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Evaluation of antibiotics consumption in therapeutic intensive care department

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Abstract

Background: Monitoring of aggregate, ward-supply data and analysis of the anatomical therapeutic chemical/defined daily dose system, adjusted for bed-occupancy, provides a clear picture of antibiotics consumption frequency and time-trends within hospitals and especially intensive care departments.
Material and methods: For this study we used data of a five-year (2010-2014) period, in therapeutic intensive care department of the Emergency Medicine Institute, which show the consumption dynamics of anti-infectives for systemic use of drugs in grams and value indexes.
Results: The defined daily doses (DDD) per 1000 occupied-bed days (DDD/OBD) of antibiotics in therapeutic intensive care department decreased from 1524 in 2010 to 1206 DDD/1000 in 2014 or by 20.87%, however, it is by 11.77% higher than medium consumption of 1052.25 DDD/1000 in intensive care units with the same activity in international hospitals. The value of 54948 lei per DDD/1000 OBD in 2010 recorded a decline to 40754 lei or by 25.84% in 2014. The cost of one medium DDD from 36.05 lei in 2010 decreased to 33.77 lei or by 6.33% in 2014. The average antibiotics annual institution consumption constituting 464.1 DDD/1000 in 2014 was higher by 1.06% comparatively with medium consumption of 459.20 DDD/1000 registered in 1706 international hospitals, and by 35.31% in comparison with global consumption of 343 defined daily doses per 1000 patient-days.
Conclusions: The decrease of DDD/1000 OBD and their cost took place as a result of efforts for rational use of antibiotics during the evaluated period. Great opportunities were found for improving rational utilization of anti-infectives for systemic use.
Key words: antibiotics, defined daily dose, consumption, rational use, hospitals.

Introduction

The main function of the Therapeutic intensive care department of Emergency Medicine Institute consists in providing measures to recover patients after anesthesia of surgical, neurosurgical, traumatological and other investigations as well as from other possible critical conditions of hospitalized patients. Often these patients are exposed to multiple invasive procedures and have to administrate a multiple broad spectrum of antibiotics. At the same time, the prescriptions are often empiric and lead to overuse or misuse of antibiotics, unnecessary side effects, growth of pathogenic microbes resistance to antibiotics and increasing treatment costs. The above mentioned requires surveillance, stringent consumption control and suppose rational antibiotic prescription [1, 2, 3, 4]. Unfortunately, in the Republic of Moldova the information about antibiotics prescription, consumption patterns, and cost analysis in hospitals with only few scientific publications [5, 9, 10, 20] is rather limited.

National Scientific-Practical Centre of Emergency Medicine of the Republic of Moldova reorganized in 2014 into Emer-

gency Medical Institute (EMI), was founded in 1959. Clinical Services of EMI include: Orthopedic-Traumatology Clinic for 150 beds, Surgery Clinic for 140 beds, Neurosurgery Clinic for 80 beds, Neurology Clinic for 70 beds, Maxillo-facial clinic for 30 beds, Urology Clinic for 40 beds, Gynecology Clinic for 30 beds, Microsurgery Clinic for 30 beds, Municipal center for hemodialysis with 8 seats and 9 beds, Clinical intensive care unit for 30 beds including and Therapeutical intensive care department for 12 beds, in total the above services of the EMI include 600 beds overall. In addition to the above mentioned services include 5 emergency medical help substations and 4 out-patient Departments of traumatology and orthopedics [6].

The primary aim of the study was to evaluate institutional representative data on antibiotics utilization for five-year (2010-2014) period, in accordance with World Health Organization (WHO) requirements, directed to determine the value of Defined Daily Doses per 1000 Occupied-Bed Days (DDD/1000). That study was carried out and with the support of other two programs that were effectuated in the institution: analysis program of consumption and stocks of drugs in Anatomical Therapeutical Chemical (ATC) and pharmacotherapeutic software [7, 8]. Based on obtained data, it aimed to make conclusions on the use of anti-infectives for systemic use in the Therapeutical intensive care department and to propose recommendations for ensuring their optimization.

