## FARMACIA DE SPITAL

### RATIONALISATION OF DRUGS GROUPS A05 BILE AND LIVER THERAPY &A06 FOR CONSTIPATION OF ALIMENTARY TRACT AND METABOLISM IN HOSPITALS

#### **Emilian Bernaz**

Public Health Institution Emergency Medicine Institute, Chisinau, Republic of Moldova

#### Rezumat

## Raționalizarea medicamentelor din grupele a05 terapia biliară și hepatică și a06 terapia constipației a tractului digestiv și metabolism în spitale

Conform datelor Organizației Mondiale a Sănătății (OMS) în prezent în lume sunt mai mult de 2 miliarde de oameni sau circa 30%, care suferă de diverse maladii ale ficatului și vizicei biliare. În Republica Moldova, în anul 2010, rata standardizată a mortalității prin boli cronice ale ficatului și ciroză hepatică a crescut de 3 ori în raport cu cea din țările europene Eur-B+C, de 10 ori – din țările grupei Eur-A și de 5,8 ori – din cele ale Regiunii Europene. Conform unor estimări de specialitate, prevalența persoanelor cu hepatite cronice, ciroză a ficatului și constipații în secțiile medicale ale Institutului de Medicină Urgentă variază între 35 și 45% din totalul persoanelor spitalizate. Reieșind din numărul mare de pacienți internați cu diferite maladii în spitale, la care prevalează incidența maladiilor ficatului, calității digestiei și motoricii intestinelor, remediile medicamentoase din grupele farmacoterapeutice terapia biliară și hepatică, precum și cele laxative sunt administrate pe larg.

Situația dată determină sistemul de sănătate din republică să acorde o atenție primordială organizării unui tratament calitativ al acestor tipuri de maladii și utilizării raționale a medicamentelor, evaluând consumul de remedii medicamnetoase utilizate pentru aceste scopuri în corespundere cu cerințele internaționale. Vom menționa, că în Republica Moldova estimarea consumului acestor grupe de remedii medicamentoase în instituțiile medicale nu este studiată în deajuns. În articolul de față ne-am propus să măsurăm de o manieră apliucativ-științifică dinamica cunsumului în indici naturali și valorici, în doze definite pentru o zi, ca unitate de bază internațională în evaluarea consumului de medicamente administrate pentru o perioădă de timp la o mie de zile-paturi, realizate prin rotație pe parcursul unui an.

Studiul prezintă un interes fundamental atât sub aspect științific, cât și practic, dat fiind necesitatea tranzitării instituțiilor medicale curative la consumul de remedii, evaluat în unități de măsură internaționale în vederea optimizării utilizării raționale a medicamentelor. **Cuvinte cheie:** remedii medicamentoase, terapia biliară, hepatică, laxative, doze definite pe zi, zile-pat ocupate, spitale, indici naturali și valorici.

#### Abstract

According to the WHO, nowadays worldwide there are more than two billion people, or approximately 30% of the world population suffering from various diseases of the liver and gallbladder. Standardized death rate by chronic liver disease and cirrhosis in Republic of Moldova compared to EU countries in 2010 exceeded 3.0 times the European countries Eur-B+C, 10 times countries Eur-A group and 5.8 times the level of European Region. The prevalence of people with chronic hepatitis, cirrhosis and suffering from constipation according to some estimates provided in the Institute of Emergency Medicine varies between 35-40% of all hospitalized people.

This situation causes significantly the health system to organized qualitative treatment of these kinds of illnesses and rational used of medicine, based on assessment at international level of consumption drugs for these purposes.

Taking in the consideration the number of patients admitted to hospital with different diseases, but with the other concomitant health problems that are belonging to the liver, digestion and intestinal bowel peristalsis irregularities, drugs of these pharmacotherapeutic groups are widely administered. It is necessary to mentioned, that in hospital institutions of Republic of Moldova the consumption of drugs in bile and liver therapy, as well as laxatives is not enough studied. The article is dedicated to estimate the consumption dynamics in nature and values indices and in defined daily dose like an international recognized unite of drug consumption measurement, determining at the same time the number of defined daily doses administered drug for a period of time to a number of occupied bed days. The study is of an interest for both practically and scientifically, in terms of practical, organization and optimization that would ensure the rational drugs use in health facilities.

