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# Surveillance of antimicrobials use in Emergency Medicine Institute

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#### Abstract

**Background**: Antibiotics have had a profound impact on humanity's health, by improving our ability to prevent, cure and reduce the transmission of many infectious diseases. It is widely known, that the unnecessary or inappropriate use of antibiotics, occurs up to 50% of prescriptions only in the United States and Canada. Fortunately all negative impact on the human health can be roughly imagined.

Material and methods: For this study we used the data of a six-year (2009-2014) period in the Emergency Medicine Institute and their main subdivisions which show the consumption dynamics of antibacterials use in natural indexes.

**Results:** The total annual medium consumption of antimicrobials was registered as the following: ICD 1796.98 DDD/1000, SSOTD 566.12 DDD/1000 and EMI 584.05DDD/1000, with the parenteral to enteral forms share of respectively 94.67% to 5.33%, 85.62% to 14.38% and 83.52% to 16.48%. Five from nine main groups: beta-lactam antibacterials, penicilins, other beta-lactam, aminoglycoside, other antibacterials and quinolone antibacterials registered around 90% of all antibiotics consumption. Comparatively to Australian hospitals and hospitals other worldwide countries in EMI consumption per DDD/1000 was lower: by 3.39 and 2.22 times for tetracyclines, by 5.1 and 4.63 for beta-lactam and penicilins, as well as by 2.55 and 1.63 for macrolides and lincosamides.

**Conclusions:** The obtained data about the dynamics of antibacterials consumption in EMI and their main departments, in comparison with hospitals from other worldwide countries, represents important arguments and reserves for improving quality treatment, planning, rational prescription and utilization of antibiotics in hospitals.

Key words: antibacterials, defined daily dose, consumption, hospitals, utilization, occupied-bed days.

### Introduction

Many surveillance drugs consumption programs, [1, 2, 3, 4] and strategies, [5, 6, 7] are used to achieve a prudent use of antibiotics in medical care institutions and quality of the anti-infective treatment of hospitalized patients. Nevertheless, a large proportion of antibiotic prescriptions is inappropriate, and constitutes up to 50% of prescriptions only in the United States and Canada. That's why, it is important to reduce the misuse and overuse of these important resources [8]. The primary aim of the study was to evaluate the institutional representative data on utilization of main antibacterial groups like tetracyclines, amphenicols, beta-lactam antibacterials and penicillins, other beta-lactam antibacterials, macrolides and lincosamides, aminoglycoside antibacterials, quinolone antibacterials, other antibacterials and antymicotics in accordance with the World Health Organization (WHO) requirements, which are directed to determine the value of Defined Daily Doses per 1000 Occupied-Bed Days (DDD/1000) [9] in the dynamics per total institution and most important departments, and to be compared with the same published data in international scientific journals.

## **Material and methods**

For this study we used the data of a six-year (2010-2014) period consumption of antibacterials in Emergency Medicine Institute (EMI) and its main subdivisions: Intensive care departments (ICD), that include (Reanimation, Intensive Therapy and intensive "STROKE" departments) as well as SSOTD (Septic surgical and Septic Orhtotraumotology departments) which show the dynamics of consumption of main groups of antiinfectives for systemic use drugs as classified by Anatomical Therapeutic Chemical (ATC), classification system of the World Health Organization (WHO) indicated in grams and value indexes. Statistical, analytical, mathematical, comparative, logical and descriptive were used as the methods of study.

### **Results and discussion**

For determining the number of DDD/1000 we used data about total annual consumption of antimicrobials and the statistics data concerning the number of treated patients (only patients with health insurance and other free treated by the state categories of citizens) [10].

