# EVALUATION OF ANTIMYCOTICS FOR SYSTEMIC USE CONSUMPTION IN EMERGENCY MEDICINE INSTITUTE

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#### Rezumat. Evaluarea consumului de antimicotice de uz systemic în Institutul de Medicină Uregentă

În ciuda faptului, că utilizarea antimicoticelor în multe țări ale lumii a fost deja descrisă în detaliu, date referitoare la utilizarea derivaților de imidazol și de triazol sunt limitate. Prezentul studiu a avut ca scop evaluarea dinamică și determinarea locului consumului antimicoticelor în cele mai importante departamente ale IMU. În perioada evaluată s-a înregistrat o creștere a consumului de antimicotice pentru uz sistemic în IMU de la 12.1 până la 21.6 sau cu 78,51%, a fost înregistrată în perioada evaluată, și vice-versa în secțiile de asistență medicală intensivă o scădere de la 158,65 la 31,27 sau cu 80,29%, așa cum și în secțiile septice de la 16.00 până a 7.55 DDD/1000 sau cu 52,81%. Consumul mediu anual pe instituție este 18.68 DDD/1000 și, respectiv, 79.04 și 15.71 DDD/1000 în secțiile de asistență medicală intensivă a fost de 435.19 lei, în secțiile septice de 158.67 lei, iar în întregime pe IMU respectiv de 106.41 lei. Consumul de antimicotice pentru uz sistemic pe parcursul a 6 ani în EMI a înregistrat o creștere și vice-versa, o scădere în departamentele evaluate. Datele obținute în urma evaluării prezină interes practic și științific în

Cuvinte-cheie: antimicotice sistemice, doză definită de zi cu zi, consumul, utilizarea rațională, spitale, glicopeptidici, imidazol și derivați de triazol

#### Summary

Despite the fact, that the use of antymicotics in many countries of the world has been already described in detail, data concerning the use of imidazole and triazole derivatives are scarce. The study was designed to determine the place, analyze the use of antymicotics in the most important departments of EMI. An increase in consumption of antimycotics for systemic use in EMI from 12.1 to 21.6 or by 78.51% was recorded during the evaluated period, and vice versa in ICUD departaments a decrease from 158.65 in 2009 to 31.27 or by 80.29%, as well as in SSOTD from 16 to 7.55 DDD/1000 or by 52.81% was registered. When the annual medium consumption determined from 6 years per institution recorded 18.68 DDD/1000 and respectively 79.04 and 15.71 DDD/1000 in ICUD and SSOTD departments. In 2014 was recorded a cost of 435.19 lei per DDD/1000 in ICUD departments, and respectively 158.67 lei registered in SSOTD departments as well as 106.41 lei per EMI. Consumption of antimycotics for systemic use during 6 years in EMI registered a step increase and vice versa, a decrease in all the important departments. The obtained results presents interest for optimizing the planning and improving management of rational use of antibiotics in all other hospitals.

Key words: antimycotics, defined daily dose, consumption, rational use, hospitals, glycopeptide, imidazole and triazole derivatives

### Резюме. Изучение расхода противогрибковых средств для системного действия в Институте Ургентной Медицины

Несмотря на то, что использование противогрибковых средств во многих странах описаны подробно, данные об использовании имидазола и триазола ограничены. Настоящее исследование, направленно на изучение

