

Evaluation of Tetracyclines and Aminoglycosides consumption

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Abstract

Background: Tetracyclines and Aminoglycosides antimicrobials hold the last positions among all main antibiotic subgroups used yearly in hospitals. Nevertheless, without these medical remedies a qualified treatment of patients with different illnesses cannot be well organized or even would be impossible. **Material and methods:** For this study we used data of a six-year (2009-2014) period, in the Emergency Medicine Institute and their subdivisions where happened main consumption of antibiotics such as: Reanimation, Therapeutic intensive care, Therapeutic «stroke» intensive care, septic Surgery and septic Orthopedic-Traumatology departments - which show the consumption dynamics of Tetracyclines and Aminoglycosides antimicrobials use in grams and value indexes.

Results: The defined daily doses (DDD) per 1000 occupied-bed days (DDD/1000) in Emergency Medicine Institute in 2009 and 2014 for Tetracyclines registered an increase from 8.2 to 20.8 or a share of 1.24% and 4.48% from the total annual consumption. Aminoglycosides recorded a decrease from 83.1 to 43.7 that represents a share of 12.55% and 9.42% from the total annual consumption. The same data in Intensive care departments recorded for Tetracyclines an increase from 3.61 to 53.98 DDD/1000 or 0.27% and 4.48% and respectively for Aminoglycosides from 494.49 to 134.4 or 15.12% and 11.16%. Septic departments recorded from 3.56 to 17.63 DDD/1000 or 0.57% and 3.44% and respectively for Aminoglycosides from 142.83 to 137.04 DDD/1000 or 22.64% and 26.77%. In the mentioned period medium consumption in international hospitals of Tetracycline's increased from 27.00 to 70.00 DDD/1000 or by 2.59 times, and comparatively with the EMI in 2014 was higher by 3.36 times. Aminoglycosides consumption in international hospitals decreased from 50.00 to 40.00 DDD/1000 or by 20% and in 2014 year was similar with the data recorded in EMI. Cost of DDD/1000 in Emergency Medicine Institute during 2009 and 2014 years, for Tetracyclines registered 1.89 and 5.57 lei, for Aminoglycosides respectively 461.19 and 460.83 lei. In Intensive care departments costs recorded 0.98 and 14.44 lei and 2793.61 and 2634.39 lei, and in Septic departments 0.4 and 4.75 lei and 536.61 and 329.23 lei respectively.

Conclusions: We found an increase in consumption of Tetracyclines DDD/1000 during the evaluated period, at the same time consumption in international hospitals in 2014 was in medium 70.00 DDD/1000 or 3.36 times more than 20.8 DDD/1000 recorded in EMI. Aminoglycosides in the evaluated period decreased in DDD/1000 consumption in EMI and international hospitals and in 2014 was around the same.

Key words: antibiotics, tetracycline, aminoglycoside, defined daily dose, consumption, rational use, hospitals.

Introduction

Despite the fact that shares of Tetracyclines and Aminoglycosides in acute-care hospitals hold the last position among other antibiotics subgroups, they remain an important component in patients' antimicrobial treatment. Around 5% of patients admitted to acute-care hospitals acquire nosocomial infections [1, 2]. Antibiotic treatment of severe acute respiratory diseases (SARS), included tetracyclines (91.0%), aminoglycosides (83.3%), quinolones (79.2%); 18.8% of the patients received a combination of tetracyclines and aminoglycosides, while 11.5% received a combination of tetracyclines and quinolones, and 63.5% received a combination of tetracyclines, aminoglycosides and quinolones [3, 4]. The mortality rate of SARS worldwide is approximately 10.5%. The mortality rate of severe acute respiratory syndrome (SARS) patients admitted to the intensive care units (ICU) ranged from 5% to 6% [5, 6]. In international hospitals medium consumption for Tetracyclines recorded 0.5-27-70,00 DDD/1000 and for Aminoglycosides from 40.00 to 50,00 DDD/1000 or no more than 5% of all amount of antibiotics. Consumption in ICU for critically ill patients that received only gentamicin or amikacin is higher and varied between 38%-66% [7, 8, 9]. A higher consumption of Aminoglycosides from 25% to 45% of the total annual amount of antibiotics occurs in septic orthotraumatology department of EMI [10]. The above mentioned supposes surveillance, stringent consumption control and rational antibiotic prescription [11, 12, 13, 14].

