

The role of apheresis in the management of Philadelphia-negative chronic myeloproliferative syndromes following drug shortages

El papel de la aféresis en el manejo de los síndromes mieloproliferativos crónicos Philadelphia negativos ante el desabastecimiento de fármacos

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To the Editorial Board of *Sangre* journal,

Recently, a new problem of drug shortages for the treatment of hematological patients has emerged. In the last 3 months, at least 937 drugs have been affected¹. This time, it concerns hydroxyurea (Hydrea[®], in its usual commercial presentation), indicated for the treatment of patients with sickle cell disease (without another approved option and outside of clinical trials), and patients with myeloproliferative neoplasms. However, this is not the first time this has happened (it occurred previously in 2018). Although the notice was published in early July, Laboratorios Rubió S.A. had informed the Spanish Agency of Medicines and Medical Devices (AEMPS) about “a supply problem of the drug Hydrea 500 mg Hard Capsules” on April 14². This problem is expected to be temporarily resolved by early August through a “foreign drug application.”

In the face of difficulties in the supply of hydroxyurea, both the Federation of Spanish Scientific-Medical Associations (FACME)³ and the Spanish Society of Hematology and Hemotherapy (SEHH)⁴ issued informative notes including SEHH recommendations for patient management. Among them, for patients diagnosed with polycythemia vera, the following was stated: “In situations of hydroxyurea shortage or restriction, it

is temporarily recommended to: - Perform additional phlebotomies to maintain hematocrit < 45%; - Add Anagrelide[®] to control thrombocytosis; - In high-risk patients with a previous history of thrombosis, consider initiating pegylated interferon (if < 50 years), or ruxolitinib (if > 50 years); - In patients with polycythemia vera difficult to control with hydroxyurea, consider switching to pegylated interferon (if < 50 years), or ruxolitinib (if > 50 years); - Optimize general measures for controlling inflammatory symptoms such as itching: use of antihistamines, hygienic-dietetic measures, etc.”³ For the management of adult, adolescent, and pediatric patients older than 2 years with symptomatic sickle cell anemia, the AEMPS recommends “prescribing and adjusting the drug Siklos film-coated tablets as needed.”

We want to congratulate the SEHH for its rapid response to the problem and for obtaining explicit support from FACME. Hopefully, other problems that arise, such as the supply of immunoglobulins, can be resolved as quickly and effectively as this one.

However, we wish to emphasize the therapeutic role of therapeutic erythrocytapheresis as an alternative to phlebotomy, or traditional bloodletting, not only for its greater efficacy but also for its better safety profile, for the return of plasma and other components, and in case

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of a need for volume replacement, becoming an isovolemic technique⁵. This allows young, active patients to lose fewer days of work, minimize travel, and hospital visits, and older, or cardiac patients to undergo the procedure with a safer hemodynamic profile^{5,6}. In addition, in cases accompanied by symptomatic thrombocytosis, it would allow the removal of platelets to reach a safer platelet count (recommendation: grade 2C; category: II)⁷. In 2011, the document endorsed by SEHH entitled “Urgent indications for therapeutic apheresis. Recommendations of the Spanish Apheresis Group”⁸ included symptomatic thrombocytosis in myeloproliferative syndromes among the 10 medical conditions or situations in which “it should be considered as an urgent treatment (urgent indication for apheresis) and instituted within 24 hours following the indication.”

The latest evidence-based guidelines from the American Society for Apheresis again grant the highest evidence possible to the use of therapeutic erythrocytapheresis in polycythemia vera⁷ (recommendation: grade 1B; category: I), and hereditary hemochromatosis (recommendation: grade 1B; category: I), as also mentioned in the pocket guide of the Spanish Apheresis Group endorsed by the SEHH. Both therapeutic cytapheresis regimens are also included in the latest edition of the Manual of the Spanish Group on the Management of Philadelphia-Negative Chronic Myeloproliferative Diseases (GEMFIN)⁹.

Drug shortage is a global problem that affects countries with low, medium, and high incomes and harms all the parties involved (on the financial, social, clinical, and especially humanistic levels). One contributing factor to this situation is the lack of global standardization in the definition of drug shortages. A study conducted in the European Union 20 reported 26 definitions, while the World Health Organization (WHO) found 56 definitions worldwide¹⁰. With this work, we aim to collaborate with WHO plan to mitigate the consequences of this situation by presenting alternative therapeutic strategies supported by high-quality scientific research¹⁰.

Authors' contribution

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Conflicts of interest

None.

Ethical disclosures

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Confidentiality of data. The authors declare that no patient data appear in this article. Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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