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ORIGINAL ARTICLE

The First Discrete Choice Experiment On Usage of Bypassing Agents in Hemophilic Patients in Iran

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ABSTRACT

Background: Bleeding events in hemophilic patients with inhibitors are managed by bypassing agents. Currently available agents in Iran are recombinant activated factor VII (rfVIIa; Aryogen, Aryoseven) and Feiba (factor eight inhibitor bypassing agent). No standardized and accurate assay is currently available for monitoring the effectiveness of bypassing agents. We suggested that history of the patients' response and also their preference could be a reliable method for assessing the efficacy of bypassing agents; therefore, we designed a multi-centric discrete choice experiment study to assess the factors that affect the efficacy of bypassing agents.

Methods: Hemophilic patients older than 2 years with inhibitors who required bypassing agents for the treatment of bleeding episodes were eligible to participate in the study. Patients' preference toward treatment with either Feiba or Aryoseven was measured with a DCE (discrete choice experiment) design on a phone interview.

Results: 80 patients were enrolled from 5 centers in Iran. At enrollment, the mean age was18.6 years (range, 2-50 years). 47 patients (58%) preferred to receive FEIBA, 21 patients (21.2%) favored Aryoseven and 12 (14.8%) patients claimed no difference between the two products.

Conclusion: Our results indicated that according to the DCE method, patients preferred Feiba to Aryoseven while the main reason was their higher efficacy. In addition, adverse reactions in both groups were almost equal. As a result, it seems that presence of both products in the market for hemophilic patients with inhibitors is absolutely essential.

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Introduction

Hemophilia A and B are X-linked disorders are the result of low levels or absence of the factor VIII (FVIII) and factor IX (FIX), respectively.[1] The mainstay of treatment in both hemophilia disorders is factor replacement therapy. As a result of replacement therapy, 20 to 35% of patients affected with hemophilia A and 6% of those with hemophilia B develop inhibitory antibodies.[2] Bleeding events in patients with inhibitors used to be treated by bypassing hemostatic agents during the lase decades.[1,3] Currently available bypassing agents in Iran are recombinant activated factor VII (rfVIIa;

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Aryogen Aryoseven) and Feiba VH (Baxter, Deerfield, IL). Clinical observation of the patients' response to bypassing agents is still a significant task for monitoring the effectiveness of bypassing agents as no standardized and accurate assay is currently available for it. It seems that past history of the patients' response and preference could be a reliable measurement for the effectiveness of the type of the treatment.[4,5]

The cost of managing bleeding episodes in patients with inhibitors is high and the expenses associated with bypassing therapy represents a significant liability to the patients. Considering patient's drug preference can lead to promising consequences in supplying the required products for providing better care for the hemophilic patients with lesser expenditures.[5] The focus on discrete-choice experiment (DCE) in medical research in recent years has heightened the awareness of the patient's perspective of health outcomes.[6] According to this approach we designed a multicentric DCE study to assess the factors that may be associated with hemophilic patients' preferences towards Aryoseven or Feiba.

Study Design

The main research question of this study was to assess hemophilic patients' preferences over the two available bypassing agents (Feiba or Aryoseven) in patients who have developed inhibitors.

Hemophilic patients older than 2 years with known inhibitors from Mofid children's hospital, "hemophilia comprehensive care center", Tehran and Imam Khomeini hospital of Tehran, Shiraz, Isfahan and Zahedan, who were in need to receive bypassing agents for the treatment of bleeding episodes were eligible to participate in this study. Patients' preferences towards treatment with either Feiba or Aryoseven was measured with a DCE (discrete choice experiment) design through a phone call interview. DCE is a quantitative method for illusttrating the individual preferences. It permits researchers to demonstrate how responders value the selected attributes of a program or a product by asking them to state their choice over different hypothetical alternatives (8).

It is noteworthy to mention that Aryoseven or Feiba have been prescribed in the customary manner in accordance with the terms of the marketing authorization. In order to prevent the bias in the mentioned study, assignment of the patients to a particular therapeutic strategy was made retrospectively and decision to prescribe these agents had been made at least 3 months prior to the enrollment in the study. The objective of this study was to reach the following answers in a cross-sectional survey. A) Which aspect of a medication upon patients' view was considered important and B) Are the hemophilic patients qualified to have a preference over Aryoseven or Feiba considering the objective results of their medication.

