Direct Oral Anticoagulants For The Treatment Of Venous Thromboembolism: An Umbrella Review Of Meta-Analysis And Economic Studies

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Introduction: Direct oral anticoagulants (DOACs) are the recommended standard of acute and extendend treatment of venous tromboembolism (VTE) based on similarly effective anticoagulation with the same or reduced risk of bleeding compared with warfarin.
Objectives: To present a comprehensive review of accumulated evidence from meta-analysis and economic studies for each DOAC and to consider the potential implications these agents have for the management of VTE.
Methods: A systematic review of meta-analysis comparing DOACs to VKA and placebo and economic studies identified from searches of MEDLINE, EMBASE and Cochrane databases with no restriction on year/language. Two authors independently screened titles/abstracts for inclusion and methodological evaluation.
Results: We identified 23 meta-analysis; 17 compared DOACs to warfarin. Most of them found similar efficacy and risk of bleeding; two reported reduction in mortality and recurrence of VTE with DOACs (Castellucci-2013, Sardar-2013). Chai-Adisaksopha-2014 concluded that DOACs are associated with lower risk of major, intracranial and clinically relevant bleeding, without increasing in gastrointestinal hemorrhage; Sardar-2013 showed increased risk of bleeding with dabigatran and rivaroxaban and Hirschl-2014. is conclusive that this is smaller with the use of apixaban. Di Minno-2015 reported the same efficacy of DOACs as warfarin in overweights patients . Four meta-analysis compared DOACs to warfarin and placebo, showing that DOACs are associated with lower risk of recurrence of VTE, being apixaban the safer therapy with respect to risk of bleeding.
We analized 14 economic studies of DOACs performed in USA and United Kingdom. Six of these were cost-effectiveness studies; three reported rivaroxaban as the most cost-effective strategy. Edoxaban was analyzed in other trial (Preblick-2015), showing an equally cost-effective option and Lanitis-2016 reported apixaban within DACOs as the treatment with better cost-effectiveness profile with respect to acute VTE treatment and prevention of recurrence.
We found 3 cost-analysis studies in which rivaroxaban was associated with lower hospitalization rate, recurrence of VTE and risk of bleeding comparing to warfarin (Mody-2014, Bookhart-2014, Patel-2015) but a cost-utility study evidenced that dabigatran was the dominant strategy compared with rivaroxaban.
One economic model (Amin-2014) documented that DACOs were associated with lower medical costs compared to warfarin providing the greatest reductions with apixaban.
Conclusions: Current evidence form meta-analysis and economic studies demonstrates the safety and efficacy of DOACs in the treatment of VTE compared to standard therapy, due to lesser bleeding complications. DOACs represent the most cost-effective strategy in high income countries; the evidence regarding this outcome is scarce in developing countries.

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