by patient's clinical condition, replacement of the empirical antibiotic therapy according to antibiogram results, inclusion of targeted antibiotic therapy based on antibiogram and other clinical situations which justify the usage of antibiotics.

Due to differences in accessibility in the Group IV it has been divided into a Group IV *a* and a Group IV *b*. The Group IV *a* contains of antibiotics which are in stock of the hospital pharmacy. The Group IV *b* contains of antibiotics which will be delivered from outside to the hospital pharmacy and therefore the access to them may be extended in time.

ADDITIONAL RECOMMENDATIONS

1. In each case of suspected infection a material should be taken for microbiological tests in accordance with the instructions before administering antibiotics.
2. It is recommended to use primarily antibiotics of the Group III based on antibiogram.
3. As far as possible the principles of sequential therapy should be applied (transition from parenteral to per-oral) observing the principle of antibiotic therapy in the same group and generation.
4. Cases which will raise diagnostic or therapeutic doubts, and has not met the requirements of antibiotic usage especially in the Group IV should be consulted by Hospital Epidemiologist.
5. It is recommended that antibiotic prophylaxis has not exceeded 48 hours and antibiotic therapy of the Group II, III and IV has been carried out for at least 10 days.

The Hospital Infection Control Team has developed an algorithm of procedure for the process of the quality

Rules of antibiotic therapy

Does the patient require antibiotic therapy?

Determining type of antibiotic therapy

Sampling material for microbiologic tests

deterioration

Group I
Application of preventive antibiotic therapy when:
- there are no infection markers,
- risk factors are present,
- an operation is planned,

Group II
(available 24h a day)
Application of empirical antibiotic therapy in case of:
- critical clinical condition of the patient,
- clinical manifestation of the infection,

Group III
Application of the first-choice antibiotic therapy, when:
- the clinical condition of the patient requires introduction of antibiotic

Evaluation of the clinical condition

improvement

Interpretation of the test result

Negative result

Positive result

Evaluation of the clinical condition

deterioration

improvement

Sampling material for microbiologic tests

Change of antibiotic into one compliant with antibiogram

Consultancy with an epidemiologist

Group IV – restricted use antibiotics
(available upon the Manager acceptance)
Application of the first-choice antibiotic therapy.

Application of antibiotic of Group III

Continuation of the therapy

Group IV a
(available in the hospital chemist's)

