Educational Interventions to Enhance Adherence to Prophylactic Treatment in Korean Hemophilia Patients

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Background: A patient’s adherence to prophylactic treatment is one of the most significant factors to achieve desired outcomes, in regards to the quality of life and treatment cost-effectiveness. The aim of this study is to evaluate the effectiveness of educational interventions in enhancing adherence to prophylactic treatment in Korean hemophilia patients.

Methods: The Validated Hemophilia Regimen Treatment Adherence Scale-Prophylaxis (VERITAS-Pro) was used to measure adherence. The study design consisted of two groups. One group was not educated with the education card which presented the morning administration of clotting factor concentrates and self-infusion skill. The other group was educated with the card. The scores of each subscale in the two groups and scores focused on the ‘Timing’ subscale were compared.

Results: Participants were recruited from five hemophilia treatment centers in Korea with 95 eligible patients forming the uneducated group and 123 patients in the educated group. The mean total score was 40.4 and 39.9, respectively. The subscale mean scores of the uneducated group and educated group were 8.43 and 7.90 (Timing), 6.12 and 5.88 (Dosing), 6.43 and 6.33 (Planning), 5.99 and 6.35 (Remembering), 6.22 and 6.25 (Skipping), and 7.23 and 7.24 (Communicating), respectively.

Conclusion: Results showed that education programs on prophylactic treatment for hemophilia patients need to be well-designed with precise and subject-appropriate contents. Although the mean total scores of VERITAS-Pro could not be improved, the appropriate timing of injection with the educational intervention was administered. Results suggest that this whole process can enhance Korean hemophilia patients’ adherence to prophylactic treatment.

Key Words: Adherence, Prophylaxis, Hemophilia, Education
Introduction

Currently, prophylactic treatment is considered as standard management for patients with severe hemophilia [1,2]. A patient’s adherence to prophylactic treatment is one of the most important factors to achieve good results of quality of life and cost-effectiveness [3-6]. In Korea, primary prophylaxis for children with severe hemophilia is strongly recommended treatment [7,8]. However, the difficulties of measuring adherence to treatment regimen were the other challenge to the hemophilia treaters. Duncan et al. [9] in 2010 introduced Validated Hemophilia Regimen Treatment Adherence Scale-Prophylaxis (VERITAS-Pro) as a new measure of adherence to prophylactic regimens in hemophilia patients. The aim of this study is to improve the adherence to prophylactic treatment in Korean hemophilia patients. To improve the adherence, the adherence levels and weaknesses of our patients needed to be known for the purposes of the first step. According to the results of the first step study, educational interventions were developed to enhance adherence and applied to patients’ education programs. Afterward, the effectiveness of educational interventions upon the educated group’s adherence to prophylactic treatment was evaluated.

Materials and Methods

1) Adherence measuring method

VERITAS-Pro questionnaire was developed and validated by the Indiana Hemophilia and Thrombosis Center (USA). It was provided to the Hemophilia Working Party of Korean Society of Hematology for use and translated into Korean during three times expert meetings of the Korean Hemophilia Working Party.

VERITAS-Pro contains the 6 subscales of timing, dosing, planning, remembering, skipping and communicating, to evaluate adherence to treatment. Each subscale has 4 items with each item quantified on a 5-point scale ranging from ‘always’ to ‘never’. Total scores can range from 24 to 120, with higher scores indicating poorer adherence [6].

2) Patients in 2 steps measurements

Between October 2015 and December 2015, the patients who underwent prophylactic treatment and treated in the 5 hemophilia treatment centers of Seoul Clinic of Korean Hemophilia Foundation, Daegu Catholic University Hospital, Kyungpook National University Hospital, Ulsan...
University Hospital, and Inha University Hospital, participated in the first step study. This was performed with VERITAS-Pro questionnaires.

Between June 2016 and July 2017, the educational interventions of the hemophilia treatment centers’ education programs for patients developed according to the results of the first step study were applied (Fig. 1).

Between June 2017 and November 2017, the same questionnaires of VERITAS-Pro were used in the second step study with patients who had experienced the educational interventions in above 5 hemophilia treatment centers’ education programs.

3) Statistical analysis

The individual total score of adherence and the mean scores of six subscales of the patients were calculated. The difference between the scores of the uneducated group and the educated group was analyzed with two sample t-test in IBM SPSS 19.0. The level of significance of P was <0.05.

This study was approved by our Institutional Review Boards and written informed consent was obtained from all participants.

### Table 1. The comparison of scores of 6 subscales in VERITAS-Pro between the uneducated group and educated group

| Subscale      | Uneducated group (mean±standard deviation) | Educated group (mean±standard deviation) | P-value |
|---------------|---------------------------------------------|------------------------------------------|---------|
| Timing        | 8.43±3.42                                    | 7.90±3.26                                | 0.246   |
| Dosing        | 6.12±2.35                                    | 5.88±2.38                                | 0.463   |
| Planning      | 6.43±2.50                                    | 6.33±2.41                                | 0.751   |
| Remembering   | 5.99±2.34                                    | 6.35±2.81                                | 0.314   |
| Skipping      | 6.22±2.77                                    | 6.25±2.66                                | 0.933   |
| Communicating | 7.23±2.94                                    | 7.24±3.04                                | 0.976   |

