9th Annual CBS/ORBCoN Transfusion Medicine Videoconference Symposium: April 9, 2014
Question and Answer Period

Morning Session:

Directed to Dr. Carrier from Dr. Bormanis
Q: If the half-lives are similar for the new oral anticoagulants, why is Rivaroxaban taken only once a day while the others need to be taken twice a day?
A: The story behind once a day for Rivaroxaban is that Phase 2 trials looking at DVT showed no difference between twice daily and once a day when looking at effectiveness and safety. The second trial looking at dosing, 20 mg was the best dose but there was no difference between 20 mg once a day or 10mg twice daily. From a compliance point of view, it is probably better to take once a day. Phase 3 trials have been done using once a day or twice daily and they are both safe and effective. Dr Carrier stated that low molecular weight heparin (LMWH) is used once a day all the time without any concern and its half-life is about the same.

Directed to Dr. Carrier from Dr. Meek
Q: One of the trials that you reviewed assessing acute treatment of DVTs and PEs used low molecular weight heparin (LMWH) for 5 days prior to Dabigatran. Is this standard care?
A: Two of the trials used Rivaroxaban and Apixaban from the start but at a much higher dose. For the Dabigatran trial, they decided to go with 5 days of LMWH followed with usual dose of Dabigatran. The risk of recurrence is always highest in the early days after diagnosis, so that is the rationale behind using a much higher dose or LMWH.

Directed to Dr. Carrier from NBRHC audience
Q: In patients with GI Bleed history, would you suggest Apixaban for newly diagnosed patients with PEs or DVTs despite it not being licensed in Canada?
A: Apixaban shows less GI bleeding, but 10 mg tablets are unavailable which requires using the 5mg tablets for off label use. Once approved and indicated in Canada, Dr Carrier would use Apixaban.

Directed to Dr. Carrier from Timmins and District Hospital, Timmins ON
Q: What are the indications for thromboprophylactic use of NOACs in joint replacement?
A: None of these trials included patients with hip fractures because they are at higher risk. Therefore it is currently not indicated. LMWH might be better indicated.

Directed to Dr. Carrier from Sault Area Hospital, Sault Ste. Marie ON
Q: Can we use any of the NOAC during pregnancy, ante- or post- partum?
A: No, these drugs should not be used in pregnancy or post partum as they cross the placenta and are excreted in breast milk.

Directed to Dr. Carrier from Pembroke Regional Hospital, Pembroke, ON
Q: Is there a recommendation for testing timelines for Warfarin when dose adjustments have been made?
A: No formal recommendation but it depends on why you are checking (i.e. new medication). As the patient stabilizes, increase time between testing (Dr. Carrier suggested 6 weeks, maybe 12 in a very stable patient).

Q: Is it reasonable to check every day after a dose adjustment of Warfarin?
A: No, it won't change that quickly. It will take 2-3 days to see changes in the coagulation parameters.

Directed to Dr. Carrier from Dr. Lesley
Q: He gave an example of a 70-75 year old male, hypertensive, diabetes, atrial fibrillation (AF). Give the patient his options (pros and cons of all NOACs as well as Warfarin). If the patient doesn't have money for new products, which would Dr. Carrier suggest?
A: Try 3 months with Warfarin first and if unstable, then the patient can get coverage. When well controlled, Warfarin is safe and very effective. We can't afford to have everyone on the NOACs, therefore they should do a 3 month trial of Warfarin first.

Directed to Dr. Carrier from NBRHC audience
Q: Can you comment on the RELY trial sub-group analysis that showed the patients on Warfarin did just as well?
A: The sub-group analysis from the RELY trial that looked at time and therapeutic range and the effectiveness and safety outcome measure as published in the Lancet. The recommendation of OBB based on this trial was that if you have a time and therapeutic range of over 65% for Warfarin, then superiority of Dabigatran for efficacy and safety disappears. No sub group analysis was done for any other trials.

Directed to Dr. Carrier via email
Q: Why have the trials for the new oral anticoagulants so far failed miserably in anticoagulation for mechanical heart valves?
A: One trial of Dabigatran shows less effective than Warfarin independent of the doses on mechanical heart valves. The reaction is different to those with foreign valves therefore Warfarin is safer and more effective. The new oral anticoagulants seem to be less effective they inhibit the contact activation pathway of the coagulation cascade.

