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PHARMACOECONOMIC ANALYSIS OF CELLEX APPLICATION IN THE TREATMENT OF CEREBROVASCULAR ACCIDENT

Kulikov A. Yu., Abdrashitova G. T.

I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation

Summary: A pharmacoeconomic study of cerebrovascular accident treatment with Cellex was conducted at the background of routine clinical practices in comparison with routine clinical practices only. It was found that in the first case the therapy is dominant in comparison with the second one as it shows better therapeutic effectiveness and is characterized by a lower cost-effectiveness ratio. It was also defined that transfer of one patient from routine clinical practices to Cellex treatment at the background of routine clinical practices is supported with the economy of 7 313 rubles.

Key words: pharmacoeconomic analysis, effectiveness, cost analysis, cost-effectiveness, budget impact, cerebrovascular accident, Cellex.

Introduction

Cerebrovascular accident (CVA) implies quickly appearing focal and diffuse violations of cerebral functions of vascular origin. CVA is a pathological process in the brain related to insufficient cerebral blood supply (cerebral infarction) or spontaneous (non-traumatic) intracranial hemorrhage (hemorrhagic stroke) [1, 2].

CVA is a relevant problem for the present-day society as it is widespread and its incidence increases every year. According to the World Federation of Neurological Societies, about 15 mln. CVA cases are annually registered in the world. In the Russian Federation (RF), CVA incidence amounts to 3.4 per 1,000 persons a year, with about 30% CVA resulting in lethal outcomes in the acute period [3, 4]. 10-15% more patients die in the subsequent year [5].

Currently there are about 62 mln. persons that suffered a brain stroke, with only 10-20% of patients returning to work, 60% experiencing stable neurological dysfunctions, and 30% requiring physical assistance. About 70% of patients have major cognitive defects after the acute phase of the stroke [6,7-11]. It should be noted that CVA is one of the main causes for population incapacitation. Widespread disability of patients that suffered a stroke is contributed by a small share of patients urgently taken to hospital (no more than 15–30%). About 20% of those that suffered a stroke remain almost completely disabled until the end of their lives [12, 13, 14, 15].

A high incidence, death and incapacitation rate make this disease a considerable economic burden for the state and society, composed of expenses on treatment, medical rehabilitation, losses in production sphere, expenses on medical and social support of the disabled and their relatives.

At present, pharmacoeconomic studies which serve as a basis for defining the most economically efficient therapy are gaining more and more importance in RF. On the basis of the above, the aim of this work was to determine the most balanced medical technology in CVA treatment (comparison of routine clinical practices with the use of Cellex and without) in terms of pharmacoeconomic analysis based on the analysis of correlation between expenses and efficiency, safety of drugs, quality of life for the patients specified.

The following problems were consistently solved to achieve the goal set:

1. Collection and analysis of information on CVA therapy clinical practices in Cellex groups + routine clinical practices and routine clinical practices only.
2. Selection of efficiency criteria in CVA treatment.
3. Analysis of expenses on compared treatment schemes in CVA therapy.
4. Using the following methods as part of pharmacoeconomic study: cost-efficiency analysis and analysis of influence on the budget.

Effectiveness Analysis

The information search by publications that conform to the subject of this study covered PubMed database, Medlink, Cochrane, «Russian Medicine» of the Central Scientific Medical Library, I.M. Sechenov First Moscow State Medical University, elibrary.ru, free search resources, such as Yandex, Google, etc. The search request was formulated in such a way as to find publications with the following key words: acute ischemic stroke, clinical trial, neuroprotectants, Cellex, cerebrovascular accident, apoplexy, efficiency.

The information search revealed only one study which represented the results of double blind placebo-controlled randomized multi-center clinical trial of Cellex efficiency in treatment of ischemic type CVA patients. This clinical trial involved 480 patients diagnosed ischemic CVA (in carotid and vertebrobasilar systems) in accordance with ICD-10 criteria, taken to hospital within the first 48 hours from the moment of disease development. The main purpose of this study was to test the efficiency of Cellex: controlled assessment of Cellex application efficiency (by clinical indicators) in patients in early and acute rehabilitation period of the stroke; determination of Cellex influence on the dynamics and terms of CVA patients lost functions recovery at the background of routine clinical therapy in the acute ischemic stroke period as compared to placebo with routine clinical practices in the acute period of ischemic stroke [16, 17].