The primary aim of the study was to evaluate institutional representative data on Tetracyclines and Aminoglycosides utilization in accordance to the World Health Organization (WHO) requirements, directed to determine value of Defined Daily Doses per 1000 Occupied-Bed Days (DDD/1000) [15, 16].

Material and methods

For this study we used the data of a six-year (2009-2014) period, DDD/1000 consumption of Tetracyclines and Aminoglycoside antibacterials in Emergency Medicine Institute (EMI) in used rates are demonstrated. EMI intensive care unit (ICU) – reanimation, therapy intensive care and “stroke” intensive care departments, septic surgical and septic orthotraumatology departments (SSOD) – which show the dynamics of consumption of anti-infectives for systemic use drugs, as classified by Anatomical 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 number of DDD/1000 we used data about total annual consumption of Tetracycline's and Aminoglycosides antibacterials and the statistics data concerning the number of treated patients (only patients with health insurance

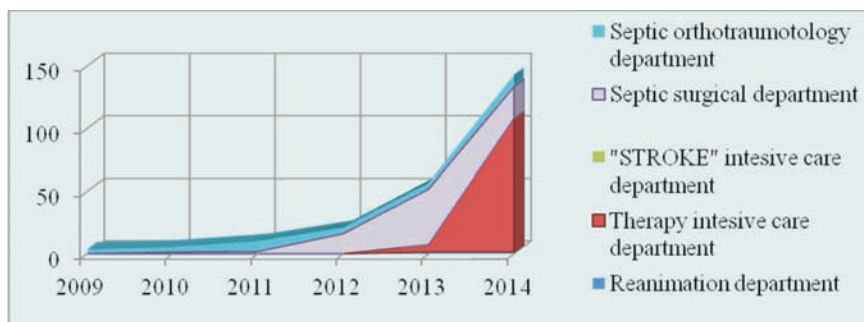


Fig. 1. Total Tetracyclines consumption in DDD/1000 during 2009–2014.

and other free treated by the state categories of citizens). The total number of occupied bed/days in the institution was 188762 in 2009, 191556 in 2010, 186246 in 2011, 199816 in 2012, 193019 in 2013 and 187558 in 2014, and respectively for the corresponding departments of EMI: reanimation intensive care unit (2009 = 3990; 2010 = 6551; 2011 = 6985; 2012 = 9051; 2013 = 7384; 2014 = 7361), therapeutical intensive care (2010 = 2922; 2011 = 3327; 2012 = 3239; 2013 = 3407; 2014 = 3388), "stroke" intensive care (2013 = 2553; 2014 = 4193), septic surgical (2009 = 14030; 2010 = 14212; 2011 = 12875; 2012 = 12372; 2013 = 12464; 2014 = 12104), septic orthopedic-traumatology (2009 = 10664; 2010 = 10017; 2011 = 9540; 2012 = 10178; 2013 = 9701; 2014 = 9535) [17, 18, 19, 20]. Total Tetracyclines consumption in DDD/1000 during 2009-2014 is shown in figure 1.

Tetracyclines consumption is characterised by the use of Doxycyclinum with 0.1gr defined daily doses. As can be observed from figure 1 in the evaluated period was recorded an increase of the average consumption annual rate in septic orthopedic-traumatology department from 3.6 to 9.7, in septic surgical department from 1.41 to 25.6, therapeutical intensive care department from 5.9 to 106.6 and reanimation department from 1.35 to 1.36 DDD/1000. In the "stroke" intensive care department consumption of Tetracyclines was not registered at all. In figure 2 the total consumption of Aminoglycosides in DDD/1000 during 2010-2014 is shown.

Aminoglycosides antibacterials are presented with the use of Streptomycinum 1.0, Gentamycinum 0.2, Kanamycinum 1.0 and Amikacinum 1.0 and respectively defined daily doses. Reanimation department recorded the higher from 494.49 to 219.13 DDD/1000 consumption with a decline by 55.69%. The consumption in septic orthotraumatology department was more stable and varied from 245.2 to 243.52 DDD/1000. The last third positions hold "stroke" intensive care depart-

ment where was recorded a decline from 206.03 to 124.73 DDD/1000 or by 39.46%, followed by therapy intensive care department with an increase from 35.25 to 59.33 DDD/1000 or by 68.31% and ended the list septic surgical department with a decrease from 40.45 in 2009 to 30.56 DDD/1000 or by 24.45%. The total consumption in intensive care units and septic departments in 2014 was 677.27 DDD/1000, from which the share of reanimation department represents 32.36%, Therapy intensive care department 8.76%, "stroke" intensive care department 18.42%, septic surgical department 4.51% and septic orthotraumatology department 35.96%.