**Keywords:** drugs, bile and liver therapy, lipotropic, drugs for constipation, defined daily doses, occupied-bed days, hospitals, nature, values, indices.

#### Introduction

Is knowledgeable fact that approximately 30% of the world population suffering from various diseases of the liver and gallbladder [1]. Morbidity and mortality from liver disease (cirrhosis) in the population of Moldova exceeded 3 times the European countries Eur-B + C, 10 times - the Eur-A countries group and 5, 8 times - European Region [2]. In some neighboring countries with Moldova, like Ukraine, prevalence of chronic hepatitis and liver cirrhosis in the last10 years has increased by at least 2.3-fold [3] with share of the elderly population (60-75 years), who at the same time are at risk of suffering from constipation of 23.3%, and the young age population (12-29 years) of 8.1%, or 3 times lower than in older [4, 5]. In all the hospital-like institutions the drug consumption subgroups of group referred to liver therapy, lipotropic, bile acids and laxatives (contact, volume and osmotic) is conditioned largely by the considerable number of concurrent systemrelated to liver disease and gastrointestinal. The evaluation of medicinal remedies' consumption should mention the above subgroups in units recommended by the World Health Organization and international recognition such as DDD - defined daily dose [6, 7] carries a practical and important scientific work connotation of doctors and pharmacists permanently concerned of rational planning of the medication needed for consumption and administration. In this context it is worth to mention that the recommended doses of the World Health Organization will use the abbreviation (DDD), and that doses determined in the Institute of Emergency Medicine will apply (DDDEMI)

abbreviation. The purpose and the principle of the work are concentrated around this question.

This is the third scientific study conducted at the Institute of Emergency Medicine with the intention of assessing consumption of medicinal remedies, the compartment of main group A0 – alimentary tract and metabolism according to the classification ATC (Anatomical Therapeutic Chemical classification the system).

#### Materials and methods

For this study we used data on a five-year period 2009 – 2013 in the Public Health Care Institution, Institute of Emergency Medicine (EMI), which shows the dynamics of consumption of medicinal remedies pharmacotherapeutic subgroups of biliary and liver, as well as laxatives of the main group A – alimentary tract and metabolism, according to ATC classification indicating the nature and value indices. As the statistical methods was used, analytical, mathematical, comparison, logical and descriptive.

#### **Results and discussion**

It is worth to mention that the level of consumption of medicinal remedies in the digestive tract and metabolism group in 2013 was 1 089 189 lei /182 360 grams, of which 20 633 lei / 1 327 grams or 1.9% / 0.8% is medication of A05subgroup Bile and Lever therapy, and A06 Laxative respectively 16,378 lei / 18 240 grams or 1.5% / 10%. The data presented above are for only patients with health insurance and other free treated by the state categories of citizens.

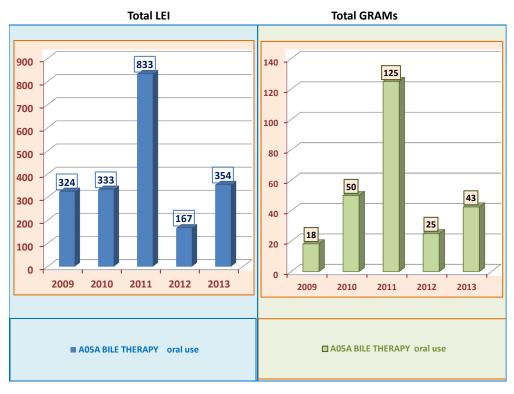


Fig. 1. Consumption of A05A Bile therapy for enteral use during the years 2009 - 2013

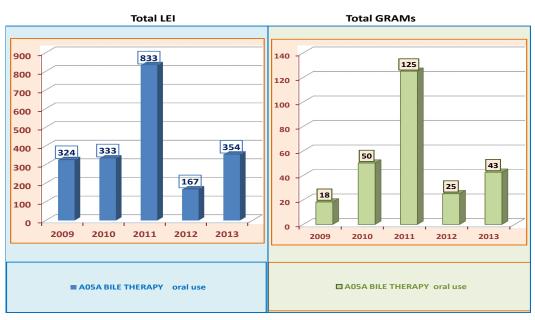


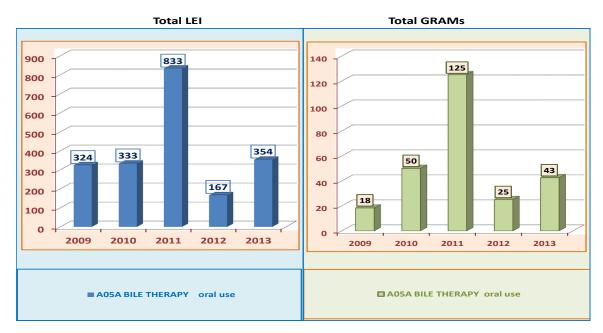
Fig. 2. A05B Liver and lipotropic therapy for parenteral and enteral use

