Novel Oral Anticoagulants and Antiplatelet Agents in Vascular Surgery: Where do we Stand Today?

Arterial and venous thrombosis affect a significantly underreported number of people worldwide, leading to million deaths per annum [1]. Cardiovascular disease is the leading cause of death, especially in low- and middle-income population [2]. Venous thromboembolism (VTE) is the cause for half a million deaths per year in the European Union, alone.

A plethora of different mechanisms involving the coagulation cascade and platelets play various roles in thrombosis. The coagulation mechanism consists of activation, adhesion, and aggregation of platelets along with deposition and maturation of fibrin.

For decades, acetylsalicylic acid, warfarin and heparin were the only available pharmaceutical agents to prevent arterial and venous thrombosis. Despite the fact that these medications saved millions of lives, they had – and still have - significant side effects; warfarin had a narrow therapeutic window, the need for regular monitoring, risk of bleeding and numerous interactions with other medication. Unfractionated heparin also requires continuous monitoring and had a short half-life. Acetylsalicylic acid is available for oral administration and its intravenous form is only a precursor molecule and not an active ingredient.

The development of novel pharmaceutical agents answers to the clinical need for better control over the anti-thrombotic effect, improved hemodynamics and safer outcomes for patients.

Novel oral anticoagulants (NOACs or DOACs from Direct Oral Anticoagulants) and novel antiplatelets (NAs) are new additions to the clinical armament for cardiac and vascular patients. These new drugs have been developed in order to address the limitations of the previous generation of anti-thrombotic medication. They do not need routine monitoring and interact less frequently with other medications. In 2010, the Food and Drug Administration (FDA) approved its first NOAC, dabigatran (Boehringer Ingelheim) [3]). By 2015, FDA had approved three more NOACs: rivaroxaban (Johnson & Johnson and Bayer Healthcare AG), apixaban (Bristol-Meyers Squibb & Pfizer Inc.); and edoxaban (Savaysa/Lixiana, Daiichi Sankyo). At present, clinical data and patients’ outcomes are being collected and the different NOACs and NAs are supported by different levels of evidence leading to fine differences in national guidelines on their use [4-7].

Despite the fact that the clinical use of most NOACs and a number of NAs is already regulated by the continuously updated guidelines, questions remain about the safety and the indication of their use on vascular patients presenting with peripheral arterial disease (PAD), VTE, and symptomatic or asymptomatic carotid disease. Vascular patients frequently present with various synchronous comorbidities and are often required to undergo more than one surgical or endovascular procedures in relatively short periods of time. As a result, the perioperative management of NOACs and NAs is still under careful assessment for this group of patients. Krasinski et al. [8] examine the administration of NOACs in patients with chronic kidney disease (CKD), a comorbidity frequently present in vascular patients.

PAD affects approximately 10% of patients over 60 years of age [9]. Until recently, patients affected by PAD have traditionally been prescribed antplatelets (acetylsalicylic acid and/or clopidogrel) and in cases of intermittent claudication cilostazol. Koutsoumpelis et al. [10] provide us with the latest updates on how the COMPASS and other trials are currently altering our existing knowledge on pharmaceutical treatment of PAD. The COMPASS trial mentions for the first time that adding a NOAC (rivaroxaban) to the established treatment of PAD improves patient outcomes, but it leaves some pending questions on which subgroup of patients are benefited the most [11]. Tsilimigras et al. [12] comment further on the clinico-economical impact of the COMPASS trial.

It is essential for anaesthesists and vascular surgeons to know the properties of NOACs and NAs. The perioperative period is associated with significant prothrombotic and bleeding risks, both potentially leading to complications or death, if not efficiently and timely addressed. The peri-operative management of the NOACs in arterial surgery is discussed by Kouvelos et al. [13]. Regarding the peri-operative management of NOACs in venous procedures, Drebes et al. [14] focus on interventions for ilio-femoral deep vein thrombosis.

As long as NOACs are concerned, peri-operative and post-traumatic bleeding is thought to be more complicated to control compared to traditional anticoagulants, although recent publications do not support this hypothesis [15]. Not all NOACs have a fully reversible effect or a direct inhibitor of their action. The management of post-traumatic or peri-operative bleeding is addressed in two publications by Zimmermann et al. [16] and Palaiodimos et al. [17].

Resistance to older antplatelet agents is well known and recorded in previous publications [18]. Markel et al. [19] described how this resistance can be quantified and measured. NAs are capable of addressing this limitation of classic antplatelet agents and providing better outcomes for vascular patients. Patelis et al. [20] provides an update on the use of already established NAs and also reports on experimental NAs.

REFERENCES


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