In table 1 comparison of average DDD/1000 consumption of Tetracyclines and Aminoglycosides antibacterials in intensive care and septic departments of EMI is shown.

Table 1

Average DDD/1000 consumption of Tetracyclines and Aminoglycosides antibacterials in intensive care and septic departments of E

Units	2009	2010	2011	2012	2013	2014
Tetracyclines						
ICU					3.61	53.98
SSOD	3.56	2.7	5.13	10.54	24.88	17.63
EMI	8.2	26.8	15.1	7.1	13.5	20.8
Aminoglycoside antibacterials						
ICU	494.49	85.63	174.79	292.74	222.19	134.4
SSOD	142.83	74.13	187.45	93.54	157.84	137.04
EMI	83.1	37.60	76.90	103.20	112.30	43.70
Total antibiotics consumption in EMI						
EMI	662.4	558.2	662.1	542.4	546.9	464.1

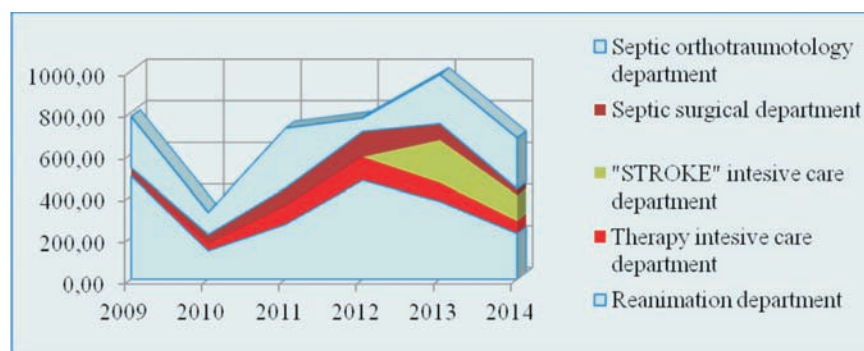


Fig. 2. Total consumption of Aminoglycosides in DDD/1000.

Table 2

Total DDD/1000 consumption of Tetracyclines and Aminoglycosides in EMI and some international acute hospitals

Total DDD/1000 consumption of Tetracyclines in international acute hospitals						
	2009	2010	2011	2012	2013	2014
Emergency Medicine Institute	8.20	26.80	15.10	7.10	13.50	20.80
Large acute Australian public hospitals [21]	27.00	41.50	52.00	60.00	60.00	70.00
The number of hospitals	16	18	22	32	42	51
Medium acute Australian public hospitals	52.00	42.50	42.00	61.50	71.00	80.00
The number of hospitals	9	9	10	13	24	26
South Australian metropolitan hospitals	40.00	38.70	37.60	41.70	37.20	
SAAUSP 37.2, NAUSP 44.00, NETHMAP 18.00 in 2013; SWEDRES 54.00, DANMAP 15.80 in 2012 [21]						
Total DDD/1000 consumption of Aminoglycosides in international acute hospitals						
	2009	2010	2011	2012	2013	2014
Emergency Medicine Institute	83.1	37.60	76.90	103.20	112.30	43.70
Large acute Australian public hospitals [22]	50.00	50.00	45.00	43.00	43.00	40.00
The number of hospitals	16	18	22	32	42	51
Medium acute Australian public hospitals	53.00	58.00	51.00	50.00	42.00	38.00
The number of hospitals	9	9	10	13	24	26
South Australian metropolitan hospitals	65.50	66.50	64.20	58.70	55.50	
SAAUSP 55.5, NAUSP 42.1, NETHMAP 39.00 in 2013 and SWEDRES 12.00, DANMAP 21.4 in 2013 [22]						

As can be seen from table 1 average DDD/1000 consumption of Tetracyclines antibacterials in intensive care and septic departments in the evaluated period increased respectively by 14.9 (53.98:3.61) and 4.9 (17.63:3.56) times, and totally for the institution by 2.4 (20.8:8.2) times. For Aminoglycoside the data conversely recorded a decrease by 3.6 (494.49:134.4) times and 5% (142.83:137.04), and totally for the institution by 1.9 (83.1:43.7) times. In table 2 is shown Tetracyclines and Aminoglycosides antimicrobial use in EMI and many different international surveillance programs, such as: SAAUSP (South Australian Antimicrobial Utilization Surveillance Program), NAUSP (National Antibiotic Utilization Surveillance Program), NETHMAP (Netherlands Monitoring Antimicrobial Resistance Program), SWEDRES (Swedish Antimicrobial Utilization and Resistance in Human Medicine), DANMAP (Danish Integrated Antimicrobial Resistance Monitoring and

Research Program).