Despite the fact that the use of tetracycline in hospitals holds some of the last positions in consumption among other antibiotics subgroups, antimicrobial therapy treatment of severe acute respiratory diseases (SARS) includes tetracycline (91.0%) and its combination with other antibiotics: tetracyclines and aminoglycosides in 18.8% of the patients, tetracyclines and quinolones in 11.5%, also 63.5% received a combination of tetracyclines, aminoglycosides and quinolones, [11, 12]. In some hospitals from other countries medium consumption for tetracycline recorded the following 0.5-27-70.00 DDD/1000 [13]. Tetracyclines consumption in EMI is characterised by the use of doxycyclinum with 0.1g defined daily doses. In the last 3 years of the evaluated period a total considerable increase of consumption was recorded: from 21.07 to 143.22 DDD/1000 or by 6.80 times in all departments, from 5.9 to 106.6 in intensive Therapeutical department and from 1.41 to 25.6 DDD/1000 in septic Surgical department.

During the last decades in many countries of the world, Amphenicol consumption was limited from 0.62 to 0.01% or totally absent [14, 15]. Notwithstanding, due to the increase of antimicrobial resistance to all antibiotics, in some countries has been renewed the interest to old drugs that have fallen into disuse. One of such examples is Israel, where Chloramphenicolum with susceptibility is routinely assessed in 44.4% – 83.3% of hospitals mostly for the treatment of aspiration pneumonia, [16]. In EMI the medium institutional amphenicols consumption constitued less than 1 DDD/1000 and recorded an increase during the years 2009-2014 from 0.5 to 0.8 DDD/1000 or by 40%, as well all in the evaluated departments of 5.37 to 9.45 DDD/1000 or by 175.98%.

The beta-lactam antibiotics remain the most heavily used antibacterials in clinical medicine. The annual consumption in US is estimated to be in the range of 10–30 million tons, which continues to increase, [17, 18]. From all antibiotics in hospitals, the use of beta-lactam recorded in mean 30-50%, [19, 20]. In EMI consumption of this group is characterised by use of parenteral (P) and enteral (E) forms of Ampicillinum with DDD 2.0 P and 2.0E, Amoxicillinum DDD 1.0 P and 1.0 E, Amoxicillinum+ Acidum clavulanicum ICD with DDD 3.0 P and 1.0 E, Ticarcillinum DDD with 15.0 P. Total beta-lactam antibacterials and penicillins consumption in main departments of EMI in DDD/1000 during 2009-2014 is shown in figure 1.

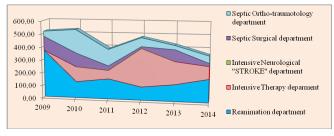


Fig. 1. Total beta-lactam antibacterials and penicillin consumption in DDD/1000 during 2009–2014.

From figure 1, it could be observed a total decrease of consumption of the group of antibiotics from 516.88 in 2009 to 356.82 DDD/1000 in 2014 or by 25.40%. From the annual medium consumption of 562.51 DDD/1000 could be placed as follows: the first – Reanimation department with 178.08 DDD/1000 or 31.66%, the second – Intensive Therapy department with 131.82 DDD/1000 or 23.43%, the third – "STROKE" intensive care department with 105.25 DDD/1000 or 18.71%, the fourth – septic Orhtotraumotology department with 84.37 DDD/1000 or 15.00% and septic Surgical department with 62.99 DDD/1000 or 11.20% on the fifth position.

All around the world in hospitals the consumption of other beta-lactam antibiotics recorded in mean 15-20% of all antibiotics, [21, 22, 23], whereas in EMI 50-60%. That situation determined a higher attention for this group of anti-infectives for systemic use. Total other beta-lactam antibiacterials consumption in DDD/1000 during 2009-2014 is shown in figure 2.



Fig. 2. Total other beta-lactam antibacterials consumption in DDD/1000 during 2009–2014.

