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Newsletter

Imagine that your mother, father, sibling or close friend is diagnosed with an acute DVT. Knowing you are who you are, and that you do what you do, they obviously call you for advice. What medicine should they be on? They ask questions like: "Is Coumadin safe, isn't that rat poison? What about Xarelto or Eliquis, I've seen those 1-800 bad drug commercials for those?" So what do you tell them and if they are the analytical, research minded people, what evidence do you have to support your choices?

As Vitamin K antagonists (VKA) such as warfarin have been out long before I even considered medical school, I will only mention them briefly. It should be noted however, that the current Chest guidelines recommend the Novel Anticoagulants (NOACs) over VKA for DVT in non-cancer patients and in cancer patients LMWH is recommended over the other options.

When using VKA therapy, it should be started with parenteral therapy (lovenox, UFH or fondoparinux). The parenteral therapy should be continued for 5 days and until the INR is greater than or equal to 2.0 for 24 hours. We all know that Coumadin has been out for a long time. It is effective and reversible but requires the initial parenteral treatment with lovenox or others. Furthermore, Coumadin requires ongoing monitoring and therapeutic levels can be affected by diet and by many prescription and otc drugs.

We currently have four novel anticoagulants (NOACs) available as options for treating DVT. Dabigatran exolate (Pradaxa) is a direct thrombin inhibitor. Rivaroxaban (Xarelto), Apixaban (Eliquis) and Edoxaban(Savaysa) are all factor Xa inhibitors.

For dabigatran (Pradaxa) and edoxaban (Savaysa) it is recommended that a parenteral anticoagulant (lovenox, UFH) be given before initiation, just like with VKA therapy. Conversely, rivaroxaban(Xarelto) and apixaban (Eliquis) are approved for initial therapy without any need for parenteral anticoagulants. As xarelto and Eliquis do not require initial parenteral therapy, they tend to be the most common first choices for initial outpatient DVT therapy. All of the Xa antagonists have relatively short half-lives (7-14 hours). Xarelto has the advantage of once daily dosing so compliance may be better but it has 80% renal excretion and therefore must be used with caution in patients with renal failure.

Studies have not shown any of the NOACs to be significantly better than the others at preventing recurrent DVT or PE but currently only dabigatran has a reversal agent so

risk of GI or other major bleeding remains a concern. In reference to all major bleeds, apixaban (Eliquis) had significantly lower rates of bleeding than either rivaroxaban (xarelto) or dabigatran (Pradaxa). Furthermore, of the three, rivaroxaban (Xarelto) had the highest rate of bleeding.
In summary, the obvious first choices would be either Eliquis or Xarelto as one of the major benefits of NOACs is the avoidance of lead in parenteral anticoagulants. Xarelto has the advantage on ease of dosing but requires more caution in patients with renal or liver impairment. As we don't yet have reversal agents for the Xa antagonists, Eliquis wins out in that it had lower rates of significant bleeding and there is less concern in patients with renal insufficiency. Furthermore, it is recommended that Xarelto be taken with food and there is no such requirement for Eliquis. Below is a quick summary for easy reference:

Medication	Action	Dosage
Dabigatran(Pradaxa)	direct thrombin inhibitor	Requires lead in parenteral, has reversal agent (Idarucizumab/ Praxbind) DVT dosing: 150mg PO BID, start ASAP after unfractionated heparin infusion of if transitioning from LMWH, give 0-2 hours before next dose of LMWH would have been given.
Edoxaban (Savaysa)	factor Xa inhibitor	Requires lead in parenteral. DVT dosing (for patients over 60kg): 60mg PO QD, start 4 hours after unfractionated heparin infusion is discontinued or if transitioning from LMWH give at the time when the next dose of LMWH would have been given
Rivaroxaban (Xarelto)	factor Xa inhibitor	No lead in, once daily dosing, caution in renal failure, slightly higher bleeding rates, take with food. DVT dosing: Start 15mg PO BID x21 days then 20mg QD
Apixaban (Eliquis	factor Xa inhibitor	No lead in, BID dosing, slightly lower rates of significant bleeding. DVT dosing: Start 10mg PO BID for 7 days and then 5mg PO BID

References:

1. Antithrombotic therapy in VTE disease: CHEST Guideline and expert panel report. Chest 2016;149(315-352) Kearon C, Akl EA, Omelas J, et al.
2. Do novel oral anticoagulants do better than standard therapy in the treatment of deep vein thrombosis? Hemostaseologie 2013/3 M Brodmann
3. Comparing Dabigatran, Apixaban, and Rivaroxaban in the absence of head to head trials. Chest 2106, Dec 31 Noseworth PA et al.
4. Dosing recommendations taken from epocrates