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Patient blood management interventions do not lead to important clinical benefits or cost-effectiveness for major surgery: a network meta-analysis

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Patient blood management (PBM) or blood saving programmes are a set of interventions aimed at reducing bleeding and the need for transfusion, in order to improve clinical outcomes (decrease morbidity and mortality). In order to compare the scientific evidence for two interventions (for example, tranexamic acid [TXA] vs placebo in bleeding) systematic reviews and meta-analyses can be useful. However, there are scenarios (as in PBM) in which we find multiple interventions for the same disease (for example, bleeding in major surgery). When comparing the scientific evidence for three or more interventions (for example, TXA and administration of iron vs placebo in bleeding in major surgery) a more appropriate approach is that of the “network meta-analysis” (NMA), also called an analysis of multiple comparisons. NMAs should include randomised controlled trials (RCTs), that are not heterogeneous (¹²) (variability between the effects of the treatments that are combined is considered high heterogeneity if >75%), but are similar (similar population, intervention, comparator, objectives and study design) and consistent (when the effect analysed in direct comparisons is similar to that obtained in indirect comparisons).

Returning to the article to comment, the authors posed the following questions (objectives):

- A Is PBM effective? Does it decrease bleeding, transfusion and re-operation for bleeding?
- B Is PBM effective? Does it reduce the incidence of organ dysfunction and mortality?
- C Does the use of resources decrease? Does it decrease ICU and hospital stay?

To address these questions the authors used a NMA, 393 RCTs (last search June 1, 2019) with 54,917 patients were included. The PBM strategies included two or more of the following interventions vs placebo:

- √ Administration of oral or intravenous iron prior to surgery
- √ Surgical blood-saving devices (cell-saver type)
- √ Use of antifibrinolytic drugs such as TXA
- √ Restrictive policy for the transfusion of packed red blood cells (RBCs)
- √ Use of transfusion algorithms directed by viscoelastic test

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The answers they found are as follows:

- PBM is effective (but with very heterogeneous studies) in terms of blood loss assessment and transfusion risk. Effective because there was a decrease in:
 1. Blood loss. RR: -1.06 (95% CI: -1.16 to -0.96), $I^2 = 94\%$
 2. RBC transfusion risk. RR: 0.6 (95% CI: 0.57 to 0.63), $I^2 = 77\%$
 3. Transfusion of fresh frozen plasma (FFP). RR: 0.74 (95% CI: 0.63 to 0.86), $I^2 = 49\%$
 4. Platelet transfusion. RR: 0.88 (95% CI: 0.78 to 0.99), $I^2 = 18\%$
 5. Need for re-operation. RR: 0.85 (95% CI: 0.74 to 0.97), $I^2 = 0\%$

- PBM is not effective (with very homogeneous studies) because there is no reduction in the incidence of:
 1. Mortality. RR: 0.93 (95% CI: 0.81 to 1.07), $I^2 = 0\%$
 2. Renal failure. RR: 0.97 (95% CI: 0.83 to 1.12), $I^2 = 0\%$
 3. Acute brain injury. RR: 1.00 (95% CI: 0.87 to 1.15), $I^2 = 0\%$
 4. Acute myocardial infarction. RR: 0.95 (95% CI: 0.84 to 1.06), $I^2 = 0\%$
 5. Infection and sepsis. RR: 0.97 (95% CI: 0.91 to 1.03), $I^2 = 9\%$

- PBM reduces ICU and hospital stays but with very heterogeneous RCTs:
 1. Stay in ICU. RR: -0.13 (95% CI: -0.2 to -0.06), $I^2 = 90\%$
 2. Hospital stay. RR: -0.38 (95% CI: -0.5 to -0.26), $I^2 = 87\%$

The authors conclude that PBM does not improve the clinical outcomes of patients with bleeding during major surgery, although it does reduce bleeding and transfusion.

Due to the heterogeneity of the included RCTs, I agree that PBM does not improve clinical outcomes, but we cannot say whether or not it reduces bleeding or the risk of RBC transfusion. It does decrease the transfusion of FFP, platelets and the need for re-operation.

It is clear that high-quality RCTs are still needed to answer some of the questions and to define which is the most optimal set of interventions for PBM in major surgery.