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Original Research Article

An analytical study of annual bleeding rates in haemophilia patients receiving low dose factor prophylaxis and those receiving episodic factor doses

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ABSTRACT

Background: This study aimed to assess the impact of low dose factor prophylaxis on haemophilia patients with respect to annual bleeding rates and severity of bleeding events.
Methods: This is an analytical study. All patients of HAEMOPHILIA A AND B who are registered with CPRH haemophilia treatment centre from January 2022 to December 2022 were included and were followed up every month from January 2022. The study population was divided into two groups: those receiving regular low dose factor prophylaxis and those receiving episodic factor treatment. Both the group participants were matched for severity of factor deficiency and age. The collected data was compared with respect to the annual bleeding rate as well as severity of bleeding episodes in the two defined groups.
Results: There were 100 study patients, and 16 of them are receiving regular low dose factor prophylaxis. The average bleeding episodes were found to be more in patients receiving episodic factor doses (ABR in moderate haemophilia= 3.511+/-0.81, ABR in severe haemophilia=5.38+/-4, 53) as compared to those receiving prophylactic factor doses (ABR in moderate haemophilia = 0.16+/-0.32, ABR in severe haemophilia=0.3+/-0.29). The incidence of severe bleeds (those requiring hospitalisation) was higher in patients receiving episodic factor therapy (15) as compared to those receiving regular low dose factor prophylaxis (1).
Conclusions: Haemophilia patients receiving episodic factor doses have higher Annual Bleeding Rate as compared to patients receiving regular low dose factor prophylaxis. Also, patients receiving prophylaxis face less severe forms of bleeding episodes as compared to other group of patients.

Keywords: Annual bleeding rate, Factor replacement therapy, People with haemophilia, Prophylactic factor doses

INTRODUCTION

Hemophilia is a hereditary X-linked recessive disorder characterized by the deficiency of factor VIII or IX coagulant activity.[1] A bleeding disorder caused by single gene mutations in either factor 8 or factor 9 encoding genes.[2] In India, prevalence of hemophilia A (factor 8 deficiency) is 0.7 per 1 lakh, and that of hemophilia B is 0.3 per 1 lakh population.[3] Varied bleeding manifestations occur in patients of hemophilia due to coagulation factor deficiencies viz.- joint bleeds, muscle hematomas, gastrointestinal bleeds, intracranial bleeds, hemoperitoneum.[4] These acute bleeds if not managed promptly can lead to chronic complications especially in cases of joint bleeds like arthropathy, pseudotumor etc.[2] Hence it is extremely important to address bleedings in such patients and also prevent the bleeding episodes in order to prevent disability and improve quality of life in these patients.[2]

METHODS

Study design

This was an analytical study. Total 100 patients were included in the study.

Study place

This study was conducted at RCSM GMC, Kolhapur (a tertiary hemophilia treatment center).

Study period

This study was conducted from 1st May 2022 to 1st May 2023.

Inclusion criteria

Hemophilia Patients with at least one spontaneous bleeding episode till date, patients and parents willing to participate in the study, patients not likely to relocate elsewhere in the advised study period were included.

Exclusion criteria

Patients non complaint to follow up schedules advised, and patients and parents not willing to participate in study were excluded.

Data collection

Patients were divided in 3 categories- mild, moderate and severe disease based on factor activity (<1%-severe, 1-5%-moderate and 5-40%-mild). Two groups were formed based on type of treatment given to the patients- prophylactic factor infusions and episodic factor infusions. Total 16 patients received prophylactic factor infusions and 84 patients received episodic factor infusions. Long term records of hospital visits and hospital admissions for various complications in all these patients were maintained and referred to during the study period. Treatment charts for each patient including episodic factor treatment and prophylactic factor doses were meticulously maintained and analyzed with respect to their corresponding groups.

Ethical committee approval was taken before starting the study from Institutional Ethics Committee.

Data analysis

Data analysis was done using SPSS 20 software.

RESULTS

Age wise distribution of patients in our study was present in Table 1.

Total 22 paediatric patients and 78 adult patients enrolled in study as shown in the Table 1.

Table 1: Age wise distribution of patients in our study.

