SURVEILLANCE OF ANTIBIOTICS CONSUMPTION IN HOSPITALS

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Abstract. The strategic action plan on antibiotic resistance with the slogan "No action today, no cure tomorrow" was marketed at the World Health Organization Day in 2011. From this event the key strategic actions started to mitigate, prevent and control antibiotic consumption and resistance. These include: promoting the prudent multifaceted use of antibiotics; strengthening surveillance systems, monitoring the use of antibiotics to bacteria resistance and others. In the EMI a considerable decrease of antibiotics consumption was registered in the evaluated period from 662.4 to 464.1 DDD/1000.

Keywords: drug supplies, antibiotics, defined daily dose, consumption, rational use, hospitals, occupied-bed days, indices, values, natural

Rezumat

Supravegherea consumului de antibiotice în spitale

La aniversarea Zilei Organizaţiei Mondiale a Sănătăţii pe data de 7 aprilie 2011, petrecută sub sloganul "Nu vom acţiona astăzi, nu vom trata mâne" a fost aprobat Planul strategic de retenţie antimicrobiană. Ca cheie a planului s-a lansat atenuarea şi controlul asupra consumului asigurarea utilizării raţionale de antibiotice, precum şi controlul asupra rezistenţei antimicrobiene şi altele. În IMU în perioada evaluată s-a înregistrat o descreştere a consumului de antibiotice de la 662.4 până la 464.1 DDD/1000.

Cuvinte cheie: medicamente, asigurare, antibiotice, doza definită pentru o zi, consum, utilizare raţională, spitale, zi pat ocupat, indice, valoare, natural

Introduction

In developing and transitional countries, in primary care less than 40% of patients in the public sector are treated in accordance with standard treatment guidelines, [1]. There are numerous sources of data that include drugs dispensed in hospitals, [2-5]. Nevertheless in the Republic of Moldova analysis in DDD, as an important indicator of optimal rational use of drug remedies generally, and of anti-infective for systemic use ones, in particular, is not studied enough and highlighted by scientific research literature.

National Scientific-Practical Centre of Emergency Medicine of the Republic of Moldova reorganised in 2014 in Emergency Medical Institute (EMI), was founded in 1957. The whole Institution include 650 beds overall. There are 4 outpatient departments of traumatology and orthopaedics as well, [6].

The primary aim of the study was to evaluate institutional representative data on antibiotics utilization for six years (2009-2014) period, in accordance to World Health Organization (WHO) requirements, projected to determine value of Defined Daily Doses per 1000 Occupied-Bed Days (DDD/1000), [7]. That study was carried out in accordance with World Health Organization (WHO) DDD program and with the support of other two programs that were effectuated in the institution "Analysis program of consumption and stocks of drugs Anatomical Therapeutical Chemical" and "Pharmacotherapeutic software". Based on the obtained data, it aimed to make conclusions on the use of anti-infective for systemic use in the medical institutions and to propose recommendations for ensuring their optimization.

Material and methods

For this study we used data on a six-year (2009-2014) period, in the Public Health Institution, Emergency Medicine Institute (EMI), which show the dynamics of consumption of medicinal remedies pharmaco - therapeutic group J – Anti-infective for systemic use, as classified Anatomical Therapeutic Chemical classification system of World Health Organization (ATC) indicating the nature and value indexes. Statistical, analytical, mathematical, comparisons, logical and descriptive were used as the methods of study.

The results of the investigation and their analysis

To determine DDD and to compare the consumption of anti-infective for systemic use drugs for the period of 2009-2014, the statistics data concerning the number of treated patients (for only patients with health insurance and other free treated by the state categories of citizens), the number of bed/days and total annual quantities of medicines were

used. Consumption of antibiotics in value indexes "leis" in EMI for the 2014 year is presented in figure 1.