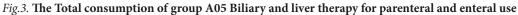
In figure 1 is presented the evaluation results of drug remedies consumption of subgroup A05A in usingenteral therapy for biliary and natural value indices, for a period of five years.

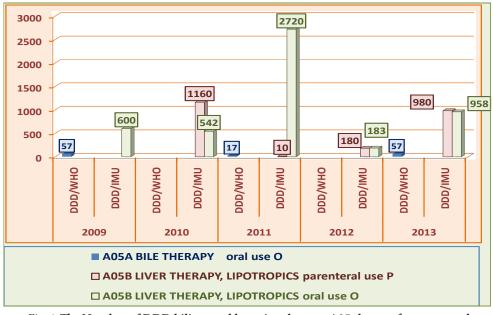
Drugs that subgroup is represented by Acidum ursodeoxycholicum DDD = 750 mg (Ursofalk c. 250 mg) [8]. During assessed period, the consumption increased in value indices from 324 lei to 354 lei, and nature indices – from 18 to 43 grams.

In Fig. 2 is presented the medicinal remedies consumption evaluation results of subgroup A05B and liver therapy lipotropic for parenteral and enteral use in values and natural indices for a period of five years. To this subgroup of drugs are belonging such drug remedies as well Essentiale combination with DDD(EMI) = 750 mg and trade name (Essentiale sol. inj. 250 mg / 5 ml); Phospholipidum with DDD(EMI) = 1800 mg and trade name (Rezalut Pro 300mg jutty Pro c. 300 mg); Argininum + Sorbitolum with DDD(EMI) = 2500 mg and trade name (Arginine-Sorbitol powder. / Sol.inj. / Perf.250 or 500 ml), Extractum chole + Extractum Cynarae scolimus) with DDD (EMI) = 3000 mg and trade name (Choliver c.); Kali orotas with DDD (EMI) = 1250 mg and trade name (Orotate K c. 500 mg); Silymarinum with DDD(EMI) = 300 mg and trade name (Lagos dr.150 mg).

Consumption of medicinal remedies subgroup A05B





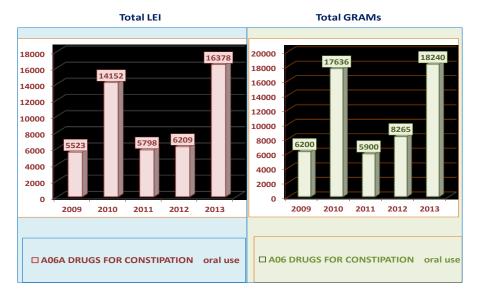


*Fig. 4.* The Number of DDD biliary and hepatic subgroup A05 therapy for parenteral and enteral use

Liver and lipotropic therapy of parenteral and enteral use for a period of five years is characterized by the decreasing tendency of value indices and increasing one in natural indices. For medicinal remedies of this subgroup used in institution, is not identified any DDD index, proposed by the World Health Organization. The consumption analysis of each drug remedy for the specified subgroup was made in their absence. Therefore, the DDD of the subgroup medicinal remedies was estimated evaluating a number of 300 to 500 cases treated in different profile sections and different time periods. To determine the number of DDD per year during the period 2009–2013 was performed dividing the annual consumption of natural indices (milligrams) in DDD(EMI) for a day and summing these data. In figure 3 is presented the data on the total consumption of medicinal remedies subgroup A05 therapy and hepatic bile for parenteral and enteral use.

The consumption of medicinal remedies subgroup A06 Drugs for constipation has higher values of 3.300 units DDD and consumption is characterized as unstable, varying considerably in 2009 and 2012 comparing to the years 2010, 2011 and 2013.

