ОРГАНІЗАЦІЯ ТА ЕКОНОМІКА ФАРМАЦІЇ

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PHARMACOECONOMIC ESTIMATION OF THE STANDARD TREATMENT REGIMENS OF PATIENTS WITH THE STOMACH AND RECTAL CANCER

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Key words: pharmacoeconomic evaluation; stomach cancer; colorectal (rectal) cancer; regimens; cost – minimization analysis; cost – effectiveness analysis

The article presents the results of pharmacoeconomic evaluation of pathogenic drug therapy regimens of the most common malignant pathologies that take the first places in the structure of cancer death – stomach cancer and colorectal cancer. The analysis of the current regulatory framework for approaches to treatment and standard regimens of basic and additional lists for treatment of these diseases are given. The authors summarized results of the research of the standard chemotherapy for stomach and colorectal cancer by the methods of pharmacoeconomic analysis of "cost – minimization" and "cost – effectiveness". It has been found that from the standpoint of saving among the standard regimens of stomach cancer it is the most appropriate to use doxorubicin in the monotherapy, and for treating colorectal cancer tegafur is used. The volumes of possible savings per course of treatment for a patient have been calculated. It has been determined that the ratio of the cost – effectiveness of the most rational therapy in treating stomach cancer is the use of doxorubicin, and in treating rectal cancer it is tegafur. Thus, the results obtained allow to choose a regimen for therapy based on the needs of savings, which is extremely important in view of the shortage of healthcare financing.

In Ukraine by the end of 2012, 1,052,333 patients were registered with cancer (2 315,2 per 100 thousand of the population), including 368,403 men (1 756,2 per 100 thousand of the male population) and 683,930 women (2 794,2 per 100 thousand of the female population) [2]. The population structure of patients with malignant neoplasms (MN) among men stomach (gastric) cancer (SC) and colorectal cancer (CRC) ranked the fourth and sixth places – 8.4% and 6.1 %, respectively, among women – those diseases took the seventh and sixth places – SC – 5.1%, CRC – 5.2%, indicating a significant morbidity among the population of Ukraine in MN of the abdominal profile [2].

The best efficiency of medical and pharmaceutical care, lower costs are the priorities of the 17-th World Meeting of the International Society of Pharmacoeconomic Research (ISPOR), the scientists of the National University of Pharmacy are its full members. Taking into account the high cost of cancer treatment and peculiarities of oncological patients (aided persons, high disability, etc.) the need of pharmacoeconomic approaches in the treatment of cancer patients is indisputable. Therefore, the aim of our study was pharmacoeconomic evaluation of standard regimens of chemotherapy of SC and CRC used in domestic medical practice.

Materials and Methods

In accordance with the order of the Ministry of Public Health of Ukraine from 17.09.2007 No. 554 the national standards for diagnosis and treatment of patients with SC and CRC were approved [1]. From 2007 until today pharmacotherapy of SC in Ukraine consists of four main and three additional regimens of chemotherapy (ChT). Pharmacotherapy of CRC includes two major and five additional treatment regimens. The pharmacoeconomic evaluation included the use of two of the most common methods of analysis in medical practice – "cost – minimization" and "cost – effectiveness". To calculate the cost of regimens of ChT the data of wholesale offers of distributors from the analytical base "Morion" as of April – September 2013 were used, retail prices were formed based on 10% of trading margin. For calculations by the "cost – effectiveness" method the results of randomized clinical trials were used; as the unit of effectiveness the likelihood of achieving the objective effect (objective response) from the application of mono- or polychemotherapy regimens was taken [4-10].

Results and Discussion

The results of the comparative evaluation of the main regimens of ChT of SC by the "cost – minimization" analysis has revealed that doxorubicin monotherapy is the most economically grounded from the standpoint of minimizing the cost of treatment. The cost of treatment for one patient with SC with doxorubicin was 204,5 UAH (or $ 25,6, $ 1 eq. 7,993 UAH), which was almost 28 times lower than the cost of treatment with the standard

Table 1

Analysis of costs for the standard regimens of chemotherapy of stomach cancer

No.	Regimen	Costs of treatment per one course of one patient, UAH/$*
The main list of regimens		
1	Mayo: Fluorouracil (single dose 425 mg/m^2, course dose – 2125 mg/m^2) Ca folinate (single dose 20 mg/m^2, course dose – 100 mg/m^2)	5 671,9 / $ 710
2	Fluorouracil (single dose 300 mg/m^2, course dose – 1500 mg/m^2)	2 442,4 / $ 306
3	Doxorubicine (single dose 40 mg/m^2)	204,05 / $ 25,6
4	Cisplatine (once 40 mg/ m^2)	238,39 / $ 30
The additional list of regimens		
1	Capecitabine (2000 mg twice a day, per os, 14 days)	3 726,6 / $ 466
2	Tegafur (1200 mg/day, per os, 20 days)	745,8 / $ 93
3	Imatinib (400-600 mg/day; duration is determined individually)	-

* 1 USD corresponds to 7,993 UAH (as of October 2013)

regime of Mayo clinic (fluorouracil + Ca folinate), which cost of treatment was the highest among the four major regimens of SC ChT – 5 671,9 UAH (or $ 710) (Table 1).

