NATIONAL SURVEY OF PATIENTS WITH HEMOPHILIA AND OTHER CONGENITAL BLEEDING DISORDERS IN THAILAND

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Abstract. A national survey of patients with hemophilia and other congenital bleeding disorders in Thailand was conducted in the years 2000 to 2002. Questionnaires were sent to physicians working at hospitals throughout the country. Although the overall response rate to the questionnaires was 19%, the two highest rates of 80% and 73.7% were found at university and regional hospitals, respectively, where most of the patients received their diagnosis and treatment. A total of 1,450 patients comprised of hemophilia 1,325 cases, von Willebrand disease, 69 cases, congenital factor VII deficiency, 15 cases, hereditary platelet dysfunction, 22 cases, and undefined causes of congenital bleeding disorders, 19 cases. Most were pediatric patients <15 years of age. Treatment was mainly given on demand for a bleeding episode, while only 8.6% received additional home treatment for early bleeding episodes. Replacement therapy primarily relied on fresh frozen plasma, cryoprecipitate and cryo-removed plasma. Factor concentrate was seldom used because of the high price. As a result, hemophilia care services in Thailand should be strengthened by providing comprehensive education for medical personnel, making available simple laboratory kits to determine hemophilia A and B, ensuring an adequate supply of blood components and affordable factor concentrate, and establishing home care treatment.

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INTRODUCTION

The prevalence of patients with congenital bleeding disorders varies from 1 to 500,000 population, found in congenital factor VII deficiency (Mariani and Mazzucconi, 1983), to up to 1 to 1,000 population found in von Willebrand disease (Werner *et al*, 1993). However, severe bleeding disorders are commonly found in hemophiliacs with a prevalence of 1 to 13,000 in the Thai population (Isarangkura *et al*, 1980), similar to western countries. It is estimated that at least 4,500 people with hemophilia live in Thailand. Hemophilia care services have been integrated into the existing infrastructure of the medical health care system (Isarangkura and Chuansumrit, 1991). They can be classified into four levels, operating with primary hemophilia care centers: 8,842 health stations and 695 district hospitals, hemophilia treatment centers in 73 provincial hospitals, comprehensive care centers in 19 regional hospitals, and reference centers for hemostatic disorders in 10 university hospitals. The majority of patients often see hematologists at university hospitals for definite diagnosis and treatment. However, hemophilia care facilities are not exclusively for patients with hemophilia, but are utilized by patients with other congenital and acquired bleeding disorders. The present study reports a national survey of patients with hemophilia and other congenital bleeding disorders in Thailand, from 2000 to 2002.

MATERIALS AND METHODS

Questionnaires concerning gender, age, bleeding manifestations, diagnosis and treatment were collected from physicians, pediatricians and internists in the district, provincial, regional and university hospitals throughout Thailand in the years 2000 to 2002.

RESULTS

The response rates for the questionnaires varied from 14.3% to 80%, with an average of 19%, as shown in Table 1. The two highest response rates, of 80% and 73.7%, were from university and regional hospitals, respectively. A total of 1,450 patients, comprised of hemophilia, 1,325 cases, von Willebrand disease, 69 cases, congenital factor VII deficiency, 15 cases, hereditary platelet dysfunction such as Glanzmann thrombasthenia, 22 cases, and undefined causes of congenital bleeding disorders, 19 cases. Males were predominant among patients with hemophilia, but both males and females were found in patients with other congenital bleeding disorders. Most (80%) were in the pediatric age group of <15 years old. Although hemophilia was the prominent diagnosis, hemophilia A and B were determined in 70% of patients. The majority of patients with hemophilia were treated at university and regional hospitals, as shown in Table 2.

The laboratory investigation for determining the status of hemophilia and other congenital bleeding disorders at different treatment centers is shown in Table 3. Complete facilities are available at university hospitals. The factor assay for determining the status of hemophilia A and B is performed at the university hospital and some

Table 1
Questionnaires response rates.

Type of hospital	Total	Responses	%
University	10	8	80
Regional	19	14	73.7
Provincial	73	28	38.3
District	695	100	14.3
Others[a]	10	3	30
Total	807	153	19.0

[a]Private hospitals, government sector hospitals

Table 2
Number of patients with hemophilia being treated by physicians in different hospitals.

Type of hospital	Number of patients	%
University	1,025	77.3
Regional	185	14.0
Provincial	79	6.0
District	28	2.1
Others[a]	8	0.6
Total	1,325	100

[a]Private hospitals, government sector hospitals

regional hospitals.

Detailed information on bleeding manifestations and replacement therapy was obtained from 465 patients receiving treatment at Ramathibodi Hospital (n=252), regional hospitals (n=106), provincial hospitals (n=79), and district hospitals (n=28), as shown in Tables 4 and 5. However, bleeding in the central nervous system was mainly treated at university and regional hospitals, while less-severe bleeding episodes were treated at provincial and district hospitals. Replacement therapy mainly relies on fresh frozen plasma and cryoprecipitate. Very minute amounts of commercial factor concentrate were used. Of note, desmopressin was used in university hospitals only. In addition, patients with inhibitor exhibiting bleeding, were predominantly treated at university hospitals. None of the patients at regional, provincial or district hospitals received home care treatment for early bleeding, except for 8.6% of patients from Ramathibodi, Songklanagarind and Chulalongkorn hospitals. However, these patients were also treated by physicians and medical personnel at provincial and district hospitals, and health stations.