From figure 2, it could be observed a total increase of other beta-lactam antibacterials consumption for all departments from 1893.69 DDD/1000 in 2009 to 2373.49 DDD/1000 or by 25.30%. According to the all departments annual medium consumption of 2701.58 DDD/1000 is placed as following: the first - Reanimation department with 970.38 DDD/1000 or 35.92% and a decrease from 1416.54 to 886.7 DDD/1000 or by 37.34%, the second - Intensive Therapy department with 794.95 DDD/1000 or 29.43% and a decrease from 974.67 in 2010 to 597.7 or by 38.68%, the third - Intensive Neurological "STROKE" department with 467.76 DDD/1000 or 17.31% and a decrease from 509.6 in 2013 to 425.95 or by 16.42%, the fourth - septic Surgical department with 237.92 DDD/1000 or 8.81% and a decrease from 310.05 to 187 DDD/1000 and septic Orhtotraumotology department with 230.57 DDD/1000 or 8.53% and an increase from 167.1 to 276.14 DDD/1000 or by 65.25% on the fifth position.

Consumption of macrolides and lincosamides antibacterials in EMI is characterised by use of parenteral (P) and enteral (E) forms as folowing: Erytromycin DDD 1.0 E, Midecamycinum DDD 1.0 E, Clarithromycinum DDD 0.5 EP, Azithromycinum DDD E0.3, P.5, Lincomycinum DDD 1.8 P.

A total decrease of macrolides and lincosamides consumption for all departments constituted from 108.77 in 2009 to 26.56 DDD/1000 in 2014 or by 75.58% and varied considerably in every subdivision during the evaluated period.

In hospitals from other countries, medium consumption for aminoglycosides recorded the following: 40.00 to 50.00DDD/1000 or not more than 5% of all amounts of antibiotics. At the same time consumption in ICD for critically affected patients is higher and varied between 38-66%, [22, 23]. In EMI, aminoglycoside antibacterials are presented by use of parenteral forms of the following antibiotics: Streptomycinum 1.0 P, Gentamycinum 0.2 P, Kanamycinum 1.0 P and Amikacinum 1.0 P defined daily doses.

In figure 3 the total consumption of aminoglicosides in DDD/1000 during 2010-2014 is shown.

Figure 5 demonstrates a total decrease in consumption of aminoglycosides for all departments during 2009 and 2010 from 780.30 to 677.89 DDD/1000 and a steep increase to 982.25 DDD/1000 in 2013, followed by a spontaneous

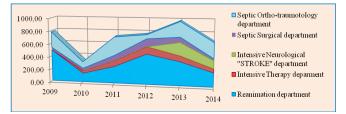


Fig. 3. Total consumption of aminoglycosides in DDD/1000 during 2010-2014.

decrease to 677.27 DDD/1000 in 2014 or by 31.05%. From the annual medium consumption of 832.24 DDD/1000, in all departments, the standings are the following: the first – Reanimation department with 326.37 DDD/1000 or 39.21%, the second – septic Orhtotraumotology department with 196.80 DDD/1000 or 23.64%, the third – intensive Neurological "STROKE" department with 165.38 DDD/1000 or 19.17%, the fourth – intensive Therapy department with 76.31 DDD/1000 or 9.17%, and septic Surgical department with 67.47 DDD/1000 or 8.11% on the fifth position.

Quinolone, is a broad-spectrum antibiotic, which plays an important role in the treatment of severe bacterial infections, especially hospital-acquired infections and has one more priority recommended as first-line therapy [24]. Consumption in EMI is characterised by the use of parenteral (P) and enteral (E) forms as the following: first-generation: Acidum pipemidicum ICD DDD 0.8 E,P, second-generation: Ofloxacinum DDD 0.4 E, Ciprofloxacinum DDD 1.0 E, 0.5 P, fourth-generation: Gatifloxacinum DDD 0.4 E,P and Mofloxacin with DDD 0.4 E,P. During the period 2009 to 2013 a total steep decrease from 583.42 to 185.63 DDD/1000 in consumption of quinolone antibacterials, followed by a significant increase to 469.65 DDD/1000 in 2014. In comparison with the annual medium consumption of 468.16 DDD/1000 the main three positions could be placed as the following: the first place - Reanimation department with 213.16 DDD/1000 or 45.62%, the second - intensive Neurological "STROKE" department with 84.04 DDD/1000 or 17.95% and the third - Intensive Therapy department with 80.26 DDD/1000 or 17.14%.