Material and methods

For this study we used the data of a five-year (2010-2014) period in therapeutic intensive care department of EMI for 12 beds, which show the dynamics of consumption of anti-infectives for systemic use drugs, as classified by ATC classification system of World Health Organization 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 amount of DDD/1000 data about total annual consumption of antibiotics 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 number of bed/days (2010 = 2922; 2011 = 3327; 2012 = 3239; 2013 = 3407; 2014 = 3388) during the evaluated period in Therapeutical intensive care department were used. All in all, 36 antimicrobial remedies with different dosage of administration (both for parenteral and enteral use) for hospitalized patients' treatment in the evaluated period were used entral forms – 7 names; parenteral forms – 29 names and 3 names of both forms, which represent 23 active antimicrobial substances.

Parenteral consumption forms rate of antibiotic subgroups evaluated in DDD/1000 during 2010-2014 is shown in figure 1.

As can be observed from figure 1 in the evaluated period the average consumption annual rate of all antibiotic subgroups records a decline from 1504 in 2010 to 1082 DDD/1000 in 2014 or by 28.06%. The main consumption of 1378.16 (974.67+285.42+118.07) or 97.63% from the total in 2010 to 951.01 DDD/1000 (597.7+97.11+256.20) or 87.89% in 2014 by a decrease of 427.15 DDD or 31% during the mentioned years was registered for three subgroups: other beta-lactam antibacterials (Cefazolinum 3.0, Cefuroximum 3.0, Cefotaximum4.0, Ceftazidimum 4.0, Ceftriaxonum 2.0, Cefoperazonum 4.0), other antibacterials (Vancomycinum 2.0 and Metronidazolum 1.5) and beta-lactam antibacterials, penicillins (Ampicillinum2.0, Amoxycillinum 2.0, Amoxicillinum + Acidumclavulanicum 3.0, Ticarcillinum + Acidumclavulanicum 15.0). The mean consumption of 105.75 (35.25+65.02+5.48) or 7.03% of the total in 2010 to 125.74 DDD/1000 (59.33+51.06+15.35) or 11.62% from the total in 2014 by an increase of 19.99 DDD/1000 or 18.90% was recorded in the same period by other three subgroups: aminoglycoside antibacterials (Streptomycinum 1.0, Gentamycinum 0.2, Kanamycinum 1.0, Amikacinum 1.0), quinolone antibacterials (Gatifloxacinum 0.4, Acidumpipemidicum 0.8) and antimycotics for systemic use (Fluconazolum 0.2). The lowest consumption of 21.53 (1.37+21.53) or 1.43% of the total in 2010 to 6.61 DDD/1000 (2.07+3.54) or 0.61% from the total in 2014, with a decrease 14.92 DDD/1000 by 3.26 times was recorded in that period by other two subrgoups: amphenicols (Chloramphenicolum 3.0) and macrolides, lincosamides and streptogramins (Clarithromycinum 0.5, Azithromycinum 0.5, Lincomycinum 1.8).

In figure 2 consumption rate of enteral forms of antibacterials for systemic use in DDD/1000 during 2010-2014 is shown.

As it is seen from figure 2 the average consumption annual rate of antibiotics for oral usage increased from 19.85 in 2010 to 123.72 DDD/1000 OBD in 2014 or by 6.23 times. The highest consumption of 19.85 DDD/1000 or 100% of the

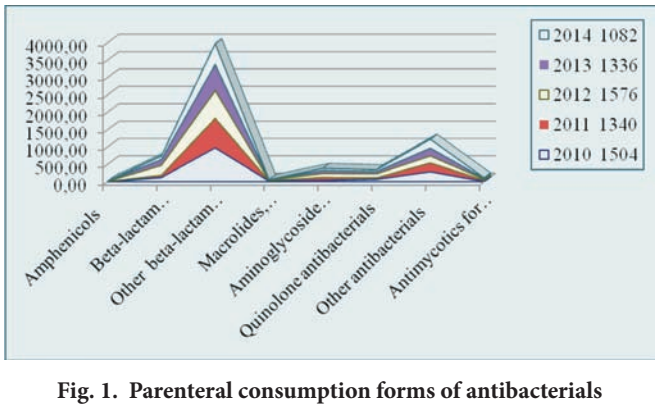

Fig. 1. Parenteral consumption forms of antibacterials for systemic use in DDD/1000.

