COMENTÁRIO EDITORIAL

João Rocha Neves
Department of Biomedicine - Unity of Anatomy, Faculdade de Medicina da Univ. do Porto, Portugal
Department of Angiology and Vascular Surgery, Centro Hospitalar Univ. de São João, Porto, Portugal
Department of Surgery and Physiology, Faculdade de Medicina da Univ. do Porto, Portugal

Gaps in evidence and role of direct oral anticoagulants

This current issue of Revista Portuguesa de Cirurgia Cardiotorácica e Vascular presents a critical review on the current evidence and clinical utility of Direct Oral Anticoagulants (DOACS). Antunes L.[1] sheds light in areas who are still fuzzy on the literature, as the subject cancer and deep venous thrombolembolism.

The author concludes DOACs are the first option of treatment in cancer patients with low risk of bleeding (exclusion of oesophageal, gastrointestinal and genitourinary cancers), and LMWHs in patients with high risk of bleeding, referring to the randomized trials and guidelines on the subject.[2,3]

In other several indications such as atrial fibrillation, DOACs almost completely replaced VKA for treating and preventing first or recurrent events. However, there seems to be pathologies where DOAC are inferior to VKA, and conditions where a gap in evidence seems deep-seated.

Given the paucity of information regarding the use of DOACs, observational data is vast and should be viewed as hypothesis-generating. Exposing a crippling failure of these drugs, current practice guidelines also stipulate that DOACs are contraindicated in patients with mechanical heart valves largely on the basis of a single phase 2 trial of dabigatran which was stopped prematurely because of excess harm associated with this oral antithrombin.[4]

Conditions such as severe Antiphospholipid syndrome or extreme obesity presumably require more care on the selection of the specific antithrombotic treatment. On this matter, the author addresses specifically the failed TRAPS Trial.[5] The study reports the use of rivaroxaban in high-risk patients with antiphospholipid syndrome was associated with an increased rate of events compared with warfarin, thus showing no benefit and excess risk. Antunes points some of the reasons why the trial failed, regarding the higher levels of anticoagulation practised with warfarin. Perhaps higher doses of DOACs, or a twice daily DOAC could perform differently.

Currently, there are five DOACS in clinical use, including four factor Xa inhibitors (apixaban, edoxaban, betrixaban, and rivaroxaban), and one direct thrombin inhibitor (dabigatran). None of these has EMEA approval for use in children. The preliminary results from EINSTEIN Junior (NCT02234843), revealed equivalent efficacy and safety profile of rivaroxaban vs warfarin in a paediatric population with VTE. The final manuscript is yet to be published, thus the medical community awaits anxiously.

A broad discussion of results within the medical community has been standing out for the past 10 years regarding anticoagulation, and no area has been the target of so much RCTs, fortunately, since anticoagulation is an appealing resource in a panoply of specialties. Science and clinical interests have been correctly blended with pharmaceutical interests, however, the first DOAC patent is going to fall in 2021, which means clinicians will have to make an additional and joint effort to fill the recurring and ever-growing gaps in evidence with quality investigation. More pragmatic randomized trials are necessary, beyond doubt, knowledge comes with experience.

REFERENCES

1. Antunes L. New oral anticoagulants (NOACs) are the gold standard in Venous Thromboembolism. Rev Port Cir Cardiotorac Vasc. 2020;27(1)
2. Young AM, Marshall A, Thirlwall J, Chapman O, Lokare A, Hill C, et al. Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D). J Clin Oncol. 2018;36(20):2017-23.
3. Li A, Garcia DA, Lyman GH, Carrier M. Direct oral anticoagulant (DOAC) versus low-molecular-weight heparin (LMWH) for treatment of cancer associated thrombosis (CAT): A systematic review and meta-analysis. Thromb Res. 2019;173:158-63.
4. Eikelboom JW, Connolly SJ, Brueckmann M, Granger CB, Kappetein AP, Mack MJ, et al. Dabigatran versus warfarin in patients with mechanical heart valves. N Engl J Med. 2013;369(13):1206-14.
5. Pengo V, Denas G, Zoppellaro G, Jose SP, Hoxha A, Ruffatti A, et al. Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome. Blood. 2018;132(13):1365-71.