Group IV b
brought for an individual patient
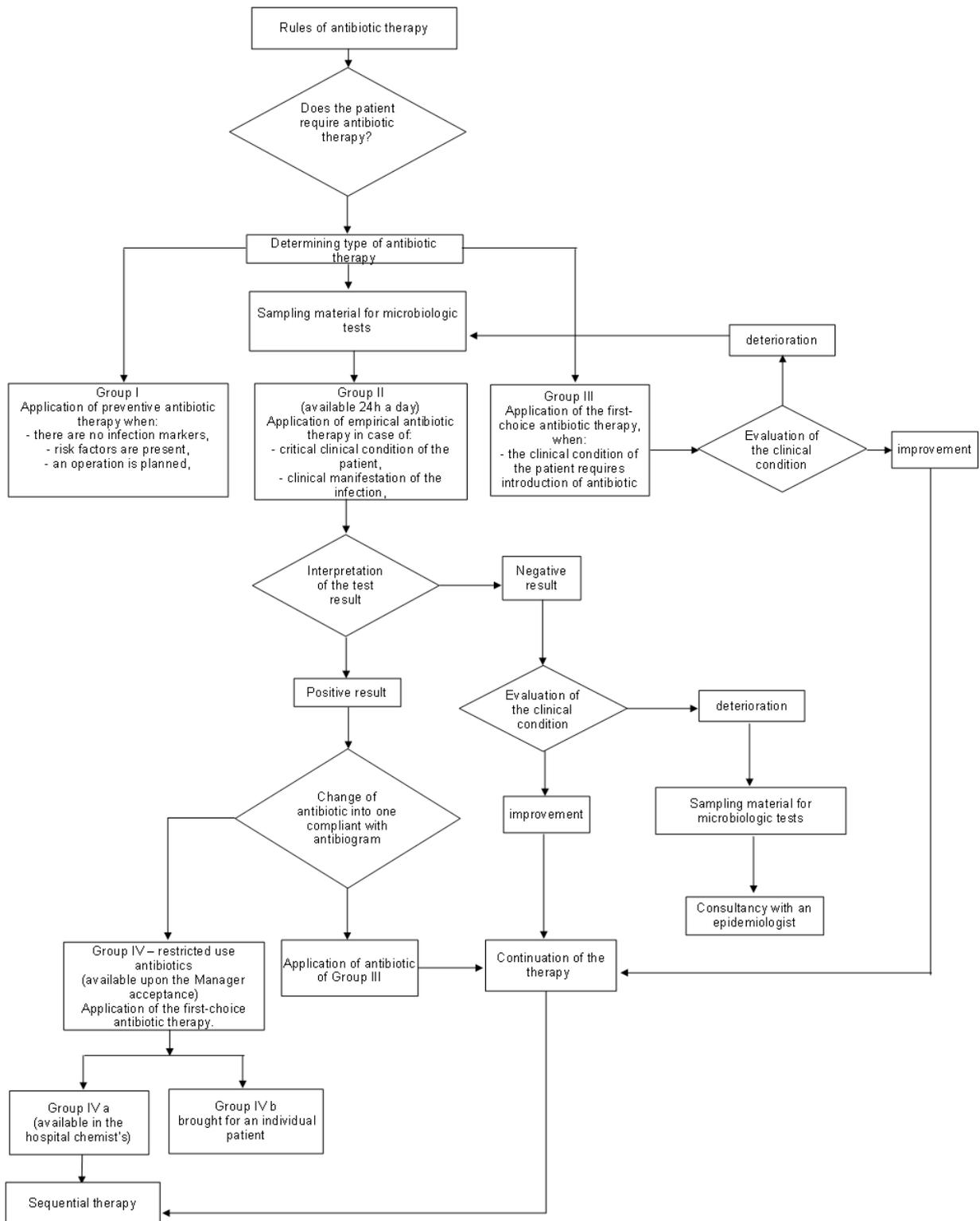
Sequential therapy

Fig. 1.   Algorithm of antibiotic therapy rules

management system ISO 9001:2008, which is shown in Figure 1. The principles of rational antibiotic therapy were introduced by decree of the hospital Director on 1 October 2008.

Hospital microbiological maps, comparisons of antibiotic cost, specification of microbiological tests made before and after introduction of the principles of a rational antibiotic therapy have been analyzed. The number of microbiological tests was converted into one bed and one patient, based on data from 2007 to 2012. In order to compare the costs, the percentage of antibiotics has been calculated in relation to drug general budget and percentage of various antibiotics in relation to antibiotic budget. The costs of antifungals and antivirals drugs have not been calculated in the antibiotic therapy cost. Annual antibiotic consumption has been counted

according to the defined daily dose (DDD) index created by the WHO. The Microsoft statistical program has been used for calculation.

