



## Cost Components of Treatment Protocols of Haemophilia Patients with Inhibitors Using Bypassing Agents in Iran

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### Abstract

Bypassing agents are the most commonly used medicines for the treatment of hemophilia patients with inhibitors. The aim of this study is to identify the cost components of management of bleeding vents in hemophilia patients with inhibitors in Iran. This study is a cross-sectional study using a bottom-up approach to determine the cost components of treatment of hemophilia patients with inhibitors via ascertaining of all direct medical and non-medical costs. The evaluation of cost components of 20 patients with 40 episodes of bleeding showed that the price of medicines used is responsible for more than 96% and 97% of costs in treatment of hemophilia patients using FEIBA<sup>®</sup> and AryoSeven, respectively. The results of this study showed that cost of treating one bleeding episode in hemophilia A patients with high antibody titer using FEIBA is 376 USD compared to 857.3 USD for AryoSeven<sup>®</sup>. Despite the small number of hemophilia patients with inhibitor in Iran, due to high cost of treating these patients, it is very important to choose the cost-effective treatment protocol for the treatment of these patients.

**Keywords:** bypassing agents, cost components, hemophilia, inhibitor.

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## 1. Introduction

Treatment of hemophilia patients with inhibitor is mostly based on using bypassing agents. These medicines are very expensive and usually impose substantial burden on the patients and health care systems. Treatment of hemophiliacs in Iran is free of charge for patients and Iran health system covers most parts of their treatment, including both clotting factors and bypassing medicines [1-3]. Currently, the protocol of treatment of the hemophilia patients with inhibitors against factor VIII is based on using either APCC (activated prothrombin complex concentrates) or rFVIIa (recombinant activated factor VII). Although recently an Iranian pharmaceutical company marketed a Biogeneric version of rFVIIa, AryoSeven® in Iran, APCC is imported under the trade name of FEIBA®. Clinical efficacy and safety of AryoSeven® have been shown to be comparable with Novoseven® for the management of hemophilia patients with inhibitors in Iran [4-5]. In order to develop a treatment protocol for management of hemophilia patients with inhibitor, considering the limited resources available in the health care system, cost analysis of available treatment options is very important [6]. Due to high costs of these medicines in Iran

this study has been designed to compare the cost components of these medicines from Iran health sector perspective. The aim of this study was to ascertain the cost of components of caring for Iranian patients with hemophilia A with high titers of inhibitors who are treated with bypassing agents including AryoSeven® and FEIBA®.

## 2. Materials and Methods

This study is a Cross-Sectional study for analyzing cost components of treatment for hemophilia patients with inhibitors. Due to the high share of costs of bypassing agents in the treatment of these patients, in this study only the direct medical and non-medical costs were analyzed. Therefore, indirect costs, including productivity lost were not considered. For an analysis of the costs, bottom-up techniques have been used [7]. By using from the bottom-up approach the sub-population who are exposed to the actual disease selected, and all costs associated with the disease ascertained. Same number of events which were treated successfully with each of the mentioned bypassing agents - AryoSeven (protocol A) and FEIBA (protocol F) - have been studied in eligible patients. This study was carried out using a validated questionnaire which contains 35 items over a period of 3 years with a bottom-up approach. The reliability of questionnaire was confirmed by the CVI and CVR (Cronbach's alpha = 0.85). The questionnaire included direct medical and non-medical costs. Direct medical

expenses including physician visits, diagnostic care (imaging, ultrasound, CT scans, MRI, bone scan, blood tests,...) and direct non-medical costs including travel costs, adaptation cost, including costs related to the adapting to the environment of home and workplace and nursing care costs have been calculated. The clinical study received approval by an ethical committee of the Shahid Beheshti University of Medical Sciences and all patients signed an informed consent form for entering the study.

### *2.1. Study Population*

The study population consists of the eligible hemophilia A patients with high inhibitor titer (greater than or equal to 5 Bethesda Unit) in four hemophilia comprehensive care centers who are treated using bypassing agents based on on-demand treatment protocol. Following initial assessment of patients for inclusion and exclusion criteria, a validated questionnaire was used for collecting demographic data as well as the medical and non-medical direct costs for patients.

### *2.2. Data Collection*

In addition to data collected by the questionnaire clinical data and medicines used were obtained from patients' clinical records. All cost components, including hospitalization costs, outpatient and drug costs have been included. The time required for management of each

bleeding event was considered as the study time horizon. All patients were followed for 24 hours, post admission following a bleeding event.

### *2.3. Calculating Direct Costs*

In this study direct medical costs were considered as all cost incurred by patients, such as costs of bypassing agents, outpatient costs and hospitalization costs. Therefore, all costs related to any other medications used, hospital costs, costs of diagnostic, and other costs from the health care system perspective were included. In recounting to the direct non-medical costs were weighed in the cost of nursing home care, adaptation (home and/or workplace) costs, and traveling costs. All costs converted to USD based on official exchange rate in 2014 (1 USD= 25,430 Iranian Rial). Drug prices were obtained from the Iran Food and Drug Administration (FDO). FDO is the official pricing body for setting medicines prices before entering the Iranian market.

