

## ФАРМАЦЕВТИЧНІ НАУКИ

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**RATIONAL CHOICE OF MONOTHERAPY FOR THE TREATMENT OF TYPE 2 DIABETES MELLITUS BASED ON THE PHARMACOECONOMICAL ANALYSIS**

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*Research was conducted to scientific justification of rational choice of monotherapy diabetes mellitus (DM) type 2 based on the pharmacoeconomical analysis. It has been found that the unit of efficiency was the cheapest in the scheme of the monotherapy with gliclazide and most expensive – in the scheme of the monotherapy with metformin*

**Keywords:** diabetes mellitus, retrospective analysis, monotherapy, cost-effectiveness analysis, sensitivity analysis

*Було проведено дослідження з метою наукового обґрунтування раціонального вибору монотерапії цукрового діабету 2 типу на основі фармакоєкономічного аналізу. Встановлено, що схема монотерапії гліклазидом мала найдешевшу одиницю ефективності, найдорожчу – з метформіном*

**Ключові слова:** цукровий діабет, ретроспективний аналіз, монотерапія, аналіз ефективності витрат, аналіз чутливості

**1. Introduction**

The formulary system is introduced in medical establishments of Ukraine. It provides the optimization of pharmacotherapy of the patients and meant to provide the highest possible quality of care and optimal use of available financial resources. This optimization can be achieved by the introduction of pharmacoeconomical component of formulary system of medicines and protocols of treatment. Unfortunately, a shortage of pharmacoeconomical studies in medicine in Ukraine leads to the absence of pharmacoeconomical component in the protocols of treatment. This problem also applies to diabetes mellitus (DM) regimens. DM is one of the actual medical and social problems in Ukraine. DM acquires the character of non-infectious epidemics now that puts the DM in problems of state importance. 1264500 patients were registered in 2011 with DM in Ukraine, 1311335 patients – in 2012, and 1380470 patients – in 2013 [1]. 90 % of them are patients with DM type 2 [2]. Metformin is the first-line drug for the treatment of DM type 2 at present time [2–4]. But in case of intolerance to metformin, the contraindications, the need for rapid therapeutic reaction and for patients without overweight sulfonylurea drugs are used [5–7]. Patient takes the hypoglycemic therapy constantly, and it requires a significant amount of money. Therefore it is important the pharmacoeconomical evaluation of the therapy.

**2. Analysis of literature data**

Results of pharmacoeconomical researches in the treatment of DM type 2 are available in contemporary literature. Review of conducted researches in pharmacotherapy of DM type 2 was made by professor Yakovleva L.V. [8], the pharmacoeconomical investigations in therapy of DM type 2 were studied by Yagudina R. I.,

Kulikov A. Y. in Russia (cost-effectiveness analysis, cost-benefit analysis, budget impact analysis) [6], Giwa Abdulganiyu, Tayo Fola have investigated this problem in Nigeria (cost minimization analysis) [9]. Nevertheless, in Ukraine are no conducted the complex pharmacoeconomical research of schemes of treatment of DM type 2. Moreover, there are no complex pharmacoeconomical studies in which the object is monotherapy of DM type 2. The foregoing causes necessity of this research.

**The purpose of the research** was a scientific justification of rational choice of monotherapy of DM type 2 based on pharmacoeconomical analysis.

**3. Research objectives**

The following objectives were set to achieve the research purpose:

1) retrospective analysis of 1792 medical histories and treatment sheets of in-patients with DM type 2 that were treated in specialized hospitals of Podolsky region in 2011-2013;

2) frequency analysis of the used treatment regimens;

3) analysis of the patient parameters: age, body mass index (BMI), fasting plasma glucose (FPG) when admission to hospital, duration of DM, duration of hospital stay and complications of DM;

4) ATC/DDD-analysis of OHD included in the studied schemes of pharmacotherapy;

5) cost-effectiveness analysis using the minimal and maximal prices of OHD in the context of generics at the regional pharmaceutical market;

6) sensitivity analysis for the determination of stability of the pharmacoeconomical analysis results.

**The object of the study:** the monotherapy of the in-

patients with DM type 2.

**4. Results of research**

The retrospective analysis showed that monotherapy was used in 25, 1 % of cases. Of these, 16, 2 % (290 patients) were treated by metformin (the first group), 5 % (91 patients – the second group) – glimepiride, 3, 9% (70 patients – the third group) – gliclazide.