Cognitive disorders make a considerable negative contribution to incapacitation of patients after the stroke as they often define the severity of patient's condition and difficulties in the process of his/her personal and professional adaptation in absence of clear focal symptoms, the NIHSS-based degree of recovery was selected as one of the efficiency criteria. (NIHSS – evaluation of focal symptoms – disability, contribution of cognitive disorders – other MoCA and MMSE scales, information, concentration of attention).

According to the found trial, the degree of recovery under NIHSS on the 21st day using Cellex + routine clinical practices scheme makes up 84.6%, and with routine clinical practices only – 67% [17].

It should also be noted that a special form of cognitive disorders is aphasia, a violation of formed speech that arises in case of focal diseases of cortex and adjoining subcortical area of the dominant brain hemisphere, and which is a systemic disorder of different speech activity forms with preservation of elementary forms of hearing and movements of speech apparatus. Any form of cognitive disorders on the whole and speech in particular results in personality

changes, violation of general and verbal communication. The patient's behavior, emotional state and quality of life change. In connection with this, we selected the second efficiency criterion related to speech recovery. The found clinical trial determined the dynamics of average grade using the Speech Questionnaire test based on 21 days of treatment for a group of patients with pronounced speech disorders of 0-1 points on the first day of treatment. As a result, the analysis of average test values in patients with 0-1 points before treatment showed that the value of this indicator in patients taking Cellex reached 8.94 points on the 21st day, which practically means speech recovery, while this indicator corresponded to 3.25 points in the control group [16]. The Number-Needed-to-Treat (NNT) method was applied to use this effectiveness in this pharmacoeconomic study. This method proposes to measure the effect of the drug or therapy by evaluating the number of patients that should be cured to influence one person [18]. Consequently, we calculated the number of patients that need to be treated to achieve one case of speech recovery on the 21st day in the Cellex application group at the background of routine clinical practices and no-Cellex group, which amounted to 1.12 and 3.08, respectively.

Table 1. The results of analyzing the efficiency of Cellex + routine clinical practices and routine clinical practices schemes in treatment of patients with CVA

Effectiveness Criterion	Cellex + routine clinical practices	Routine clinical practices
Degree of recovery under NIHHS scale on the 21st day	84.6 %	67.0%
The number of patients required to be treated to achieve 1 case of speech recovery on the 21st day (in the group of patients with pronounced speech disorders)	1.12	3.08

Cost Analysis

In the course of this pharmacoeconomic study, the expenses on the treatment of one CVA patient were calculated. It should be noted that both direct and indirect expenses on CVA treatment were taken into account during the study.

An average cost of active ingredient unit for Cellex was calculated on the basis of analysis methodology used for expenses and data obtained in the course of analyzing the cost of stock keeping units. Further, we calculated the cost of Cellex course dose in accordance with basic prescribing information for CVA. The analysis of Cellex pharmacotherapy cost also took into account the cost of hypodermic injection.

At the next stage of the expenses analysis, the cost of CVA patients treatment was calculated, including assessment of expenses on diagnostics, treatment and drug therapy in accordance with:

- Order of the Ministry of Healthcare of Russia No. 1740n dated 29.12.2012 «On Approval of Specialized Medical Aid Standard for Cerebrovascular Accident» [19]
- Order of RF Ministry of Healthcare and Social Development No. 534 dated 22.08.2005 «On Measures to Improve Organization of Neurorehabilitation Aid to Patients with Consequences of Stroke and Brain Injury» [20]
- Order of RF Ministry of Healthcare and Social Development No. 236 dated 22.11.2004 «On Approval of Medical Aid Provision Standard to Patients with Stroke by Outpatient Institutions» [21]

At the first stage of indirect expenses assessment, the costs related to disability pension and monthly monetary payment were calculated. The amount of disability pension and monthly monetary payment depends on the disability group [22]. At the next stage, GDP losses due to disability of CVA patients were assessed on the basis of CVA incidence among the economically active population and average GDP per capita. The source of annual GDP value per capita was the information of RF State Statistics Service for 2015 [23]. Sick lists were calculated only for patients of working age, making up 34% from all CVA patients [24].

As the efficiency data was obtained on the 21st day, we calculated the expenses on one average CVA patient treatment for 21 days for cost-efficiency analysis. The final value of the expenses analysis included the cost of Cellex pharmacotherapy (only for Cellex + routine clinical practices therapy scheme) and the expenses on emergency and hospital care.