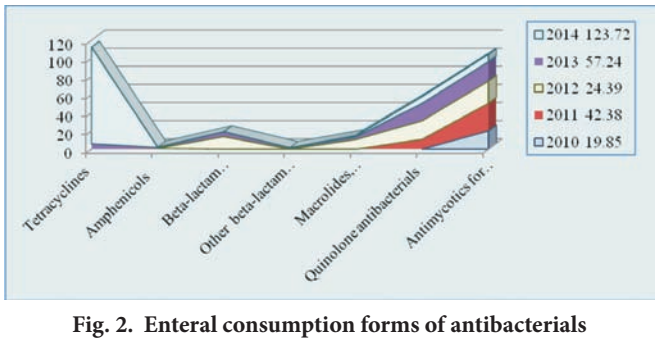

Fig. 2. Enteral consumption forms of antibacterials for systemic use in DDD/1000.

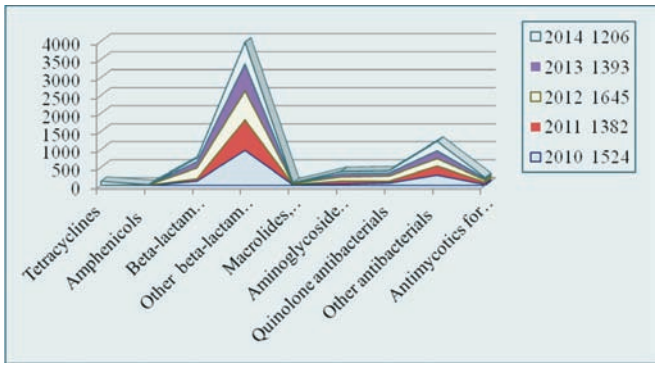

Fig. 3. The total consumption of antibacterials for systemic use in DDD/1000.

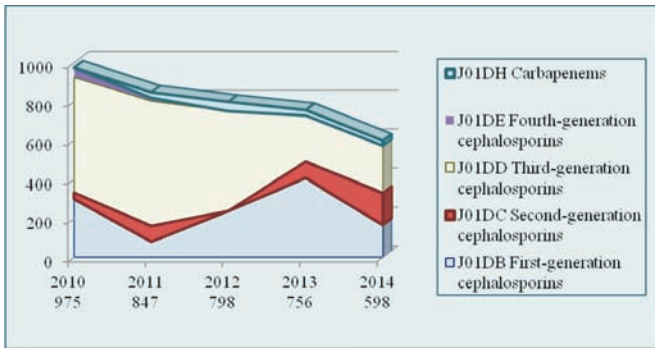

Fig. 4. Total consumption forms of other beta-lactam antibacterials for parenteral use in DDD/1000.

total in 2010 was registered for antimycotics for systemic use and 106.6 DDD/1000 or 86.16% of the total in 2014 for tetracyclines. In figure 3 the total (parenteral and enteral forms) antibiotic subgroups used rates are demonstrated.

As it can be observed from figure 3 the average aggregated annual rate for total antibiotics consumption in the evaluated period decreased from 1524 in 2010 to 1206 DDD/1000 in 2014 or by 20.87%.

The highest yearly consumption for the first 3 subgroups during mentioned years remains similar to parenteral use (other beta-lactam antibacterials, other antibacterials and beta-lactam antibacterials, penicillins) as well as for mean (aminoglycoside antibacterials, quinolone antibacterials, antimycotics for systemic use) and lower consumption (amphenicols, macrolides, lincosamides and streptogramins).

Nevertheless, though consumption of enteral forms of antibiotics registered a significant increase during the evaluated period, the total DDD/1000 consumption wasn't influenced respectively.

