Italian consumption of plasma-derived factor VIII after the SIPPET study

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Dear Sir,

We would like to share some reflections on the findings of the SIPPET (Survey of Inhibitors in Plasma-Products Exposed Toddlers) study and the letter published in Blood Transfusion concerning the consumption of plasma-derived factor VIII (pdFVIII) in Italy and the recommendations for its use in people with haemophilia A².

We believe that the SIPPET study, which demonstrated that the risk of inhibitor development in previously untreated patients is lower with pdFVIII than with recombinant factor VIII (rFVIII), did not receive due emphasis, at least in Italy. Googling the word "sippet" we found only a dozen authoritative pages in Italian that cited the study in 2016. Thus, it is not surprising that the study went relatively unnoticed even though published in the New England Journal of Medicine. When a new drug proves to be superior to (old) alternatives, the news is most likely to be presented as an additional example of the benefits of innovation, voicing the need to ensure access to all potential patients even if the new drug is much more expensive. In the case of SIPPET, we have already speculated that since it was the old drug that turned out to be better, in addition to being less expensive, the news went almost ignored¹.

The findings of the SIPPET study had also no consequence for the higher prices of recombinant products: the Italian Medicines Agency did not renegotiate the prices of rFVIII products to get them closer to (if not below) those of pdFVIII.

Considering the limited emphasis on the study's findings, a limited impact on current clinical practice can be expected. There is no doubt that treatment decisions should be shared between doctors and patients. However, the driving force of the doctor-patient relationship should be the best available evidence. In this case, accurate communication of information should include a clear statement that one of the two products, i.e. the pdFVIII, is safer, at least for previously-untreated patients with severe haemophilia A. The fact that the transmission of human immunodeficiency virus and hepatitis B and C viruses via plasma-derived concentrates has been almost completely eliminated should also be part of the communication. An additional issue pertains to the current recommendations of the Italian Association of Haemophilia Centres (AICE, Associazione Italiana Centri Emofilia) which suggest that rFVIII is the product of choice for previously-untreated patients. We found that the guidance of the World Federation of Hemophilia, issued in 2013, "does not express a preference for recombinant over plasma-derived concentrates". Moreover, a meta-analysis of observational studies carried out by AICE, already suggested that the different types of FVIII products were not associated with different risks of inhibitor development. The additional experimental evidence provided by the SIPPET study reinforces the positive benefit-risk profile of the pdFVIII.

We are aware that periodic updating of any recommendations is a long process which requires a careful evaluation (and grading) of the systematically retrieved evidence by a multi-professional panel of experts. In the meantime, when breakthrough studies have the potential impact to redefine current practice, it may be useful for scientific associations to make their position publicly available through specific statements as those endorsed at an international level (e.g. from the World Federation of Hemophilia, the Canadian Hemophilia Society, the European Haemophilia Consortium).

Clearly, several questions are still unanswered. The extrapolation of results to previously-untreated patients with less severe haemophilia and to newly marketed rFVIII not considered in the SIPPET study remains to be investigated; furthermore, additional data should be gathered on longer follow-up and on patients switching between different products.

In conclusion, we support the idea that valid, new evidence, as it becomes available, should be incorporated, as part of a continuous process, in guiding current clinical practice, updating evidence-based guidelines, redefining regulatory decisions and establishing priorities for both commercial and independent research investments. When considering these objectives, the findings of the SIPPET study deserve much greater attention.

Disclosure

The opinions expressed in this article do not necessarily reflect the views of the Authors' institutions.
The Authors declare no conflicts of interest.

References


3) Traversa G, Trotta F. [Head to head comparisons to ascertain whether the new drug is innovative: the case of factor VIII containing products]. Ric & Pra 2016; 32: 164-5. [In Italian.]
