The Pharmacoeconomic Analysis of the Treatment Regimens of Patients Having Cardiovascular Diseases with Drugs of the Antithrombotic Action


Department of Organization and Economic of Pharmacy, National University of Pharmacy, Kharkiv, Ukraine

Abstract

Aim: The aim of our study is to conduct the pharmacoeconomic analysis of the treatment regimens of patients having cardiovascular diseases (CVDs) with antithrombotic drugs, namely clopidogrel and acetylsalicylic acid, in Ukraine. Materials and Methods: The results of a randomized, blind Clopidogrel versus Aspirin in Patients at Risk of Ischemic Event study (clopidogrel, n = 9599 and acetylsalicylic acid, n = 9588) and materials of unified clinical protocols in the specialty “Cardiology” and data of the “Available medicines” reimbursement program in Ukraine were used in the work. Results and Discussion: Based on available clinical studies of the effectiveness of using drugs with the antithrombotic action in patients with CVD, the direct and indirect costs for further analysis of the total cost of the disease were calculated. It was found that the direct cost of the treatment with clopidogrel was 2.16 times higher than the cost of the treatment with acetylsalicylic acid. The total cost of the treatment of one patient with clopidogrel was 20.35% higher than with acetylsalicylic acid. The analysis by the “cost-effectiveness” method showed that the cost-effectiveness ratio (CER) for acetylsalicylic acid was 13837.33 UAH/529.76 USD and for clopidogrel was 17366.66 UAH/664.88 USD. The cost of an incremental CER additional unit per one saved life when treating with clopidogrel is 5788.71 UAH/221.62 USD. Conclusion: Summing up the results of the study conducted, it has been found that the therapy with clopidogrel is more expensive; however, this drug is included in the reimbursement program in Ukraine, and therefore, the state partially compensates the patient for the expenses of it. Despite the fact that the therapy with acetylsalicylic acid should be carried out on a permanent basis in patients with CVD, it is necessary to include it in the “Available medicines” reimbursement program. The inclusion of drugs with acetylsalicylic acid in the list of reimbursed drugs will improve the health of patients with CVD and will help to save public funds that may be lost due to disability of the patient.

Key words: Cardiovascular diseases, pharmacoeconomic analysis, the “Available medicines” reimbursement program

INTRODUCTION

Cardiovascular diseases (CVDs) occupy a leading place in the world among other nosologies in the number of deaths of the working-age population [Table 1].

Thus, in the structure of the main causes of mortality of the population on the CVD in aggregate make up 48.28%, for the comparison of HIV / AIDS, cancer trachea and lower respiratory tract infections totaled 24.87%, which is 23.41% lower than that of the CVD. Each year, more than 18.5 million people die in the CVD from around the world. In Europe, approximately 3 million people die each year from CVD, and in the USA, more than 1 million people die; moreover, more than half of the deaths are persons under 65 years of age.

According to the Ministry of Health of Ukraine, annually more than two million people diagnosed with CVD are registered for the first time with a family physician; of them, every

Address for correspondence:
A. S. Nemchenko, Department of Organization and Economic of Pharmacy, National University of Pharmacy, Kharkiv, Ukraine.
E-mail: asnemchenko@ukr.net

Received: 21-11-2018
Revised: 09-05-2019
Accepted: 16-05-2019
second person is of working age. Therefore, the “Available medicines” reimbursement program was introduced in Ukraine; its goal is to provide all segments of the population with the necessary qualitative and effective drugs for the treatment of nosologies such as CVD, bronchial asthma, and type II diabetes.\(^2\) The pharmacotherapy of CVD is rather expensive and prolonged due to the peculiarity of the disease course and the presence of concomitant nosologies in the patient. The data of unified clinical protocols in the specialty “Cardiology” indicate that the treatment with antithrombotic drugs is necessary throughout the life of patients with chronic conditions of CVD; they are also used for prevention in the early stages of the disease.\(^3\)

Therefore, the aim of our study is to conduct pharmacoeconomic analysis of the use of drugs with the antithrombotic action, namely clopidogrel and acetylsalicylic acid, which are used in the treatment of CVD. To achieve the goal, the following tasks were outlined: To search for the data of scientific literature on clinical studies concerning the use of drugs with the antiplatelet action and to perform the analysis by the pharmacoeconomic methods selected.

