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Commentary: We need to know more about erythropoietin

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CENTRAL MESSAGE

An important case report is presented of a Jehovah's Witness CABG patient with submassive thrombosis after treatment with high-dose EPO and parenteral iron.

Murillo-Berlioz and colleagues[1] present a case report of thrombosis after coronary artery bypass graft surgery in a patient who was a practicing Jehovah's Witness (JW). Their patient, who was without known preoperative thrombosis risk, was treated preoperatively with parenteral iron, folate, vitamin B12, and 8 daily subcutaneous doses of epoetin (EPO) Alfa-epbx 300 units/kg. The patient suffered submassive venous plus arterial thromboses on postoperative day 10, having doubled her platelet count to 424,000 on admission for thrombectomy. Hypercoagulable workup was negative. EPO is known to increase platelet as well as red cell production.

EPO is a hypoxia-induced hormone produced in the kidney that stimulates hematopoiesis in the bone marrow. As a therapeutic agent, recombinant EPO is used in treating various types of anemia, including anemia of end-stage renal disease and cancer-related anemia on chemotherapy. EPO use in heart surgery was never approved by the Food and Drug Administration based on a negative randomized controlled trial of low-dose EPO in 1997.[2] There has not been another cardiac surgical randomized controlled trial since that time. However, there have been numerous reports and case series using high-dose EPO in patients who are JW and others in whom red cell transfusion is not an option—as part of a multidisciplinary blood-conservation regimen focused on enhancing red cell mass and on reducing blood loss.

In a 144-patient retrospective case comparison study of cardiac surgical patients who were JW, Tanaka and colleagues[3] did not report increased thrombosis with the use of EPO. They presented evidence that enhancing red cell mass with preoperative erythropoietin and iron therapy to a target hemoglobin level of 12 g/dL is associated with a reduction in major adverse events in patients refusing blood transfusion.

In an editorial for the study of Tanaka and colleagues in the *Journal* we asked "why aren't we doing this for everyone?"[4]—meaning a multidisciplinary blood-conservation regimen. We also called for further comprehensive study of patients who are JW undergoing heart surgery with such blood-conservation methods as used in this present report by Murillo-Berlioz and colleagues. Murillo-Berlioz and colleagues will no doubt be cited in the future revisions of guidelines for blood conservation in cardiac surgery.[5,6]

The Society of Thoracic Surgeons database and other national registries would be ideal places to gather risk–benefit data to inform future guideline development on the use of EPO in cardiac surgery. Murillo-Berlioz and colleagues report an important critical event but cannot answer the questions raised. For that, the need for robust data is clear. The accuracy of future guideline development would be enhanced by it.

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Disclosures: The author reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication July 24, 2020; revisions received July 24, 2020; accepted for publication July 24, 2020; available ahead of print July 31, 2020.

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JTCVS Techniques 2020;4:158-9

2666-2507

https://doi.org/10.1016/j.xjtc.2020.07.024

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