Table 2. Results of expenses analysis for treatment of one average CVA patient for 21 days

	Cellex + Routine clinical practices	Routine clinical practices
Cost of Cellex pharmacotherapy, rubles.	15,361	0
Emergency medical care, rubles.	2,149	2,149
Inpatient medical care, rubles.	62,589	62,589
Total, rubles:	80,099	64,738

Further on, the expenses on treatment of one average CVA patient a year were calculated, where both direct and indirect expenses were taken into account.

Table 3. Results of expenses analysis for treatment of one average CVA patient a year

	Cellex + Routine clinical practices	Routine clinical practices
Cost of Cellex pharmacotherapy, rubles.	30,722	0
Emergency medical care, rubles.	2,149	2,149
Inpatient medical care, rubles.	66,720	89,413
Early neurorehabilitation, rubles:	31,252	31,252
Outpatient care, rubles.	14,445	14,100
Cost of incapacitation, rubles.	54,442	57,506
Loss of GDP due to incapacitation, rubles:	9,025	20,220
Payments on sick lists, rubles:	7,227	8,655
Total	215,982	223,295

As we see from Table 3, the total expenses made up 215,982 rubles on one patient taking Cellex at the background of routine clinical practices and 223,295 rubles on one patient treated with routine clinical practices only.

Cost-Effectiveness Analysis

At the next stage of the study, we conducted the cost-efficiency analysis based on the treatment of one patient using the results of expenses analysis, as well as the data found in the course of efficiency analysis.

In the course of this study, the values of cost-efficiency ratios were determined for Cellex + routine clinical practices as compared to routine clinical practices only in CVA treatment. The obtained values of cost-efficiency ratios are presented in Table 4.

Table 4. The results of cost-efficiency analysis conducted for compared healthcare technologies.

Parameter	Cellex + Routine clinical practices	Routine clinical practices
Expenses, rubles:	80,099	64,738
Degree of recovery under NIHHS scale on the 21st day	84.6%	67.0%
CER recovery under NIHHS scale	94,680	96,624
The number of patients required to be treated to achieve 1 case of speech recovery on the 21st day (in the group of patients with pronounced speech disorders)	1.12	3.08
CER speech recovery	89,711	199,394



As we see from the above results, when we use the degree of recovery under NIHSS scale as the efficiency parameter, the value of the cost-efficiency ratio is the lowest for Cellex + routine clinical practices treatment scheme, which means that this therapy requires less expenses on efficiency unit achievement as compared to routine clinical practices.

If the degree of speech recovery is used as an efficiency criterion (in the group of patients with pronounced speech disorders), the lowest value of the cost-efficiency ratio is shown by Cellex + routine clinical practices scheme. Consequently, this therapy will require the lowest expenses on one case of speech recovery on the 21st day after the disease develops.

Thus, the application of Cellex at the background of routine clinical practices is characterized by lower values of the cost-efficiency ratio as compared to the routine clinical practices alone, and so is a dominant technology from the position of the cost-effectiveness analysis.

Budget impact analysis

The budget impact analysis conducted at the final stage of the pharmacoeconomic analysis, reflects the influence of the studied therapy on the healthcare budget. In other words, this analysis makes it possible to predict the influence on the healthcare budget and determine the economic effect expressed in the economy of funds or additional expenses required for transition from comparison therapy to the evaluated therapy. Complete analysis requires taking into account all kinds of expenses. As a result, we may express the budget impact using the formula

$$BIA = Efec(1) - Efec(2),$$

where BIA is the result of budget impact in monetary terms;

Efec(1) is the total economic effect from the application of the medical comparison technology in monetary terms;

Efec(2) is the total economic effect from the application of the studied medical technology in monetary terms.

It was calculated on the basis of expenses analysis that the transfer of one patient from routine clinical practices to Cellex treatment at the background of routine clinical practices will reduce the expenses by 7 313 rubles a year.

Conclusions

The following was established in the course of pharmacoeconomic analysis of CVA patients treatment:

1. total expenses on one patient a year with application of routine clinical practices amounted to 223 295 rub., while treatment with Cellex at the background of routine clinical practices cost 215 982 rub.

2. the application of Cellex at the background of routine clinical practices as compared to the routine clinical practices alone is a dominant technology from the position of cost-efficiency analysis.

3. if one CVA patient a year is transferred from routine clinical practices to Cellex accompanied with the same, the expenses will be reduced by 7313 rubles.

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