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Short Communication

Platelet Transfusion in Patients with Chronic Liver Disease-Associated Severe Thrombocytopenia Undergoing Invasive Procedures in Spain. Challenges and Opportunities during the COVID-19 Pandemic

Isidro Jarque-Ramos[1], Maria Eva Mingot-Castellano[2], Maria Dolores Fernández-Herrera[3] and Alicia Gil[4]*

[1]Hospital Universitari i Politècnic La Fe, Valencia, Spain

[2]Hospital Universitario Virgen del Rocío, Sevilla, Spain

[3]Centro de Transfusión, Tejidos y Células, Huelva, Spain

[4]Omakase Consulting S.L., Barcelona, Spain

***Corresponding Author:** Alicia Gil, Omakase Consulting S.L., Barcelona, Spain.

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Severe thrombocytopenia (TCP), defined as a platelet count < 50 x 10^9/L, is a rare complication affecting approximately 1% of chronic liver disease (CLD) patients. Moreover, in the course of CLD, patients often undergo invasive diagnostic and therapeutic procedures. Severe TCP can increase the perioperative bleeding risk, causing morbidity and cancellations of scheduled interventions [1-3].

There are currently no clinical guidelines in Spain for the management of these patients. Nevertheless, in current clinical practice in Spain, most patients with CLD and severe TCP who undergo invasive procedures receive prophylactic platelet transfusions (PTs) [4], in line with international recommendations [5].

However, PTs can be associated with efficacy and safety problems, as well as their availability being limited by logistical and supply issues [6]. The current COVID-19 pandemic represents a challenge in all aspects, including ensuring the supply of blood products [7,8], adding to the already existing unmet needs in the management of this clinical situation and making it necessary to explore alternatives to PTs [9].

Each Spanish region has its own regional blood bank which distributes platelet therapeutic units (PTUs) to the transfusion services of the hospitals in the region and these report the use of resources to the regional blood banks [10].

The information on the use of PTs in patients with TCP associated with CLD in Spain is very limited. With the aim of obtaining data based on real clinical practice, a study was carried out with 10 haematologists from 5 Spanish regions (Andalusia, Cantabria, Catalonia, Madrid and Valencia): 5 representatives from regional blood banks (Centro Regional de Transfusión Sanguínea de Sevilla, Centro de Transfusión, Tejidos y Células de Huelva, Banc de Sang i Teixits de Catalunya, Centro de Transfusiones de la Comunitat Valenciana, Centro de transfusión de la Comunidad de Madrid), 3 representatives from hospital transfusion services (Hospital Universitario Marqués de Valdecilla, Hospital Clínic i Provincial de Barcelona, Hospital General Universitario Gregorio Marañón) and 2 clinical haematologists (Hospital Universitario Virgen del Rocío, Hospital Universitari i Politècnic La Fe).

A study questionnaire was developed by the authors and sent out to the rest of study participants to collect both quantitative and qualitative data on the use of PTs in these patients across different hospitals and regions. In May 2020, the results were discussed and validated in an online meeting where key challenges and opportunities regarding the use and opportunity cost of PTs were discussed. Data were analysed using descriptive statistics.

Key study results are presented below.

All study participants agreed that platelets represent a scarce resource due to their short shelf-life (average of five days), the lack or decrease of blood donors, the increase in their consumption, and the complexity process involved in their collection, processing, transportation and conservation. Most PTUs (approximately 94%) used in Spain come from several donors ("platelet pool"), while the rest (6%) are obtained from a single donor by plateletpheresis, with about 3% of PTUs being discarded each year.

Ninety percent of platelet consumption is associated with scheduled invasive procedures and the rest (10%) with emergency interventions. However, platelet consumption by hospital specialty service, indication or type of invasive procedure is unknown due to lack of adequate reporting.

Historically, the demand for platelets has increased over time (at a rate of approximately 3 - 5% annually) and is expected to continue due to the increased introduction of complex treatments (e.g. CAR-T therapies, solid organ and hematopoietic transplants, oncological therapies) causing shortages at certain times of the year (e.g. holiday periods). The COVID-19 pandemic crisis has only worsened the already precarious situation [8].

PTs are associated, although infrequently, with a variety of complications in terms of safety, ranging from mild adverse effects such as allergic or febrile reactions to severe adverse effects such as transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI). Given their human origin, there is also the possibility of transmission of bacterial and/or viral diseases, known or unknown. In addition, repeated PTs can lead to refractoriness (lack of response) [6].

Current reporting of both the effectiveness and safety associated with PTs has its limitations: it is not common to measure their real effectiveness in clinical practice, nor is it regularly communicated to blood banks. In addition, there is a lack of protocolization and adequate training among healthcare professionals on good haemovigilance practices and adverse effect reporting.

Although they derive from altruistic blood donations, a PTU costs between 250 - 800€, depending on the centre and method of collection, in line with another recent Spanish publication about cost associated with the management of this condition [11]. The cost of a PT must also take into account the costs associated with logistics, management of adverse events, the performance of compatibility tests, the need to hospitalise the patient the night before the scheduled intervention and the cost-opportunity of potential delays and/or cancellations of scheduled interventions due to the inability of reaching necessary platelet levels among other reasons. The cost associated with managing a patient with severe TCP undergoing an invasive procedure in Spain has been estimated to vary between 2.448,23€ and 3.986,33€ [11].

Despite its low prevalence, patients with severe TCP associated to CLD account for between 5.8% and 7.5% of the total annual consumption of PTUs in Spain. It should be considered that, in these patients, due to the hypersplenism they present, the effectiveness of PTs before an invasive intervention is limited and it is considered not cost-effective.

There is a need for effective and safe prophylactic measures for CLD patients with severe TCP undergoing invasive procedures, as well as options that avoid the use of PTs to ensure the supply and availability of an appropriate platelet stock.

The recent availability of new pharmacological treatment options for these patients, the protocolization of the use of PTs and the adequate cross-specialty training could contribute to increase and ensure the appropriate use of PTs, reserving them for patients and clinical situations without available prophylactic or therapeutic alternatives [12,13].

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