When comparing groups of patients (table 1) that received different monotherapy it has been found that the

patients of the 2<sup>nd</sup> and 3<sup>rd</sup> groups had not authentic distinctions on all other analyzed indicators. The patients of 1<sup>st</sup> and 3<sup>rd</sup> groups had authentic distinctions on the duration of hospital stay and they had not authentic distinctions on all other analyzed indicators. Patients of 1<sup>st</sup> and 2<sup>nd</sup> groups had authentic distinctions in all analyzed parameters.

Consequently, the patients that received metformin were significantly younger, they had the highest BMI, the lowest FPG on admission and the lowest duration of DM type 2 (Table 1).

Table 1

Characteristics of patients at different monotherapy

№	Indicators	Pharmacotherapy schemes			The significance of differences
		scheme 1 (metformin)	scheme 2 (glimepiride)	scheme 3 (gliclazide)	
1	The number of patients	290	91	70	
2	Age (years)	53,82±1,23	57,88±2,56	58,47±2,66	p <sub>1-2</sub> <0,05 p <sub>1-3</sub> <0,05 p <sub>2-3</sub> >0,05
3	Duration of illness (year)	5,29±0,58	7,12±1,34	6,63±1,43	p <sub>1-2</sub> <0,05 p <sub>1-3</sub> <0,05 p <sub>2-3</sub> >0,05
4	BMI (kg/m <sup>2</sup> )	34,36±0,95	29,4±2,25	27,48±1,66	p <sub>1-2</sub> <0,05 p <sub>1-3</sub> <0,05 p <sub>2-3</sub> >0,05
5	FPG on admission (mmol/L)	9,10±0,28	10,03±0,62	9,61±0,57	p <sub>1-2</sub> <0,05 p <sub>1-3</sub> <0,05 p <sub>2-3</sub> >0,05
6	Duration of hospital stay (days)	10,28±0,27	11,12±0,55	10,36±0,67	p <sub>1-2</sub> <0,05 p <sub>1-3</sub> >0,05 p <sub>2-3</sub> >0,05

DDD of OHD that was included in the studied schemes of pharmacotherapy was studied by ATC/DDD-analysis [10]. DDD for drugs with the international nonproprietary name (INN) were amounted. There were: for metformin – 2,000 mg, for glimepiride – 2 mg, for gliclazide – 60 mg. Their prices were researched in Ukrainian national currency – UAH at the regional pharmaceutical market of Vinnytsia and Vinnytsia region with calculation of value of each monotherapy regimen *in* the context of minimal and maximal values of generics. The cost of DDD was calculated according to the data register of wholesale selling prices for drugs [11]. The total number of calculated variants for the scheme with metformin was 33, for the scheme with glimepiride – 19, with gliclazide – 5. As a result of ATC/DDD-analysis it has been found that the cost of DDD of monotherapy with metformin ranges from 1,25 UAH to 4,26 UAH, with glimepiride – 1,22-3,42 UAH, with gliclazide – 1,26–3,97 UAH.

In the cost-effectiveness analysis the number of effective patients in the context of each scheme was calculated. Under the number of effective patients was the percentage of patients whose FPG level after pharmacotherapy became ≤7mmol/l [1, 2, 5, 8].

It was established that the number of effective patients with metformin monotherapy was 67 %, with glimepiride – 53,8 %, with gliclazide – 65,7 %.

To compare research schemes costs-efficiency ratios (CER1, CER2 and CER3, respectively) were calculated according to the formula [9]:

$$CER=DC/Ef,$$

where DC – cost of treatment for the course of monotherapy (DC1, DC2 and DC3, respectively), Ef – individual indicator of efficiency (Ef1, Ef2 and Ef3, respectively)

When taking into account the minimal cost of OHD-generics the effectiveness ratio (CER) has made:

$$CER1 \text{ (metformin)}=DC1/Ef1=15,50/0,67=23,13 \text{ UAH};$$

$$CER2 \text{ (glimepiride)}=DC2/Ef2=12,20/0,538=22,68 \text{ UAH};$$

$$CER3 \text{ (gliclazide)}=DC3/Ef3=12,60/0,657=19,18 \text{ UAH}.$$

Comparison of CER1, CER2 and CER3 at minimal prices of OHD in the context of generics showed that the unit of efficiency was the cheapest in the scheme of monotherapy with gliclazide and it was most expensive in the scheme of monotherapy with metformin.