**MATERIALS AND METHODS**

For further research, the method of the pharmacoeconomic analysis for the treatment of patients with CVD was developed [Figure 1].

The second stage of the pharmacoeconomic analysis included the search for the results of clinical trials in specialized scientific databases (Cochrane, PubMed, and MEDLINE) on the safety and efficacy of the antiplatelet therapy in patients with CVD.

Thus, the following studies were analyzed: Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE), CURE-percutaneous coronary intervention, Clopidogrel for the Reduction of Events during Observation trial, Clopidogrel as Adjunctive Reperfusion Therapy, and Clopidogrel and Aspirin versus Aspirin Alone for the Prevention of Atherothrombotic Events; however, a randomized, blind Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events study (CAPRIEs) was selected for calculations. In this study, they compared monotherapy with clopidogrel and acetylsalicylic acid in patients at risk for ischemic manifestations [Figure 2].

Taking into account the data of the CAPRIE study, the average duration of therapy – 1.9 years – was taken for further calculations. The number of patients participated in the study was 19185; of them, 9599 patients took clopidogrel and 9588 patients received acetylsalicylic acid.\(^4\)-\(^10\)

The third stage included the choice of methods of pharmacoeconomic analysis, first of all, the mandatory “total cost of the disease,” taking into account direct and indirect costs, separately for each of the drugs, as well as the calculation by the methods of “cost minimization” (CMA indicator) and “cost-effectiveness” (the cost-effectiveness ratio [CER] and incremental CER [ICER]).

Thus, the following studies were analyzed: Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE), CURE-percutaneous coronary intervention, Clopidogrel for the Reduction of Events during Observation trial, Clopidogrel as Adjunctive Reperfusion Therapy, and Clopidogrel and Aspirin versus Aspirin Alone for the Prevention of Atherothrombotic Events; however, a randomized, blind Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events study (CAPRIEs) was selected for calculations. In this study, they compared monotherapy with clopidogrel and acetylsalicylic acid in patients at risk for ischemic manifestations [Figure 2].

Taking into account the data of the CAPRIE study, the average duration of therapy – 1.9 years – was taken for further calculations. The number of patients participated in the study was 19185; of them, 9599 patients took clopidogrel and 9588 patients received acetylsalicylic acid.\(^4\)-\(^10\)

The third stage included the choice of methods of pharmacoeconomic analysis, first of all, the mandatory “total cost of the disease,” taking into account direct and indirect costs, separately for each of the drugs, as well as the calculation by the methods of “cost minimization” (CMA indicator) and “cost-effectiveness” (the cost-effectiveness ratio [CER] and incremental CER [ICER]).

**Table 1: The main causes of mortality in the world***

<table>
<thead>
<tr>
<th>The causes of mortality</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td>23.47</td>
</tr>
<tr>
<td>Cerebral accident and other diseases associated with cerebral circulation disorders</td>
<td>21.57</td>
</tr>
<tr>
<td>Infections of the lower respiratory tract</td>
<td>13.26</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9.58</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>6.41</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>6.85</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>6.47</td>
</tr>
<tr>
<td>Cancer of the trachea, bronchi, and lungs</td>
<td>5.14</td>
</tr>
<tr>
<td>Hypertensive disease</td>
<td>3.24</td>
</tr>
<tr>
<td>Road traffic accidents</td>
<td>4.03</td>
</tr>
<tr>
<td>In total</td>
<td>100</td>
</tr>
</tbody>
</table>

*The data are given at the beginning of 2018

**Figure 1: The method of the pharmacoeconomic analysis for the treatment of patients with cardiovascular diseases**
At the last fourth stage, the general conclusions on the results of the study were highlighted, and recommendations on the pharmacoeconomic analysis conducted were given.

RESULTS

We calculated direct costs – the cost of treatment regimens during the hospital stay and indirect costs – the costs arising from the inability of the patient to be useful to the society [Table 2]. The cost of treatment regimens was calculated using the materials of the Register of Wholesale and Retail Prices for Drugs as of 04.05.2018, and their recalculation was done in dollar equivalent at the official exchange rate of the National Bank of Ukraine (1 USD = 26.12 UAH, as of June 01, 2018).[11,12] According to the data of unified clinical protocols and guidelines, it was found that the average length of patients’ staying in the hospital was 28 bed days, and the average cost was 105.28 USD.[13] For the calculations, the data of the State Statistics Committee of Ukraine, namely the average salary as of May 01, 2018, and the nominal Gross Domestic Product (GDP) for 2017, were taken.[14]

According to the calculations, it was found that the direct cost of the treatment of one patient with clopidogrel was 2.16 times higher than the cost of the treatment with acetylsalicylic acid.