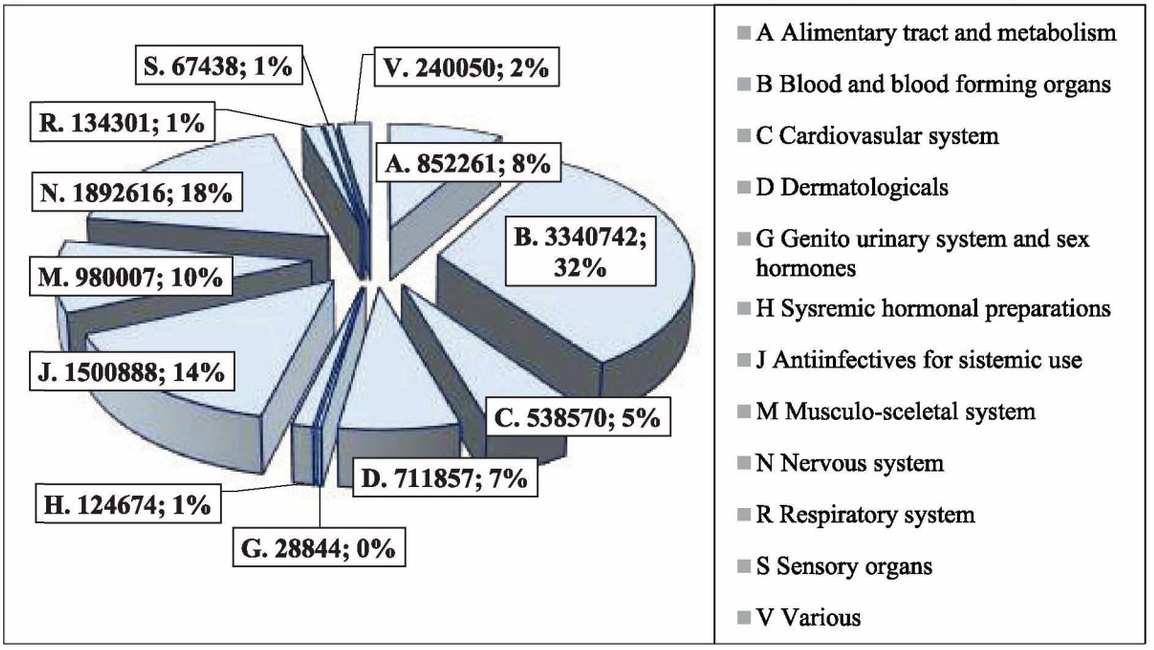

Figure 1. **The antibiotics share from all annual drugs consumption in 2014 in lei.**

From figure 1 we find that the total consumption of drugs in 2014 constituted 11 084 624 (lei), from which in accordance with ATC classification anti-infective for systemic use consisted 1 500 888 lei or 14%, that are with some deviation (2-3%) the same for more years, [8, 9].

The DDD for any drug is defined as the average dose per day for treatment the main indication for an average adult patient.

$$\text{Number of DDD} = \frac{\text{Total grams used}}{\text{WHO assigned DDD value}}$$

The World Health Organization (WHO) has determined DDDs standards for most drugs and these values have been used in calculating usage rates. To determine value of Defined Daily Doses per 1000 Occupied-Bed Days (DDD/1000) we followed 10 steps of study recommended by WHO for every antimicrobial evaluated remedies, [10]. The DDD of antibiotics publicised by World Health Organization and utilizing in EMI in table 1 is shown.

Table I

The DDD of antibiotics determined by World Health Organization and utilizing in EMI

International name of antibacterial	ROUTE	DDD (g)
J ANTIINFECTIVES FOR SYSTEMIC USE		
J01 ANTIBACTERIALS FOR SYSTEMIC USE		
J01A TETRACYCLINES		
Doxycyclinum	*O*	*0,1*
J01B AMPHENICOLS		
J01BA Amphenicols		
Chloramphenicolum	O	3
Chloramphenicolum	P	3
J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS		
J01CA Penicillins with extended spectrum		
Ampicillinum	O	2
Ampicillinum	P	2
Amoxycillinum	O	1
Amoxycillinum	P	1
J01CR Combinations of penicillinc, incl. beta-lactamase inhibitors		
Amoxicillinum + Acidum clavulanicum	*O*	*1*