As stated in table 1 in the evaluated period the ratio between antibiotics DDD/1000 parenteral to enteral forms was 75.79:1 in 2010 to 8.75:1 in 2014. The percentage of parenteral forms from the total antibiotics DDD/1000 in the mentioned period decreased from 98.70% to 89.74%, as well as the enteral forms increased from 1.3 to 10.26% of the total. Similar data for the entire institution can be found in some early publications [10]. Some publications demonstrate that in terms of switch therapy, approximately 40-50% of patients admitted for intravenous antibiotics can be switched to oral antibiotics within 2-3 days [11].

From this chart one can see in the evaluated period the total consumption of parenteral forms of cephalosporin's decreased from 975 to 598 DDD/1000 or by 38.67%. Cephalosporin's first generation (Cefalexinum and Cefazolinum) represents 300.82 DDD/1000 or a share of 30.85% from the total in 2010, and 166.77 DDD/1000 or 27.88% from the total in 2014 by a decrease of 134.05 DDD/1000 or 44.57% during 5 years. The consumption of cephalosporin's second generation (Cefuroximum, Cefaclorum) recorded an increment from 32.11 DDD/1000 to 163.81 DDD/1000 or by 5.10 times during the mentioned period. Cephalosporinț's third generation (Cefotaximum, Ceftazidimum, Ceftriaxonum, Cefixim, Cefoperazonum, Cefoperazonum + Sulbactamum) demonstrates a considerable decrease of consumption from 591.72 DDD/1000 in 2010 to 241.74 DDD/1000 in 2014 or by 2.44 times. Cephalosporins G-IV and carbapemens (Meropenemum, Imipenemum+Cilastatinum) recorded a consumption lower than 50 DDD/1000.

Comparison of total consumption data of anti-infectives for systemic use evaluated in DDD/1000 in 54 intensive care units of international hospitals with the similar data of Therapeutical intensive care department of EMI is presented in figure 2.

As we can see from table 2 the average annual rate for total-hospital antibiotics utilization period in EMI decreased from 662.4 in 2010 to 464.1 DDD/1000 in 2014 or by 30%. That result was higher by 67.65 DDD/1000 or by 14.58% than the medium consumption of 396.45 DDD/1000 registered in case of 1256 international hospitals and lower by 112.66 DDD/1000 or by 36.68% in case of 450 international hospitals where the

Table 1

The ratio between DDD/1000 for parenteral to enteral antibiotic form

Years	2 010	2011	2012	2013	2014	
Parenteral	1504.44	1339.95	1576.11	1336.06	1082.36	
Enteral	19.85	42.382	68.85	57.239	123.715	
The ratio of parenteral to oral	75.79:1	31.62:1	22.89:1	23.34:1	8.75:1	
Total	1524.29	1382.33	1644.96	1393.30	1206.08	
Percentage from total	Parenteral	98.70	96.93	95.81	95.89	89.74
	Enteral	1.30	3.07	4.19	4.11	10.26

Table 2

Surveillance studies of antibiotics use in intensive care units of international hospitals, compared with the similar data in therapeutical intensive care department of EMI

Setting	Surveillance time-period	Data source Pharmacy	Data collection	Use of antibiotics in DDD/1000 bed-days over the study period
Emergency Medicine Institute	6 years (2010–2014)	dispensing records (PDR)	Annual	662.4 hospital-wide in 2010 464.1 hospital-wide in 2014
Therapeutical intensive care department of EMI	5 years (2010–2014)	(PDR)	Annual	1524.29 in 2010 1206.08 in 2014
ICU Tertiary level in Northern India [12]	In 2008	(PDR)	Annual	1086.5
Neurosurgical ICU of Germany [13]	From 2002 to 2005	(PDR)	Annual	652.0
40 ICU of Southwestern Germany non university regional general hospitals [14]	From 2001 to 2002	(PDR)	Annual	1056.0 (in medical ICU) 1169.0 (in surgical ICU) 1127.0 (in mixed ICU)
8 Tertiary intensive care unit in Hungary [15]	In 2008	(PDR)	Annual	1013.0
ICU of Military Medical Academy hospital of Bulgaria [16]	In 2011	(PDR)	Annual	1052.0
ICU of 1 university hospital in Switzerland [17x24Loeffler, JM, Garbino, J, Lew, D, Harbarth, S, and Rohner, P. Antibiotic consumption, bacterial resistance and their correlation in a Swiss university hospital and its adult intensive care units. Scand J Infect Dis. 2003; 35: 843–850 CrossRef | PubMed | Scopus (47) See all References24]	5 years (1996–2000)	(PDR)	Annual	462.0 (in surgical ICU) 683.0 (in medical ICU) 400.0 (in the entire hospital)
ICU of 1 university hospital in Greece (personal unpublished data) [18]	5 years (1998–2002)	(PDR)	Annual	982.0 (in mixed ICU)
The global antibiotics consumption [19]	From 2006 to 2008 varied little	(PDR)	Annual	343.0

