EDITORIAL

Comprehensive Hemophilia Management in India – Miles to Go Before We Sleep

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India contributes to the maximum proportion (10%) of the global population of people with hemophilia (PwH) [1]. The perceived infrequency of the disease stands in sharp contrast to the exhaustive resource management it demands. India has a dismally low mean per capita anti-hemophilic factor (AHF) consumption, surpassed by smaller neighboring countries such as Nepal, Sri Lanka, Indonesia and Thailand [1]. Timely and comprehensive management can enable PwH to lead a productive life that is comparable to their peers [2]. Yet, inadequate knowledge of the disease among the affected families, health professionals, and health planners interposes a major hurdle for progress in hemophilia care [3]. While the West has taken strides towards ensuring a near normal quality of life for PwH, India still reckons with under-diagnosis, administration of plasma due to lack of AHF, and sub-optimal management of musculoskeletal complications.

Nevertheless, the last few years have seen the government taking an active interest in improving hemophilia care in the country [4]. Currently, 74% of the country is covered under a complete or partial AHF support [4]. Jammu and Kashmir, Uttarakhand, Haryana, Rajasthan, Delhi, Uttar Pradesh, Bihar, Orissa, West Bengal, Assam, Gujarat, Maharashtra and Tamil Nadu are the states offering complete AHF support [4]. The supply of AHF is not always consistent though. The advocacy of the Hemophilia Federation of India has played a vital role in ensuring AHF availability for PwH.

This issue of *Indian Pediatrics* carries the Consensus statement of the Indian Academy of Pediatrics (IAP) for the diagnosis and management of hemophilia [5]. Comprehensive guidelines have been published earlier by the World Federation of Hemophilia [6]. Still, recommendations that are adapted to common sociocultural factors and resource-constraints are superior to the *verbatim* adoption of International guidelines. The guidelines have been formulated by experts from across the country and amply elucidate diagnosis, prophylaxis, and management of hemophilia in children [5].

Certain issues unique to our country require emphasis. Genetic counselling of X-linked inheritance and obligate carrier status in females is tricky in the context of patriarchal nature of Indian society. Screening of carrier status in female siblings may be associated with potential stigmatization and reduced prospects of marriage [7]. Secondly, administration and accessibility of AHF under government initiative predominantly caters to on-demand requirement during an acute bleeding episode, and offering primary prophylaxis in PwH is exceptional. The multicentric, prospective MUSFIH study which included an Indian referral centre concluded that episodic AHF replacement does not alter the natural course of bleeding in hemophilia or the musculoskeletal deterioration [8]. As the country steps towards universal access to AHF, the stakeholders in hemophilia care must envisage a paradigm shift from episodic replacement to primary prophylaxis starting from a young age. The IAP guidelines rightly emphasize the superiority of low dose prophylaxis (10-20 U/kg twice- or thrice-a-week) over no prophylaxis [5]. Cost-effectiveness, efficacy in reducing hemarthrosis and improved school attendance with low dose prophylaxis was demonstrated by a randomized trial in a University-hospital in India, though the size of the cohort was small [9]. Increased prescription and administration of AHF would increase the demand and manufacture, accompanied by reduction in costs. Another issue is that the potential utility of AHF vials that have crossed expiry date is seldom discussed. It is noteworthy that the World Federation of Hemophilia (WFH) has issued a statement in this regard: After the expiry date, although the manufacturer can no longer guarantee potency, the WFH is not aware of any safety problems with clotting factor concentrates. Clinical experience reported to the WFH suggests that, under appropriate storage conditions, the loss in potency immediately after the expiry date is

negligible. Any loss in potency is gradual over months and AHF may still be used safely and effectively in many clinical situations after their labelled expiry date [10]. However, one has to note that WFH is not a regulatory agency.

Designated hemophilia centres offering multi-disciplinary management under a single roof are the need of the hour. As emphasized by the guidelines, AHF administration must be complemented by access to physiotherapy and orthopedic care to optimize musculoskeletal function and quality of life [3,5]. Although the authors expound in detail on management of inhibitors in hemophilia, one has limited opportunity to apply these to practice for a typical patient. The bypassing agents required for patients with inhibitors are exorbitantly priced.

Endeavors to disseminate this valuable document to health professionals working at all levels including primary health centers are essential. This could be in the form of half-day workshops conducted under the aegis of the state governments and IAP to provide practical information regarding AHF availability, administration and follow up of PwH. Further, such recommendations should inspire uniform management protocols across major centers as well as multicentric trials to evaluate cost-effective interventions to reduce bleeding episodes and improve musculoskeletal function in PwH. Quality of life measures need to be validated in Asian countries for assessing patient-centric outcomes [3].

There are 'miles to go before we sleep' with regards to management of PwH in India. Systematic efforts should ensure universal availability of AHF and gradually cessation of the use of plasma and blood products [11]. Low dose prophylaxis could be one stepping stone to improve the quality of life of PwH. Comprehensive haemophilia care centers must be established with state-of-art facilities including genetic diagnosis, experts from relevant fields, advanced musculoskeletal interventions and resources to manage challenging patients such as those requiring surgery and those with inhibitors. With collaborative efforts, the day would not be far when PwH live a wholesome life rather than being weighed down by a list of activities that need to be dodged and avoided.

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