Consumption of other antimicrobials in EMI is characterised by the use of parenteral (P) and enteral (E) forms as the following: glycopeptide antibacterials: Vancomycinum DDD 2.0 P, imidazole derivatives: Metronidazolum DDD 1.5 P, nitrofuran derivatives: Furazidinum DDD 0.2 E, Nitrofurantoinum DDD 0.2 E and other antibacterials: Dioxydinum DDD 0.7 P and Nitroxolinum DDD 1.0 E.

Total other antibacterials consumption in DDD/1000 during 2009-2014 is shown in figure 4.

From figure 4, it can be stated a considerable decrease of other antibacterials consumption during 2009 and 2012 from 607.50 to 312.92 DDD/1000 of the total consumption or by 48.49%, followed by a steep increase to 551.08 DDD/1000 in 2014 or by 76.11%. According to the all departments annual medium consumption of 477.3 DDD/1000, could be placed as follows: the first – intensive Therapy department

with 244.42 DDD/1000 or 51.22%, the second – Reanimation department with 167.7 DDD/1000 or 35.14%, the third – intensive Neurological «STROKE» department with 88.31 DDD/1000 or 18.5%, the fourth – septic Surgical department with 47,06 DDD/1000 or 9.86% and septic Orhtotraumotology department with 29.35 DDD/1000 or 6.15% on the fifth position.



Fig. 4. Total other antibacterials consumption in DDD/1000 during 2009–2014.

Despite the fact that the use of antibiotics in many parts of the world has been described in details, the data concerning the use of antimycotics for systemic use such as imidazole derivatives and triazole derivatives are scarce, [25, 26]. Consumption in EMI is characterised by use of parenteral (P) and enteral (E) forms as the following: imidazole derivatives: Ketoconazolum DDD 0.2 E and Triazole derivatives: Fluconazolum with DDD 0.2 E, P. A total decrease in consumption of antimycotics for systemic use for all departments during 2009 and 2010 from 190.65 to 131.48 DDD/1000 and a steep increase to 231.22 DDD/1000 in 2013, followed by a spontaneous decrease to 108.91 DDD/1000 in 2014 or by 52.88%. More than 100 DDD/1000 from the annual medium consumption of 198.54 DDD/1000 in all departments recorded only Reanimation department with 105.25 DDD/1000 or 53.01%.

Evaluation of consumption of main groups of antimicrobials for systemic use shows a medium annual (for 6 years) period for: Reanimation department of 1981 DDD/1000, intensive Therapy department of 1192 DDD/1000, intensive Neurological "STROKE" department of 965 DDD/1000, septic Surgical department of 965 DDD/1000 and for septic Orhtotraumotology department of of 657 DDD/1000. A total decrease since 2009 until 2014 of antimicrobials consumption for ICD from 3273.79 to 1281.71 DDD/1000 or by 60.85%, for SSOTD from 631.14 to 515.54 DDD/1000 or by 18.32% and for EMI from 662.4 to 464.1 or by 29.94% during the evaluated period was recorded.

To determine the correlation between parenteral and enteral forms of evaluated antibiotics, was counted total by forms DDD/1000 separately for ICD and SSOTD and divided by the number of those departments (3 and respectively 2). The results are shown in table 1.

Data from table 1 shows the total annual medium consumption during 6 years, recorded for ICD 1801.00 DDD/1000, SSOTD 581.72 DDD/1000 and EMU 584.05 DDD/1000. Parenteral and enteral forms of use from total

