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What Clinical Management Strategies Must Be Deployed to Effectively Transition From the Acute to Post-Acute Setting When a Pediatric VTE Patient Is at Risk for a Recurrent VTE?

Announcer:
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Dr. Kumar:
Hello, my name is Riten Kumar and I'm a pediatric hematologist at the Boston Children's Hospital. Today, we are going to talk about management strategies that should be deployed in effectively transitioning a patient from acute treatment for venous thromboembolism to secondary thrombo-prophylaxis. I think the first thing we need to consider while transitioning a patient from acute VT management to secondary thromboprophylaxis is the choice of the agent. And the choice of the agent for secondary thromboprophylaxis depends upon the indication of thromboprophylaxis.

In a child who has completed anticoagulation for an acute VTE and does require ongoing prophylaxis, I always look at the indication for prophylaxis. So if you're prophylaxing a patient because they had a catheter associated DVT and continue to need a catheter, there is really good data from the Einstein Junior Study suggesting that DOACs work quite well in this cohort. I will caution you that in patients with primary to standard failure or short gut syndrome, DOACs may not be effective 'cause the patient may not absorb the DOACs. In patient with cancer associated thrombosis, our standard of care has historically been to use low molecular weight heparin. In adults, the American Society of Hematology Guidelines now recommends using direct oral anticoagulants in adults who have cancer and thrombosis. We have very little experience with DOAC use in cancer, but at our centers, we have started transitioning some of our more stable patients to direct oral anticoagulants. Additionally, the Prevapix-ALL study, which is looking at Apixaban for prophylaxis in children with leukemia and lymphoma and Asparaginase associated thrombosis will be published shortly and will hopefully give us more experience in this sub cohort.

In children with cardiac disease both direct oral anticoagulants and Vitamin K antagonists may be used as secondary prophylaxis. The Universe trial has shown good safety and efficacy for Rivaroxaban in children with single ventricle physiology who've undergone a Fontan procedure. The Saxophone trial, looking at Apixaban for prophylaxis in children with congenital and acquired cardiac diseases, and the results of that are going to be published shortly. In a patient who has congenital thrombophilia such as Antithrombin Deficiency, protein C or protein S deficiency, The diversity trial has shown that Dabigatran is a good choice in this cohort. In patients with Antiphospholipid Antibody Syndrome, particularly patients with Triple Antiphospholipid Antibody Syndrome, and certain kids with mechanical valves, Vitamin K antagonist remains the anticoagulant of choice. And lastly, in patients who are on anticoagulation because of a history of a Recurrent Unprovoked Venous Thromboembolism DOACs are safe and efficacious.

One question that frequently face is what dose of anticoagulation to use in a child requiring secondary thromboprophylaxis, as in to continue therapeutic dose anticoagulation versus transitioning them to prophylactic-dose anticoagulation. Recently, Dr. Leslie Raffini in child and at the Children's Hospital of Philadelphia published a retrospective study where they looked at 373 kids with CVL or Central

Venous Line Associated Thrombosis. Of this cohort about 65% required a subsequent central venous line, and 17% developed recurrent VTE. Predictors of recurrence included: placement of another central venous line, congenital heart disease, and parental nutrition. Interestingly, in this study, patients who received therapeutic dose anticoagulation for secondary prophylaxis were less likely to develop a recurrent clot compared to patients who received prophylactic-dose anticoagulation.

Other practical considerations include patient education. At our organization we give our patients several handouts. These include handouts on where the low molecular weight heparin can be administered, and even handouts on how to read a prescription label. Our patients go home with contact information for the anticoagulation team. Close follow up in clinic is very important for this cohort. And again, all our patients are given a medical alert bracelet at the time of discharge. We also give our patient handouts on activity restriction, specifically advising against contact and collision sports while receiving thromboprophylaxis.

Other practical considerations include food interaction. I will point out that low molecular weight heparin does not have any food interaction. As we discussed in one of the previous modules, Vitamin K antagonists are affected by Vitamin K rich foods. Rivaroxaban and Dabigatran should be taken with meals, while Apixaban may or may not be taken with meals. Low molecular weight heparin and the direct oral anticoagulants are predominantly excreted through your kidneys. In the Phase Three trials of direct oral anticoagulants a creatinine clearance of less than 30 or a creatinine clearance of less than 50 for Dabigatran, the exclusion criteria. Lastly, obesity. At our center, we use actual body weight for all patients receiving low molecular weight heparin. With regards to direct oral anticoagulants the International Society on Thrombosis and Hemostasis has recommended standard dose Rivaroxaban and Apixaban for adults with a weight greater than 120 kilograms, or a BMI greater than 40.

Other practical considerations include drug interactions. We typically ask our patients to avoid NSAIDs and aspirin while on anticoagulation. Vitamin K antagonists have several drug interactions and the patient should be educated about them. Dabigatran is a substrate for P-glycoprotein, and therefore can be affected by P-glycoprotein inducers and inhibitors. Apixaban and Rivaroxaban can be affected by both P-glycoprotein and CYP3A4 inducers and inhibitors. For our patients who are on polypharmacy, we typically reach out to our Hematology pharmacists and have them do a drug interaction check before transitioning any of our patients to DOACs.

The other practical consideration is interruption of anticoagulation before a scheduled procedure. For most procedures that have a minimal bleeding risk such as a central venous line removal, dental cleaning or dental filling, no interruption of anticoagulation is required. For low risk procedures, such as a CVL placement, Arthroscopy, or dental extractions, anticoagulation should be held for a short duration of time. This includes about one day of interruption for direct oral anticoagulants and three days of interruption of Vitamin K antagonists. For high bleeding risk procedures such as lumbar punctures, major surgery, renal or hepatic biopsy, anticoagulation should be interrupted for a longer duration of time. This includes two days of interruption of direct oral anticoagulants and about five days of interruption for Vitamin K antagonists. Lastly, we'll talk about reversal agents.

As we've discussed in one of the previous modules, low molecular weight heparin is only partially reversed by protamine. Vitamin K, in combination with Fresh Frozen Plasma and Prothrombin Complex Concentrates can be used to reverse Warfarin. Idarucizumab is a humanized monoclonal and antibody which can be used as an antidote for Dabigatran. Again, there isn't much experience using this agent in children. And similarly, Andexanet Alfa which is a small decoy protein is an FDA approved antidote for patients getting Rivaroxaban and Apixaban. Unfortunately, there's very limited data on its use in children. Thank you so much. Thank you for watching this educational program.

Announcer:
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