Directed to the Panel from St. Joseph's General Hospital, Elliot Lake, ON
Q: We have heard a lot about new oral anticoagulants being used for hips and knees. Typically those patient profiles are older adults who usually ingest non-steroidal anti-inflammatory drugs (NSAIDs). Can you talk about the role of these non-steroidal antiflammatory medications causing those patients to become bleeders?
A: Small dose of Naproxen will have no impact. Dr Bormanis said that they do affect platelet function and enhance the activity of the Warfarin. Dr. Bormanis suggested looking for bruising and renal failure. Dr. Carrier suggested some precautions that can be taken to lower the risk by

controlling blood pressure and decreasing alcohol intake. Dr. Irwin suggested taking them off NSAID and putting them on Tylenol.

Directed to the Panel from North Wellington Health Care, Mount Forest, ON
Q: What effect does Dabigatran have on PTT and INR?
A: Dabigatran affects INR much less. Thrombin Time is the best test for this drug, PTT is second, and INR is not useful.

Directed to Dr. Irwin from Sault Area Hospital, Sault Ste. Marie,ON
Q: How useful is Voluven in fluid replacement?
A: Voluven (or Pentaspan) is very useful as a colloid but there have been recent findings that suggest it increases creatinine and renal failure so its use has been limited.

Directed to Panel from NBRHC audience
Q: In one of the case studies presented of the patient on Dabigatran, the patient received both PCC and FP. Is there any benefit to this intervention?
A: The plasma would increase his volume and the PCC have no effect on Dabigatran.

Directed to Dr. Carrier from Dr. Ready, North Bay Regional Health Centre, North Bay, ON
Q: If you or a loved one had a recent onset of AF, what would you recommend (without considering the cost)?
A: Dr Bormanis said he would suggest Rivaroxaban. Dr. Carrier said that if there were no other issues, he would choose either Rivaroxaban (1/day) or Apixaban.

Directed to Dr. Carrier from NBRHC audience
Q: Which would you suggest after a hip replacement?
A: After a hip replacement, Rivaroxaban or Apixaban would be suggested. Warfarin is harder to control and would not be a good choice.

Directed to Dr. Bormanis via email
Q: Dr. Bormanis suggested PCC were ineffective for Dabigatran reversal but then he suggested the use of PCC along with factor VIIa and Tranexamic acid with the suggestion of a “thrombin burst.” I did not understand that.
A: PCC provides more substrate (eg. Factors II, VII, IX, X). Factor Via activates IX and X directly to get thrombin. The large dose of VIIa generates the production of Thrombin at bleeding site. This is the likely effect. Transexamic acid is used to stabilize any clot that is formed. PCC alone is ineffective.

Directed to Dr. Carrier via fax
Q: Oncology patients with new PE/DVT are usually treated with LMWH only. Will this change with the NOACs?
A: Patients with cancer-associated PE/DVT should be treated with LMWH only and not with the NOACs.

Directed to Dr. Meek via email
Q: In your presentation the last case study was where PCC and FFP were given to the patient. Could you answer what was the %benefit of each intervention?
A: The INR normalized and the patient got better. It is unknown which treatment provided the benefit. No source of bleeding was ever identified.

Afternoon Session:

Directed to Dr. Carrier from NBRHC audience
Q: Define non-valvular AFib.
A: If you have any form of valve replacement or severe mitral disease-those would not be included. No significant abnormalities detected with a stethoscope.

Directed to Dr. Carrier from Weeneebayko Hospital, Moose Factory ON
Q: Described a case where a 40 year old female with recurrent DVT on Warfarin, 3.2 INR upon arrival at hospital, worried about a recurrent DVT. Asked whether there were any other agents
A: Dr. Carrier said when you have a patient with a recurrent event despite good therapeutic doses of oral anticoagulants, what we tend to do is stop the oral anticoagulants, depending on the INR, he would give a bit of Vitamin K, put her on LMWH for a few weeks and re-challenge her to oral anticoagulation afterwards.

Directed to Dr. Carrier from NBRHC audience
Q: Would the D-Dimer test be helpful to diagnose recurrence?
A: It would be unlikely to help with recurrence if no previous baseline.

Directed to Dr. Carrier from Health Sciences North, Sudbury, ON
Q: Is there any reason to use Pradax (Dabigatran) at 110 mg?
A: He would use 110mg of Dabigatran if there are additional risk factors of bleeding that are not modifiable and patient is over 70-75 years old because there is a significantly lower risk of bleeding than Warfarin.