When taking into account the maximal cost of OHD-generics the effectiveness ratio (CER) has made:

$$CER1 \text{ (metformin)}=DC1/Ef1=54,60/0,67=81,49 \text{ UAH};$$

$$CER2 \text{ (glimepiride)}=DC2/Ef2=34,20/0,538=63,57 \text{ UAH};$$

$$CER3 \text{ (gliclazide)}=DC3/Ef3=39,70/0,657=60,43 \text{ UAH}.$$

Comparison of CER1, CER2 and CER3 at maximal prices of OHD in the context of generics showed that the unit of efficiency was the cheapest in the scheme of monotherapy with gliclazide and was most expensive in the scheme of monotherapy with metformin.

The cost-effectiveness ratio testifies to cost-effective benefits of monotherapy with gliclazide.

Sensitivity analysis was conducted in the context of minimal cost of OHD-generics to determine the stability of the cost-effectiveness analysis results [9].

One-way sensitivity analysis showed that the scheme of monotherapy with gliclazide keeps pharmacoeconomical benefits to increased cost of DDD up to 18 %. Further increase the cost of DDD results of pharmacoeconomical benefits are lost (Table 2). Because the cost of unit effectiveness of monotherapy with gliclazide was not significantly different from the cost of unit effectiveness of monotherapy with metformin (22,9 UAH compared to 23,13 UAH).

For the two-way sensitivity analysis we assumed that the price of drugs on the pharmaceutical market will grow and efficiency will decrease. In this case the scheme pharmacotherapy with gliclazide kept pharmacoeconomical benefits to increase of cost of DDD up to 9 % and to reduction of the efficiency of treatment up to 9 % (Table 3). Because the cost of unit effectiveness of monotherapy with gliclazide was not significantly different from the cost of unit effectiveness of monotherapy with metformin (22,9 UAH compared to 23,13 UAH).

Table 2

One-way sensitivity analysis

№	increase in the cost		CER,UAH
	%	UAH	
	початкові дані	12,6	19,2
1	1 %	12,7	19,4
2	2 %	12,9	19,6
3	3 %	13,0	19,8
4	4 %	13,1	20,0
5	5 %	13,2	20,2
6	6 %	13,4	20,4
7	7 %	13,5	20,6
8	8 %	13,6	20,8
9	9 %	13,8	21,0
10	10 %	13,9	21,2
11	11 %	14,1	21,4
12	12 %	14,2	21,6
13	13 %	14,3	21,8
14	14 %	14,5	22,0
15	15 %	14,6	22,3
16	16 %	14,8	22,5
17	17 %	14,9	22,7
18	<b>18 %</b>	<b>15,1</b>	<b>22,9</b>
19	19 %	15,2	23,2
20	20 %	15,4	23,4

Table 3

Two-way sensitivity analysis

№	increase in the cost		reduced efficiency		CER, UAH
	%	UAH	%	individual effectiveness	
1.	original data	12,60	original data	0,657	19,18
2.	1 %	12,7	1 %	0,650	19,52
3.	2 %	12,9	2 %	0,644	20,03
4.	3 %	13,0	3 %	0,638	20,39
5.	4 %	13,1	4 %	0,631	20,75
6.	5 %	13,2	5 %	0,625	21,12
7.	6 %	13,4	6 %	0,619	21,65
8.	7 %	13,5	7 %	0,613	22,03
9.	8 %	13,6	8 %	0,607	22,42
10.	9 %	13,8	9 %	0,601	22,97
11.	10 %	13,9	10 %	0,595	23,36

**5. The following conclusions were made by the results of this research:**

1) The frequency analysis showed that monotherapy was used in 25,1 % cases, of which 16,2 % was used metformin, 5 % – glimepiride, 3,9 % – gliclazide.

2) The patients that received metformin monotherapy were significantly younger, they had the highest BMI, the lowest FPG on admission and the lowest duration of DM type 2. It has been found that patients who were on the glimepiride and gliclazide monotherapy had not authentic distinctions on all other analyzed indicators.

3) As a result of ATC/DDD-analysis it has been found that the cost of DDD of metformin ranges from 1,55 UAH to 5,46 UAH, for glimepiride – from 1,22 UAH to 3,42 UAH, for gliclazide – from 1,26UAH to 3,97 UAH in the context of minimal and maximal costs of OHD-generics.

4) Comparison of CER1, CER2 and CER3 at minimal and maximal prices of OHD in the context of generics showed that the unit of efficiency was the cheapest in the scheme of monotherapy with gliclazide and was the most expensive in the scheme of monotherapy with metformin.

5) A sensitivity analysis showed the stability of the pharmacoeconomical study results when fluctuations in the value of DDD were up to 18 % and change both in the value of DDD and efficiency of treatment simultaneous – up to 9 %.

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