динамики расхода и определения объема использования этой группы антибиотиков в отделениях интенсивной медицинской помощи и гнойных отделениях учреждения. За период исследования расход противогрибковых медицинских препаратов для системного применения в ИУМ увеличился с 12.1 до 21.6 ССД/1000 или на 78.51% и наоборот отделениях интенсивной медицинской помощи и гнойных отделениях произошло сокращение этого расхода с 158.65 до 31,27 в 2009 году или на 80.29%, и соответственно от 16 до 7.55 ССД/1000 или 52.81%. Среднегодовой расход ССД/1000 по учреждению составил 18.68 ССД/1000, и соответственно, 79.04 и 15.71 ССД/1000 в отделениях интенсивной медицинской помощи и гнойных отделениях. Стоимость ССД/1000 в 2014 в отделениях интенсивной медицинской помощи и гнойных отделениях. Стоимость ССД/1000 в 2014 в отделениях интенсивной медицинской помощи в году составил 435.19 лей, в гнойных отделениях 158.67 лей по учреждению 106.41 лей соответственно. Расход данной группы антибиотиков в целом по учреждению за исследуемый период увеличился, в то время как в отделениях интенсивной медицинской помощи и гнойных отделениях отделениях и оптимизации планирования, а также рациональное назначения антибиотиков во всех других больницах.

Ключевые слова: противогрибковых средств для системного действия, среднесуточная доза, расход, рациональное использование, госпиталь

## Introduction

Despite the fact, that the use of antibiotics in many parts of the world has been described in details [1. 2. 3. 4. 5] and many strategies are used to achieve a prudent use of antibiotics in medical care institutions in order to qualify anti-infective treatment of hospitalized patients, [6. 7], data on the use of antimycotics for systemic use such as imidazole derivatives and triazole derivatives are scarce, [8, 9, 10]. The primary aim of the study was to evaluate institutional representative data on antymicotics utilization in accordance to World Health Organization (WHO) requirements, directed o determine value of Defined Daily Doses per 1000 Occupied-Bed Days (DDD/1000) and value cost in the dynamics per total institution and most important departments,[11] and compare with the same published data in internationals scientific journals.

#### Material and methods

For this study we used the data of a six-year (2010-2014) period DDD/1000 consumption of other antibacterialin EMI (Emergency Medicine Institute) and their main departments as following: ICU (Re-animation, intensive Therapy and intensive Neurological "STROKE" departments) and SSOTD (septic Surgical and septic Orhtotraumotology departments) which shows the dynamics of consumption of antiinfective for systemic use drugs as classified by Ana-

tomical Therapeutic Chemical (ATC) classification system of 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 DDD/1000 we used data about total annual consumption of antimycotics for systemic 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), the total number of occupied bed/days in the institution and respectively for the evaluated departments,[12, 13, 14, 15].

Based on their antibacterial spectrum of antimycotics for systemic use are divided into generations [16] consumption of which in EMI is carecterised by use of parenteral (P) and enteral (E) forms as folowing: I midazole derivatives: ketoconazolum DDD 0.2 E and triazole derivatives: fluconazolum DDD 0.2 E .P.

Total antimycotics for systemic use consumption in DDD/1000 during 2009-2014 is shown in **figure 1**.

From **figure 1**, it could be observed a total decrease in consumption of antimycotics for systemic use per all departments during 2009 and 2010 from 190.65 to 131.48 DDD/1000 with a steep increase to 231.22 DDD/1000 in 2013, followed by a spontaneous decre-



Fig. 1. Total antimycotics for systemic use consumption in DDD/1000 during 2009–2014



Fig. 2. Total antimycotics for systemic useconsumption in DDD/1000 (parenteral forms)



Fig. 3. Total antimycotics for systemic use consumption in DDD/1000 (enteral forms)

ase to 108.91 DDD/1000 in 2014 or by 52.88%. From the anual medium consumption of 198.54 DDD/1000 in all departments for the evaluated period, the standings are as follow: first - Reanimation department with 105.25 DDD/1000 or 53.01%, second - intensive Therapy department with 42.92 DDD/1000 or 21.62%, third - intensive Neurological "STROKE" department with 19.05 DDD/1000 or 9.60%, fourth - septic Surgical department with 17.41 DDD/1000 or 8.77% and septic Orhtotraumotology department with 13.91 DDD/1000 or 7.00% on fifth position. In **figure 2** the total antimycotics for systemic useconsumptionof parenteral formsin DDD/1000 during 2010-2014 is shown.