The additional list of regimens of SC ChT, which under the law can be used with adequate providing or at the expense of the patient at his request, involves the use of monoregimens of capecitabine, tegafur or imatinib. Since the duration of imatinib treatment is determined individually for each patient, there are no guidelines that standardize the treatment course for treating SC. In further calculations the regimens with capecitabine and tegafur were compared. It has been found that the cost of treatment with tegafur per a patient is 745,8 UAH (or $ 93); it is 5 times less than the cost of capecitabine treatment that is 3 726,6 UAH (or $ 466) (Table 1).

Assessment of the main list of standard regimens for CRC ChT has revealed that from the standpoint of minimizing the cost of treatment it is more appropriate to use the De Gramont regimen (Ca folinate + fluorouracil 2) compared to the Mayo regimen, which cost is

Table 2

Analysis of costs for the standard regimens of chemotherapy of colorectal cancer

No.	Regimen	Costs of treatment per one course of one patient, UAH/$*
The main list of regimens		
1	Mayo: Fluorouracil (single dose 425 mg/m^2, course dose – 2125 mg/m^2) Ca folinate (single dose 20 mg/m^2, course dose – 100 mg/m^2)	5 671,9 / $ 710
2	**De Gramont** (or **LV/5-FU2):** Ca folinate 400 mg/m^2 i/v Fluorouracil 400mg/m^2 + 600mg/m^2	4 193,71 / $ 525
The additional list of regimens		
1	**IFI**: Irinotecane 125 mg/m^2 Ca folinate 20 mg/m^2 Fluorouracil 500 mg/m^2	18 825,6 / $ 2 355
2	**FOLFOX-6:** Oxaliplatine 100 mg/m^2 Ca folinate 400 mg/m^2 Fluorouracil 400 mg/m^2 + 2400 mg/m^2	6 039,78 / $ 756
3	**XELOX:** Oxaliplatine 130 mg/m^2 on the 1st day Capecitabine 2000 mg/m^2 i/v on the 1-14 days	8 251,2 / $1 032
4	Bevacizumab 5 mg/m^2 Irinotecane 125 mg/m^2 Ca folinate 20 mg/m^2 Fluorouracil 500 mg/m^2	-
5	Tegafur 300 mg/m^2, 28 days	472,34 / $ 60

* 1 USD corresponds to 7,993 UAH (as of October 2013)

Table 3

Results of analysis of standard regimens of SC and CRC ChT by the "cost – effectiveness" method

No.	Regimen	Objective effect, %	Source of information, authors of the study	CEA indicator, UAH ($*)
Stomach cancer:				
1	Mayo regimen	38,5	[2] Hsu CH, Yeh KH, Chen LT et al.,1997, 2004	147 ($ 18,5)
2	Fluorouracil	21	Sakamoto J. et al., 2006	116 ($ 15)
3	Doxorubicine	17	Sakamoto J. et al., 2006	12 ($ 1,5)
4	Cisplatine	19	Sakamoto J. et al., 2006	12,5 ($ 1,6)
5	Capecitabine**	26	Sakamoto J. et al., 2006	143,3 ($ 17,9)
6	Tegafur**	19	Sakamoto J. et al., 2006	39,3 ($ 5)
Colorectal cancer:				
1	Mayo regimen	33,7	Losa A., 2004	168 ($ 21)
2	LV/5-FU2	32,6	[4] De Gramont A., 1997	128,6 ($ 16)
3	IFl**	44,7	Douillard, 2000; Saltz, 2000; Kohne, 2003	421 ($ 52,7)
4	FOLFOX-6**	45	Van Custem E., 2004	134,2 ($ 16,8)
5	XELOX**	50,3	Satre, 2005	164 ($ 1820,5)
6	Tegafur**	19	Manuel Valdivieso, 1975; Sakamoto J. et al., 2006	25 ($ 3,2)

* – 1 USD corresponds to 7,993 UAH (as of October 2013); ** – additional list of regimens

4 193,71 UAH (or $ 525) and 5 671,9 (or $ 710), respectively. Thus, saving from the use of the De Gramont regime will be almost 1480 UAH (or $ 185) per the course of treatment for one patient (Table 2).

