Journal of Pharmaceutical Research International

31(6): 1-6, 2019; Article no.JPRI.53517
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Economic Analysis of an Ambulatory Care Service Delivery Model for Hemophilia a Patients; A Cost Minimization Study

Abolfazl Sadeghi[1], Majid Davari[1,2*], Zahra Gharibnaseri[3], Roya Ravanbod[4] and Peyman Eshghi[5]

[1]Department of Pharmacoeconomics and Pharmaceutical Administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
[2]Health Equity Research Centre, Tehran University of Medical Sciences, Tehran, Iran.
[3]National Institute for Health Research, Tehran University of Medical Sciences, Tehran, Iran.
[4]School of Medical Sciences, Tarbiat Modares University, Tehran, Iran.
[5]Department of Pediatrics, Shahid Beheshti University of Medical Sciences, Iran.

Authors' contributions

This work was carried out in collaboration among all authors. Author AS revised the study protocol, performed data collection and wrote the first draft of the manuscript. Author MD designed the study, managed the analyses of the study and revised the manuscript. Authors ZG, RR and PE managed the literature searches and confirmed the appropriateness of the delivery model for the patients. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2019/v31i630377
Editor(s):
(1) Dr. Jinyong Peng, College of Pharmacy, Dalian Medical University, Dalian, China.
Reviewers:
(1) Mario Schiavoni, Italy.
(2) Guenka Petrova , Medical University of Sofia , Bulgaria.
(3) Malina Jordanova, Space Research and Technology Institute and Bulgarian Academy of Sciences, Bulgaria.
Complete Peer review History: http://www.sdiarticle4.com/review-history/53517

Original Research Article

Received 24 October 2019
Accepted 27 December 2019
Published 10 January 2020

ABSTRACT

Aim: This study aimed to perform an economic evaluation of Hemophilia ambulatory service delivery model (HASDM) comparing to the traditional home-episodic treatment model.
Study Design: Tehran university of medical science, department pharmacoeconomics and pharmaceutical administration, between Jun 2016 and September 2018.
Methods: A cost-minimization analysis (CMA) was conducted for evaluating potential savings of HASDM in comparison to the traditional home-episodic treatment model. The main cost of regular episodic service delivery, basic arm, consists of the cost of recombinant factor VIII (FVIII). In the

**Corresponding author: E-mail: M-davari@tums.ac.ir;*

comparator arm, HASDM, the costs of HASDM for 1660 hemophilia A patients (HAPs) in Tehran were calculated. One-way sensitivity analysis was done to investigate the robustness of the results and to investigate the impact of uncertainty in the percentage of mistakes in bleeding sensation.

Results: There were 1660 patients with severe Hemophilia A (PWSHA) in Tehran in 2018. The mean utilization of annual per patient FVIII was 44814 international units (IUs) in Iran. The total annual cost of FVIII concentrate for 1660 hemophilic patients in Tehran was estimated at $ 11,001,816. The cost of running HASDM, personal, and equipment is equal to $ 580,956. The cost of FVIII in HASDM would be $ 4,004,661. Therefore, the total cost of HASDM is estimated at $ 4,585,617. The amount of savings was $ 6,416,199. Sensitivity analysis indicated the robustness of the results up to 94.64% of the variation in the model parameters.

Conclusions: HASDM, compared to episodic model, can save 58.32% of the funding for controlling bleeding in HAPs annually. This can save more than 38 times of HAPs annual cost over their lifetime.

Keywords: Hemophilia A; factor VIII; economic evaluation; cost-minimization analysis; efficiency.

1. INTRODUCTION

Hemophilia is a rare disease that causes bleeding as a result of deficiencies of coagulation factors. Hemophilia A (HA) and hemophilia B (HB) are the most common types of hemophilia, which are due to the low concentration of factor VIII and factor IX, respectively. HA is categorized in three levels according to coagulation factor activity, severe (<1%), moderate (1-5%), and mild (>5-30%)[1]. Hemophilia patients could have a good quality of life if they have access to adequate treatment; otherwise, they could suffer from joint destruction, disability or death [2].

