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SHORT COMMUNICATION

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Pros and Cons of Direct Oral Anticoagulants *versus* Vitamin K Antagonist

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Introduction

Direct Oral Anticoagulants (DOSCS) had become a standard practice since been approved in 2010 and almost replaced warfarin in medical and surgical patients [1]. Unlike warfarin, DOSCS have a set dose and do not require regular international normalization ratio blood testing, they also have faster onset and offset action which make it safer. Warfarin has a long half-life and narrow therapeutic window, necessitating regular blood monitoring and is a very common cause of iatrogenic hospital admission, management of perioperative anticoagulation for patients on direct anticoagulants became simple, standardized and patient does not need to hospital admission before elective surgery.

Discussion

DOSCS either antithrombin (dabigatran) or factor Xa inhibitor (apixaban, rivaroxaban, edoxaban and betrixaban)

Patient make a quick decision to go for DOSCS anticoagulation over warfarin as doses are fixed, and no need to do blood testing for monitoring and there is decreased risk of bleeding especially hemorrhagic stroke [2], again switching from warfarin to DOSCS is easy and safe given that the half-life of dabigatran, apixaban, edoxaban and rivaroxaban is 12 hours in the presence of normal kidney function, where betrixaban is 24 hours [3].

Dabigatran is 85% renally excreted that is why half-life is up to 48 hours in patients with creatinine between 30-50ml/min, other advantage of DOSCS that when going for procedures with low risk of bleed (endoscopy with no biopsies or dental work) there is no need to cease DOSCS.

Procedures with mild risk of bleed in the presence of normal kidney and liver function, DOSCS will be stopped only 24 hours before and restarted 6 hours after surgery [4].

High bleeding risk like spinal surgery, patient need to stop anticoagulants 3-5 days and restart 48 hours after the procedure [5] bleeding risk can be assessed by age, impaired kidney function, concomitant use of non-steroidal anti-inflammatory, antiplatelet, history of hemorrhagic stroke, dissecting aneurism, bleeding or coagulation disease, uncontrolled hypertension, liver failure, use of cytochrome P450 induce medication [6].

In October 19, 2010 FDA approval had been granted for dabigatran for non-valvular AF, treatment and prevention of DVT and PE, thromboprophylaxis after total hip replacement, off-label indication includes thromboprophylaxis after total knee replacement and after PCI with non valvular AF, rivaroxaban was granted approval for after total knee and hip replacement, prophylaxis in ill medical patients, and peripheral vascular diseases, apixaban granted approval for same indication [7].

DOSCS do not bind with platelet factor 4 (anti heparin) that is why it does not cause HIT (heparin induced thrombocytopenia), in fact it is a treatment option for HIT [8].

Patient with high BMI (40) will have less exposure of the drugs which increase thrombosis risk and patient with low BMI will have more exposure for the drugs and increased the bleeding risk [9].

Patient who started on dabigatran will have less risk of brain hemorrhage and probably slightly increase in gastrointestinal bleed with the higher dose 150mg BD compared with warfarin [10]. Common side effect of dabigatran is dyspepsia and gastroesophageal reflux [11].

With direct factor X inhibitor, drug monitoring can be done by measuring anti factor X inhibitor specially in patients with extreme weight, slim Asian patients should not prescribe lower doses as the Korean study did not support that [12]. Patient who develops non-life-threatening bleed due to DOACs, do not require reversal treatment because half-life of DOACs is short (12 Hours) especially in the presence of normal kidney and liver function [13]. In life threatening bleed due to dabigatran, patient can be treated with hemodialysis or hemofiltration. Because dabigatran has 35% protein bound and the rest is unbound [14]. Idarucizmab which is monoclonal antibody that can act as antidote and bind to dabigatran and clear it from the circulation within 60 seconds [13].

Bleeding from factor X an inhibitor cannot treat with dialysis or

hemofiltration because of tightly bound to the plasma protein and can't be cleared [14] from the circulation. Recombinant human factor X (andexnet alfa) was approved to reverse bleed due to apixaban and rivaroxaban in life threatening situation, it is an expensive medication and not available in resource limited hospitals. Prothrombin complex is widely used instead, although it is not FDA approved yet [15]. DOACs are not approved and strictly contraindicated in patient with mechanical valves. Patients with antiphospholipid syndrome, in pregnant or breast-feeding women.

Conclusion

Direct non vitamin K antagonist are widely prescribed by clinicians for patients who deemed before unsuitable for vitamin K antagonist because they can't afford to have regular blood monitoring, drug interactions, unpredictive INR, patients who develop complication like skin infarction due to protein C deficient, or intracranial hemorrhage,

However, ODAC's are not suitable for patients with severe kidney or liver impairment. Although the advantages of DOSCs over warfarin are modest, most guidelines recommend direct oral anticoagulants because they are easy to use and have superior safety over warfarin. Prescribing direct oral anticoagulant for older people with atrial fibrillation and DVT has increased and even for people with risk of non-serious falls [16].

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