Amoxicillinum + Acidum clavulanicum	*P*	*3*
Ticarcillinum + Acidum clavulanicum	*P*	*15*
J01D OTHER BETA-LACTAM ANTIBACTERIALS		
J01DB First-generation cephalosporins	-	-
Cefalexinum	O	2
Cefazolinum	P	3
J01DC Second-generation cephalosporins		
Cefuroximum	O	0,5
Cefuroximum	P	3
Cefaclorum	O	1
J01DD Third-generation cephalosporins		
Cefotaximum	P	4
Ceftazidimum	P	4
Ceftriaxonum	P	2
Cefixim	O	0,4
Cefoperazonum	P	4
Cefoperazonum + Sulbactamum	P	4
J01DH Carbapenems		
Meropenemum	P	2
Imipenemum+Cilastatinum	P	2
J01E SULFONAMIDES AND TRIMETHOPRIM		
J01EE Combinations of sulfonamides and trimethoprim, incl. derivatives		
Sulfamethoxazolum + Trimethoprimum	O	1,9
J01F MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS		
J01FA Macrolides		
Erytromycin	O	1
Midecamycinum	O	1
Clarithromycinum	O	0,5
Clarithromycinum	P	0,5
Azithromycinum	O	0,3
Azithromycinum	P	0,5
J01FF Lincosamides		
Lincomycinum	P	1,8
J01G AMINOGLYCOSIDE ANTIBACTERIALS		
J01GA Streptomycins		
Streptomycinum	P	1
J01GB Other aminoglycosides		
Gentamycinum	P	0,2
Kanamycinum	P	1
Amikacinum	P	1
J01M QUINOLONE ANTIBACTERIALS; J01MA Fluoroquinolones		
Mofloxacin	P	0,4
Gatifloxacinum	O	0,4
Gatifloxacinum	P	0,4
Acidum pipemidicum	O	0,8
Acidum pipemidicum	P	0,8
J01R COMBINATIONS OF ANTIBACTERIALS		
Ciprofloxacinum + Tinidazolum	O	2

J01X OTHER ANTIBACTERIALS; J01XA Glycopeptide antibacterials		
Vancomycinum	P	2
J01XD Imidazole derivatives		
Metronidazolum	P	1,5
J01XE Nitrofuran derivatives		
Furazidinum	O	0,2
Nitrofurantoinum	O	0,2
J01XX Other antibacterials		
Dioxydinum	P	0,7
Nitroxolinum	O	1
J02AB Imidazole derivatives		
Ketoconazolum	O	0,2
J02AC Triazole derivatives		
Fluconazolum	O	0,2
Fluconazolum	P	0,2

All in all 50 antimicrobial remedies (both for parenteral and enteral use) treating assistance of hospitalized patients in the evaluated period were used, from which with only enteral form 12 names, with only parenteral form 18 names and with both forms 10 names, which represents 40 active antimicrobial substances, [11]. Cephalosporins consumption rate of enteral forms in DDD/1000 during 2009-2014 is presented in figure 2.