mentioned medium was 634.34 DDD/1000 respectively. Other all medium consumption in 1706 international hospitals constituting 459.20 DDD/1000 was lower than consumption of 464.1 DDD/1000 in EMI in 2014 by 4.90 DDD/1000 or by 1.06% and lower by 121.1 comparatively to global antibiotics consumption of 343 defined daily doses per 1000 patient-days or by 20.09% [20].

DDD/1000 of antibiotics in Therapeutical intensive care department decreased from 1524 in 2010 to 1206 DDD/1000 in 2014 or by 20.87%, however, it is by 11.77% higher than medium consumption of 1064.01 DDD/1000 [(1x1086.5 + 1x652.0 + 15x1056.0 + 10x1169 + 10x1127 + 8x1013 + 1x1052 + 1x462 + 1x683 + 1x982):54] in intensive care units of 54 international hospitals with the similar activity.

The value cost of parenteral forms of antibacterials for systemic use per DDD/1000 in lei is shown in figure 5.

As we can see from figure 5 the average consumption annual rate per DDD/1000 in value indexes (lei) of all parenteral antibiotic subgroups recorded a decline from 54782 in 2010 to 40509 lei in 2014 or by 26.06%. The medium yearly consumption for the evaluated period with more than 5000 lei per DDD/1000 was registered for other beta-lactam antibacterials (31975.8 lei) and for beta-lactam antibacterials (10146.5 lei). Other subgroups as other antibacterials, macrolides, lincosamides and streptogramins, quinolone antibacterials, antimycotics for systemic use registered a medium yearly consumption less than 5000 lei per DDD/1000.

The value cost of enteral forms of antibacterials for systemic use per DDD/1000 in lei is presented in figure 6.

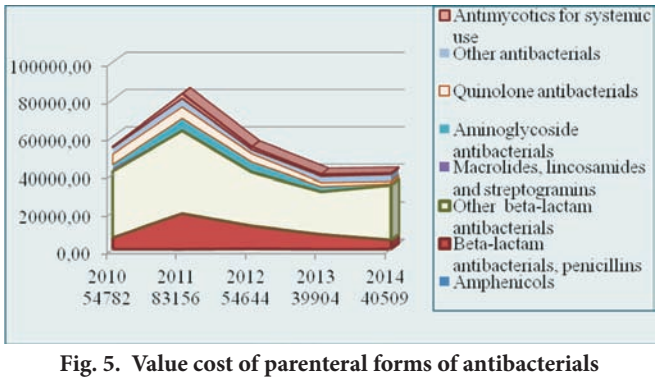

Fig. 5. Value cost of parenteral forms of antibacterials for systemic use per DDD/1000 in lei.

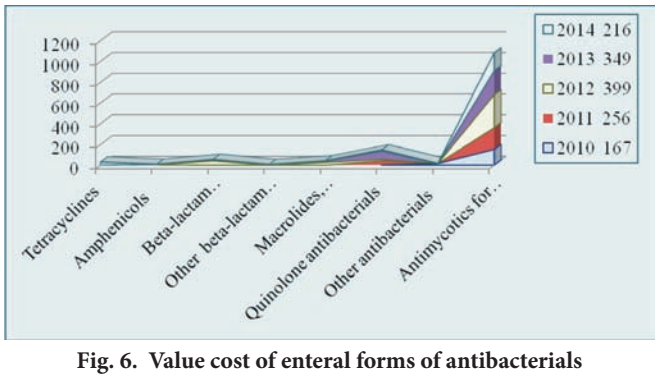

Fig. 6. Value cost of enteral forms of antibacterials for systemic use per DDD/1000 in lei.

