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Perspective

Management of hemophilia in Korea: the past, present, and future

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Hemophilia is a bleeding disorder. Although the incidence of hemophilia is very low, the World Foundation of Hemophilia (founded in 1963) has used a multidisciplinary approach to focus its efforts to improve care for patients with the disease worldwide. In Korea, however, the management of hemophilia has been supported by the Korea Hemophilia Foundation (KHF) since 1991.

The management of hemophilia in Korea benefited from the development of factor concentrates that were successfully advanced by both global and domestic pharmaceutical companies. In addition, factor concentrates are included in coverage, even in limitation, by the national health insurance. Furthermore, to improve the management of hemophilia in medical institutions around the country, the Hemophilia Working Party (HWP) and KHF published and distributed the manual for the management of hemophilia. Quantitative data has demonstrated that the support provided by these organizations has led to an improvement in the life expectancy of Korean hemophilia patients [1].

For children with severe hemophilia, primary prophylaxis, in addition to the management of bleeding episodes, is now the recommended treatment strategy [2]. The HWP and KHF have made efforts to convince the government and primary prophylaxis for the patients under 18 years old could be supported by the national health insurance since 2013. However, prophylaxis for adult patients is also important and necessary to improve the quality of life; therefore, we, HWP and KHF, have prepared to show the clinical evidence regarding the benefits of prophylaxis in adult patients.

In the management of hemophilia, the development of inhibitors, the alloantibodies to factor concentrates, can cause severe complications. Once a patient develops inhibitors, he will experience more frequent and severe bleeding episodes and will need more factor concentrates or bypassing agents (e.g., activated prothrombin complex concentrates and activated recombinant factor VII). Some inhibitors may disappear spontaneously but when the inhibitors persist and show high titer, immune tolerance induction (ITI) is needed to eradicate inhibitors [3]. However, ITI costs a lot, and it is allowed and performed limitedly by the several hemophilia centers in Korea. Furthermore, financial and practical issues make prophylaxis with the bypassing agents very difficult for patients with inhibitors to obtain.

Although much progress has been made in regards to the management of hemophilia, there are still several issues to solve. For example, according to the KHF 2012 annual report, the number of patients with hemophilia A and hemophilia B was 1,579 and 365, respectively [4]; however, hemophilia A occurs in about 1 in 5,000 male births while hemophilia B is 4–6 times less common. Given the size of the general population of Korea, these numbers are much lower than expected. A national registration system and more accurate diagnosis methods are needed to adequately measure the incidence and prevalence of hemophilia in the Korean population.

Furthermore, although we do not fully understand why, the number of hemophilia patients with inhibitors in Korea is lower than that of other countries [4]. Therefore, we plan to conduct genetic analyses in order to manage and

predict the development of inhibitors and construct a database for future analyses.

In addition, the adoption of prophylaxis as the gold standard poses significant challenges. Young patients, for example, need frequent intravenous injections; however, venous access is often difficult in these patients. In light of these challenges, research has focused on the production of factors with a prolonged half-life. Several products have already undergone clinical trials and reported the study results [5-8].

Primary prophylaxis is defined as the regular administration of factor concentrates for preventing joint bleeds. Research has shown that patients with factor levels over 1% rarely suffer from spontaneous joint bleeds and arthropathy; therefore, maintaining a trough level above 1% might convert severe hemophilia to moderate hemophilia and abolish joint bleeds [9]. Thus, primary prophylaxis can prevent the development of arthropathy and may increase a patient's quality of life. However, the optimal regimen for personalized prophylaxis is based on different individual pharmacokinetics (PK) to factor concentrates and bleeding tendency [10, 11]. In Korea, primary prophylaxis for children with severe hemophilia is the standard treatment; however, individual PK studies are needed to tailor prophylaxis for individual patients. Tailoring can make prophylaxis more effective, factor concentrate consumption more cost-efficient, and can improve the quality of life [12]. With a view to the management of the patient with inhibitors which still has limitation with financial and practical issues, individual PK study will help assessing the full tolerance at the end of ITI. If PK-based dose tailoring is to be used in routine clinical practice, methods that use reduced and convenient sampling points are needed [10].

The levels of diagnosis and treatment provisions vary widely across the world. For example, in developing countries, access to health care is very limited and very few people can be tested for hemophilia. Developed countries, on the other hand, use personalized prophylactic therapy to optimize outcomes and work towards zero bleeds. Individualizing prophylaxis allows for inter-individual differences and enables patient-centered therapy. In addition, the management of hemophilia becomes more holistic through the involvement of a multidisciplinary team working together to guide patients towards self-management. Furthermore, patient-centered therapy focuses on shared decision-making, heightening the awareness regarding the importance of every bleed as well as the use of prophylaxis, and emphasizes the need for adherence to the prescribed treatment regimen [13].

Comprehensive care of hemophilia includes the treatment and prevention of bleeding, the long-term management of hemophilic arthropathy and other bleeding complications, the management of significant complications from treatment (e.g., the development of inhibitors and transfusion transmitted infections), as well as the psychosocial support and education required to manage the disorder. Therefore, comprehensive care requires a multidisciplinary team approach to provide management for the patient and family through continuous supervision of the medical and psychosocial aspects of the disease [14]. In Korea, several medical centers and clinics of KHF provide management for hemophilia patients. However, these centers are not always able to offer a multidisciplinary team approach; therefore, government supported hemophilia treatment centers are needed to provide comprehensive care for hemophilia patients. As the leading hemophilia care organizations, the HWP and KHF will participate in international collaboration focused on improving care for all hemophilia patients.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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