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BLEEDING RISK IN SUBJECTS WITH SEVERE HEMOPHILIA ON VERY LOW DOSE AHF PROPHYLAXIS- AN OBSERVATIONAL STUDY

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ABSTRACT

Background: In order to strike a balance between cost-effectiveness and bleeding prevention, very low dose prophylaxis of AHF (antihemophilic fever) in individuals with hemophilia uses lower and more frequent doses. In addition to cost-effectiveness, a customized strategy, preventing overtreatment, and enhancing QoL (quality of life) in hemophilic people, close monitoring of these subjects guarantees sufficient protection.

Aim: The purpose of this study was to evaluate the risk of bleeding in individuals with severe hemophilia who are receiving very low doses of AHF prophylaxis. The study evaluated hemophilics' yearly AHF usage as well. The SF (social functioning) 36 questionnaire was used in the study to measure the patients' quality of life. FISH (Functional Independence Score in Hemophilia) was used to measure functional disability and to gauge the subjects' adherence to the preventive regimen.

Methods: The current study evaluated individuals who had been diagnosed with hemophilia, reported to the Institute within the specified study period, and were scheduled for surgical treatment. Participants in the study had to be at least 13 years old. The SF-36, FISH scores, annual AHF use, and bleeding risk were evaluated in each participant.

Results: FISH scores, SF-36 scores, the amount of AHF ingested, and ABR (annual bleeding rate) all showed statistically significant differences between the two research groups with $p<0.05$.

Conclusion: The current investigation comes to the conclusion that very low-dose prophylaxis considerably reduces the abnormal bleeding rate in hemophiliac patients. Significant gains in SF-36 scores are observed with AHF, while functional independence deteriorates in those who are not on AHF. Additionally, AHF is more effective and preferable than on-demand medication for low-dose prophylaxis.

Keywords: AHF, anti-hemophilic factor, hemophilia, low-dose prophylaxis, on-demand therapy

INTRODUCTION

Hemophilia is a bleeding illness characterized by excessive and prolonged bleeding in individuals with a deficit in clotting factors, mainly factors VIII and IX. One newborn out of every 10,000 births is reported to have hemophilia. Affected individuals have mild, moderate, and severe forms of the condition, which are described by factor plasma levels of 1% or less, 2-5%, and 6-40%, respectively. Coagulation factors are essential for both intrinsic and extrinsic pathways of coagulation.[1]

Prophylaxis is a widely acknowledged and preferred treatment for hemophilic patients. It has been shown to be more effective than episodic treatment (ET) in lowering the overall risk of bleeding and enhancing joint health and quality of life.[2]

A very low dose of AHF (anti-hemophilic factor) prophylaxis is essential for preventing bleeding, long-term financial benefits, improving quality of life, and preserving joint health. Additionally, it contributes to the improvement of psychological aspects, allowing for a more customized treatment strategy.[3]

The literature has documented the effectiveness and benefits of very-low dose prophylaxis in comparison to traditional PT (prophylaxis therapy) and ODT (on-demand therapy). However, there aren't many trials on very low-dose AHF prevention in the literature.[4]

Therefore, the goal of the current study was to evaluate the bleeding risks in individuals with severe hemophilia who are receiving very low dosages of AHF prophylaxis. The study evaluated hemophilics' yearly AHF usage as well.

MATERIALS AND METHODS

The SF (social functioning) 36 questionnaire was used in the study to measure the patients' quality of life. FISH (Functional Independence Score in Hemophilia) was used to measure functional disability and to gauge the subjects' adherence to the preventive regimen. The goal of the current study was to evaluate the risk of bleeding in individuals with severe hemophilia who are receiving extremely low dosages of AHF prophylaxis. The study evaluated hemophilics' yearly AHF usage.

The SF (social functioning) 36 questionnaire was used in the study to measure participants' quality of life. FISH (Functional Independence Score in Hemophilia) was used to measure functional disability and to gauge individuals' adherence to a preventive regimen. The Institute's Department of Pharmacology provided the study subjects. Prior to participation, each subject provided both written and verbal informed consent.