Iran has the ninth-largest population of hemophilic patients in the world [3]. The prevalence rate of HA and HB in Iran is estimated as 14 and 2.5 in 100,000 males, respectively [4]. Eighty two percent of hemophilia (HA) patients in Iran are suffering from factor VIII (FVIII) deficiency, and 60 percent of them are severe [3]. HA is a high-cost disease as it is a lifetime, and FVIII is a high-cost medicine [5]. All of HA patients are being treated with recombinant FVIII in Tehran. The average annual health care cost for every patient was USD 15,130 in Iran in 2018, 67% of it referred to medication [6]. All factor concentrates (medications), diagnostic tests and other health care services of patients with hemophilia A (PWHA) in Iran are covered by the ministry of health and health insurance organizations so that all facilities are free for the patients [3].

Intra-articular bleeding is the most regular problem of HA [7]. Hemorrhage happens in 13% of muscle and 80% joints [8]. To manage muscle-skeletal bleeding in PWHA, two protocols are being used in PWHA; episodic (on-demand treatment) and prophylaxis. In episodic therapy, any bleeding episode could be managed by the patients in their home [9]. As in the other developing countries, episodic therapy is the most common therapeutic strategy to manage the joint bleeding episodes in Iran [3,10].The most part of the medical costs of PWHA is because of FVIII consumption [6]. Hence, governments should pay more attention to utilize their resources to improve hemophilia' treatment.

Episodic therapy is being managed based on the patients' perception [9]. It is showed that using FVIII based on patients' perception of bleeding can have a 63.6% error rate [11]. Indeed, they are taking FVIII mistakenly, as the sensation of pain in their joints could be a result of hemarthrosis [11]. This model of treatment can lead to a significant waste of economic resources. For solving this problem, we developed and introduced a Hemophilia Ambulatory Service Delivery Model (HASDM) for PWHA in Tehran, to manage the hemorrhagic conditions effectively [12]. Although we expect the health outcome of HASDM to be better than the episodic model in hemorrhage management, since we still do not have evidence for that, we assumed that its health outcomes are equal. Thus, the aim of this study was to perform a cost-minimization analysis of FVIII consumption of HASDM comparing to the traditional home-episodic treatment model (without implementing ultrasonography).

2. METHODS

A cost-minimization analysis (CMA) was conducted for evaluating potential savings of HASDM as a telehealth intervention in comparison to the traditional episodic home-treatment model. All costs were calculated from the perspective of the health care payer. The

prices were converted to US dollars based on the exchange rate of Iranian Rial to the US dollar in 2017 (one US dollar equals to 37,600 Iranian Rial). The cost data were collected from documented data in Iran food and drug administration (IFDA), Central Bank of Iran (CBI), and experts' opinions, where there was no recorded data. The main cost of traditional episodic service delivery, primary arm, consists of the cost of FVIII for 1660 HAPs in Tehran. In the comparator arm, HASDM, all running costs of HASDM for 1660 HAPs in Tehran were calculated. For this purpose, we first calculated the types and numbers of required personnel and equipment in HASDM, and then the annual costs of running HASDM plus the cost of FVIII were calculated. The details of the HASDM are presented elsewhere [12]. We used the following formula to calculate the cost savings due to the use of the HASDM model:

$\Delta C = C1 - C2$

Where ΔC is the total saving cost, C1 is the cost of the traditional episodic service delivery model, and C2 is the total cost of HASDM. The total annual cost of FVIII resulting from traditional service care delivery model (C1) for the primary study, arms was calculated as follows:

C1= annual consumption of FVIII in Tehran * the price of FVIII

C2= Cost of HASDM + Cost of FVIII

A one-way sensitivity analysis was done to investigate the robustness of the results and to investigate the impact of uncertainty in the percentage of mistakes in bleeding sensation. This percentage was reduced to the extent which the delta cost becomes equal to zero. As the economic evaluation was done for one year, discounting was not applicable in this analysis.