From table 2 as one can see in the evaluated period the total consumption of Tetracycline's in large acute international public hospitals increased by 2.59 (70:27) times and respectively in EMI by 2.5 times, at the same time in 2014 these data in EMI were less than recorded in international large acute hospitals in medium by 3-4 times. Aminoglycosides in EMI registered an instable consumption, nevertheless, in the end of the evaluated period comparatively with international acute hospitals recorded in medium the similar data.

In fig. 3 the total DDD/1000 Tetracyclines consumption in lei during 2010-2014 is shown.

As we can see from figure 3 the average consumption annual rate per DDD/1000 in value indexes

- for Tetracyclines in all departments recorded an increment, even so these data are low in the beginning and

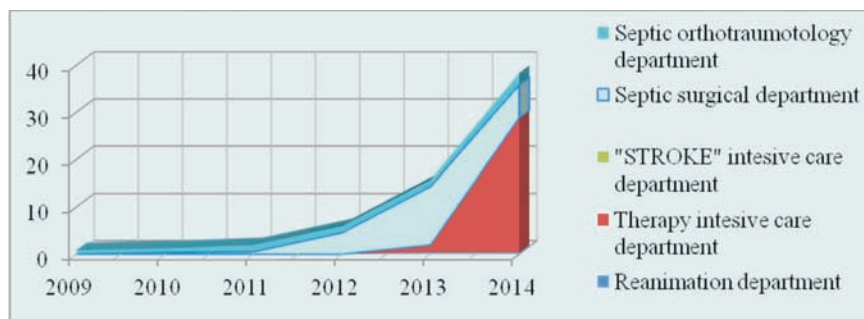


Fig. 3. Total value cost of Tetracyclines use per DDD/1000 in lei.

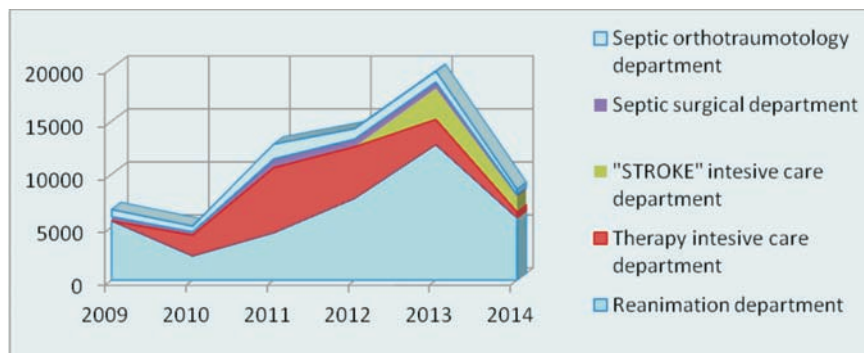


Fig. 4. Value cost of Aminoglycosides antibacterial for systemic use per DDD/1000 in lei.

the end of the evaluated period for therapeutic intensive care department registered

- 1.59 and 28.51 lei, septic surgical department – 4.54 and 6.92 lei, septic orthotramotology department – 0.81 and 2.58 lei as to reanimation department – 0.37 and 0.36 lei.

The value cost of Aminoglycosides antibacterials use per DDD/1000 in lei is presented in figure 4.

As can be observed from figure 4 during the evaluated period the main value cost of DDD/1000 recorded reanimation department from 5587.22 to 5879.70 lei, with the highest results in 2013 of 12780 lei and consequently the second position holds «stroke» intensive care department from 2950.30 lei to 1468.60 lei and respectively therapy intensive care department from 1980.60 to 554.87 lei, with the highest results in 2011 of 6160.50 lei is placed on the third position. The last position, is divided between septic orthotraumatology department with the cost of DDD/1000 from 670.63 to 459.92 lei, with the higher cost of 1395.50 lei in 2011, and respectively septic surgical department from 402.58 to 198.54 lei and the higher cost of 824.77 lei in 2011.