Subjects with additional bleeding diseases, such as kidney illness, liver disease, or Von Willebrand's disease, were excluded from the study, which evaluated participants older than 13. The determination of ABR (annual bleed rate) in severe hemophilia was the study subjects' major outcome, and the computation of AHF and the evaluation of functional impairment using FISH were the study subjects' secondary outcomes.

In the end, 88 participants were enrolled in the experiment after meeting the inclusion and exclusion criteria. Of these, 48 were placed in the demand group and 40 in the prophylaxis group, which received extremely low-dose prophylaxis of factor VIII/IX after giving informed consent. Both groups were critically assessed.

In order to evaluate any joint deformity or bleeding that may have happened during the prophylactic period, a thorough history and clinical examination were performed at routine checkup. ABR was used to assess hemorrhage. The FISH score was used to evaluate the joint functioning. The SF-36 questionnaire was taken into consideration in order to evaluate the subjects' general well-being. The possible benefits of very low-dose prophylaxis for individuals with severe hemophilia were examined in terms of quality of life in each patient.

While the control group received just on-demand medication, 40 test group participants received a very low dose prophylactic of 20 IU/kg/week in addition to ETs as needed. During the prophylactic phase, the participants were monitored for a year and their ABR was compared. FISH scores were used to evaluate functional impairment. A standardized SF-36 questionnaire was used to measure MH (mental health) and QoL. All of the domain scores were combined and labeled as 0 to 100.[5,6]

Fisher's exact test, Mann-Whitney U test, Chi-square test, and SPSS (Statistical Package for the Social Sciences) software were used to statistically analyze the collected data. The mean, standard deviation, frequency, and percentages were used to express the results. A p-value of less than 0.05 was taken into account.

RESULTS

The goal of the current prospective randomized controlled clinical study was to evaluate the bleeding risks in individuals with severe hemophilia who are receiving extremely low dosages of AHF prophylaxis. The study evaluated hemophilics' yearly AHF usage as well. The SF (social functioning) 36 questionnaire was used in the study to measure the patients' quality of life. FISH (Functional Independence Score in Hemophilia) was used to measure functional disability and to gauge the subjects' adherence to the preventive regimen. Following inclusion and exclusion criteria, the study evaluated 88 participants, of whom 48 were assigned to the demand group and 40 to the prophylaxis group, which received extremely low-dose prophylaxis of factor VIII/IX.

According to the study's findings, the amount of hemophilic factor consumed and the annual bleed rate, After prophylaxis, the test group's mean ABR was 8.8±19.4, which was considerably lower than the control group's mean ABR of 22.3±10.97 ($p=0.01$). The test group's consumption of AHF was measured and found to be considerably lower. Additionally, the test group's AHF utilization dropped by almost 50%, from 84000 to 47000 MU, while the control group's usage did not decrease.

The test group's functional independence ratings for hemophilia were found to be 29.73 and 30.63, respectively, before and after prophylaxis. Before and after prophylaxis, the control group's scores were 30.623 and 29.12, respectively. With p=0.01 and 0.02, respectively, the findings were statistically significant.

The two groups' mean SF-36 scores before and after prophylaxis were not significantly different (p=0.363 and 0.212). Following prophylaxis, the test group's role emotional (RE) and role physical (RP) scores significantly increased (p=0.04 and 0.03). Before and after prophylaxis, all other metrics showed non-significant results with p>0.05. GH (general health), BP (bodily pain), SF (social functioning), MH (mental health), VT (vitality), and PF (physical functioning) had p-values of 0.844, 0.343, 0.165, 0.202, 0.633, and 0.249, respectively, in the test group (Table 1).

DISCUSSION

This study assessed the risk of bleeding in people with severe hemophilia who were given very low dosages of AHF prophylaxis. The study also assessed the annual use of AHF by hemophilics.