From figure 6 it can be found that the average consumption annual rate in value indexes of all antibiotic subgroups records an increase from 167 in 2010 to 216 lei per DDD/1000 in 2014

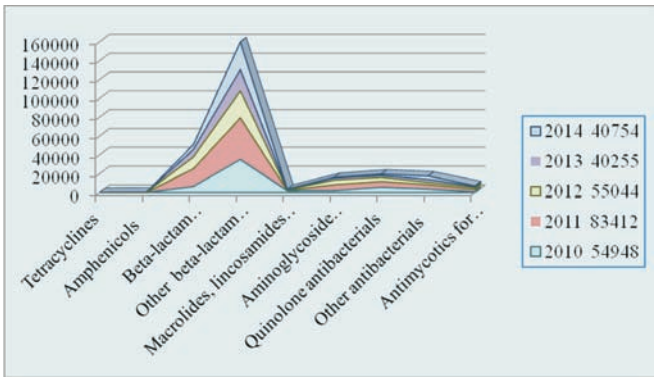

Fig. 7. Total value cost of antibacterial for systemic use per DDD/1000 in lei.

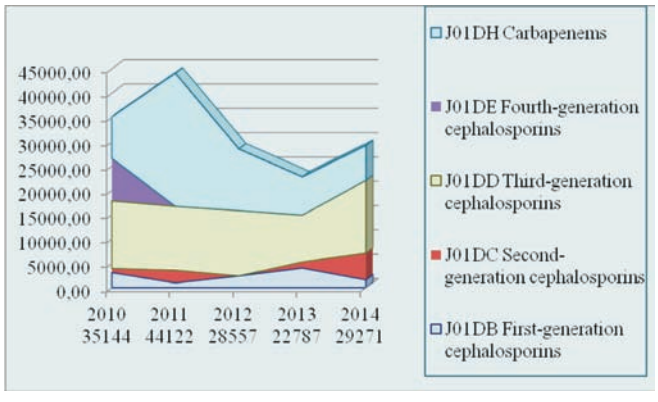

Fig. 8. Total value cost of other beta-lactam antibacterials for parenteral use of DDD/1000 in lei.

or by 29.34%. All other subgroups recorded consumption per DDD/1000 less than 100 lei. Total value cost of antibacterials for systemic use per DDD/1000 in lei is shown in figure 7.

In this chart the presented data demonstrate that the average consumption annual rate in value indexes of total antibiotics record a decline from 54948 in 2010 to 40754 lei per DDD/1000 in 2014 or by 25.84%. The highest yearly cost of DDD/1000 of the total antibacterials for systemic use represents other beta-lactam antibacterials and beta-lactam antibacterials. Introduction of coordinated cost control program and prescribed protocols established by consensus as guidelines for a rational policy in antibiotics therapy in some institutions result in decreasing of value cost during 2 years by more than 40% [21, 22].

Total value cost of other beta-lactam antibacterials for parenteral use of DDD/1000 in lei is presented in figure 8.

Figure 8 shows that the cost of DDD/1000 in value indexes (lei) of antibiotic subgroups for parenteral use recorded a decline from 35144 in 2010 to 29271 lei in 2014 or by 16.72%. As an exception from the decline was 2011 year with the higher consumption of 44122 lei per DDD/1000. An increment in cost per DDD/1000 was recorded by the second generation of cephalosporin's from 859.24 in 2010 to 5525.00 lei in 2014 or by 6.43 times. Third cephalosporin's generation slightly increased cost per DDD/1000 from 13884.1 in 2010 to 14948 lei in 2014 or by 7.66%. A decrement in the evaluated period was recorded by the first generation of cephalosporins from 3113.05 lei per DDD/1000 to 1605.5 or by 48.43% and carbapenems from 8508.83 lei per DDD/1000 to 7192.70 or by 18.29%.

