Journal of Pharmacoeconomics & Pharmaceutical Management
Journal Homepage: jppm.tums.ac.ir

Cost-Minimization of Availability of Fusidic Acid in the Treatment of Topical Infection in Iran

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Citation Seyedifar M, Khorasani E, Taheri F, Soleymani F. Cost-Minimization of Availability of Fusidic Acid in the Treatment of Topical Infection in Iran. Journal of Pharmacoeconomics and Pharmaceutical Management .2018; 4(1-2):10-18.

Running Title Cost-minimization analysis of fusidic acid

Article Type Original Article

Article info:

Received: 13.06.2017

Revised: 14.08.2017

Accepted: 05.10.2017

Keywords:

Fusidic acid, Topical infections, Antimicrobial resistance, Impetigo, Cost-effectiveness, Iran

ABSTRACT

Background: Since at the time of this study fusidic acid was not available in the pharmaceutical market of Iran, this study was designed to investigate the economic aspects of the availability of fusidic acid for the treatment of topical infection in Iran.

Methods: A decision tree model was used to compare circumstances, in which only mupirocin and fusidic acid were available. Medical and hospitalization costs were considered as direct medical costs. Budget impact analysis and sensitivity analysis were performed to examine the robustness of the base-case analysis.

Results: It was assumed that a 50/50 ratio exists between burn patients to other patients. The treatment cost of 1000 cohort hypothetical patients was estimated at $54766 when mupirocin was the only available treatment choice and $15951 when fusidic acid was available as well. In other words, overall, $39 per patient was saved when physicians could consider fusidic acid as another choice of treatment.

Conclusion: The availability of fusidic acid appears to be reasonable because it reduces the costs of skin infection treatment. It also improves antibiotic consumption appropriateness.

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1. Introduction

Skin and soft tissue infections account for about 14.2 million ambulatory care attendances in the United States in 2005. Also, in the United Kingdom in 2015, these complications account for 4.7 million prescriptions [1-3]. Skin infections vary in severity, ranging from superficial, mild, and self-limiting conditions to severe life-threatening infections of deep tissue [1].

Impetigo is a common type of cutaneous infection that is caused by opportunistic microorganisms, namely Staphylococcus aureus and Streptococcus pyogenes [3, 4]. These microorganisms also cause secondary infections in injuries and burns. Skin burns provide a suitable condition for microbial flora and make other bacteria grow. Therefore, it is not surprising that antibiotics are commonly prescribed in such conditions. However, like all other infectious diseases therapy, the unnecessary and excessive use of Antibiotics Cause Antimicrobial Resistance (AMR), which is a common problem in skin infections [3, 5-11].

Microorganisms with multiple resistances to antibiotics cause considerable problems in patients with skin burns, who are hospitalized in burn wards [12, 13]. Therefore, the development of a new therapeutic regimen and appropriate use of antibiotics, including topical antibiotics, should be considered to reduce AMR rate and its related costs [3, 14-16]. Studies show a 2-3 fold increase in mortality and hospitalization stay. Therefore, a considerable economic burden owing to AMR is reported [17-24].

Typically two topical antibiotics of mupirocin ointment and fusidic acid cream are used to treat topical infections [2, 3, 25]. Both are equally effective and slightly superior to oral erythromycin [1-3]. At the time of this study, mupirocin was the only available choice of physicians in Iran for the treatment of topical infections. As reported in burn wards in Iran, resistance to this medicine has developed with a prevalence of 2.7% to 40% because of over-prescription, over-the-counter dispense, and the irrational use of mupirocin in recent years [16, 26, 27].

In a study, resistance to mupirocin among burn ward personnel was as high as 60% [28]. Accordingly, since mupirocin is prone to AMR, it is prudent to consider alternatives such as fusidic acid cream [1-3]. Fusidic acid in ointment and cream forms have been used in other countries as an effective choice in the treatment of primary and secondary skin infections since 1965 [29]. In some countries, topical fusidic acid is recommended as the first-line treatment for impetigo and primary skin infections [29].

