Who is going to do well on anticoagulants?

Anticoagulants are very good at preventing recurrent disease in patients with deep vein thrombosis and pulmonary embolism. This is important because venous thrombosis frequently causes long-term complaints such as pain, edema, fatique and dyspnea. Moreover, 4% of the patients die within 30 days after diagnosis.

The main side effect of anticoagulants is bleeding. This risk sharply increases when anticoagulants are overdosed. On the other hand, a too low dose increases the risk of a new thrombosis. The level leading to the optimal risk benefit ratio is called the therapeutic range. Vitamin K antagonists (VKA) are still the most commonly used type of anticoagulants. It depends on several factors such as diet, comedication, physical activity and genes what VKA dose is needed. Therefore, the optimal dose of VKA varies between but also within patients over time.

The degree of anticoagulation can be measured by the International Normalized Ratio (INR). To keep the INR within the therapeutic range, frequent blood measurements and dose adjustments are performed. When all or most INRs are within the therapeutic range, the efficacy and safety of VKA are optimal. Unfortunately, patients with many INRs outside the therapeutic range or large differences between the INRs are less protected against thromboses and suffer more bleeds.

The aim of our study was to predict who will have poor VKA control and who will have adequate VKA control. We used data from two large trials, called EINSTEIN-DVT and EINSTEIN-PE studies. In these studies, patients were assigned to VKA therapy or another type of anticoagulant called Rivaroxaban. We only included patients who used VKA. Subsequently, we determined what information available at start of VKA therapy could help to distinguish between patients with poor and adequate VKA control. From previous studies we knew that we could also use the treatment information from the first 4 weeks, but we didn’t know whether this was of additional value. Finally, we wanted to know whether the predictors of poor VKA control could also predict premature treatment discontinuation, bleeds and thrombotic events.

We found that patients with a bodyweight below 50kg, active cancer, and/or a venous thrombosis due to a temporary risk factor all had a higher risk of poor VKA control. Patients for whom VKA management deviated from the guidelines also had more often poor VKA control. The course of VKA therapy during the first four weeks turned out to contain valuable extra information. Warfarin and acenocoumarol are two types of vitamin K antagonists, warfarin having a longer half-life. Interestingly, for patients on warfarin it was mainly relevant how much the INRs differed from each other. For acenocoumarol users, the patients with many INRs in the therapeutic range had better subsequent VKA control than the others, but it mattered less how much the INRs differed. Many of the predictors of poor VKA control could also predict whether VKA treatment would be discontinued sooner than planned. However, none of the above mentioned predictors could also predict bleeds and thrombotic events.

Knowing which patient and treatment characteristics predict poor VKA control could aid clinicians to identify patients who might need extra medical attention. Also, alternative treatment options could be considered such as non-VKA oral anticoagulants (NOACs) or another type of VKA. NOACs have the advantage that they can be used in fixed dose without the risk of large fluctuation in the degree of anticoagulation. However, further research would be needed to find out whether switching to any other treatment would really benefit these patients.

Publication

Independent predictors of poor vitamin K antagonist control in venous thromboembolism patients. Data from the EINSTEIN-DVT and PE studies.
Kooistra HA, Gebel M, Sahin K, Lensing AW, Meijer K
Thromb Haemost. 2015 Jul 30