PROPHYLACTIC TREATMENT FOR HEMOPHILIA A PATIENTS : A PILOT STUDY

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Abstract. Prophylactic treatment with factor VIII concentrate was given to six hemophilia A boys whose factor VIII:C ranged from 1% to 3.5% at Ramathibodi Hospital. The age ranged from 11 to 16 years with the median age of 12 years old. Each patient received factor VIII concentrate twice a week in the dosage of 8-10 unit per kg for one year. During the prophylactic period, bleeding episodes seldom occurred. They did not need hospitalization. The absence from school was reduced. They became muscular from regular daily exercise. They could join the activity at school and lived a near normal life. The patients and family were very happy since they did not have to worry about bleeding. No adverse effect was found. The only constraint was the cost. It cost 180,000 baht (US$ 7,200) per year or 15,000 baht (U$$ 600) per month for a 25 kg hemophiliac boy.

INTRODUCTION

Hemophilia A and B are X-linked recessively inherited bleeding disorders affecting 1 in 13,000 to 20,000 population in Thailand which is similar to other western countries (Isarangkura *et al*, 1980). The blood component which is routinely used among the hemophiliac patients in Thailand is local preparation of single unit preparation of fresh frozen plasma (FFP), cryoprecipitate, fresh dry plasma (FDP). FDP is a lyophilized form of FFP that can be kept at a 4°C home refrigerator for one year (Isarangkura *et al*, 1987). These blood components are not virus-inactivated product. The patients are vulnerable to contract blood transmitted diseases (Isarangkura *et al*, 1991, 1993). However, accepted blood donors have negative tests for HIV antigen, anti-HIV antibody, VDRL and hepatitis B surface antigen.

In Ramathibodi Hospital, most of the hemophiliac patients receive replacement therapy on demand during each bleeding episode combined with modified home care therapy using FDP whenever the early bleeding occurs. The rate of deformative arthropathy is 20%, which is similar to that of western countries over the last 20 years (Chuansumrit *et al*, 1993). Therefore, prophylactic treatment has been considered for these young hemophiliac patients. The local blood components are not suitable for prophylactic treatment since they are not virus-inactivated. In 1992, the virus-inactived factor concentrate was kindly supplied by a pharmaceutical company for this pilot study. This paper reports an assessment of the effectiveness of prophylactic treatment.

PATIENTS AND METHODS

Patients

Six hemophiliac patients who attended the Hematology Clinic, Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital were included. They received treatment on demand of bleeding episode combined with modified home care therapy using FDP or FFP. The patients and parents were trained to dissolve the factor concentrate and venipuncture with sterile technique.

Each patient received factor VIII concentrate twice a week in a dosage of 8-10 units per kg for one year in 1992. The patients were advised to have regular daily exercise such as muscle stretching, swimming, bicycling. The patients wrote their records of factor VIII concentrate administration, bleeding episodes, number of venipunctures as well as adverse reactions such as utricaria, itching. They attended the Hematology Clinic every 3 months for physical examination, blood testing for factor VIII inhibitor, liver function tests, hepatitis B surface antigen and anti-HIV antibody testing.

Method

The coagulogram was performed by the standard method. The factor VIII clotting activity (FVIII:C) in fresh samples was determined by a one-stage method based on the partial thromboplastin time with human lyophilized factor VIII deficient plasma (Stago) as

substrate (Hardisty and Macpherson, 1962). The FVIII:C was expressed as percentage activity in relationship to normal plasma. Inhibitor titers against human factor VIII were determined by Bethesda system (Kasper *et al*, 1975). The other parameters were determined by standard methods.

RESULTS AND DISCUSSION

Table 1 presents the descriptive data of six patients who were moderate or severe hemophilia A patients. The factor VIII clotting activity ranged from 1% to 3.5%. The age ranged from 11 to 16 years with the median age of 12 years old. The distance from home to Ramathibodi Hospital varied from 20 to 890 kilometers.