To determine DDD and compare the consumption of alementary tract and metabolism drugs for the period of 2009-2013, 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 me-



*Fig. 5.* The consumption results in value and natural indices of medicinal remedies for the subgroup A06A laxatives enteral use

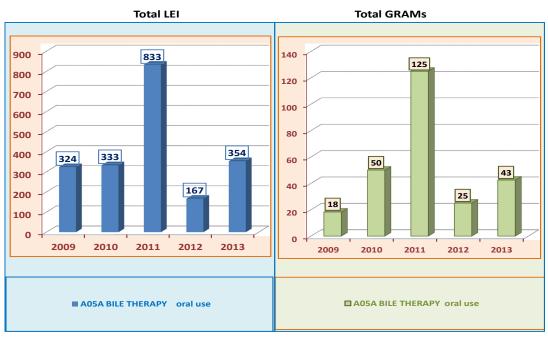


Fig. 6. The number of DDD for group A06 Drugs for constipation enteral use

dicines were used. The number of patients treated in the institution was 20 946 in 2009 with the median treatment duration of 8.62 days corresponding to 188 762 occupied bed/days; and respectively in 2010 was 21 341 and the ave-

rage duration of treatment 8.64 days which corresponds to 191 556 occupied bed/days; in 2011 was 19 913 patien-ts with an average duration of treatment 8.66 days corresponding to 186 246 occupied bed/days; in 2012 was 20

Table 1

# Number of DDD / 1000 and DDD (IMU) / 1000 occupied beds of the subgroup biliary, hepatic and the laxatives therapy, for parenteral and enteral form administered in the years 2009-2013

Forma de		2009		2010		2011		2012		2013	
	ĺ		DDD/				DDD/		DDD/		DDD/
administrare	de măsură	WHO	EMI								
	Anual	AO5	A06								
Parenteral (EMI)	DDD			1160				180		980	
Enteral (EMI)	DDD	600	20	542		2720	315	183		958	20
Enteral (OMS)	DDD	57	30		3289	17	3213		665	57	2654
Enteral total	DDD	657	50	542	3289	2720	3528	183	665	1015	2674
Total	DDD	657	50	1702	3289	2737	3528	363	665	3010	2674
Divizare		• •		• •		• •				• •	
Zile pat		188762		191556		186246		199816		193019	
Înmulțire		x 1000		x 1000		x 1000		x 1000		x 1000	
Rezultatul		11		11		11		11		11	
Parenteral (EMI)	DDD/1000			6.1				0.9		5.1	
Enteral (EMI)	DDD/1000	3.2	0.1	2.8		14.6	1.7	0.9		5.0	0.1
Enteral (OMS)	DDD/1000	0.3	0.2		17.2	0.1	17.3		3.3	0.3	13.7
Enteral total	DDD/1000	3.5	0.3	2.8	17.2	14.6	18.9	0.9		5.3	13.8
Total	DDD/1000	3.5	0.3	8.9	17.2	14.7	18.9	1.8	3.3	10.4	13.8

664 patients with an average duration of treatment of 8.82 days corresponding to 199 816 occupied days/ bed, in 2013 was respectively 20 830 patients with an average duration of treatment 7.8 days corresponding to 193 019 occupied days/bed [9].

As shown in table 1, the total consumption of DDD/1000 for the parenteral form operated during in the evaluated period it is registered only for the subgroup A05 Drugs for liver and biliary therapy had an administration range of 6.1 (2010) and 5.1 (2013) for DDD/1000 occupied beds. The total for enteral form of administration the range of consumption DDD/1000 is limited between 3.5 (2009) and 5.3 (2013) units. The total consumption of DDD/1000 for referred subgroup was 8.9 units in 2010 and 10.4 units in 2013 respectively, marking an increase of 116.9%. The consumption of drugs subgroup A06 Laxatives was only in enteral form and in 2009 showed 0.3 DDD/1000 occupied beds, in 2010 to 17.2 DDD / 1000 occupied beds, in 2011 around 18.9 DDD / 1000 occupiedbeds, in 2012 to 3.3 DDD/1000 occupied beds and in 2013 to 13.8 DDD/1000 occupied beds.

#### Conclusions

1. The consumption of medication therapy for biliary and hepatic subgroups A05 and A06 Laxatives in 2013 was 18 152 lei / 3 426 grams or 1.7% / 1.9% respectively, 16 378 lei / 18 240 grams or 1.5% / 10% of group A – digestive tract and metabolism, which was 1 089 189 lei / 182 360 grams for the whole year.

