PREDMET:

Najnovija meta analiza koja je uključivala 28 RCT i 196 761 pacijenata otkrila je značajne razlike u KV sigurnosti između oralnih antikoagulanasa

"Dragi doktore .....,

Tokom moje posljednje posjete, pokazali ste zainteresovanost za neka pitanja, pa Vam dostavljam korisne informacije. Nadam se da će Vam biti zanimljive. Ako budete imali dodatna pitanja, slobodno kontaktirajte mene ili naš odjel za pružanje informacija o lijeku (medinfo.ba@bayer.com).

U ovom članku predstavljeni su rezultati meta analize o riziku od akutnog infarkta miokarda povezanog sa antikoagulantnim terapijama. Rezultati su pokazali da je Xarelto povezan s najnižim rizikom.

Ključne tačke:

- Rezultati koji se odnose na kardiovaskularnu sigurnost različitih DOAK-a bili su neuvjerljivi pa je meta analiza, kako bi se riješila ova sporna situacija, kombinovala rezultate 28 randomizirano kontrolisanih ispitivanja koja su uključivala skoro 197 000 pacijenata.
- Urađeno je opsežno istraživanje literature i poređenje između grupa liječenih DOAK i kontrolnih grupa (placebo, aspirin, VKA). Primarna krajnja tačka bila je frekvencija MI analizirana Bayesovom hijerarhijskom komparativnom meta analizom mjesovitog liječenja.
- Vaskularna doza rivaroksabana obrađena je odvojeno jer sigurnosni profil i efikasnost antikoagulansa može ovisiti o dozi.
- Rizik od MI je najniži kod rivaroksabana, pa onda kod apiksabana i edoksabana, dok je najveći rizik kod VKA i dabigatrana. Izračunata vrijednost da će biti prvi najbolji izbor liječenja bila je 61,8% za rivaroksaban.
- Autori zaključuju da razlike u riziku od MI mogu uticati na izbor liječenja i trebaju biti uzete u obzir u razvoju personaliziranih antitrombocitnih režima.

Publikacija

Kupó, P et al. Direct anticoagulants and risk of myocardial infarction, a multiple treatment network meta-analysis. Angiology. 2020 Jan;71(1):27-37. doi: 10.1177/0003319719874255

LONG ABSTRACT

Direktni oralni antikoagulansi i rizik od infarkta miokarda, mrežna meta-analiza višestrukih tretmana

Kupó, P; Szakács, Zs; Solymár, M; Habon, T; Czopf, L; Hategan, L; Csányi, B; Borbás, J; Tringer, A; Varga, G; Balaskó, M; Sepp, R; Hegyi, P; Bálint, A; Komócsi, A.

Angiology. 2020 Jan;71(1):27-37. doi: 10.1177/0003319719874255

The cardiovascular safety of long-term anticoagulation therapies is of utmost importance. Due to the lack of direct comparisons, a meta-analysis was performed to assess the safety and efficacy profile of various anticoagulants, including warfarin and direct oral anticoagulants (DOACs). The different DOACs were also compared to each other. Except for dabigatran, DOACs were favourable compared to placebo, aspirin or vitamin K-agonists, with rivaroxaban having the highest net clinical benefit.

Coronary heart disease is a leading cause of death worldwide. The coagulation cascade has an important role in the evolution of acute events, and long-term anticoagulation therapy has been widely used for secondary prevention after acute myocardial infarction (MI). Vitamin K antagonists (VKAs) in monotherapy or in combination with aspirin were found to be superior to aspirin alone for this purpose and had been the choice of treatment. However, since the introduction of direct oral anticoagulants (DOACs) as an alternative treatment option, they became widely adopted as DOACs have been proven to have similar or higher efficacy in preventing ischemic events and similar or lower risk for major bleeding, bleeding-related case fatalities, and intracranial bleeding. DOACs are easier to use as there is no need for regular laboratory monitoring and the chance of drug/food interactions is reduced. However, various DOACs showed different results regarding cardiovascular safety: while rivaroxaban showed favorable outcomes when combined with aspirin (among patients with stable atherosclerotic disease), and it also reduced ischemic risk in ACS, some signals were detected in prior studies regarding dabigatran in relation to MI risk associated with the treatment. Still, the results are not conclusive. As direct comparative trials are not available, the authors performed a Bayesian multiple treatment network meta-analysis to summarize the available information from trials and to evaluate the cardiovascular safety of DOACs.

For this, medical literature databases were manually searched for randomized clinical trials assessing the clinical safety and/or efficacy of anticoagulant regimen including at least one DOAC (dabigatran, rivaroxaban, apixaban, edoxaban); including at least one control group either treated with oral anticoagulants, antiplatelet agents or placebo; and reporting the frequency of MI or the rate of acute coronary syndrome. The primary endpoint was the frequency of MI, analysed in a hierarchical Bayesian mixed-treatment comparison meta-analysis. Inferences were based on random-effects models, as these account better for interstudy differences, while fixed-effects

models were used as a sensitivity test. Subgroup analyses were carried out based on identical risk groups and the MI definition. The secondary endpoint was overall mortality. The incidence of major bleeding was measured to assess safety.

A total of 28 studies (trials in nonvalvular atrial fibrillation, including those scheduled for elective cardioversion, trials in patients after embolic stroke of undetermined source, trials in VTE- pulmonary embolism or deep vein thrombosis, as well as cases at high risk for CHD including ACS), involving nearly 197 000 patients in total were included and divided into 8 groups according to the applied anticoagulant (control arm: placebo, aspirin, or warfarin; treatment arm: dabigatran, edoxaban, apixaban, rivaroxaban, rivaroxaban in vascular dose). Most direct comparisons were available between dabigatran or rivaroxaban versus warfarin. Analysis of bias revealed high quality of the information with low probability of bias and no obvious publication bias.

The total number of MIs in the studies was 3554, the lowest rate observed in the VKA arm of studies (1.25%), the highest rate in the placebo arm (4.55%). Results were consistent within treatment groups, but DOAC subgroups showed high heterogeneity.

Apixaban was associated with a 24% relative risk reduction of Mis compared to dabigatran, and VKAs with a 19% reduction compared to dabigatran.

Rivaroxaban reduced the relative risk of MI when compared to either dabigatran (31%) or placebo (21%).

Rivaroxaban in vascular-dose was handled separately because the safety and efficacy profile of anticoagulants might be dose-dependent, however, similar results were obtained when compared to either placebo (16%) or dabigatran (27%).

When mortality or major bleeding were considered, treatment ranking was the same with MI or mortality, while there was opposite tendencies with the risk of major bleeding (the higher the rank for MI, the lower the rank for major bleeding) – although this was not significant.

The computed probability of being the first best choice of treatment was 61.8% for rivaroxaban, 17.4% for vascular dose rivaroxaban, and 14.2% for apixaban. The lowest probability was for placebo and dabigatran, i.e. <0.1%.

The results of this analysis support the notion that anticoagulants can reduce ischaemic events, and that DOACs have a potential as preventive therapy, however, this potential is heterogeneous among various DOAC agents. This extended analysis revealed that important differences in MI risks were found, favouring the most rivaroxaban, followed by apixaban and edoxaban while it is highest for VKA and dabigatran.

Sažetak karakteristika lijeka je javno dostupan na Internet prezentaciji Agencije za lijekove BiH, odnosno dostupan je na sljedećem linku:

http://lijekovi.almbih.gov.ba:8090/FileDownload.ashx?attachID=420447