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Bleeding news

Reversal of anticoagulation: Haemostatic efficacy or clinical benefit?

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The growing use of anticoagulants, particularly in elderly patients with multiple comorbidities, has turned its urgent reversal in a common clinical challenge. In this excellent review, Rocca and ten Cate analyse the available antidotes, their mechanisms of action and the evidence supporting their use, highlighting a fundamental issue: **an effective pharmacological reversal does not always translate into a proven clinical benefit.**

Of particular relevance is the analysis of **andexanet alfa**, with an ability to reverse the activity of factor Xa inhibitors, yet some uncertainties surrounding its safety. In the ANNEXA-I trial, andexanet showed an improved haemostatic efficacy compared with the conventional treatment (67% versus 53.1%), but without significantly reducing mortality and with a higher incidence on thrombotic events (10.3% versus 5.6%). Its withdrawal from the US market in December 2025, while retaining conditional authorisation in Europe, illustrates the difficulties in establishing a favourable risk-benefit balance.

In this scenario, **four-factor prothrombin complex concentrates** represent a pragmatic alternative, particularly in cases of severe haemorrhage or emergency surgery. However, their use to reverse the effects of direct oral anticoagulants is still based on limited evidence, and neither the optimal doses nor their comparative efficacy against specific antidotes have been conclusively established.

The review also points out that even well-established treatments, such as protamine or idarucizumab, still have unresolved issues, particularly related to dosing, monitoring and a potential rebound of anticoagulant activity.

From the perspective of perioperative haemostasis, the **lack of evidence available for patients requiring emergency surgery**—an under-represented population in clinical trials—warrants particular attention. Furthermore, there are still significant limitations in monitoring reversal. Viscoelastic testing and point-of-care systems offer interesting possibilities, but they still require specific validation for this purpose.

The main strength of this article lies in its balanced analysis of the efficacy and safety of available treatments, but since it is a narrative review, it does not provide a systematic assessment of the certainty of the evidence. Besides, a better integration of antidotes would be desirable into overall strategies to treat haemorrhage, including control of the source of bleeding and the resumption of anticoagulation.

Thus, this review reminds us that reversing anticoagulation doe not necessarily improve the prognosis. The real challenge lies in identifying which patients benefit from reversal, selecting the most appropriate strategy, and ensuring that the attempts to control a haemorrhagic complication ends up leading to another complication of a thrombotic nature.

The availability of increasingly specific antidotes is undoubtedly a step forward, but their use should always be guided by clinically relevant outcomes and not exclusively by the normalisation of analytical parameters.