Commentary

Haemophilia in 21st Century Singapore
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The recognition that a bleeding diathesis can arise as an inherited disorder was documented as far back as the 2nd century ACE in Talmudic writings. Our current understanding of haemophilia as a deficiency of clotting factors is, however, a more recent establishment dating to the 1940s.1 Haemophilia A, or congenital factor VIII deficiency, is the most common of the inherited bleeding disorders and afflicts 1 in 5000 live births. Less common is factor IX deficiency or haemophilia B, which occurs in one in 30,000 live births.2 Deficiencies of other clotting factors are much rarer.

As we mark World Haemophilia Day this month, it is apt for us to reflect upon the issues that we face collectively as patients, their families and clinicians, in striving to make living with haemophilia as normal as possible. The hard figures on the number of haemophiliacs in Singapore are not daunting. The Singapore Haemophilia Registry currently lists a total of 185 haemophilia A and 32 haemophilia B patients as of January 2009. Measured against a population estimate of 3.5 million,3 this statistic seems unworthy of further scrutiny, until one realises the tremendous burden of this lifelong disorder, an understanding that only haemophiliacs, their families, and a few discerning clinicians and paramedical staff are privy to. A near normal life is, however, achievable with the appropriate resources.

Appreciating the clinical implications of a clotting factor deficiency is simple enough. Affected individuals bleed excessively and such events lead to significant short- and long-term morbidity and potential early mortality. The condition places a disproportionate strain on clinical resources, and on both the quality of life of patients and their ability to contribute economically. Replacement of clotting factor is a simple solution to this problem.

The real life situation is, however, more complex. Haemophiliacs in Singapore share many similar challenges with their brethren in both the developed and developing world. Not least are the following issues: affordability of treatment for acute bleeding and prophylactic therapy, inhibitor development and the management thereof, and blood-borne infections associated with plasma-derived blood products. Access to rehabilitative services to limit the morbidity of repeated bleeding episodes, especially in target joints, and to optimise residual function are all too often under-emphasised. Let us also not forget psychosocial support for patients and their families.

These issues are most pressing in haemophilia A patients, who have greater exposure and more significant bleeding episodes. The goal of comprehensive haemophilia care is the successful integration of patients into society, such that this disorder becomes like other chronic conditions that many people will acquire at some point in their lives.

The overwhelming majority of our patients do not receive prophylactic clotting factor replacement, unlike their counterparts in some developed nations. That this preventive strategy is effective in reducing bleeding episodes and their short- and long-term complications is irrefutable. What is uncertain is how this can ever be a standard of care in our setting. Surmounting this step requires a persistent and concerted effort on the part of healthcare providers, healthcare authorities and funding bodies, as well as the pharmaceutical industry to produce a sustainable model that gels with the interest of all parties. The lack of a near-term solution should not deter us from constantly exploring and pursuing options to provide prophylactic therapy to our patients.

Fortunately, haemophiliacs in Singapore were spared from the ravages of the human immunodeficiency virus (HIV) infection that affected a high proportion of haemophiliacs in the western world in the 1980s.4 However, the same cannot be said of hepatitis C, as it affects 60 patients, or more than one-half of all the 118 haemophilia A patients tested here. The potential in hepatitis C carriers for developing liver cirrhosis and hepatocellular carcinoma adds a further dimension to the long-term care of these patients. Undoubtedly, our exclusive use of plasma-derived clotting factors and, previously, cryoprecipitate, contributed to this blood-borne menace.

The safety of current plasma-derived clotting factors has, however, improved by leaps and bounds in recent years through the meticulous selection of plasma donors, and new technology in detecting and inactivating infectious organisms. Nevertheless, we are vulnerable to other, as yet
undiscovered, blood-borne infections in the future. Another potentially calamitous blood product-born epidemic has certainly served as the business argument for manufacturers of recombinant clotting factors and other blood derived products.

Two recombinant factor VIII products are currently marketed in Singapore for haemophiliacs. Their tangible benefits are difficult to disregard, but their cost only serves to aggravate the headaches of all concerned, as we struggle to provide even the least exorbitant of clotting factors to patients. Due credit must, however, go to the industry for attempting to reduce the price difference between the plasma-derived and the recombinant clotting factors. The retort of supporters of plasma-derived clotting factors is that the latter are less likely to induce the generation of inhibitors. Indeed, inhibitor development is the bane of haemophilia treatment, as they nullify the usual replacement products. The issue of which product type is the more immunogenic remains unresolved, and is the subject of intense clinical study by both proponents and opponents of this hypothesis.5

Other factors that determine the development of inhibitors are less controversial. These include the genotype and clinical severity of haemophilia, family history of inhibitors, age at first exposure, and the number of exposure days.6 Regardless of the causation, inhibitors further raise the bar in the management of bleeding episodes in haemophiliacs. Available treatments such as recombinant activated factor VII, and factor eight bypassing agent (FEIBA), are effective,7 but very costly. A possible solution to the inhibitor problem is immune tolerance therapy, but most treatment protocols require continued and prolonged exposure to clotting factors. This approach returns us to the fundamental issue – the affordability of clotting factors. We therefore need to find other cheaper and equally safe protocols that are within the reach of most patients in the developing world.

The optimum care of the haemophilia patient is a multidisciplinary, comprehensive effort which should bring together the patient, his family, the haematologist, orthopaedic surgeon, gastroenterologist, physiotherapist, occupational therapist, dentist, social worker, hospital administrators, and support groups. Haemophilia treatment centres like the one in Singapore General Hospital are entrusted with this task of coordinating all activities necessary for the care of haemophiliacs, and must therefore keep all parties engaged and interested.

While the holy grail of haemophilia treatment is to correct the genetic defect through gene therapy, this approach remains an unrealised potential.8 As we reflect on this topic in the 21st century, we should not ask ourselves if we should do more for haemophilia in Singapore. To do so would be disrespectful to our haemophiliacs as we know the answer too well.

REFERENCES