**Figure 2** demonstrates a consumption decline of parenteral forms of antimycotics for systemic use from 78.20 to 29.38 DDD/1000. Calculation of anual medium consumption from total medium anual consumption of 63.01 DDD/1000 per all departments is placing on the first position Reanimation department with 39.56 DDD/1000 or 62.79%, second - intensive Therapy department with 22.01 DDD/1000 or 34.92%, third - intensive Neurological «STRO-KE» department with 1.34 DDD/1000 or 2.13% and septic Surgical department with 0.11 DDD/1000 or 0.17 % on the last position. In **figure 3**, consumption of antimycotics for systemic use (enteral forms) in DDD/1000 during 2009-2014 is shown.

From **figure 3**, it could be stated a decrease in the total consumption of antimycotics for systemic use

for all departments during the evaluated period from 112.45 in 2009 to 79.54 DDD/1000 in 2014 or by 29.27% From the total medium anual consumption of 135.53 DDD/1000 per all departments in the evaluated period is placesing on the first position Reanimation department with 65.68 DDD/1000 or 48.47%, second - intensive Therapy department with 20.92 DDD/1000 or 15.43%, third - intensive Neurological «STROKE» department with 17.72 DDD/1000 or 13.07%, fourth - septic Surgical department with 17.30 DDD/1000 or 12.77% and septic Orhtotraumotology department with 13.91 DDD/1000 or 10.26% on the last position.

To determine the medium consumption of other antibacterial DDD/1000 the total of DDD/1000 was counted separately for ICU and SSOTD and divided to the number of those departments (3 and respectively 2). The results are shown in **table 1**.

The data in **table 1** shows that in the evaluated period consumption of DDD/1000 in ICU departaments of antimycotics for systemic use decreased by 80.29%, with P to E forms share from the medium yearly consumption of 62.89% and 37.11%, respectively in SSOTD by 52.81with P to E forms share of 0.7% to 99.30% and vice versa the total EMI increase by 80% with P to E forms share of 7.76% and 92.24%. Consumption in ICU comparatively to SSOTD departments in 2014 was (31.27:7.55) = 4.14 times more.

From table 2, it could be observed that during the evaluated period consumption of antimycotics for

systemic use in EMI recorded an increase from 12.1 to 21.60 DDD/1000 or by 78.51% and calculated the yearly medium of 18.51 represents a share of 3.27% from the 6 years medium annual total of 566.02 DDD/1000. The consumption of this group of drugs in Belgian hospitals in 2006 and 2007 was 21 and 22 DDD/1000 respectively representing a share of practically of 4% in both years from the total of 525 and respectively 549 DDD/1000. Taking into consideration the connection between different indicators that caractherised consumption of antimicrobial, [18], was determined DDD/1000 of antimycotics for systemic use for other international hospitals and devised with the consumption: more than 50 DDD/1000: Denmark 51.11, from 30 to 50: Italy 42.79, Norway 31.69 and a medium of 37.24, from 10 to 30: Sweden 14.58, Finland 18.45, Slovenia 27.53 and a medium of 22.50

from 0 to 10: Estonia 9.90, Bulgaria 6.56, Hungary 5.63 and a medium of 7.36 DDD/1000 (Table 2). The yearly calculated medium consumption of 29.53 DDD/1000 for other international hospitals, represents 5.32% from yearly medium total consumption of 555.25 DDD/1000 determined as yearly medium consumption of total other international hospitals in 2008. So, the yearly medium of 18.51 DDD/1000 in EMI is by 16.15% less than 21.5 DDD/1000 yearly medium recorded in Belgium hospitals and by 59.54% of 29.53 DDD/1000 yearly medium recorded in others international hospitals. The total value cost of other antibacterial use per DDD/1000 in lei is presented in **figure 4**.