DISCUSSION

Although the overall response rate to the questionnaires was 19%, the two highest rates of 80% and 73.7% were from university and regional hospitals, respectively, where most of the hemophiliacs received diagnosis and treatment. Only 29.4% (1,325/4,500) of the estimated hemophiliac

Table 3
Laboratory investigation for patients with hemophilia and other congenital bleeding disorders at different treatment centers.

Hospital	Venous clotting time	Coagulogram	Factor assay	Platelet function test
University	+	+	+	+
Regional	+	+	±	+
Provincial	+	+	-	-
District	+	±	-	-
Government sector	+	+	±	-
Private	+	+	-	-

+ = available, - not available, ± may be available in some hospitals

Table 4
Common bleeding episodes among 465 patients with hemophilia treated at four different treatment centers.

Bleeding manifestation	University[a] n = 252	Regional n = 106	Provincial n = 79	District n = 28	Total n = 465
Hemarthrosis	50	66	34	11	161
Hematoma	58	38	25	8	129
Gum and teeth bleeding	10	45	27	10	92
Ecchymosis	7	40	20	14	81
Epistaxis	3	16	9	9	37
CNS bleeding	24	13	2	-	39
Others	31	12	11	1	55
Total	183	230	128	53	594

[a]Ramathibodi Hospital

Table 5
Replacement therapy for patients with hemophilia in Thailand.

Type	Heat-treated dried cryoprecipitate	Frozen cryoprecipitate	Cryo-removed plasma	Fresh frozen plasma	Commercial factor concentrate
Hemophilia A	+	+	-	+	Occasional
Hemophilia B	-	-	+	+	Occasional
Unclassified	-	-	-	+	-

+ = yes, - = no

patients in Thailand received diagnosis and treatment. Most were pediatric patients, <15 years of age. Unfortunately, 70.6% of estimated hemophilia patients were still undiagnosed because of limited health care resources in rural areas. They lived with intense pain, disability, and debility. They fought a lonely battle resulting in a loss of their limbs or their lives. The patients who received little or no treatment often succumbed to bleeding episodes in their early life and seldom reached adulthood. In fact, in a previous study, 103 out of 139 males (74.1%) with a presumptive diagnosis of hemophilia by history-taking, died from bleeding episodes at a mean age of 8 years, 9 months (Krasaesub and Chuansumrit, 2001). It is clear that comprehensive education related to hereditary bleeding disorders should be provided to all health personnel, identify more patients with congenital bleeding disorders.

However, the determination of hemophilia A and B was not consistently carried out at these hospitals. In the present study, 30% of patients received a presumptive diagnosis of hemophilia without determining the status of hemophilia A and B, since the assay of factor VIII and IX clotting activities was not routinely performed. The main constraint in performing the assay is that the substrate of commercial factor VIII or IX deficient plasma is expensive. Of note, factor VIII or IX deficient plasma obtained from patients with severe hemophilia is recommended as the in-house prepared substrate for the factor assay. The shelf life is 3 months if kept at -70ºC, and decreases to 1 month if kept at -20ºC. In the future, an in-house laboratory kit for distinguishing hemophilia A and B should be created and distributed, especially to hospitals in rural areas.

The clinical manifestations of bleeding episodes of hemophiliacs treated at the regional, provincial and district hospitals did not differ from the previous study of university hospitals (Chuansumrit *et al*, 1993). They mainly received fresh frozen plasma and cryoprecipitate on demand for bleeding episodes. Factor concentrate was seldom used because of the high price. Inadequate replacement therapy is the main constraint in hemophilia care services. Moreover, fresh frozen plasma and cryo-removed plasma are both insufficient to raise the desirable levels of factor VIII or IX clotting activity, especially in patients with a body weight > 30 kg. Additionally, volume overloaded, pulmonary edema and renal impairment are found in patients receiving large amounts of plasma transfusion (Moran and Kapsner, 1987). Therefore, an adequate supply of blood component and affordable factor concentrate are essential for maintaining hemophilia care.

Home-care treatment was only provided to patients of Ramathibodi, Songklanagarind and Chulalongkorn hospitals. In fact, home-care treatment for early bleeding episodes is essential, especially in developing countries with limited health care resources. Low literacy is no barrier to the establishment of home care treatment (Chuansumrit *et al*, 1999). Bleeding, if promptly treated at home, is less extensive compared with delayed treatment, and fewer blood components are utilized than with delayed treatment (Dietrich, 1996).

In conclusion, the hemophilia care services in Thailand should be extended to the majority of patients in rural areas by strengthening four aspects: comprehensive education related to heredi-

tary bleeding disorders should be provided to medical personnel; the availability of simple laboratory testing kits for determining hemophilia A and B should be distributed nationwide; an adequate supply of blood components and affordable factor concentrates should be maintained; and home-care treatment for early bleeding episodes should be established and promoted. As a result, medical outreach services will gradually bring about better outcomes for patients with hemophilia all over Thailand. Hopefully, they will be able to live out their lives as healthy adults and continue to contribute to our society.

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