The current study was carried out when fusidic acid cream was not available in Iran. However, after submitting the study and owing to little evidence for fusidic acid resistance in Iran and other countries [24, 30-33], the health authorities were convinced to enter fusidic acid cream to the pharmaceutical market of Iran. It is currently accessible nationwide.

This study aims at investigating the economic impact of the availability of topical fusidic acid in the treatment of skin infections in Iran.

2. Methods

The current study utilized the secondary data of the published studies, interviewing specialists, and national statistics so that ethical approval is waived.

Study design and model

A decision tree model was used to compare the cost of different therapeutic strategies of skin infections in the hospitals of Iran (Figure 1). The common therapeutic regimen in Iran was based on interviewing specialists. The literature was reviewed for other treatment strategies. A total of 15 physicians, including infectious disease specialists and dermatologists, were purposefully selected and interviewed to develop the model. The relevant literature was also reviewed. Through searching PubMed, EMBASE, Scopus, and the Cochrane Library, relevant studies were retrieved, using specific keywords such as “Fucidin, topical infections, AMR, impetigo, cost-effectiveness, fusidic acid, and topical antibiotics”.

The study has been carried out from the payer’s perspective. The costs of treatment were calculated based on the official medicine price lists published by the Food and Drug Administration (FDA) of Iran. The average cost per hospital bed-day was extracted, using the approved price lists of the governmental and private sectors [34, 35]. Indirect costs were not included. The direct cost of fusidic acid and mupirocin treatment was calculated based on the rate of consumption and the price. The cost of mupirocin was extracted from the FDA price list. Fusidic acid was not available in the market of Iran and it had not been entered into the FDA price list at the time of this study. The price of fusidic acid was revealed by manufacturer representatives in

Iran. According to the clinical guidelines, the common doses of mupirocin and fusidic acid were similar. Both medicines are administered 3 times a day for 7 to 12 days [17, 19].

Method of the economic evaluation of the decision-making model

A total of 1000 hypothetical cohort patients were considered. The ratio of patients of burn ward to the patients of other wards was considered 1:1. Subsequently, the two following conditions were compared for 500 hypothetical cohort patients in burn wards and 500 hypothetical cohort patients hospitalized in the other wards:

A condition, in which mupirocin was available, while fusidic acid was not available. A condition, in which both mupirocin and fusidic acid were available. For the first condition in each of the mentioned wards, mupirocin was the only choice of prescription. The rate of failure was extracted from references and interviewing the specialists.

In the second condition, fusidic acid was assumed to be available in each of the mentioned wards. Based on our survey and specialists' interview, mupirocin was considered the first choice of prescription for 80% of the patients and fusidic acid was considered the first choice for 20% of hypothetical patients.

The probabilities and assumptions of the model were extracted and finalized, using the results of other stud-