Results

80 patients were enrolled from 5 centers in Iran. At enrollment, the mean age was 18.6 years (range, 2-50) years. 47 patients (58%) preferred Feiba, 21 patients (27%) preferred Aryoseven and 12 (15%) patients disclosed no difference over the two products. In terms of efficacy, 18 out of 47 patients (38%) who preferred Feiba described it as excellent, 21(44%) as very good, 4 (1%) mentioned as good and 1 patient as average, respectively. Data from 3 patients was not available. On the other hand, among patients who favored Aryoseven as drug of choice, 5 patients (24%) described it as excellent, 11 (52%) as very good and 5 (24%) as average. Patients who were satisfied with Aryoseven, mentioned that their bleeding episodes were controlled with more than 3 doses of Aryoseven in 54.5%; whereas in group of patients who preferred Feiba, bleeding events were controlled with 3 doses of Feiba in 46.8% of the cases, respectively.

Features of the products which were considered by the patients to favor each drug is shown in figure 1.

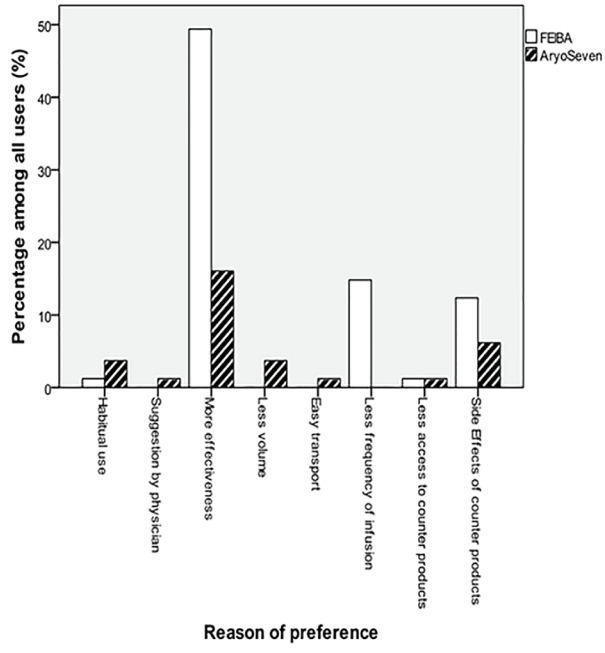

Figure 1: Features considered by the patients to assign the preference of bypassing agents in hemophilic patients with inhibitors.

59% of the patients had experienced total relief of their symptoms with 3 or more doses of Feiba, 10.6% with 2 doses and %25.5 with only one dose of it; on the other hand, in Aryoseven group 59% had relief with more than 3 doses, 36.4% with 2 and 4.5% with 1 dose of the drug. In patients who received Feiba, longer injection intervals (22.5%) and side effects (21.3%) were the main reason to prefer this product.

In Aryoseven group, side effects were reported in 22.7%, longer injection intervals in 13.6% and transportability of the drug in 4.5%, respectively.

Discussion

Interpreting the preferences of the patients by health professionals could be beneficial in the field of policy making and treatment planning.[6] A DCE is a quantitative technique for explaining the individual's preferences in different fields.[7] It allows researchers to unveil how individuals' priorities selected particular attributes of a program or a product by asking them to share their

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choices over different hypothetical alternatives. These include the elicitation of views on diagnosis, treatment and supportive care.[7,8] In a DCE point of view, respondents are asked to choose the most-preferred alternative from a set of hypothetical profiles, assuming that these are the only alternatives available.[8]

As a matter of fact, bypassing agents do not restore the normal pathway of hemostasis in hemophilia, hence the routine laboratory coagulation assays do not assess precisely the hemostatic activity of bypassing agents, and also no validated assay is available to measure their in vivo efficacy or predict individual's response to the treatment. As a result, the patient's preference methods could provide an alternative and clinical method for characterizing patients' needs or priorities. In a study from Iran, Golestani et. al reported similar effects in reducing joint bleeding episodes in comparison between the two bypassing agents.[9] Additionally, there were also other features which prompted the patients to make such preferences which included the rate of occurrence of side effects and interval of injections.

In developing countries, the idea of application of DCE to elicit the questions of health policy and treatment planning is relatively recent, but appears to be of growing interest and could be used as a resolving method unless there is more objective measures to determine the efficacy of some therapeutic options.[6]

Conclusion

To the best of our knowledge this study is the very first one based on DCE method which compares hemophilic patients' preference over the two available bypassing agent product (Aryoseven versus Feiba) for treatment of their bleeding episodes due to high titers of inhibitors. Our results indicated that according to the DCE method analysis, patients preferred Feiba to Aryoseven and the most significant reason was the more efficacy.

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Conflict of Interest: None declared.

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