Age group	Haemophilia A	Haemophilia B	Total
0-12 years	16	6	22
12-60 years	62	16	78
Total	78	22	100

All patients were residents of rural areas of Western Maharashtra, residing around Kolhapur. Among all the 100 patients included in study, 78% had hemophilia A and 16% had hemophilia B (comparable to the national data of both the diseases). Patients with mild, moderate and severe disease based on deficient factor activity were found to be as follows in Table 2.

Table 2: Severity of disease based on factor activity levels.

Severity	Patient number	Percentage of total hemophilia patients in the study, %
Mild (5-40%)	17	17
Moderate (1-5%)	49	49
Severe (<1%)	34	34

Distribution of the patients in 2 study groups wiz. - prophylaxis and episodic. Total 16 patients included in prophylaxis arm and 84 patients in episodic treatment arm (Table 3).

Table 3: Distribution of the patients in 2 study groups.

	Prophylaxis	Episodic treatment	Total patients
Mild	0	17	17
Moderate	6	43	49
Severe	10	24	34

Annualized bleeding rates in the 2 groups were compared and found to be as follows. In mod hemophiliacs, prophylaxis caused reduction in ABR to 0.16±0.32 while those with episodic treatment had ABR of 3.511±0.81. Similarly, in severe hemophiliacs, prophylaxis caused reduction in ABR to 0.3±0.29 while those with episodic treatment had ABR of 5.38±4.53 (Table 4).

In mod hemophiliacs, prophylaxis caused reduction in ABR to 0.16±0.32 while those with episodic treatment had ABR of 3.511±0.81. Similarly, in severe hemophiliacs, prophylaxis caused reduction in ABR to 0.3±0.29 while those with episodic treatment had ABR of 5.38±4.53 (Figure 1).

Table 4: Annualized bleeding rates in 2 groups expressed in terms of Mean±SD.

Mean (+/- SD) ABR	Mild hemophilia	Moderate hemophilia	Severe hemophilia
Prophylactic treatment	0	0.16±0.32	0.3±0.29
Episodic treatment	3.062±0.76	3.511±0.81	5.38+/-4.53

Patients receiving prophylaxis experienced lesser severe bleeds as compared to patients on episodic treatment (The severity of bleeding episode was defined for this study purpose as episode requiring hospitalization). Total 15 hemophilia patient hospital admissions were noted over one year in the group receiving episodic treatment while that in prophylactic group, 1 hospital admission was noted.

DISCUSSION

The age group in our study ranged from 0-60 years of age compared to 0-7 years in The ESPRIT study[5], less than 15 years by Uddin MM and Karim et al and less than 18 years of age by Hazewinkel et al.[6-8]

The study period was much shorter-one year in our study as compared to 10 years in The ESPRIT study, 5 years in Aronstam et al study.[5,9]

Hemophilia A (78%) was the most common type of hemophilia as compared to hemophilia B. The ratio of hemophilia A/hemophilia B has been reported between 78/22 and 87/13 throughout the world.[10]

We have found mild disease in 17%, moderate disease in 49% and severe disease in 34% as compared to 25.19% mild, 38.84% moderate and 33.93% in severe haemophilia in the Bhopal study by Nigam et al.[4]

The no of bleeding episodes per person over 1 year in our study was found to be lesser in the group receiving prophylaxis as compared to the group receiving episodic treatment which is comparable to all the similar studies.[5,11,12]

The mean ABR in prophylaxis group in our study was 0.16 and 0.3 in moderate and severe hemophilia as compared to 1.32 in The ESPRIT study and that in episodic treatment group in our study was 3.0, 3.5 and 5.3 in mild, moderate and severe hemophilia respectively as compared to 5.76 in The ESPRIT study. [5]

The differences in results may be attributed to the duration difference and different age groups included in the study.

The primary outcome in our study was considered to be the frequency of bleeding episodes.

Most of our patients on prophylaxis are receiving low dose regular prophylaxis started after 2-3 episodes of joint bleeds- i.e. on secondary prophylaxis.

Due to scarcity of resources and social barriers in patients' and parents' reaching the facility on regular basis, we have comparatively lower no of patients in prophylaxis group.

CONCLUSION

We conclude that with low dose regular factor prophylaxis, many bleeding events can be prevented successfully owing to better quality of life in patients of haemophilia. As compared to episodic management of haemophilia patients, prophylaxis is better in terms of low ABR, lower rates of hospitalizations. This eventually will lead to better quality of life, better joint scores and is a cost-effective way of managing haemophilia patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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