<table>
<thead>
<tr>
<th>Table 2: The total cost of cardiovascular diseases treatment regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>International non-proprietary name</strong></td>
</tr>
<tr>
<td>Dosage regimens</td>
</tr>
<tr>
<td>The wholesale and retail price of drugs, UAH</td>
</tr>
<tr>
<td>The cost of a daily dose, UAH</td>
</tr>
<tr>
<td>The total cost of the treatment of a patient for 1.9 years, UAH/USD</td>
</tr>
<tr>
<td>Direct costs</td>
</tr>
<tr>
<td>The cost of therapy regimens+the cost of bed days per one patient, UAH/USD</td>
</tr>
<tr>
<td>Indirect costs</td>
</tr>
<tr>
<td>Expenses for payment of incapability days+loss of GDP due to disability per one patient, UAH/USD</td>
</tr>
<tr>
<td>Total costs per one patient, UAH/USD</td>
</tr>
</tbody>
</table>

*US dollar exchange rate as of 01.06.2018. GDP: Gross domestic product

Figure 2: Characteristics of the results of Clopidogrel versus Aspirin in Patients at Risk of Ischemic Event clinical trial

CAPRIE

• (Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events).
• The number of patients – 19185; the average duration of the study – 1.9 years.

Adverse reactions when taking the regimen with Clopidogrel:
• - rash – 6.0%;
• - diarrhea – 4.5%;
• - liver abnormality – 3.0%;
• - intracranial bleeding – 0.35%;
• - any bleedings – 9.3%.
• The number of lives saved: when taking the regimen with Clopidogrel – 943 per 1000 patients

Adverse reactions when taking the regimen with Acetylsalicylic acid:
• - rash – 4.6%;
• - diarrhea – 0.23%;
• - liver abnormality – 3.2%;
• - intracranial bleeding – 0.49%;
• - any bleedings – 1.4%.
• The number of lives saved: when taking the regimen with Acetylsalicylic acid – 940 per 1000 patients
The total amount for pharmacotherapy with clopidogrel is 16411.71 UAH/628.32 USD and with acetylsalicylic acid is 13007.23 UAH/497.98 USD. Thus, if the cost-effectiveness indicator CMA (by the method of “cost minimization”) is calculated, the treatment with acetylsalicylic acid is less expensive by 3404.48 UAH/130.34 USD (by 26.0%) than with clopidogrel.

Next, the “cost-effectiveness” analysis (CEA) requiring the calculation of CER and ICER was conducted [Table 3].

It should be noted that when receiving the regimen with clopidogrel, the number of additionally saved lives is 3.

Thus, it has been found that CER for acetylsalicylic acid is 13837.33 UAH/529.76 USD, and for the drug clopidogrel, it is 17366.66 UAH/664.88 USD, i.e., 25.5% higher. The cost of an ICER additional unit per one saved life when treating with clopidogrel is 5788.71 UAH/221.2 USD.[15]

### Table 3: The results of the pharmacoeconomic analysis of therapy with clopidogrel and acetylsalicylic acid by the method of “cost-effectiveness”

<table>
<thead>
<tr>
<th>The name of the drug</th>
<th>Clopidogrel</th>
<th>Acetylsalicylic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs per 1000 patients, UAH/USD</td>
<td>16411718.4/628320*</td>
<td>13007237.6/497980*</td>
</tr>
<tr>
<td>The number of lives saved per 1000 patients, (Ef)</td>
<td>943</td>
<td>940</td>
</tr>
<tr>
<td>The CER USD per one saved life, UAH/USD</td>
<td>17366.66/664.88*</td>
<td>13837.33/529.76*</td>
</tr>
</tbody>
</table>

*US dollar exchange rate as of 01.06.2018. GDP: Gross domestic product, CER: Cost-effectiveness ratio

REFERENCES


Source of Support: Nil. Conflict of Interest: None declared.