A brain haemorrhage during anticoagulant therapy: what therapy next?

We read with interest the articles by Ntaios and by Ricci et al. concerning pros and cons of restarting oral anticoagulants (drugs that work to prevent the coagulation (clotting) of blood) after intracerebral hemorrhage. While we appreciate the review of available data that both Authors provided, we were surprised that neither of them took into consideration the INR value (assays used to determine the clotting tendency of blood) at the time of bleeding on warfarin as a factor in deciding whether or not to resume anticoagulation.

It is well known that bleeding risk with warfarin increases with INR augmentation, and that an INR lower than 3 (or 3.5 in patients with mechanical prosthetic heart valves) is sufficient to provide an effective anticoagulation with reasonable bleeding risks in most patients. Very often bleeding during warfarin therapy occurs when INR exceeds the therapeutic window (between 2 and 3 in patients with atrial fibrillation). For example, Anthony et al. found that 50% of patients who presented to the Emergency Room for bleeding while on warfarin had INR above the therapeutic range. Similarly, Uygungül et al. studied warfarin users admitted to the Emergency Department. They found that those who were admitted for bleeding had a significantly higher INR than those who were admitted for causes other than bleeding.

An INR above the therapeutic target can be considered a modifiable risk factor for bleeding while on warfarin, and the possibility of modifying it should be taken into account when deciding if and when to restart warfarin after cerebral bleeding. If the bleeding had occurred at a time when INR was significantly elevated above the therapeutic range, restarting warfarin while attempting to improve INR control should be a viable option. As an example, attempts to obtain a better control on INR may include a more frequent laboratory check of INR, or the use of one of the computerized programs that assist in warfarin dosing. This is true among else in patients with non-valvular atrial fibrillation. However, we agree with Ntaios that in this specific group of patients one might consider replacing warfarin with a novel anticoagulant, because they have a lower day-to-day variability in anticoagulant effect and, perhaps also for this reason, they carry a bleeding risk lower than warfarin. However, in patients with non-valvular atrial fibrillation use of the novel anticoagulants is not always possible. For example, in Italy the National Health System provides the novel anticoagulants only to atrial fibrillation patients having a HAS-BLED score greater than 3, or who cannot for various reasons undergo warfarin treatment. In atrial fibrillation patients who cannot receive the novel anticoagulants, restarting warfarin while attempting to better control INR is a viable option, too.

We agree that controlled, randomized trials are lacking, thus no strong evidence-based recommendations can be given. However, for the time being we believe that in making the difficult decision on whether or not to resume warfarin in a patient who had cerebral bleeding one cannot avoid taking into consideration what was the likely cause of the bleeding. If a modifiable cause is

found, removing it may make restarting anticoagulation a safe option. With this in mind, we suggest that in patients who (1) had a cerebral bleeding on warfarin (2) had an INR above the therapeutic range at the time of bleeding and (3) no other major bleeding risk factors are apparent, warfarin may be restarted while implementing a strategy to better control INR value. Alternatively, and if possible, the new oral anticoagulants provide a viable option in these patients, too.

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