RESULTS

In 2007 the hospital microbiological maps showed that among all bacterial isolates derived from clinically relevant material, the strains of staphylococcus, enteobacteriacae, acinetobacter and pseudomonas dominated. According to drug resistance determination of bacterial strains, the following mechanisms of resistance have been detected: methicillin-resistant Staphylococcus aureus (MRSA), extended-spectrum beta-lactamases (ESBL) among Enterobacteriaceae especially Klebsiella pneumoniae and carbapenemases produced by the strains of Acinetobacter and Pseudomonas. After 6 years of implementation of the rational antibiotic therapy principles, the decrease in number of isolated strains which are resistant to Klebsiella pneumoniae ESBL and Acinetobacter baumanii (resistant to carbapenems) has been indicated. The number of the Pseudomonas aeruginosa isolates has increased approximately three times, and the number of resistant isolates to carbapenem has grown six times. The number of methicyllin-resistant staphylococcus strains (MRSA) has not changed significantly (Table III). The cost of antibiotics has been gradually decreased in 2012 in order to represent 9,66% of all drug budget (without drug programs) (tab. IV). Detailed analysis of antibiotic consumption has showed that after the implementation of rational antibiotic therapy principles the consumption of meropenem has increased twice in comparison to the all drugs. The cost of meropenem comparing to the antibiotic budget has increased from 10% to 27.95% (tab. V) within 5 years. About 90% of meropenem consumption has been generated by four units: neonatal and adult intensive care, general surgery and hematology. The number of microbiological tests was made from clinically relevant materials and have increased from 10.8 to 18.34 per one bed in 2007-2013. The number grew from 0,20 to 0,25 per one patient (tab. II), which Percentage of antimicrobial resistance testing increased from 22,78% in 2007 to 28,23% in 2013 (tab. I). Annual DDD index calculated on 100 person-days has been reduced from 59,552 in 2007 to 39,90 in 2009, and it is 47,88(tab. VI) in 2013. Currently, the hospital uses 35 kinds of antibiotics.

DISCUSSION

The modern medicine problems in the treatment of infections are caused by increasing resistance among pathogens and poor pharmaceutical sector performance

Table I.   The number of drug resistance tests made in 2007 – 2013 (clinically relevant material)

Years	Cultures	Positive	%
2007	7965	1815	22.78
2008	8811	2105	23.89
2009	9643	2312	23.97
2010	9243	2322	25.12
2011	8736	2250	25.75
2012	9910	2639	26.62
2013	11120	3140	28.23

Table II.   The number of microbiological tests made in 2007-2012 per one bed and one patient (clinically relevant material).

Year	Number of tests	Number of beds	Number of patients	Number per bed	Number per patient
2007	7965	737	39437	10.80	0.20
2008	8811	725	41745	12.15	0.21
2009	9643	715	42555	13.50	0.23
2010	9243	692	39880	13.35	0.23
2011	8736	621	37765	14.06	0.23
2012	9910	609	38504	16.27	0.25
2013	11120	606	37869	18.34	0.29

Table III. The most commonly isolated bacteria with drug resistance in 2007-2012 (clinically relevant material)

Years	Staphylococcus MRSA	Eneterobact. Kl pneumoesbl.	Ac./ resistant to carbapenems	Pseud/ resistant to carbapenems
2007	17	12	0	13
2008	4	33	5	12
2009	10	47	3	35
2010	16	17	10	26
2011	24	29	7	50
2012	11	26	6	67
2013	17	56	13	44

Table IV. The costs of antibiotics and their percentage in drug budget in years 2001-2013

Years	Drug budget	Cost of antibiotics	Percentage
2001	7.096.788	1.524.369	21.48
2002	6.980.660	1.536.604	22.01
2003	6.252.751	1.686.217	26.96
2004	5.774.295	1.063.754	18.42
2005	6.684.140	1.850.286	27.68
2006	8.667.276	1.346.957	15.54
2007	6.466.332	1.469.321	22.72
2008	7.968.523	1.813.735	22.76
2009	9.778.334	1.658.792	16.96
2010	10.786.412	1.489.959	13.81
2011	11.581.386	1.381.773	11.93
2012	13.042.577	1.260.450	9.66
2013	13.627.975	1.391.744	10.21

Table V.   Percentage of meropenem in the drug and antibiotic budgets in 2007-2013

2007	2008	2009	2010	2011	2012	2013
9.82%	19.92%	18.89%	16.61%	22.94%	27.95%	22.54%

Table VI. Antibiotic consumption according to DDD100 person – days in 2007 - 2012

