Acute Coronary Syndrome in Patients With Thrombocytopenia. Response

Síndrome coronario agudo en pacientes con trombocitopenia. Respuesta

To the Editor,

In relation to the views expressed in our scientific letter,[1] we would like to mention the following considerations, which we also believe to be of interest. Platelets are essential mediators of hemostasis and thrombosis. The normal platelet count in humans is around 250×10^9/L, but it is still not entirely clear how platelet numbers affect hemostasis and the development of thrombotic events.

How many platelets are needed to achieve hemostasis? Several observations provide evidence that counts as low as 7 to 10×10^9/L suffice to maintain vascular integrity in humans.[2] Before the availability of platelet transfusions, severe bleeding was not observed in patients undergoing chemotherapy while platelet counts remained above 5×10^9/L. Furthermore, in primary immune thrombocytopenia (ITP), spontaneous bleeding does not usually occur (beyond blood extravasation into the skin) even with counts below 10×10^9/L.

Why is it that thrombocytopenic patients with comparable platelet counts do not have the same bleeding risk? Age, genetic susceptibility, environmental factors, traumatic events, comorbidities, and the etiology of thrombocytopenia all have an impact on this question. Following immunologic destruction of the majority of circulating platelets in ITP, a population of young platelets develops. Although these do not change overall platelet function, they may have a disproportionate role in maintaining hemostasis when platelet count is very low.[3] Nonetheless, this population of young platelets is not produced in acute thrombocytopenia with a central origin, such as acute leukemia or bone marrow aplasia. Platelet functional defects, rather than thrombocytopenia, are the main cause of the bleeding phenotype in hereditary thrombocytopenia, and the same is true in uremia and in ITP following administration of nonsteroidal anti-inflammatory drugs or antiplatelet agents. In contrast, the imbalance between prohemostatic and antihemostatic factors in liver disease, although abnormal, can ultimately achieve a maintained hemostatic balance.

There is less certainty regarding the relationship between thrombocytopenia and thrombosis. How many platelets are needed to form a pathological clot that leads to ischemia? That is: Can thrombocytopenia protect against thrombosis? Studies in murine models have shown that with 10% to 30% of the normal platelet count, thrombosis can occur in small, medium, and large vessels.[4] In humans, an increase in thromboembolic risk has been observed in ITP. Why do ITP patients experience stroke or acute coronary syndromes, which are not seen in other acute thrombocytopenias? The answer may be related to the release of huge amounts of highly thrombogenic microparticles during immunologic platelet destruction. Then, should primary prophylaxis be used in patients with ITP and significant cardiovascular risk factors? Which antiplatelet agents and what platelet counts would be safe in this situation? And if thrombosis occurs, how can we treat it without dangerously increasing the risk of bleeding?

In clinical practice, there is considerable experience but little published information to respond to these questions. Clearly there is a need to create guidelines based on the most robust evidence available to provide recommendations on appropriate treatment for these patients.

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