3. RESULTS

According to the documented information in the Iranian Ministry of Health, there were 1660 hemophilic patients in Tehran in 2017. Based on the documented information in IFDA, the unit cost of FVIII was $ 0.15 and then the total annual cost of factor concentrate for 1660 HAPs in Tehran was estimated as follows:

1660 HAPs * Annual IU of FVIII per patient * Cost of one IU of FVIII = $ 11,001,816

In the HASDM arm, all of the 1660 HAPs are benefited from the new ambulatory service. The costs of human resources and equipment were calculated to measure the C_{HASDM} (Table 1).

15% of fixed costs= $ 27,207

Variable costs= $ 553,749

C_{HASDM} = 15% of Fixed Costs + Variable Costs = $ 580,956

The equipment does not need to change over the time. So, they were considered fixed costs and their depreciation rate was considered 15%. Indeed, the running cost of HASDM was waived for better comparison.

C_{F8} = Cost of FVIII according to HASDM: $ 4,004,661

C2: $C_{HASDM} + C_{F8}$ = $ 4,585,617

$\Delta C = C_1 - C_2$ = $ 6,416,199

The savings and related costs components of the CMA are shown in Table 2.

Sensitivity analysis: In a one-way sensitivity analysis, we continuously reduced the patients' error rate (63.6%), which has been considered as the main cause of cost-wasting, until the delta cost reached to zero.

The results of sensitivity analysis confirmed that the delta cost will be zero if the patients' error rate (63.6%) is reduced by 94.64%. This means if the patients' error reduced to 3.38%, the total cost of HASDM would be equal to the traditional model, but at any rate above 3.4, the new model will be cost-saving. Therefore, HASDM is very robust and reliable and is not sensitive to the rate of patients' error by 94.64%.

4. DISCUSSION

The objective of this study was to perform a cost-minimization analysis of HASDM comparing to the traditional service care delivery. Without performing ultrasonography at the point of care, it was previously shown that in the traditional home therapy, 63.6% of patients' bleedings sensation was incorrect [11]. Thus, the same percentage of the medication (FVIII) was used incorrectly. Besides, hemophilia need continuous high-cost treatment [5]. The studies' results show the importance of HAPs' economic burden. Duncan et al. and Valentino et al. illustrated that the

coagulation factors usage has been increased in some countries like Korea [13,14]. The prescription compliance for the coagulation factor (CF) was reported at 80%, which might trigger in financial waste if CF was used incorrectly [15]. The mean per-patient annual direct cost of severe hemophilia was estimated at € 173,102, € 313,068, € 210,025, € 132,329, and € 116,963 for France, Germany, Italy, Spain, and the UK, respectively [16]. These are approximately 48, 79, 87, 65, and 34 times higher than the mean per-capita health expenditure in these countries [16]. Any new idea like HASDM could be useful for them to utilize their limited resources efficiently.

A practical and innovative HASDM was proposed for hemophilia A patient in Tehran in 2018 [12] to manage the wasteful medication and prevent losing economic resources. As the Iranian government, like many other developing countries, has economic limitation for implementing prophylaxis protocol, the on-demand protocol was considered for designing HASDM. The actual difference between HASDM and traditional home-episodic treatment is that in HASDM, the HAPs take medicine after implementing ultrasonography. Indeed, they do not use FVIII before effective diagnosis. However, in the traditional model they take FVIII just according to their sensation without correct evaluation of their aura in their joints. HASDM is a home care model with five care centers in Tehran. In this model, the patients after bleeding sensation do not inject the FVIII immediately. Instead, they call one of the five centers to receive an accurate examination. After the arrival of a trained-care-giver to the patients' location and implementing the ultrasonography, he or she will send the result of ultrasonography online to the radiologists which are based in Care centers. The radiologists will diagnose and order medication if it would be the real bleeding. HASDM is designed so that the HAPs take their required medication/s in less than one hour. The details of this model including the type and number of human resources and equipment, the duration of one service according to treatment guidelines, location of the centers in the city, are presented elsewhere [12].