In table 3 is presented the medium cost DDD/1000 of Tetracyclines and Aminoglycosides for ICU and SSOD in lei. To determine the medium cost of DDD/1000 was counted total cost of DDD/1000 separately for ICU and SSOD and divided by the number of these departments (3 and respectively 2) in the evaluated period.

Table 3

Cost of medium DDD/1000Tetracyclines and Aminoglycosides in lei

Tetracyclines						
	2009	2010	2011	2012	2013	2014
ICU					0.98	14.44
SSOD	0.4	0.61	11.45	2.96	6.89	4.75
EMI	1.89	6.13	3.76	1.98	3.73	5.57
Aminoglycosides						
ICU	2793.6	2126.8	5308.7	6297.5	6036.3	2634.39
SSOD	536.61	419.62	1110.2	845.63	801.64	329.23
EMI	461.19	286.64	664.02	716.28	812.72	460.83

As we can see from table 3 in the evaluated period the medium cost of DDD/1000 for Tetracyclines in 2014 recorded for SSOD 4.75 lei, or less by 3 times than cost of 14.44 lei in

ICU and respectively 329.23 lei cost for Aminoglycosides in SSOD in 2014 or less by 8 times than 2634.39 lei recorded ICU.

Conclusions

1. Consumption of Tetracyclines in DDD/1000 in the evaluated period increased in all evaluated departments of EMI as follows: therapeutical intensive care department from 5.9 to 106.6, septic surgical department from 1.41 to 25.6, septic orthopedic-traumatology department from 3.6 to 9.7 and reanimation departmet from 1.35 to 1.36 DDD/1000, that reprezents respectively a share from the total departments consumption of 142.6 DDD/1000 in 2014 of 74.3%, 17.9%, 6.8% and 0.9%. Despite entire institution growth from 8.2 to 20.8 DDD/1000, the difference of consumption is more than 3 - 4 times comparatively with 70 – 80 DDD/1000 recorded in international hospitals.
2. The decrease of the value cost of DDD/1000 in lei for Tetracyclines in the end of evaluated period was recorded for therapeutic intensive care department 28.51 lei, septic surgical department – 6.92 lei, septic orthotramotology department – 2.58 lei as to reanimation – 0.36 lei, when for the entire institution – 5.57 lei.
3. Consumption of Aminoglycosides in the evaluated period was recorded in all departments as follows: reanimation department from 494.49 to 219.13 DDD/1000, septic orthotraumatology department from 245.2 to 243.52 DDD/1000, "stroke" intensive care department from 206.03 to 124.73 DDD/1000, therapy intensive care department from 35.25 to 59.33 DDD/1000 and from 40.45 to 30.56 DDD/1000 septic Surgical department, that represents respectively a share from the total departments consumption of 677.27 DDD/1000 in 2014 of 32.36%, 35.96%, 18.42%, 8.76% and 4.51% respectively. An unstable consumption recorded in EMI from 83.1 at the beginning to 43.7 DDD/1000 in the end of the evaluated period, which in the medium is similar comparatively to international acute hospitals records.
4. The decreased records of value cost of DDD/1000 in lei for Aminoglycosides in 2014 were for reanimation department 5879.70 lei, „stroke” intensive care department – 1468.60 lei, therapy intensive care department – 554.87 lei, septic orthotraumatology department – 459.92 lei, septic surgical department – 198.54 lei.
5. The average DDD/1000 consumption of Tetracyclines in intensive care departments and septic departments during

the evaluated period increased respectively by 14.9 and 4.9 times, and totally for institution by 2.4 times. For Aminoglycoside the data conversely recorded a decrease by 3.6 times and 5%, and for the total institution by 1.9 times.

6. In 2014 the medium cost of DDD/1000 for Tetracyclines in SSOD recorded 4.75 lei, or less by 3 times than cost of 14.44 lei in ICU and respectively of 329.23 lei for Aminoglycosides in SSOD or less by 8 times than 2634.39 lei recorded in ICU.
7. According to some scientific researches antibiologic therapies treatment of severe acute respiratory diseases (SARS), included tetracyclines (91.0%), aminoglycosides (83.3%), quinolones (79.2%); 18.8% of the patients received a combination of tetracyclines and aminoglycosides, while 11.5% received a combination of tetracyclines and quinolones, and 63.5% received a combination of tetracyclines, aminoglycosides and quinolones.