### Table 2. The comparison of scores of 4 items of subscale ‘timing’ in VERITAS-Pro between uneducated group and educated group

| Items                                           | Uneducated group (mean±standard deviation) | Educated group (mean±standard deviation) | P-value |
|------------------------------------------------|---------------------------------------------|------------------------------------------|---------|
| I do prophylaxis infusions on the scheduled days. | 1.66±0.75                                    | 1.84±0.89                                | 0.127   |
| I infuse the recommended number of times per week. | 1.75±0.92                                    | 1.18±1.17                                | <0.001  |
| I do prophylaxis infusions in the morning as recommended. | 2.83±1.39                                    | 2.12±1.16                                | <0.001  |
| I do infusions according to the schedule provided by the treatment center. | 2.21±1.34                                    | 2.15±1.19                                | 0.745   |

### Results

1) Adherence of the uneducated group

Ninety-five eligible patients were recruited for participation from the 5 hemophilia treatment centers. Of the 95 patients, eighty-two patients had hemophilia A and 13 patients had hemophilia B. The median age of the patients was 15 years (range: 1-63). The mean total score was 40.4 (range: 24-75). Subscale mean scores were 8.43 for timing, 6.12 for dosing, 6.43 for planning, 5.99 for remembering, 6.22 for skipping, and 7.23 for communicating (Table 1).

2) Adherence of the educated group

One hundred and twenty-three patients were recruited from 5 hemophilia treatment centers. Of the 123 patients, one hundred and four patients had hemophilia A and 19 had hemophilia B. The median age of the patients was 18 years (range: 2-75). The mean total score was 39.9 (range: 24-77). Subscale mean scores were 7.90 for timing, 5.88 for dosing, 6.33 for planning, 6.35 for remembering, 6.25 for skipping, and 7.24 for communicating (Table 1).

3) Comparison between the uneducated group and the educated group

The difference of the mean total score between the uneducated group and the educated group was not significant (P=0.783). However, the mean scores of 2 items in subscale ‘timing’ showed a statistically significant difference between two groups (P<0.001) (Table 2). These 2 items were “I infuse the recommended number of times per week” and “I do prophylaxis infusions in the morning as recommended”.

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Discussion

Prophylactic treatment, regular interval replacement of clotting factor concentrates is now a standard treatment for patients with severe hemophilia [1,2]. Although prophylactic regimens are variable, the effects of prophylactic treatment were sufficiently told in many studies [10-14]. As a lifelong disease, patient’s adherence to the treatment of hemophilia has a strong influence upon clinical outcome and quality of life [15,16].

Schrijvers et al. [17] defined the adherence of patients with hemophilia mainly by skipping, dosing, and timing of infusion during a 4-week assessment period and they used a 3-step part classification: adherent, sub-optimally adherent, and non-adherent. In Korea, it was a challenge for hemophilia treaters to measure adherence to the treatment regimen in clinical practice.

Since VERITAS-Pro was introduced as a new measure of adherence to prophylactic regimens in hemophilia in 2010, many other studies were performed to survey or analyze the adherence in hemophilia patients with this method, VERITAS-Pro [9,18-20].

In this study, we also used VERITAS-Pro to assess our patients’ adherence levels. As planned, the evaluation of patients’ weakest points was prioritized. With the first step study, results showed that timing was a pitfall. Infusion of clotting factor concentrates was not administered according to prescriptions or recommendations of time and frequency. Morning infusion was recommended by treaters, however, patients’ infusion time varied and infusion number did not abide to recommendations.

Although there were many barriers of adherence to prophylactic treatment, efforts were made to overcome issues outlined in previous studies [15,21-23]. In efforts to promote self-management and adherence during prophylaxis, Schrijvers et al. [16] made evidence-based recommendations for hemophilia treatment specialists. They emphasized acceptance of the disease and self-management skills were important aspects that may require tailored professional support. This study developed the education card based on the first step study and used this card to administer education programs in each hemophilia center. The card focused on morning infusion and self-infusion or home infusion.

Contrary to predictions in this study’s initial hypothesis, the mean total score of VERITAS-Pro was unchanged in educated group compared with that in uneducated group. We had to considered that our patients had relatively high scores of communicating with hemophilia centers, and it means they had poor adherence in communication. This could be explainable to the unchanged the mean total score and remained necessities to improve the communication issues.

Recently, Giordano et al. [4] reviewed the current management of the hemophilic child, and they also emphasized the importance of close relationships among patients and families with medical teams and the influence of psychological support. This study shed light upon the issue of multidisciplinary management in Korea. Although the mean total score of VERITAS-Pro in educated group could not be improved, proper timing of injection with the educational intervention was enhanced. The proper timing of injection is essential to keep necessary trough level of factor activity.

Limitations of this study include the lack of direct comparison of the same patient group’s change before and after educational interventions and that participants did not represent all Korean patients with hemophilia.

Recent studies have focused on and developed methods according to the timing of injection based on individual pharmacokinetics [24-26]. Additionally, we, the Hemophilia Working Party of the Korean Society of Hematology have planned further studies using methods to enhance adherence in patients with hemophilia.

Conclusions

This study suggests how educational interventions during prophylactic treatment of patients with hemophilia should be designed with delicate and concrete contents. Additionally, it sheds light on the necessity for with enthusiastic efforts of hemophilia treatment centers.

Nevertheless, this whole process can enhance adherence in patients and provide an improvement of multidisciplinary approach to hemophilia treatment in Korea.
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