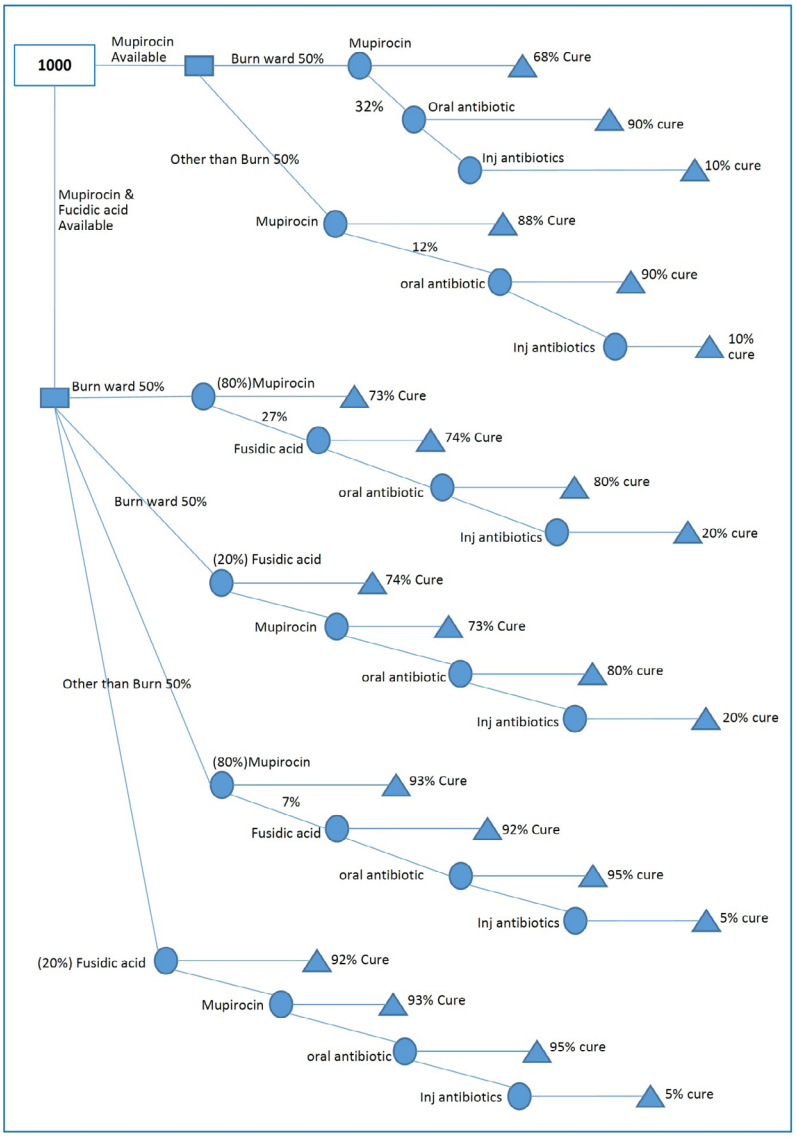

Figure 1. Decision tree structure

ies, interviewing specialist physicians, and referring to clinical guidelines.

Since resistance to each antibiotic occurs shortly after starting the treatment, in case that any resistance to mupirocin or fusidic acid was detected, half of the cost for a complete treatment would be considered because the second tube was not needed. All costs were converted to US dollar ($1=IRR42000, date of conversion: 2019-12-04) for international comparisons [36]. The duration of hospitalization for each case and the costs of systemic antibiotics were determined by guidelines and specialists' opinions.

Hospitalization costs were divided into two categories of general ward beds and skin burn wards. The hospital grade was also considered for the calculation. The current Iranian drug list was used to identify which antibiotics are currently on the market of Iran; subsequently, the average cost of pertinent oral and injectable antibiotics was calculated based on the FDA of Iran or distributor prices.

Model probabilities, assumptions, and inputs

Tables 1 and 2 present the estimated amounts of each condition, transition, and probability, as well as the reference.

Costs

Table 3 presents the costs for the study.

Sensitivity analysis and budget impact analysis

After running the model, a one-way sensitivity analysis was performed to assess the sensitivity of results to various parameters. The results were, then, assessed and calculated with the change in each of the following parameters: 1. Fusidic acid price; 2. The ratio of skin burn patients to other patients; 3. The increase in the positive response to mupirocin ointment when applied after topical fusidic acid

A budget impact analysis was performed. The number of mupirocin annually prescribed in Iran was obtained from the Research Center of Rational Use of Drugs. The number of patients was estimated by prescription number. Then, the model was run for 1 year with an estimated patient number. After all, the observed cost variation was used to predict the amount of fusidic acid consumption.

As a result, by comparing the costs in the two cases, the budget impact of adding fusidic acid to Iran Drug List was calculated through the model with an assumed ratio of 50% burn indications to other uses.