To determine the cost of one medium DDD of antibacterials for systemic use separately for parenteral and enteral forms, the cost sum of DDD/1000 per DDD/1000 was divided respectively. The cost of one medium DDD of antibiotics in lei for parenteral and enteral forms and total is shown in table 3.

As we can see from table 3 in the evaluated period the cost of one medium DDD recorded a slow increase from 36.41 lei in 2010 to 37.43 lei in 2014 or by 2.80% for parenteral forms, a decrease from 8.41 to 1.75 lei or by 4.80 times for enteral forms and from 36.05 to 33.77 lei or by 6.33% for one total DDD. In chronological way for the evaluated years the ratio between the cost of one medium DDD of parenteral to enteral forms was respectively 4.32:1; 9.78:1; 5.97:1; 4.81:1 and 21.38:1.

Treatment patterns, antibiotics stewardship activity, potential opportunities for early switch from intravenous to oral formulations [23] and measures necessary for preventing and strengthening antimicrobials resistance and nosocomial infections will lead to potential cost savings per every eligible patient [24, 25, 26].

Table 3

Cost of 1(one) DDD of antibiotics in lei for parenteral and enteral forms and total

Year/ cost (in lei)	2010	2011	2012	2013	2014
Parenteral cost in lei per DDD/1000	54781.50	83156.00	54644.40	39904.00	40509.00
Enteral cost in lei per DDD/1000	166.88	255.99	399.13	355.18	216.23
Total cost in lei per DDD/1000	54948.38	83411.99	55043.53	40259.18	40725.23
Parenteral DDD/1000	1504.45	1339.95	1576.11	1336.06	1082.36
Enteral DDD/1000	19.85	42.382	68.85	57.239	123.715
Total DDD/1000	1524.29	1383.83	1644.95	1394.77	1206.07
Cost in lei per 1(one) DDD	36.05	60.43	33.61	28.89	33.77
Parenteral cost in lei per 1(one) DDD	36.41	62.06	34.67	29.87	37.43
Enteral cost in lei per 1(one) DDD	8.41	6.04	5.80	6.2	1.75

Conclusions

1. The DDD/1000 of antibiotics in therapeutical intensive care department decreased from 1524 in 2010 to 1206 DDD/1000 in 2014 or by 20.87%, however, it was by 11.77% higher than medium consumption of 1052.25 DDD/1000 in intensive care units of 54 international hospitals. The consumption of parenteral forms constituting 1504.44 or 98.70% from the total in 2010 and 1082.36 DDD/1000 or 89.74% from the total in 2014 had an overall decrease of 29.06%. For enteral forms the stated data were 19.85 or 1.30% from the total in 2010 to 123.72 DDD/1000 or 10.25% from the total in 2014 or an increase by 6.23 times respectively.

2. The value of 54948 lei per DDD/1000 OBD in 2010 recorded a decline to 40754 lei in 2014 or by 25.84%. The cost of one medium DDD from 36.05 lei in 2010 decreased to 33.77 lei in 2014 or by 6.33%. International experience demonstrates that introduction of coordinated cost control program and prescribed protocols can lead to a decrease of anti-microbials treatment cost during 2 years by more than 40%.

3. 36 antimicrobial remedies with different dosage of administration with: enteral forms – 7 names, parenteral forms – 29 names and with both forms – 3 names, that represent 23 active antimicrobial substances in the period from 2010-2014 were evaluated.

4. Besides the drugs consumption evaluation in DDD that permits to improve rational use of medical remedies in hospitals of the Republic of Moldova, daily practices in antimicrobial treatment of potential opportunities for early switch from intravenous to oral formulations, coordinated cost control program and prescribed protocols established as guidelines for a rational policy in antibiotics therapy, and the last but not the least the measures for preventing and strengthening antimicrobials resistance and nosocomial infections as well will lead to growing treatment quality of hospitalized patients and potentially saving institutional budgets.

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