Table 1

Departments of and EMI	ICDD			SSOTD			EMI		
Groups of antibacterials/ forms of use	Р	E	т	Р	E	т	Р	E	Т
Tetracyclines	0	9.6	9.6	0	11	11	0	15.25	15.25
Amphenicols	3.52	0.27	3.79	0.63	0	0.63	0.65	0.25	0.9
Beta-lactam and penicilins	174.39	3.9	174.39	52.21	21.48	73.69	54.4	11.1	65.5
Other beta-lactam	895.3	0.48	895.78	221.8	12.42	234.22	249.89	12.38	262.27
Aminoglycozide	192.83	0	192.83	132.1		132.1	76.23	0	76.23
Macrolides and lincosamides	14.24	4.49	18.73	38.86	1.65	40.51	33.07	1	34.07
Quinolone	161.9	13.1	175	11.6	33.6	45.2	37.4	35.6	73
Other antibacterials	209.28	21.87	231.15	36.8	2.87	39.67	34.82	3.5	38.32
Antimycotics	49.71	46	95.71	0.11	15.6	0.11	1.31	17.2	18.51
Total	1701	95.81	1796.81	494.1	72.02	566.12	487.77	96.28	584.05

Correlation between parenteral and enteral forms of consumption of maim group of antibacterials in DDD/1000 in ICD, SSOT departments and EMI

DDD/1000 consumption in ICD departamentals represent 94.46% to 5.54%, in SSOTD departments respectively 84.94% to 15.06%, as well as for EMI 83.52% to 16.48%. Five from nine main groups: beta-lactam antibacterials and penicilins, other beta-lactam, aminoglycozide, other antibacterials and quinolone antibacterials of the total medium consumption represents 1673.05 or 92.90% in ICD departments, 524.78 or 90.21% in SSOTD departments and respectively 515.32 or 88.23% in EMI. In table 2, comparative medium data of antimicrobials consumption per DDD/1000 in EMI and some international hospitals and perceptual change during 2009 to 2014 years are shown.

The results from table 2 show that during the evaluated period tetacycline consumption recorded an increament by more than 250% in EMI and Australian hospitals, when in the second case, it was recorded by 3.39 (51.75:15.25) as well as by 2.22 (33.80:15.25) times higher in other international hospitals, [27, 28, 29, 30]. The similar report by 5.1 and 4.63 times more could be mentioned for beta-lactam antibacterials, penicilins, as well as for macrolides and lincosamides by 2.55 and 1.63 times more. A decrease in consumption was recorded for aminoglycozide antibacterial, quinolone antibacterials and other antibacterials. The percentage changes in consumption of antimicrobial for systemic use for other international hospitals can't be counted, because evaluated data were for the period of 1 or not more than 2 years.

## Conclusions

1. Five from nine main groups: the beta-lactam antibacterials, penicilins, the other beta-lactam, the aminoglycoside, the other antibacterials and the quinolone antibacterials registered around 90% of all consumption. Comparatively to Australian hospitals and other hospitals in foreign countries in EMI consumption per DDD/1000 was less by: 3.39 and 2.22 times for tetacyclines, 5.1 and 4.63 for beta-lactam and penicilins, and by 2.55 and 1.63 for macrolides and lincosamides.

2. Medium annual consumption in the evaluated period recorded the following results: in Reanimation department 1981 DDD/1000, intensive Therapy department 1192 DDD/1000, intensive Neurological "STROKE" department 965 DDD/1000, septic Surgical department 965 DDD/1000 and in Septic Orhtotraumotology department 657 DDD/1000.

3. Total annual medium consumption of antimicrobials recorded for ICD 1801.00 DDD/1000, SSOTD 581.72 DDD/1000 and for EMU 584.05 DDD/1000, with the parenteral and enteral forms share respectively 94.46% to 5.54%, 84.94% to 15.06% and 83.52% to 16.48%.

4. A total decrease during the evaluated period of antimicrobials consumption for ICD from 3273.79 to 1281.71 DDD/1000 or by 60.85%, for SSOTD from 631.14 to 515.54 DDD/1000 or by 18.32% and for EMI from 662.4 to 464.1 or by 29.94% was recorded.

5. Obtained data about consumption dynamics of antibacterials in EMI and its main departments in comparison with hospitals from worldwide countries represents an important argument, which encourages to improve the quality of the treatment, planning, rational prescription and utilisation of antibiotics in hospitals.

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