Although HASDM is designed for HAPs in Tehran, but based on the number of patients, geographical distribution and facilities available, it can be adapted and used in other cities and countries; particularly in those in which episodic therapy is being used for controlling hemorrhage in HAPs.

Table 1. The types and distribution of the HASDM costs

Cost type	Number needed	Cost type	Average total Price ($)	Data source
Injection kit	30	Fixed	731	IFDA*
Electronic devices (Mobile or tablet)	15	Fixed	11,968	DOSW**
Portable ultrasonography device	30	Fixed	98,404	IFDA
Transportation vehicle **(**Motorcycle**)**	30	Fixed	51,196	DOSW
Location of deployment	5	Fixed	13,296	IMH***
Required equipment (Refrigerator)	5	Fixed	1,462	DOSW
Bed for staff	25	Fixed	4,321	DOSW
Total fixed costs	-	-	181,378	-
Annual depreciation of the fixed costs **(**15%**)**			27,207	-
Staff wages of courier of care	25	Variable	344,441	TUMS**** financial office
Specialist online visits	69720	Variable	209,308	IMH
Total Variable costs			553,749	
HASDM annual cost			580,956	
Total HASDM annual cost			4,585,617	

**Iranian Food & Drug administration*
*** Digikala Online shopping website*
**** Iranian ministry of health*
*****Tehran University of medical science*

Table 2. The savings and related costs components of CMA

Type of service delivery	Total cost ($)	Cost/patient ($)	Cost saving/ patient ($)	Total saving ($)	Percentage saving
Episodic	11,001,816	6,627.60	-	-	-
HASDM	4,585,617	2,762.42	3,865.18	6,416,199	58.32

In HASDM, ultrasonography was considered to distinguish the correct bleeding as a reliable method [13]. Although we supposed that the goal and outcomes of both models, HASDM and episodic, are similar in managing muscle-skeletal bleeding [9], but we expect better health outcomes in HASDM because of more patients' satisfaction and fewer complications of FVIII. Nonetheless, as we have not documented evidence yet to prove this expectation, we assumed that both models have the same effects and did a CMA. Likewise, as the main impact of HASDM is on the utilization of FVIII, we assumed that the costs of diagnostic and laboratory services are the same in both models.

Other cost savings, such as a reduction in the rate of inhibitory patients, preventing drug smuggling, and direct non-medical costs, were also not considered in our analysis. This means that, if they were considered, they would have significantly increased the amount of cost-saving. Nevertheless, it is illustrated that HASDM could improve the efficiency of treatment of bleeding episodes significantly.

As the health expenditure are increasing in all countries, there is increasing pressure on health care managers to improve efficiency and quality of health care delivery. Our study shows that the episodic model of health care delivery for managing hemorrhage is not an efficient manner. One of the sources of inefficiency in this model is wrong sensation of bleeding in HAPs. This could be responsible for more than 63% of the wastage in this model (Table 2). The second source of inefficiency could be attributed to the rate of development of FVIII inhibitors in HAPs. Several studies have showed the relationship between the frequency of treating with FVIII and increasing the risk of development of FVIII inhibitors [17-20]. As the number of injection FVIII will decrease in HASDM, it is expected that HASDM can reduce both sources of inefficiency more than 60%.

The figures in Table 1 show that HASDM can run at 5.28% of the cost of the FVIII in episodic model. In fact, by 5.28% of expenses allocated to the hemophilic patients in Tehran, the annual costs can be reduced by 58.32% in each year. Considering the fact that hemophilia is a lifelong disorder (around 65 years in Iran), the total savings per patient would be about 38 times their annual cost.

Sensitivity analysis is showing the robustness of the outcomes by about 94.64%. The source of the HASDM could be supplied by the substitution of the traditional model. During evaluating the feasibility and reliability of the HASDM, it was shown, the high range of patients' compliance regarding this alternative, moreover, clinicians, and health politicians proved its feasibility.