During the prophylactic period, the bleeding episodes seldom occurred. They did not need hospitalization as compared to 7-35 days of hospitalization per year in the previous year. The absence from school was reduced. Five out of six patients became muscular and gained 1.5 to 6 kg per year (Table 2). The patient (No. 1) who was obese reduced the weight from 62 to 59 kg by controlling diet plus exercise. No additional deformative joint was detected by the physical examination.

The patients could join the activity at school and lived a near normal life as their friends and siblings. The patients and the family were very happy since they did not have to worry about bleeding and its consequence. For example, the patient (No. 1) who could give factor VIII concentrate himself properly went abroad with his family for one week. It was the first trip in his life. He used to stay home quietly with the housekeeper when the family went abroad for vacation. He did not join them because he was worried about bleeding. By the prophylactic treatment,

Table 1

Descriptive data of six hemophilia A patients.

No.	Age	FVIII:C (%)	Venipuncture	FVIII concentrate (unit/kg)
1	12	2.6	patient	8
2	13	3.5	father	10
3	11	< 1	father	10
4	16	< 1	patient	9.6
5	11	1.6	nurse	8
6	13	2.2	nurse	10

Table 2

The comparison of body weight, bleeding episode and hospitalization before and after the prophylactic treatment.

No.	Body weight (kg)		Bleeding (episodes/yr)		Hospitalization (d/yr)	
	Before	After	Before	After	Before	After
1	62	59	24	3	7	-
2	25	29.5	18	3	35	-
3	24	26.5	7	2	20	-
4	40.5	43	17	6	23	-
5	31	34	2	-	7	-
6	38	44	1	-	3	-

he confidently joined them because he could take care of himself properly.

Two fathers who have been trained to give FDP could give factor VIII concentrate to their sons. Two patients were trained to inject themselves. No adverse complication was detected. Another two hemophiliac boys who were siblings dare not to perform the venipuncture. They had a nurse nearby their house assisting them. Most of the factor VIII concentrate was given via one injection.

During one year of prophylaxis and one year later, the patients had no factor VIII inhibitor, the liver function tests were normal, the anti HIV anti-body testing and hepatitis B surface antigen were negative.

Prophylactic treatment has been shown to be the best treatment for hemophiliac patients (Nilsson *et al*, 1981; Heijnen, 1986). The earlier the prophylactic treatment starts, the better the outcome. Prophylactic treatment is beneficial to both physical and psychosocial aspects. In this study, the patients had a good chance to exercise during the prophylactic treatment, they became muscular. A muscular patient will have lesser chance of bleeding. And if the bleeding occurs, the severity is less than a weak patient. The deformative arthropathy is minimized, the hospitalization as well as absence from school is reduced. The patients have good self-esteem. The most impressive benefit is the patient's psychological independence of well-being and much improvement of quality of life. The parent's absence from work is reduced too. The patients and their families can live a near-normal life happily.

The factor VIII inhibitor among the hemophilia A patients varies from 5% to 20%, most of them are severe degree (FVIII:C < 1%) (Shapiro and Hultin, 1975; Fulcher *et al*, 1985). In this study, factor VIII inhibitor was not detected during one year of prophylaxis and one year after. The regular infusion of factor VIII concentrate in this prophylactic program is similar to the low dose regimen of immune tolerance in hemophilia A patients with inhibitor (van Leeuwen *et al*, 1986).

Blood-transmitted diseases are another hazards among the hemophiliac patients who received blood products. However, the solvent-detergent treated factor VIII concentrate has been proved to be an effective virus-inactivated product (Bloom, 1991). In this study, no evidence of HIV and hepatitis B infection were detected. The safety and effectiveness of solvent-detergent treated factor VIII concentrate in the prophylactic treatment is comfirmed. The greatest constraint is the cost. The factor concentrate is expensive. The cost for a hemophiliac boy who weights 25 kg is 180,000 bahts (US$ 7,200) per year or 15,000 baht (US$ 600) per month. It is too high for most parents to afford. In the near future, the National Red Cross Blood Center will produce lyophilized, heat-treated cryoprecipitates which will be an alternative blood product for prophylactic treatment.

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