3. Results

Model results

Using the documented assumptions, the model was used for 1000 cohort hypothetical patients having an

Table 1. The state transition probabilities in the burn ward and other wards

Conditions	Transition	Probability (%)	Reference
Not including fusidic acid in the drug list (in burn ward)	Positive response to mupirocin	68	[27]
	Positive response to one oral antibiotic after resistance to mupirocin	90	Survey
Not including fusidic acid in the drug list (in other wards)	Positive response to mupirocin	88	[37]
	Positive response to one oral antibiotic after resistance to mupirocin	90	Survey
With fusidic acid availability (in burn ward)	Positive response to mupirocin	73	[24, 27, 31]
	Positive response to fusidic acid	74	[30]
	Positive response to one oral antibiotic after resistance to mupirocin and fusidic acid	80	Survey
With fusidic acid availability (in other wards)	Positive response to mupirocin	93	[24, 27, 31]
	Positive response to fusidic acid	92	
	Positive response to one oral antibiotic after resistant to mupirocin	95	Survey

Table 2. Assumptions and input data for the model

Subject	Amount	Reference
The proportion of the first-line antibiotic to the second-line choice	80%	Assumed
The change in microbial resistance to mupirocin after providing access to fusidic acid	5%	Assumed
The change in response to the systemic antibiotic in the non-burn ward	The change is considered 10%	Survey
Duration and dosage of treatment with mupirocin Duration and dosage of treatment with fusidic acid	Two 15 mg tubes for the positive response and 1 tube for the negative response	
Duration of treatment with an oral antibiotic (average of selected drugs)	7 days	
Duration of treatment with a parenteral antibiotic (average of selected drugs)	7 days	
Hospital stay for patients receiving oral treatment in the burn ward	1 day	Survey
Hospital stay for patients receiving oral treatment in other wards (non-burn)	0 day	Survey
Hospital stay in patients receiving parenteral antibiotic in the burn ward	7 days	Survey
Hospital stay in patients receiving parenteral antibiotic in other wards (non-burn)	5 days	Survey

indication for topical antibiotic treatment. The results were obtained assuming a 50/50 ratio for burn patients to other patients. The treatment cost of 1000 patients was estimated at $54766 with mupirocin only and $15951 with mupirocin while fusidic acid was accessible in the market as well. Since the efficacy of both topical ointments is equal, the lower cost in the fusidic acid arm means entering fusidic acid to the market of Iran is cost-saving.

Based on the results of the model, $39 was saved for each patient when fusidic acid, in addition to mupirocin, was available. The model was run for skin burn patients and other indications, as well. The costs in skin burn treatment were more than other indications, but in both groups, fusidic acid led to a reduction in treatment costs (Table 4).

Sensitivity analysis

Figure 2, in a tornado diagram, shows the results of costs in patients of each group and the difference after adding fusidic acid as a treatment option in various cases.

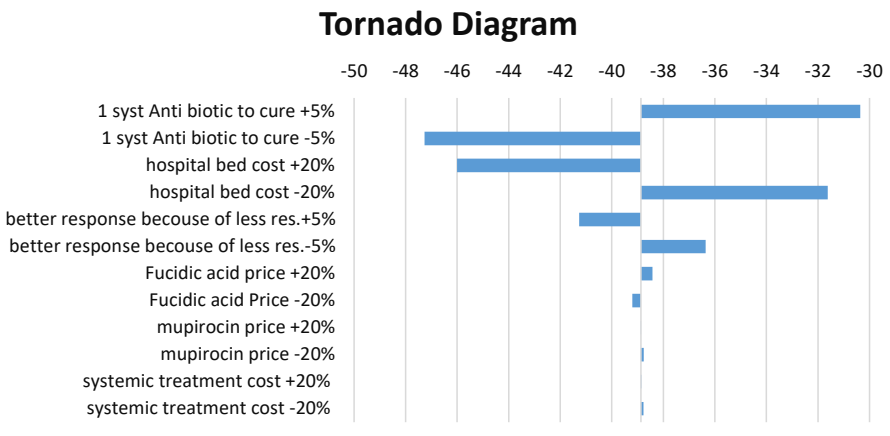

Figure 2. Tornado diagram comparing the differences after adding fusidic acid as a treatment option