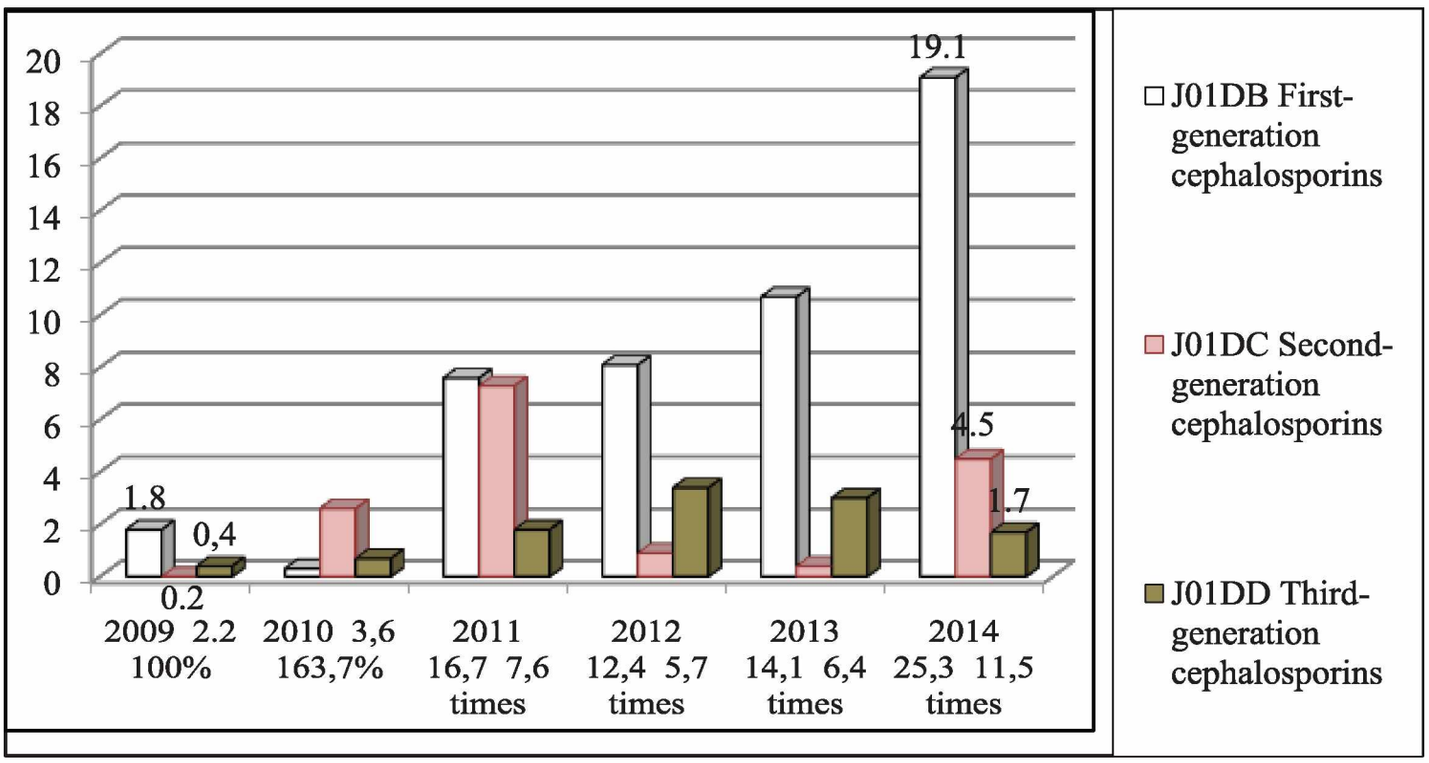

Figure 2. **Cephalosporins consumption rate of enteral forms in DDD/1000 during 2009-2014.**

From this figure as one can see the intake of enteral forms cephalosporins G-I (first generation) reveals an increment by 10.7 times, G-II the second generation by 22.2 times, G-III the third generation) by 4.3 times and increase for whole groups has changed from 2.2 in 2009 to 25.3 DDD/1000 in 2014 or by 11.5 times. Cephalosporins consumption rate of parenteral forms in DDD/1000 during 2009-2014 in figure 3 is presented.

In figure nr. 3 consumption of parenteral forms of cephalosporins is shown. A decrease by 2.45 times was registered for cephalosporin's G-I, and an increment for G-II and G-III by 2 and 2.79 times respectively. All in all, the consumption of three generation groups of cephalosporin's faces to a slight decrease from 268.5 to 247.3 DDD/1000 or with 7.9%. In figure 4 the cephalosporins consumption rate of parenteral and enteral forms in DDD/1000 during 2009-2014 it is presented.