According to the results of the calculations it has been determined that among the five regimens of the additional list for the treatment of CRC in order to minimize the cost the application of the tegafur monoregimen is the most appropriate; its cost of treatment for one patient is 472,34 UAH (or $ 60). Possible savings compared to the use of other regimens will be from 5,57 thousand UAH to 18,4 thousand UAH (or 0,7-2,3 thousands $) for a patient per the course of treatment. Considering the fact that during the research period there were no drugs of bevacizumab at the domestic pharmaceutical market, the cost of the regimen with this drug was not calculated.

In modern medicine, with the imperative need of cost savings and minimization of the cost of treatment, the quality and the outcome of therapy play the important role. Therefore, in recent years in the field of healthcare, particularly in oncology, the priority is the pharmacoeconomic evaluation of approaches to treatment that considers the clinical effectiveness of the regimens used. That is why the next stage of the study was the pharmacoeconomic evaluation of the standard regimens of SC and CRC ChT by the "cost – effectiveness" method [3].

As an indicator of clinical efficacy the likelihood of achieving the objective effect of therapy was taken. The analysis was determined the ratio of the cost for each medical technology (standard chemotherapy regimens) to its effectiveness – the index of CEA (cost – effectiveness analysis) per a course of treatment for one patient (Table 3) [4-10].

As evidenced by the calculations, among the regimens of SC ChT the use of doxorubicin is characterized by the lowest cost – CEA corresponds to 12 USD for one patient per a course of treatment. At the same time it should be noted the lowest indexes of clinical effectiveness of the treatment with this drug in monotherapy (17% of the objective effect achievement). It should be noted that the highest cost of the efficacy unit in SC ChT corresponds to the basic regimen – Mayo which according to the results of clinical studies demonstrates the highest effectiveness in the treatment of SC.

The lowest cost per unit of clinical effectiveness (probability of achieving the objective effect) in ChT of CRC corresponds to the use of the tegafur monoregimen, which is referred to the additional list of CRC regimens – CEA is 25 UAH for one patient per a course of treatment. The IFl regimen (irinotecan, calcium folinate, fluorouracil) has the highest indexes of clinical effectiveness and the cost of unit of CRC therapy effectiveness. Therefore, the results of the study should be used considering the priority of treatment – either from the standpoint of the highest efficacy, or with the purpose of rationalization and optimization of costs based on the ratio of the cost of therapy to its clinical efficacy.

CONCLUSIONS

1. It has been found that for SC treatment in Ukraine the current legislation provides for seven standard regimens of chemotherapy, for CRC therapy there are also seven standard regimens used.

2. The research results of standard SC regimens by the "cost – minimization" analysis indicate that it is the most appropriate to use doxorubicin (204,5 UAH, or $ 25,6); its cost of treatment is almost 28 times lower than the cost of treatment with the standard regimen of the Mayo clinic.

3. From the standpoint of minimizing the cost of treatment it has been determined that among the standard CRC chemotherapy the monoregimen with tegafur is the most appropriate, the cost of treatment of one patient is 472, 34 UAH, or $ 60. Possible savings can range from

5,57 thousand UAH (compared to the Mayo regimen) to 18,4 thousand UAH (compared to the Ifl regimen), or 0,7-2.3 thousand $ per a course of treatment for one patient with CRC.

4. The analysis by "cost – effectiveness" method allows to calculate that among the standard SC regimens of Cht the doxorubicin monoregimen is characterized by the lowest costs of the unit of clinical effectiveness (probability of achieving the objective effect) (CEA corresponds to 12 UAH for a patient per one course of treatment); among the CRC regimens of treatment the tegafur monoregimen is the best (CEA is 25 UAH for a patient per one course of treatment).

Thus, our study has allowed to determine the regimens for chemotherapy of SC and CRC, which use is the most appropriate in order to minimize costs and the regimens, which use is the most rational from the standpoint of the ratio of the cost and clinical effectiveness. The results of the present study can be used in planning of the drug purchasing at the level of government institutions and by patients to select the optimal therapy for the treatment at their own expense.

REFERENCES

1. *Наказ МОЗ України від 17.09.2007р. №554. [Електронний ресурс]. – Режим доступу: http://www.moz.gov.ua/ua/portal/dn_20070917_554.html*
2. *Рак в Україні, 2011-2012. 14 вид. – К., 2013. [Електронний ресурс]. – Режим доступу: http://www.ncru.inf.ua/publications/BULL_14/index.htm*
3. *Фармацевтична енциклопедія. [Електронний ресурс]. – Режим доступу: http://www.pharmencyclopedia.com.ua/article/288/farmakoekonomichnij-analiz*
4. *Buyse M.E., Pignon J. // J. Clin. Oncol. – 2010. – Vol. 1. – P. 246-276.*
5. *De Gramont A., Bosset J.F., Milan C. et al. // J. Clin. Oncol. – 1997. – Feb; Vol. 15 (2). – P. 808-815. Resource of Access: http://www.ncbi.nlm.nih.gov/GCbmed/9053508*
6. *Hsu C.H., Yeh K.H., Chen L.T. et al. // Oncol. – 1997. – №54. – P. 275-280.*
7. *Kang Y.K., Kang W.K., Shin D.B. et al. // Ann. Oncol. – 2009. – №20. – P. 666-673.*
8. *Norman G., Soares M., Peura P. et al. // Health Technol. Assess. – 2010. – №14. – P. 11-17.*
9. *Okines A.F.C., Norman A.R., McCloud P. et al. // Ann. Oncol. – 2010. – №20. – P. 1529-1534.*
10. *Vincenzo C. // Histopathol. – 2011. – №58. – P. 669-678.*