As it could be observed from **figure 4**, during the evaluated period the cost per DDD/1000 of antimycotics for systemic use recorded a decrease for

Table 1

$f_{i} = f_{i} = f_{i$									
Department	Administration /time	2009	2010	2011	2012	2013	2014	Procent 2009/ 2014	Medium yearly consumption
ICUD	Parenteral	78.20	23.73	34.19	30.36	21.98	9.79	-87.48	49.71
	Enteral	80.45	29.01	52.2	51.75	41.11	21.48	-73.3	46.00
	Total	158.7	52.74	86.39	82.11	63.09	31.27	-80.29	79.04
SSOTD	Parenteral	0	0	0.31	0.24	0.08	0	0	0.11
	Enteral	16	13.01	18.68	17.47	20.92	7.55	-52.81	15.60
	Total	16	13.01	18.99	17.71	21.01	7.55	-52.81	15.71
Total EMI	Parenteral	0.5	1.5	1.9	1.9	2	0.9	80	1.45
	Enteral	11.5	18.5	18.2	14.2	20.3	20.7	80	17.23
	Total	12	20	20.1	16.1	22.3	21.6	80	18.68

Antimycotics for systemic use (parenteral and enteral forms) consumption of DDD/1000 in ICUD and SSOTD departments of EMI

Table 2

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Institution/data/year	2009	2010	2011	2012	2013	2014	Medium
Emergency Medicine Institute	12.1	20.0	20.1	15.0	22.3	21.6	18.51
Total	662.4	558.2	622.1	542.4	546.9	464.1	566.02
Percentage	1.83%	3.58%	3.23%	2.77%	4.08%	4.65%	3.27%
International hospitals	2006	2007					
Belgian hospitals,[17]	21	22					21.5
Total	525	549					537
Percentage	4%	4.01%					4%
Other international hospitals[18]							
Denmark hospitals more than 50			51.11				
Italy, Norway hospitals (from 30 to50)				37.15			
Sweden, Finland, Slovenia hospitals (from					22.50		29.53
10 to 30)					22.30		
Estonia, Bulgaria, Hungary hospitals from						7 26	
(0 to 10)						7.30	
Total			460	787	595	380	555.25
Percentage			11.1%	5.55%	3.78%	1.94%	5.32%



Fig. 4. Total value cost of antimycotics for systemic use per DDD/1000 in lei



Fig. 5. Valuie cost of antimycotics for systemic use in DDD/1000 of parenteral forms in lei



Fig. 6. Valuie cost of antimycotics for systemic use in DDD/1000 (enteral forms) in lei

all departments from 10101.76 to 1593.81 lei or by 6.34 times.

The main medium yearly value cost of 3530 lei for DDD/1000 that belongs to Reanimation department represents 64.89% from the medium total cost of 5440 lei in all departmental, the second position with 1404 lei or 25.80% belongs to intensive Therapy department, the third one with238.8 lei or 4.39% to intensive Neurological "STROKE" department, followed by septic Orthotraumotology department with 142.90 lei or 2.63% lei and the last position to the septic Surgical department with 124.7 lei or 2.29%. In **figure 5** the total valuie cost antimycotics for systemic use in DDD/1000 (parenteral forms) is presended.

As it could be seen from **figure 5**, during the evaluated period the cost per DDD/1000 of antimycotics for systemic use recorded decrease for all departments from 9143.57 to 1183.07 lei or by 7.73 times.

The main medium yearly value cost of 3143 lei for DDD/1000 or 69.46% calculated from the medium total all departmental cost of 4525 lei belongs to Reanimation department, second - intensive Therapy department with 1187 lei or 26.24%, third - septic Surgical department with 76.83 lei or 1.70%, followed by septic Orthotraumotology department with 71.68 lei or 1.58% lei and the last one to intensive Neurological «STROKE» department with 46.17 lei or 1.02%. In figure 6 the value cost DDD/1000 in lei of antimycotics for systemic use enteral forms is shown (**fig. 6**).