## **3. Results and Discusiion**

After excluding patients who did not complete the study due to either lack of willingness to run or incomplete data records, cost data were calculated for 20 patients with 40 episodes of bleeding. Data are shown in Tables 1-3. Considering the cross- over nature of the study direct non-medical costs of two products are similar to each other.

**Table1.** Cost components of treatment of hemophilia patients with inhibitors in protocol A (USD).

Time Points during treatment course	Direct Medical Costs			Direct Non-medical Costs			
	Drugs Cost		Out-patient costs	Hospitalization costs	Nursing home care Cost	Adaptation Cost	Traveling Cost
	Bypassing agents drug costs	Other drugs					
1	1629	9	79	0	0	35	<b>45</b>
3	1511	0	39	0	0	0	<b>0</b>
6	4023	0	85	87	0	0	<b>0</b>
9	4048	0	86	0	2.5	0	<b>0</b>
12	3172	0	67	0	0	0	<b>0</b>
18	2143	0	45	0	0	0	<b>0</b>
24	0	0	42	0	0	0	<b>0</b>

**Table 2.** Cost components of treatment of hemophilia patients with inhibitors in protocol F(USD).

Cost Components Points during treatment course	Direct Medical Costs			Direct Non-medical Costs			
	Drugs Cost		Out-patient *costs	Hospitalization costs	**Nursing Home care Cost	***Adaptation Cost	Traveling Cost
	Bypassing agents drug costs	Other drugs					
1	3314	9	98	0	0	35	<b>45</b>
3	0	0	7	0	0	0	<b>0</b>
6	0	0	0	87	0	0	<b>0</b>
9	3820	0	62	0	2.5	0	<b>0</b>
12	0	0	0	0	0	0	<b>0</b>
18	0	0	0	0	0	0	<b>0</b>
24	0	0	42	0	0	0	<b>0</b>

\*Outpatient costs including imaging cost, ultrasound and CT scan cost, MRI, bone scan, blood tests costs and vein therapy cost.

\*\*Nursing home care cost including costs associated with home care and the cost of child care in home.

\*\*\*Adaptation cost including costs related to the adapting of the environment of home and workplace

The results of this study showed that the cost of bypassing medicines is the most important

component of the costs of managing bleeding events in hemophilia patients with inhibitors.

Table 3 shows that the price of medicines used is responsible for more than 96% and 97% of the costs of the treatment using FEIBA and

hemophilia A patients with high antibody titer using FEIBA is 376 USD compared to 857 USD for Aryoseven. A variety of factors,

**Table 3.** Average costs (USD) per patients (n=20) for hemophilia A with inhibitor.

<b>Bypassing agents drugs</b>	16,526	7,135
<b>Drugs: other</b>	9	9
<b>Out-patient costs</b>	443	209
<b>Hospitalization costs</b>	87	87
<b>Total direct medical costs</b>	17,065	7,440
<b>Total direct non-medical costs</b>	82.5	82.5
<b>Total costs</b>	17147.5	7515.5
<b>Average costs per bleeding episode</b>	857.3	376

Aryoseven respectively. Previously published results [1] also reported that the medicines costs play a crucial role and contributed to about 98 percent of direct costs [8]. Since the cost of treating hemophilia patients with inhibitor is already reported to be at least 1.3 higher than patients without inhibitors [9], Pharmacoeconomics analysis can be used for selecting cost effective therapeutic options for the management of hemophilia patients.

In Iran the costs of treatment of hemophilia patients are paid fully by Iran national health system. Despite the low number of hemophilia patients in general and particularly hemophilia patients with inhibitor against factor VIII in Iran, the burden of the management of these patients on national health system is significant. Therefore, it is very important to select a cost effective treatment protocol for these patients [10]. The results of this study showed that total costs of treating one bleeding episode in

including the patient's age, the severity of bleeding, inhibitor development, time management and first-line therapy's effectiveness have contributed to the treatment costs of hemophilia [11] and these issues should be considered in determining costs as has been reviewed elsewhere [12]. This primary result underlines the importance of comparative cost-effective prospective study design for two bypassing agents in Iran in the separate study.

#### 4. Conclusion

However, in order to find a cost effective treatment strategy, we need to also include efficacy of these two medicines and based on the comparative cost effectiveness ratio of these medicines draw a final conclusion for selecting the most cost effective treatment alternatives. Despite the small number of hemophilia patients with inhibitor in Iran, due to high cost of treating these patients, it is very

important to choose the cost-effective treatment

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protocol for the treatment of these patients.

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