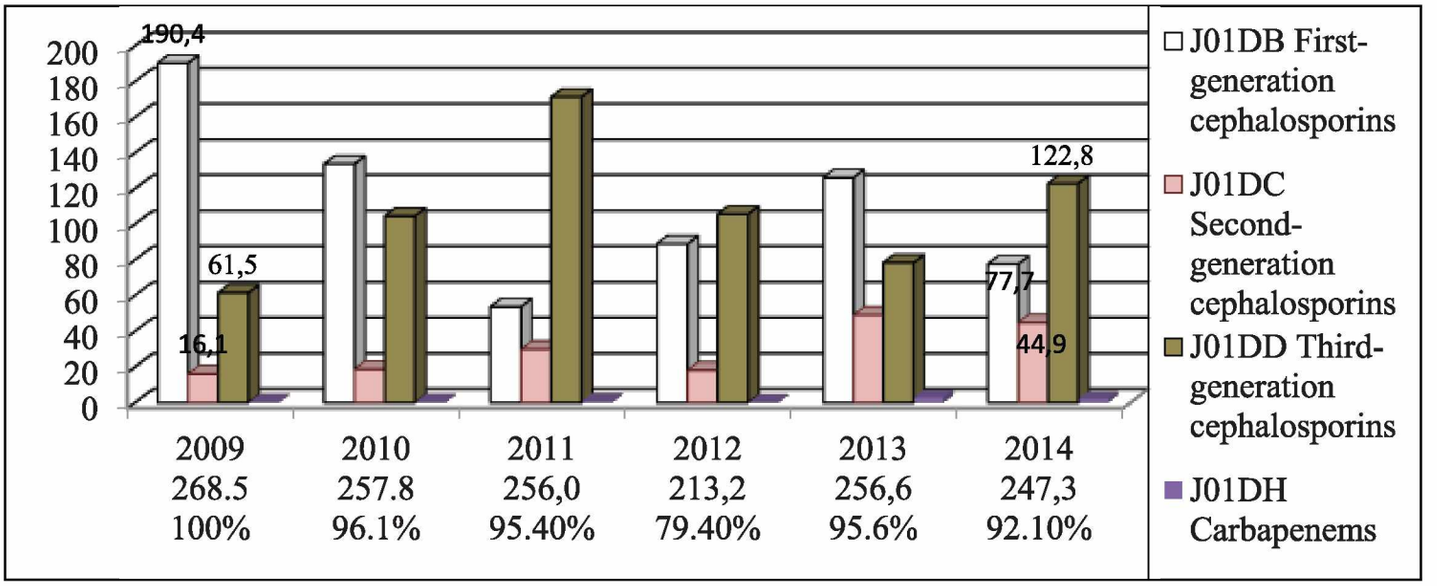

Figure 3. **Cephalosporins consumption rate of parenteral forms in DDD/1000 during 2009-2014.**

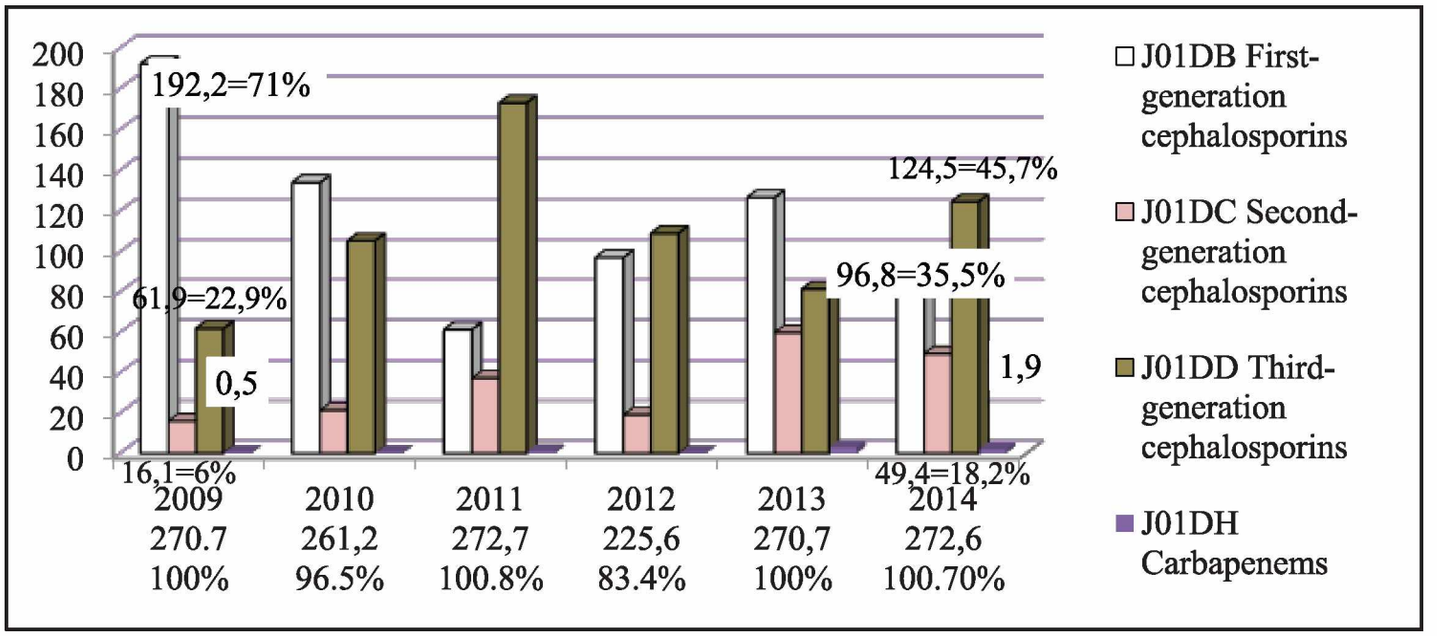

Figure 4. **Cephalosporins consumption rate of parenteral and enteral forms in DDD/1000 during 2009-2014.**