References

1. Swartz M. N. Hospital-acquired infections: diseases with increasingly limited therapies. Proceeding of the National Academy of Sciences of the United States of America PNAS. Current Issue. 1994;91(7):2420-2427.
2. Lobritz Michael A, Belenky Peter, et al. Antibiotic efficacy is linked to bacterial cellular respiration. Proceeding of the National Academy of Sciences of the United States of America PNAS. 2015;112(27):8173-80.
3. Wu W, Wang J, et al. A hospital outbreak of severe acute respiratory syndrome in Guangzhou, China. *Chinese Medical Journal*. 2003;116(6):811-818.
4. Finberg RW, et al. The importance of bactericidal drugs: Future directions in infectious disease. *Clin Infect Dis*. 2004;39(9):1314-1320.
5. Manocha S, Walley KR, Russell JA. Severe acute respiratory distress syndrome (SARS): a critical care perspective. *Critical Care Medicine*. 2003;31(11):2684-2692.
6. Franco-Paredes C, Kuri-Morales P, et al. Severe acute respiratory syndrome: a global overview of the epidemic. *Salud publica de Mexico*. 2003;45(3):211-20.
7. Salehifar E, et al. How aminoglycosides are used in critically ill patients in a teaching hospital in North of Iran. *Caspian J Intern Med*. 2015;6(4):238-242.
8. Meyer E, Schwab F, et al. Surveillance of Antimicrobial Use and Antimicrobial Resistance in German Intensive Care Units (SARI): A Summary of the Data from 2001 through 2004. *Infection*. 2006;34(6):303-309.
9. Bernaz EP. Evaluation of the antimicrobials used in defined daily doses in hospitals of the Republic of Moldova. *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale [Bulletin of the Moldovan Academy of Sciences. Medical Sciences]*. 2014;44(3):189-200.
10. Bernaz EP. A six year evaluation of antibiotics consumption in DDD in septic orthopedic-traumatology department. *Curierul medical*. 2015;6:10-16.
11. The world medicines situation - 2011. Centre for Drug Statistics in Oslo, Norway. www.who.int/.../WMS_ch14_wRational.pdf: <http://www.who.no>.
12. Surveillance of antimicrobial consumption in Europe 2010. <http://ecdc.europa.eu/en/publications/Publications/antimicrobial-antibiotic-consumption-ESAC-report-2010-data.pdf>. 2010;3-59.
13. Esposito S, Leone S. Antimicrobial treatment for intensive care unit (ICU) infections including the role of the infectious diseases specialist. *Int J Antimicrob Agents*. 2007;29:494-500.
14. Paterson DL, Rogers BA. How Soon Is Now? The urgent need for randomized, controlled trials evaluating treatment of multidrug-resistant bacterial infection. *Clin Infect Dis*. 2010;51:1245-7.
15. Bernaz E, Ciobanu Gh, Mişin I, Borovic E, Rusu V. Raţionalizarea consumului de remedii medicamentoase antimicrobiene sistemice în instituţiile medicale spitaliceşti [Rationalisation of consumption with systemic antimicrobial in hospitals]. *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale [Bulletin of the Moldovan Academy of Sciences. Medical Sciences]*. 2012;35(3):212-221.
16. Bernaz EP. Evaluation of consumption in DDD of antimicrobial drugs for systemic use in hospitals. *Curierul medical*. 2015;5:10-17.
17. Bernaz EP. Antibiotics consumption evaluation in reanimation department. *Curierul medical*. 2016;1:22-26.
18. Bernaz EP. Evaluation of antibiotics consumption in therapeutic intensive care department. *Curierul medical*. 2016; 2:5-10.
19. Bernaz EP. The Evaluation of Antibiotics DDD Consumption in septic surgical department in the Republic of Moldova. *Journal of Pharmaceutical Sciences and Research (JPSR)*. 2016;8(3):141-148.
20. Bernaz EP. Evaluation of antibiotics consumption in therapeutic "stroke" intensive care department. *Archives of the Balkan Medical Union*. 2016;51(1)(supl. 1):216-221.
21. Antimicrobial use in Australian hospitals: 2014 annual report of the National Antimicrobial Utilisation Surveillance Program. Commonwealth of Australia 2015;12-16.
22. Antimicrobial use in Australian hospitals: 2013 annual report of the National Antimicrobial Utilization Surveillance Program. Sahealth. sa.gov.au; 2013;36-37.