The results of sensitivity analysis confirmed that HASDM is highly robust and reliable.

5. CONCLUSION

HASDM, compared to episodic model, can save 58.32% of the funding for controlling bleeding in HAPs annually. This can save more than 38 times of HAPs annual cost over their lifetime.

This health care delivery model can increase the efficiency of managing hemorrhage in HAPs through two mechanism; correct diagnosis of bleeding in HAPs and decreasing the rate of development of FVIII inhibitors in HAPs.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCE

1. Valleix S, et al. Skewed X-chromosome inactivation in monochorionic diamniotic twin sisters results in severe and mild hemophilia A. Blood. 2002;100(8):3034-3036.

2. Kang H-S, et al. Treatment and characteristics related to patients with hemophilia. Journal of Muscle and Joint Health. 2006;13(2):119-129.
3. Dorgalaleh A, Dadashizadeh G, Bamedi T. Hemophilia in Iran. Hematology. 2016; 21(5):300-310.
4. Mehdizadeh M, et al. Occurrence of haemophilia in Iran. 2009;15(1):348-351.
5. Unim B, et al. Haemophilia A: Pharmaco-economic review of prophylaxis treatment versus on-demand; 2015.
6. Gharibnaseri Z, et al. Health care resource utilization and cost of care for haemophilia A and B patients in Iran. 2016;54(1):122-126.
7. Radossi P, et al. Intra-articular rifamycin in haemophilic arthropathy. Haemophilia. 2003;9(1):60-63.
8. Oldenburg J. Blood coagulation and hemorrhagic diathesis. Pharm Unserer Zeit. 2006;35:20-28.
9. Rosendaal F. Definitions in hemophilia, recommendation of the scientific sub committee on factor VIII and factor IX of the scientific and standardization committee of the international society on thrombosis and haemostasis factor VII and factor IX subcommittee; 2001.
10. Meyers RD, et al. The social and economic impact of hemophilia--a survey of 70 cases in Vermont and New Hampshire. American Journal of Public Health. 1972;62(4):530-535.
11. Ceponis A. et al. Rapid musculoskeletal ultrasound for painful episodes in adult haemophilia patients. 2013;19(5):790-798.
12. Davari M. Sadeghi A. et al. An efficient and effective online ambulatory service model for hemophilia-A patients; an introduction to a novel service delivery model for developing countries; Under evaluation; 2018.
13. Duncan N, et al. A haemophilia disease management programme targeting cost and utilization of specialty pharma-ceuticals. Haemophilia. 2014;20(4):519-526.
14. Valentino L, et al. Healthcare resource utilization among haemophilia A patients in the United States. Haemophilia. 2012; 18(3):332-338.
15. Zappa S, et al. Treatment trends for haemophilia A and haemophilia B in the United States: Results from the 2010 practice patterns survey. Haemophilia. 2012;18(3):e140-e153.
16. O'Hara J, et al. The cost of severe haemophilia in Europe: The CHESS study. Orphanet Journal of Rare Diseases. 2017; 12(1):106.
17. Gouw S, van den Berg H, le Cessie S, et al. Treatment characteristics and the risk of inhibitor development: A multi-center cohort study among previously untreated patients with severe hemophilia A. J Thromb Haemost. 2007;5:1383–1390.
18. Gouw S, van der Bom J, Marijke van den Berg H. Treatment-related risk factors of inhibitor development in previously untreated patients with hemophilia A: The CANAL cohort study. Blood. 2007;109: 4648–4654.
19. Maclean P, Richards M, Williams et al. Treatment related factors and inhibitor development in children with severe haemophilia A. Haemophilia. 2011;17: 282–287.
20. Ragni M, Ojeifo O, Feng J, et al. Risk factors for inhibitor formation in haemo-philia: A prevalent case-control study. Haemophilia. 2009;15:1074–1082.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/53517