The presented data in chart 6, demonstrates that in the evaluated period value cost of DDD/1000 for all departments increased from 338.59 to 423.1 lei or by 24.96%. From the medium departments cost of 720.02 lei the first position belongs to intensive

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Department	Structure of consumption	2009	2010	2011	2012	2013	2014	
ICUD	Parenteral	4488.79	2186.5	2533	1010.2	809.21	337.27	
	Enteral	40.23	94.57	142.25	197.68	206.27	97.92	
	Total	4529.02	2281.04	2675.27	1207.88	1015.48	435.19	
SSOTD	Parenteral	0.00	0.00	28.00	10.00	3.00	94.00	
	Enteral	129.07	94.07	116.22	190.64	140.89	64.67	
	Total	129.07	94.07	144.22	200.64	143.89	158.67	
Total EMI	Parenteral	226.87	142.62	141.95	99.16	71.38	30.48	
	Enteral	107.53	100.10	98.34	195.39	134.41	75.93	
	Total	334.40	242.72	240.29	294.55	205.79	106.41	
		334.4	242.72	240.29	294.55	205.79	106.41	

Medium cost of DDD/1000 in lei of antimycotics for systemic use (parenteral and enteral forms) in EMI

Therapy department with the medium annual cost per DDD/1000 of 216.54 lei or 30.07%, second - intensive Neurological "STROKE" department with 86.08 lei or 26.75%, third - Orthotraumotology department with 93-75 lei or 17.68%, forth - septic Surgical department with 127.32 lei or 16.37% and the last one to Reanimation department with 33.28 lei or 9.12%. To determine the medium cost of antymicotics in DDD/1000 was counted the total cost of DDD/1000 separately for ICU and SSOTD and divided to the number of those departments (3 and respectively 2) in the evaluated period.

As it could see from **table 3**, total cost of DDD/1000 of antimycotics for systemic use, recorded an abrupt decrease in ICU departments from 4529.02 in 2009 to 435.19lei or by 10.41 times in 2014 and vice versa in SSOTD departments an increase from 129.07 to 158.67 lei or by 22.93%.

The total value cost of 435.19 lei recorded in 2014 in ICU departments is more than 2.74 and 3.14 times registered cost of 158.67 lei per DDD/1000 in SSOTD departments and respectively of 106.41 lei in EMI.

# Conclusions

1. During the evaluated period in EMI was recorded an increase of antimycotic for systemic use consumption from 12.1 to 21.6 DDD/1000 or by 78.51%. From annual total medium antibioics consumption of 566.02 DDD/1000, antimycotics for systemic use represents 18.51 DDD/100 or 3.27% and is by 16.15% less than 21.5 DDD/1000 yearly medium recorded in Belgium hospitals as well as by 59.54% of 29.53 DDD/1000 yearly medium recorded in other international hospitals.

2. From the anual medium consumption of 198.54 DDD/1000 in all departments, the standings are the following: first - Reanimation department with 105.25 DDD/1000 or 53.01%, second - Intensive Therapy department with 42.92 DDD/1000 or

21.62%, third - "Intensive Neurological "STROKE" department with 19.05 DDD/1000 or 9.60%, fourth - septic Surgical department with 17.41 DDD/1000 or 8.77% and septic Orhtotraumotology department with 13.91 DDD/1000 or 7.00% on fifth position.

3. Consumption of DDD/1000 in ICU departamentals of antimycotics for systemic use decreased by 80.29%, with P to E forms share from the medium yearly consumption of 62.89% and 37.11%, respectively in SSOTD by 52.81 with P to E forms share of 0.7% to 99.30% and vice versa the total EMI increase by 80% with P to E forms share of 7.76% and 92.24%.

4. A decrease cost of DDD/1000 from 334.40 in 2009 to 106.41 lei in 2014 or by 68.18% was recorded for the total institutional antimycotics for systemic use and an abrupt decrease in ICU departments from 4529.02 to 435.19 lei or by 10.41 times and vice versa in SSOTD departments an increase from 129.07 to 158.67 lei or by 22.93% was registered.

5. The fact determened by this study would serve as a significant support for hospitals to compare the data concerningantimycotics consumption with the international heath care institutions and to optimise the planning necesities, as well as to improve rational use of antimycotics.

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