ФАРМАКОЕКОНОМІЧНА ОЦІНКА СТАНДАРТНИХ СХЕМ ЛІКУВАННЯ ХВОРИХ НА РАК ШЛУНКА ТА РАК ПРЯМОЇ КИШКИ

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Ключові слова: *фармакоекономічна оцінка; рак шлунка; рак прямої кишки; схеми лікування; аналіз «мінімізація вартості»; аналіз «вартість – ефективність»*

Представлені результати фармакоекономічної оцінки схем патогенетичної фармакотерапії найбільш розповсюджених злоякісних патологій, які займають перші місця у структурі онкологічної смертності – раку шлунка та раку прямої кишки. Проаналізовано чинну нормативну базу щодо підходів до лікування, зокрема встановлено, що для лікування раку шлунка в Україні передбачено застосування семи стандартних схем терапії, з яких чотири включено до основного переліку схем лікування; для раку прямої кишки також рекомендовано застосування семи стандартних режимів терапії, з яких дві віднесені до основного переліку. У представленому дослідженні наведені стандартні схеми основного та додаткового переліків для лікування вказаних захворювань. Авторами узагальнені отримані результати дослідження стандартних схем хіміотерапії раку шлунка та раку прямої кишки за основними методами фармакоекономічного аналізу «мінімізація вартості» та «вартість – ефективність». Встановлено, що з позиції економії серед стандартних схем лікування раку шлунка найбільш доцільне застосування доксорубіцину у монорежимі, для лікування раку прямої кишки – застосування тегафуру, наведені обсяги можливої економії з розрахунку на курс лікування для одного хворого. Визначено, що у співвідношенні вартість – ефективність терапії найбільш раціональним у лікуванні раку шлунка також є застосування доксорубіцину, а у лікуванні раку прямої кишки – тегафуру. Таким чином, отримані результати дозволяють обрати схему терапії з урахуванням потреби в економії коштів, що є вкрай актуальним з огляду на дефіцит фінансування системи охорони здоров'я.

ФАРМАКОЭКОНОМИЧЕСКАЯ ОЦЕНКА СТАНДАРТНЫХ СХЕМ ТЕРАПИИ БОЛЬНЫХ РАКОМ ЖЕЛУДКА И РАКОМ ПРЯМОЙ КИШКИ

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Ключевые слова: *фармакоэкономическая оценка; рак желудка; рак прямой кишки; схемы терапии; анализ «минимизация стоимости»; анализ «стоимость – эффективность»*

Представлены результаты фармакоэкономической оценки схем патогенетической фармакотерапии наиболее распространенных злокачественных патологий, которые занимают *первые места в структуре онкологической смертности – рака желудка и рака прямой кишки. Проанализирована действующая нормативная база относительно подходов к лечению, а именно, установлено, что для лечения рака желудка в Украине предусмотрено использование семи стандартних схем терапии, из которых четыре схемы включены в основной перечень схем лечения; для рака прямой кишки также рекомендуется использование семи стандартных режимов терапии, из которых две схемы (режима) отнесены к основному перечню. В представленном исследовании приведены стандартные схемы основного и дополнительного перечней для лечения указанных заболеваний. Авторами обобщены полученные результаты исследования стандартных схем химиотерапии рака желудка и рака прямой кишки методами фармакоэкономического анализа «минимизация стоимости» и «стоимость – эффективность». Установлено, что с позиции экономии среди стандартных схем лечения рака желудка наиболее целесообразно применение доксорубицина в монорежиме, для лечения рака прямой кишки – тегафура, а также приведены объемы возможной экономии в расчете на курс лечения для одного больного. Определено, что в соотношении стоимость – эффективность терапии наиболее рациональным в лечении рака желудка также является применение доксорубицина, а в лечении рака прямой кишки – тегафура. Таким образом, полученные результаты позволяют выбрать схему терапии с учетом потребности в экономии средств, что является крайне актуальным в условиях дефицита финансирования здравоохранения.*