2. Consumption of remedies for the parenteral administration DDD / 1000 subgroup A05 biliary and liver therapy, for the evaluated period ranged from 6.1 in 2010 to 5.1 in 2013, with a decrease of 16.4% respectively.

3. The total consumption of DDD / 1000 A05 forbili-

ary and hepatic therapy subgroup was of 8.9 units in 2010 to 10.4 in 2013, an increase of 16.9%. For subgroup A06 Laxatives the total consumption of DDD / 1000 was 17.2 in 2010, an increase of up to 13.9 DDD / 1000 occupied beds in 2013 or an decrease of 19.2%.

4. It was determined the institutional DDD (DDD (EMI)) for medicinal remedies: Essential combination DDD(EMI) = 750 mg (trade name

Essential sol. Inj. 250 mg/5 ml) Phospholipidum DDD(EMI) = 1800 mg (trade name Rezalut Pro c. 300 mg); Argininum + Sorbitolum DDD (IMU) = 2500 mg (trade name Arginine-Sorbitol powder. / Sol.inj. / Perf.250 or 500 ml) Extraction tum extractumchole + + Cynaraescolimus Court DDD(EMI) = 3000 mg (trade name Choliver), Kali orotas DDD(EMI) = 1250 mg (trade name orotate K c. 500 mg), Silymarinum DDD(EMI) = 300 mg (trade name Lagos dr.150mg), which if representing the medicinal remedies subgroup A05B liver and lipotropic therapy, and, from subgroup A06 Laxatives Cassia acutifolia DDD = 140 mg (trade name Senadexin comp. 70 mg) used in the IMU.

5. Due to cirrhosis in Moldova standard death rate is 5.8 times higher than in the European Region, the morbidity is permanent growing and the total staff of hospitalization, those with concomitant diseases of bile, liver and intestinal peristaltic is more than 35-40%. Based on this, it highlights the need to provide remedies nomenclature and quantities of drug for the subgroups A05 Bellary and hepatic therapy and A06 Laxatives, to provide both qualitative treatment and disease prevention.

6. The data from the evaluation result serves as a basis for optimizing planning and the rational use of drugs remedies of the listed groups.

#### Bibliography

- 1. Т.Д. Звягинцева, С.В. Глущенко. Хронические диффузные заболевания печени: патогенетические подходы к лечению. Здоровье Украины. Медицинская газета номер 1. Медицинская Академия Биологической Медицины. Киев. 2010. стр. 1-2.
- 2. L. Solomon. Autoreferat «Impactul cirozei hepatice asupra sănătății populației Republicii Moldova «. Chișinău, 2014. p.3-4.
- 3. Ткач С.М. Эффективность и безопасность гепатопротекторов с точки зрения доказательной медицины. В: Здоровья Украины, 2009, nr.6/1, c.7-10.
- 4. R S Sandler, M C Jordan, and B J Shelton. Demographic and dietary determinants of constipation in the US population. Am J Public Health. 1990 February; 80(2): 185–189.N.C.
- 5. Talley NJ<sup>1</sup>, Fleming KC, Evans JM, O'Keefe EA, Weaver AL, Zinsmeister AR, Melton LJ 3rd. Constipation in an elderly community: a study of prevalence and potential risk factors. Am J Gastroenterol. 1996 Jan;91(1):19-25.
- 6. Guidelines for ATC classification and DDD assignment WHO, 16<sup>th</sup> edition. WHO Collaborating Centre for Drug Statistics Methodology Norwegian Institute of Public Health. Oslo, 2013: 284 p.
- 7. E. P. Bernaz. Evaluation of the antimicrobial use in Defined Daily Doses in hospitals of The Republic of Moldova. Buletinul Academiei de Ştiințe din Moldova 3(35) 2014: 212-221.
- WHO Collaborating Centre for Drug Statistics Methodology Norwegian Institute of Public Health Oslo, Norway. 2013: http://www. whocc.no/atc\_ddd\_index/? code = A05A.
- 9. Dările de seamă despre activitatea Centrului Național Științifico Practic Medicină de Urgență anii 2009 2013: http://www.urgenta.md/ Scientific\_ Activity.aspx.