Table 3. Costs of medicines and hospital bed/day

Items	Cost ($)	References
Cephalexin	0.42 (average cost)	FDA of Iran
Erythromycin		
Clindamycin		
Co-Amoxiclav		
Vancomycin (IV)	2.06 (average cost)	
Clindamycin (IV)		
Mupirocin topical	1.3	FDA of Iran
Fusidic acid topical	2.6	Company
Non-burn hospital bed/day cost	53	Average official fee according to the ministry of health (2017)
Burn hospital bed/day cost	176	

Table 4. The results of the model running in two arms for 1000 patients

Cases	Cost of Mupirocin Arm ($)	Cost of Mupirocin + Fusidic Acid Arm ($)	Cost Change Per Patient ($)
Base-case	54766	15951	-39
In-burn indication only	104808	27752	-77
With other indications only (impetigo)	4696	4150	-0.5

All costs are in US dollar.

Table 5. Budget impact results

The Changed Parameters	Number of Fusidic Acids Used in a Year	Changing in Health Budget (Million $)
Default (No change)	206000	-14
Need for hospitalization in 5% of patients resistant to topical antibiotic	206000	-11.5
Burn/other infections ratio: 75%	220000	-21
Burn/other infections ratio: 25%	192000	-7.5

The results are more sensitive to the probability of no oral antibiotic response. The least sensitivity is related to the price of fusidic acid.

Budget impact analysis

Since having fusidic acid as a treatment option, according to the model results, reduces treatment costs, it is expected that the total direct costs also go down. To calculate the budget impact, the data of mupirocin consumption were used to extract a prescription pattern and predict the extent of mupirocin prescriptions in Iran. Subsequently, using the ratio of mupirocin to fusidic acid, the utilization of fusidic acid and its budget impact for a year were calculated.

Considering fusidic acid as an available treatment option leads to the use of 206,000 tubes of fusidic acid annually in Iran, which will incur a direct acquisition cost of more than $680,000. However, since it prevents other costs and reduces overall expenditure, the direct costs reduced by $14 million in the first year. Because various circumstances are considered in the budget impact analysis, the assessment was carried out considering modified assumptions and budget analysis (Table 5).

4. Discussion

For the first time, this research evaluated the pharmacoeconomic aspects of making fusidic acid available in the treatment of skin and soft tissue infections. Prior to this study, one pharmacoeconomic study was conducted in 1993 [37] on fusidic acid, which has its own shortcomings in terms of structure and methodology.

Adding fusidic acid to the available treatment options appreciably reduces the treatment costs. Consequently, it is both economically and clinically reasonable for insurance companies and health authorities to support prescribing fusidic acid as the second-line treatment of skin infection. This approach will not only reduce the costs but also improves the care of patients needing topical antibiotics because fusidic acid is less likely to develop resistance in Iran. Having alternative therapies should also help reduce the current resistance rates to mupirocin.

Adding fusidic acid to the available treatment options reduces the costs in all circumstances, although the extent of saving in each case differs from one to another. Based on the budget impact results, considering fusidic acid as an additional available treatment option in different scenarios leads to an overall reduction of costs and saving of $7.5 to $21 million annually in direct costs. The cost-savings are generally associated with reduced hospitalization costs.

We have reduced the number of limitations in our study by undertaking a range of different scenarios. However, the robustness of any model will depend on the opinions of the specialists used in model development. Also, the costs of topical fusidic acid are based on company estimates. Despite these limitations, the findings of this study are robust and provide guidance to the authorities of Iran and other countries.

4. Conclusions

Overall, adding fusidic acid to the topical treatment options in Iran appears to be cost-saving by reducing the costs of other drugs and hospitalization. In addition, the availability of fusidic acid is clinically useful through reducing future resistance rates. Consequently, this medicine should be available among the options of treatment, especially in patients with skin infections.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article.

Funding

This study was funded by the Leo pharmaceutical company.

Authors contributions

Conceptualization, writing – original draft, writing – review & editing, resources: All author; Methodology, investigation: Meysam Seyedifar, Elahe Khorasani; Funding Acquisition: Fatemeh Soleymani; Supervision, Meysam Seyedifar, Fatemeh Soleymani.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

The authors would like to thank Dr. Mohraz, Loghman and Emam hospital that contributed in this study.

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