Directed to Dr. Carrier by Dr. Lesley
Q: If a patient came to Dr. Carrier with acute DVT and finances were an issue (i.e. no insurance etc...) which would you suggest?
A: Dr. Carrier would discuss the pros and cons of both treatment options. Rivaroxaban is covered by a LU code for the initial 6 months. From an ODB's perspective, Rivaroxaban is cheaper than Warfarin (due to the ongoing need for testing) up to 6 months of treatment. If the patient requires long-term anticoagulation (i.e. more > 6 months) Warfarin would be cheaper.

Directed to Dr. Meek from NBRHC audience
Q: How quickly would a surgeon be able to put in a central line for an anticoagulated patient?
A: Deferred to Dr. Bormanis who explained that if platelets are normal and the patient is on Dabigatran, there shouldn't be any complications based on case reports where a pace maker was put into a patient who was fully anticoagulated on Dabigatran.

Directed to Dr. Bormanis from Queen's University, Kingston, ON
Q: When you have used Factor V11a to reverse Dabigatran were there any thrombotic complications after?
A: None.

Directed to Dr. Bormanis from NBRHC audience
Q: There has been recent evidence to suggest that major bleeding in patients taking NOACs is higher than those on Warfarin; however the mortality rate for NOACs is lower than that of Warfarin. Is this true?
A: Dr. Bormanis was unsure if this is true or not. There is still very little literature for NOACs compared to Warfarin at this time. Dr. Bormanis can't understand why there would be less trouble stopping the bleeding for patients on Warfarin.

Directed to Dr. Bormanis via email
Q: What is the rationale for female being a 1+ in CHADS score?
A: This refers to the CHADS-VASC score. Women are often underdiagnosed with ischemic cardiac events and have different symptomology than men.

Directed to Dr. Bormanis via email
Q: Regarding MTP, we are a small hospital. We have an emergency department. We have RBCs, Octaplex and rV11a on hand but we no longer keep any FP here. The closest hospital is a 30 minute drive away so getting some FP or AHF (cryoprecipitate) would take about 1 hour by the time they thaw it and send it over. Dr. Bormanis mentioned that early intervention with RBCs or plasma is important in a MTP. He did not say RBCs and plasma. In our case, should we be keeping at least a few units of group AB FP or AHF on hand in the event we get a patient needing a MTP?
A: If you are a hospital that has major surgeries and receives trauma patients, Dr. Bormanis suggested keeping frozen plasma and cryoprecipitate on hand. If you are a small hospital, the likelihood of a massively bleeding patient being transferred to a larger facility before plasma or cryoprecipitate could be prepared and given is high therefore, it might not make sense to try to stock these products. Dr. Bormanis commented that stocking tranexamic acid may be more helpful to immediately address the bleed.

Directed to Dr. Bormanis via email
Q: Is there a recommended off label dose for Niastase RT in the context of Cardiovascular surgery and trauma? There is no such recommendation on the product monograph and the information provided by Novo Nordisk refers to studies and a different range depending on the situation.
A: There is no recommended dose. However pump patients are usually warm and in good acid base balance, as such I use lower doses (eg. 2mg and repeat in 20-30 minutes).

Directed to Dr. Bormanis via email
Q: What is the recommended off label dose of PCC in Cardiac surgery?
A: I have used it only in cases of shock liver and Jehovah's Witness patients. I use 60-80 cc also cryo for fibrinogen.

Directed to Dr. Bormanis via email
Q: Would you have any practical suggestions for our transfusion committee? Two MTPs were recently called on patients in the OR/CVOR which we already had compatibility testing completed and were already actively issuing products. When they called the MTP, we accordingly thaw 4 FP and get 4 units of red cells ready for issue immediately as required by the MTP policy, followed by a second pack of 6 RBCs and a platelet ready to issue. The problem is both times they didn't use the FP and didn't need all the red cells. It seems the MTP is better used as an emergency issue of product for ER trauma patients etc.
A: We always have 2 AB plasma thawed, it is good up to 5 days. We have gone to a code bleed where when called, porters are sequestered to ER and Blood Bank. We send up packs (eg. 4 RBC and 2 Plasma). Depending on urgency, we prefer to go group specific. The reason for AB is to get it up fast. Other packs contain RBC, Plasma, Cryo and platelets. The trend is to use Fibrinogen and platelets earlier (eg. 2nd pack).