From this chart as one can see the total consumption of parenteral and enteral forms of ce-phalosporin's G-I (in the evaluated period) has decreased with 49.63%, and cephalosporin's G-II and G-III has increased from 78 (16.1 + 61.9) in 2009 to 173.9 DDD/1000 (49.4 + 124.5) respectively or by 2.3 times. The total consumption of the group encounters a slight increase from 270.7 to 272.6 DDD/1000 or with 0.7%, with some deviations in 2010 and 2012.

In figure 5 it is shown the total consumption rate subgroups of antibiotics (enteral and parenteral forms) in DDD/1000 during 2009-2014.

In this figure the total (parenteral and enteral forms) antibiotic groups used rates is demonstrated. The average aggregated annual rate for total-hospital antibiotics utilization period decreased from 662.4 in 2009 to 464.1 DDD/1000 OBD in 2014 or by 30%.

The rate of parenteral form (P) to enteral (O) from and total (T) consumption of antibiotics in DDD/1000 during 2009-2014 is shown in figure 6.

From this figure as one can see a decline with 11.1 % (85.9% - 74.8%) for parenteral and an encrease oral usage with 11.1 % (14.1% - 25.2%) had been recorded. That fact could be observed from this chart.

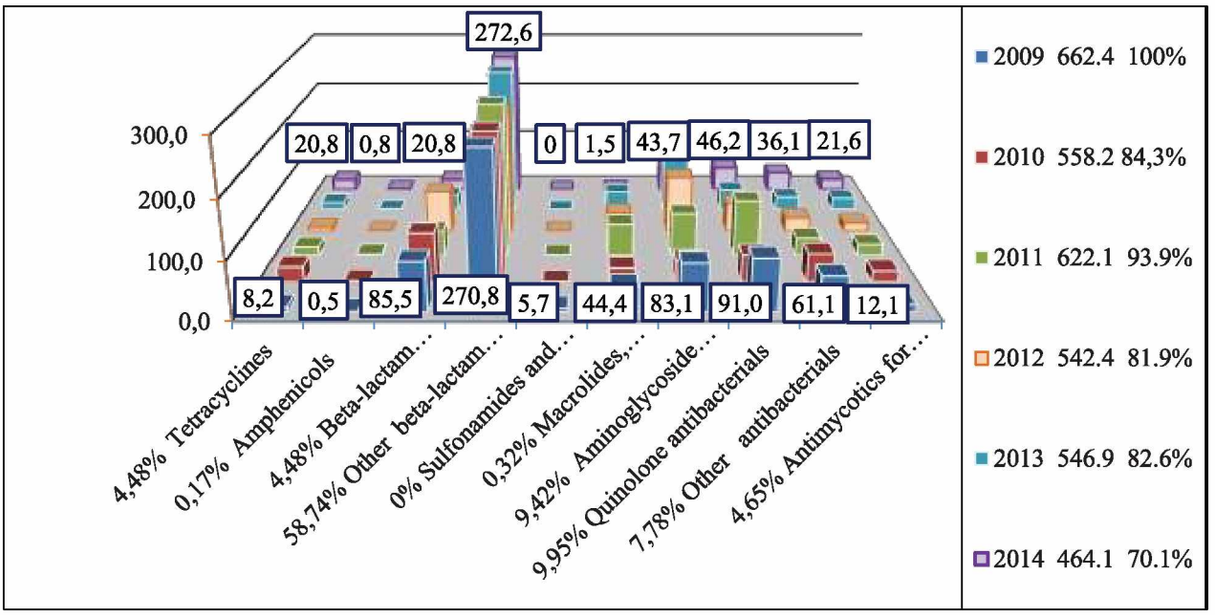

Figure 5. **Total consumption rate subgroups of antibiotics (enteral and parenteral forms) in DDD/1000 during 2009-2014.**