Lata	2007	2008	2009	2010	2011	2012
DDD	59.52	57.17	39.90	42.38	47.18	47.88

in synthesizing new antibiotics. The stand of the WHO was determined in 2001 and European Union legislation followed it (6,7). The aim of administrative action was suppression of antibiotic use, incremental drug resistance, increase in the number of hospital infections and better surveillance of this phenomenon in outpatient centers (8,9,10). An example of antibiotic overage was the index of antibiotic use per 59,52 DDD/100 person-days in Dr Jan Biziel University Hospital No 2 in 2007. In Poland, the Hospital Infection Control Teams are responsible for these tasks (10). The Hospital Infection Control Team (HICT) of Dr Jan Biziel University Hospital No 2 in Bydgoszcz was established in 1999. HICT developed and implemented the principles of a rational antibiotic therapy in 2008. A behavior algorithm has worked since 01.10.2008. Implementation of the principles of a rational antibiotic therapy was part of the hospital antibiotic policy (1,2,3,4,5). The hospital administration, the hospital pharmacy and the microbiological diagnostic unit were engaged in realization of assumptions about the hospital antibiotic policy. In contrary to other similar projects, the implemented algorithm of antibiotic therapy points the code of conduct for physicians, and allows them not to limit the level of their decisiveness and their responsibility for infection treatment. A consultation with a clinical microbiologist and / or a hospital epidemiologist is the last element of the algorithm. It is reserved for the most difficult cases. Division of antibiotics into four groups has differentiated accessibility to them. The goals were achieved after five years from implementation of principles of a rational antibiotic therapy.

The number of microbiological tests has increased twice per 1 bad, and the number of drug resistance testing is 50% higher per year. This is a proof that physicians keep the algorithm of antibiotic therapy and limit the usage of empirical antibiotic treatment. The PPS studies which were carried out in May and June 2014 showed that the algorithm principles were ignored only in two cases, and antibiotic consumption was applied among 29% patients (438 patients). The percentage index of hospital infections is 5,25 %.

These are results below average for this type of domestic and foreign epidemiological study (9). Antibiotic therapy cost calculated as a percentage share in hospital drug budget has decreased to 10 %, which is at similar level for the last two years. In 2011 antibiotic consumption per year, according to DDD/100 person-days, was 35,68. It was counted without peri-procedural antibiotic prophylaxis. This value is close to the consumption of antibiotics which has been shown at score-based study in 2014. Negative effect of principles of a rational antibiotic therapy has been Meropenem consumption growth. The costs went up from 10% to 27%. Wards with the highest incidence of hospital infection have had about 80% of Meropenem consumption. However, in 90% cases this antibiotic has been implemented on the basis of drug resistance results.

In order to change this tendency, the Infection Control Committee held talks with heads of the wards. In 2013 Meropenem consumption was decreased. Analysis of microbiological maps have not showed growth in the number of drug resistant isolates except for Pseudomonas aeruginosa producing carbapenemases. Probably it is the effect of Meropenem consumption growth.

Antibiotic division into four groups has caused simplification in tender procedures. The hospital is using 35 types of antibiotics now. An intravenous form of amoxicillin was retreated from hospital formulary in 2012 because of low efficiency that was proven by science. The principles of rational antibiotic therapy in comparison with the other elements of antibiotic policy in hospital have caused positive changes in antibiotic ordinance. The base of these changes is the drug resistance result. It has significantly increased the antibiotic costs. Index DDD/100 person-days has fallen by 11,64. Negative phenomenon was carbapenem consumption growth in twice. It may have influenced on the 6 times growth in number of the Pseudomonas aeruginosa isolates which produce carbapenemases.

CONCLUSIONS

1. It is required to adhere to the principles of a rational antibiotic therapy by medical staff mainly on the administrative restriction of access to antibiotics.
2. Monitoring changes in drug resistance of hospital flora is an essential element of the principles of a rational antibiotic therapy modification..

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