The SF (social functioning) 36 questionnaire was used in the study to measure participants' quality of life. FISH (Functional Independence Score in Hemophilia) was used to measure functional disability and to gauge individuals' adherence to a preventive regimen. The study evaluated 88 participants based on inclusion and exclusion criteria, with 40 participants in the prophylaxis group receiving extremely low-dose prophylaxis of factor VIII/IX and 48 participants assigned to the demand group. These findings were similar to those of Gulshan S et al. (2020) and Collins PW et al. (2028), whose authors used a similar study methodology to the current investigation.

The test group's mean ABR after prophylaxis was 8.8±19.4 for annual bleed rate and hemophilic factor amount consumed, which was considerably lower than the control group's mean ABR of 22.3±10.97 with p=0.01. The test group's consumption of AHF was measured and found to be considerably lower. The test group's AHF utilization also decreased by over 50%, from 84000 to 47000 MU, but the control group's usage did not reduce. These results were in line with the findings of Fischer K et al. (2002) and Windyga J et al. (2014), who found similar annual bleed rates and amounts of hemophilic factor eaten.

According to the study's findings, the test group's functional independence ratings in hemophilia before and after prophylaxis were 29.73 and 30.63, respectively. Before and after prophylaxis, the control group's scores were 30.623 and 29.12, respectively. With p=0.01 and 0.02, respectively, the findings were statistically significant. These results were consistent with those of Verma SP et al. (2016) and Sidharthan N et al. (2017), whose authors found functional independence ratings in hemophilia that were similar to the current study. There was no significant difference between the mean SF-36 scores of the two groups before and after prophylaxis (p=0.363 and 0.212).

Following prophylaxis, the test group's role emotional (RE) and role physical (RP) scores significantly increased (p=0.04 and 0.03). Before and after prophylaxis, a non-significant outcome with p>0.05 was observed for all other parameters. GH (general health), BP (bodily pain), SF (social functioning), MH (mental health), VT (vitality), and PF (physical functioning) all had p-values of 0.844, 0.343, 0.165, 0.202, 0.633, and 0.249 in the test group. These outcomes were consistent with the SF-36 scoring provided by the authors of Manco-Johnson MJ et al. (2007) and Carcao M et al. (2010) was comparable to the results of the present study.

CONCLUSIONS

The current study concludes, within its limitations, that extremely low-dose prophylaxis greatly reduces the abnormal bleeding rate in hemophiliac patients. Significant gains in SF-36 scores are observed with AHF, while functional independence deteriorates in those who are not on AHF. Additionally, AHF is more effective and preferable than on-demand medication for low-dose prophylaxis.

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S. No	Parameters	Before prophylaxis	After prophylaxis	p-value	Before prophylaxis	After prophylaxis	p-value
1	**Mean**	75.26±5.02	83.92±3.77	0.363	69.574±14.04	66.60±11.76	0.212
2	**GH**	65.43±5.02	65±13.76	0.844	61±15.57	57.3±14.36	0.113
3	**BP**	79.30±4.35	80.21±13.96	0.343	68.73±18.84	61.3±8.80	0.155
4	**SF**	70.43±8.45	77.25±20.03	0.165	68.73±18.84	67.3±19.70	0.341
5	**MH**	59.61±7.04	64.34±4.69	0.202	68.6±16.1	61.0±13.19	0.169
6	**VT**	68.16±4.09	69.53±10.81	0.633	70.3±13.61	69±11.71	0.392
7	**RE**	36.33±11.40	51.49±31.13	**0.04**	49.97±39.27	43.31±44.56	0.166
8	**RP**	52.25±13.23	61.34±12.75	**0.03**	60±39.42	55±32.89	0.342
9	**PF**	58.16±7.12	65.7±3.33	0.249	52±20.55	50±21.19	0.341

Table 1: Comparison of social functioning-36 scores between test and control subjects