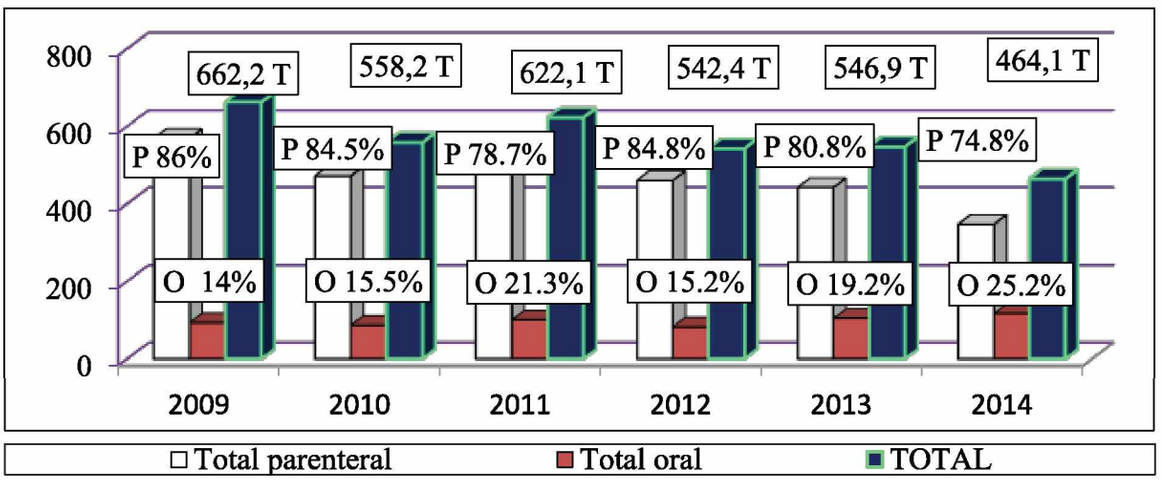

Figure 6. **The rate of parenteral form (P) to enteral (O) from total (T) consumption of antibiotics in DDD/1000 during 2009-2014.**

In figure 7 the average maximum and minimum consumption of antibiotics of DDD/1000 in European Union countries hospitals and EMI is shown.

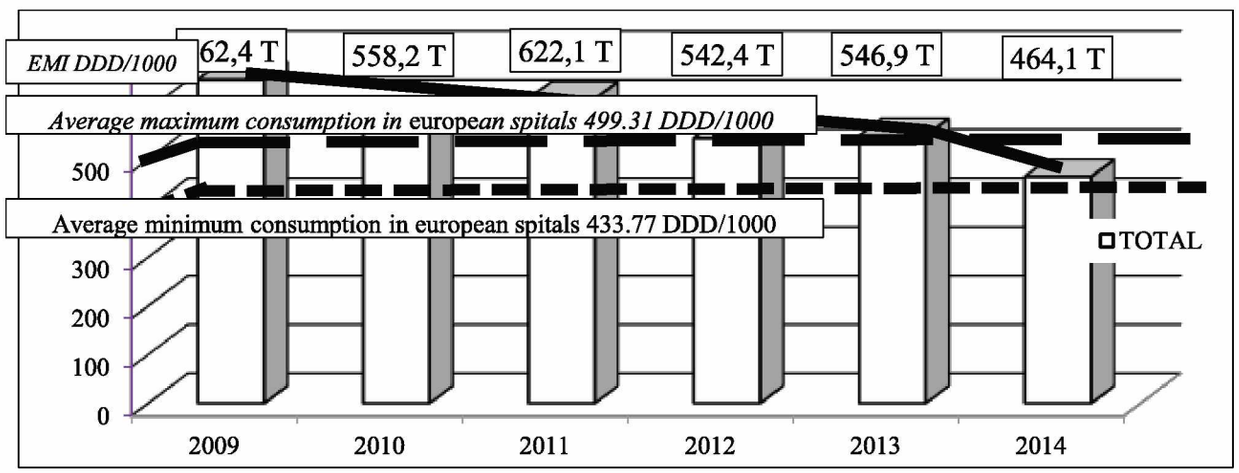

Figure 7. **The average maximum and minimum consumption of antibiotics of DDD/1000.**

In this chart the average maximum and the minimum consumption of antibiotics in DDD/1000 is shown in the period 2009-2014 between Public Health Care Institution EMI and more than 1500 European Union hospitals in comparison. As one may see the total consumption of antibiotics was recorded 662.4 DDD/1000 in 2009, which was more than average maximum consumption, registered in some hospitals of EU countries, consisting 162.4 DDD/1000. In 2014 the consumption was reduced to 464.1 or in other words the decrease was up to 198.3 DDD/1000 or by 30% in comparison with 2009. In figure 8 it is shown the seasonal pattern - the antibiotic use depending on the strength of Escherichia *Coli.*

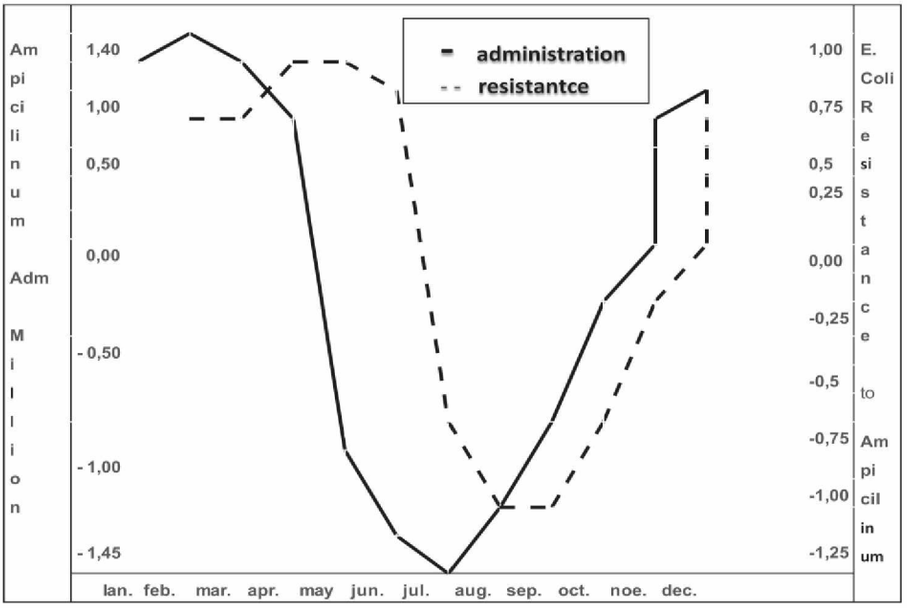

Figure 8. **The seasonal pattern - the antibiotic use depending on the strength of Escherichia Coli.**

The study of pathogenic microbes' resistance in dependence on the seasonal temperature throughout the year is an important direction in the achieving high progress in antimicrobial treatment. As one may see at this chart, the thorough analysis performed by American scientists in more than 300 hospitals in the US in the period of 1999-2007, the consumption of aminopenicillins for treatment infected patients caused by *E.coli* is much higher during cold period (November, December, January, February, March and a part of April), than hot period of the year (May, June, July, August, September and November) [12].

Because of different opinions on the preoperative antimicrobial prophylaxis under the leadership of professor Gheorghe Ciobanu, chief of Urgent Medicine Department of SMFU by "N. Testimitanu" was elaborated the institutional guide of "Antibiotic prevention of surgical infection" [13].

The content of the guide confirmed that the cephalosporin's I and II generations are used in 85 – 90% cases for preoperative antimicrobial prophylaxis in surgery and traumatology investigations.

Conclusions:

1. In EMI a considerable decrease of antibiotics consumption was registered in the period 2009 –2014. The DDD/1000 in 2009 constituting 662.4 unites was with 162.4 unites more than the medium maximum in more hospitals of EU countries. In 2014 DDD/1000 constituting 464.1 unites was with 36 unites less than mentioned medium, or in other words with 30% (198.3 unites) less than consumption in 2009.
2. The rate of parenteral forms compared with entral forms of consumption was changed significantly from 86% and 14% in 2009 to 74.8% and 25.2% in 2014 respectively. For cephalosporin's this rate constituted only 9.3% in 2014.
3. Estimation of consumption of antimicrobial medical remedies for systemic use in DDD per day and 1000 occupied bed days has permitted an appreciation of therapeutical effect on 1000 patients (or occupied bed days) and the comparison with the consumption of antibacterial in hospitals worldwide.
4. Information of institution team doctors and other measures about optimization antibiotic usage changed significantly the attitude towards the treatment of all groups of the antimicrobial medical remedies.

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