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CLINICAL VIGNETTE

Warfarin Initiation and Monitoring in the Elderly: A Clinical Vignette

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Case Report

An 86-year-old man was discharged from the hospital following a new splenic infarct and atrial fibrillation. He was started on Warfarin 5 mg on the day of discharge and bridged with Enoxaparin. Home health was ordered, and he was enrolled in an anticoagulation management program at the time of discharge. He was scheduled to have an INR drawn three days later, but the home health nurse was unable to obtain blood and, after consultation with patient's primary care physician, it was agreed that the blood would be drawn the next day.

An INR was drawn on the next day, but the anticoagulation program was closed for a holiday. The home health agency did not report the result to the on-call physician. Four days later, the home health agency again drew the blood, but results were not available. The primary care physician repeated the test at a post-hospitalization follow-up visit, and the result was an INR of 6.3.

Discussion

Initiation of Warfarin in Outpatients

When rapid anticoagulant effect is required, it is recommended that a rapidly acting, parenteral anticoagulant (e.g., low-molecular-weight heparin, or unfractionated heparin) be started at time of Warfarin initiation and be discontinued after at least 5 days of concomitant therapy[1,2] and after the INR has been in the therapeutic range for at least 2 measurements approximately 24 hours apart.[1] If there is no urgent need for immediate anticoagulant effect (e.g., chronic stable atrial fibrillation), Warfarin administration can be started without concurrent use of a rapid acting parenteral anticoagulant.[1]

In clinical practice, it is common for Warfarin to be initiated at a fixed dose for the first several doses. The half-life of Warfarin varies among individuals and is on average 36-42 hours; it can take more than a week to reach a pharmacokinetic steady state when starting a maintenance dosage.[1] INR levels need to be monitored closely to prevent both under- and over- dosing of Warfarin during initiation. Although Warfarin dosing based on genotype during the early phase of treatment can lead to fewer adverse events, and a higher portion of time in which the patient is within the narrow therapeutic window, this has yet to become the standard of care.[1,3]

According to the American College of Chest Physician (ACCP) 9th edition guidelines (2012), for patients who are starting treatment as outpatients, it is recommended that Warfarin be initiated at 5 mg or 10 mg daily for the first 2-3 days, followed by an INR measurement.[4] In elderly patients or in patients with malnutrition, liver disease, congestive heart failure, or high bleeding risk, a starting dose of Warfarin 5 mg or less is often appropriate.[1] Initial monitoring is recommended once every few days until a stable dose response has been achieved.

The American Family Physician (AFP) Point-of-Care Guidelines on evidence-based initiation of Warfarin (2005) include a 5 mg algorithm and a 10 mg initiation algorithm. In the 5 mg algorithm, patients are given Warfarin 5 mg daily for the first 2 days, and INR is measured on days 3, 4, and 5; subsequent Warfarin dose adjustments are made using previously validated nomograms.[5,6] With the 10 mg algorithm,10 mg was given the first 2 days of therapy, and INR is assessed on days 3 and 5 during the first week of therapy.[6] If a patient does not have a therapeutic INR by day 5, the INR is measured daily until therapeutic.[5] The AFP 2005 guidelines indicated that both the 5 mg and 10 mg algorithms are reasonable options in the initiation of Warfarin therapy as there are no data demonstrating that one or the other algorithm is better.[6]

There are very few Warfarin initiation studies in regards to the elderly population. A prospective study used a "geriatric dosing-algorithm" for initiation of Warfarin in patients aged 75 and older. (The study population was hospitalized Caucasians.) Warfarin 4 mg was given for three days, and INR is measured on days 3 and 6.[7] Warfarin dose of less than 5 mg was chosen due to concerns that empiric starting dose of 5 mg daily would lead to over-anticoagulation in elderly patients.[7,8] The Canadian Family Physician (2013) recommends that elderly patients start a low initial dose of Warfarin (2 or 3 mg) daily for 2 days and checking INR on day 3 and 5.[9] The *College of American Pathologists* (1998) recommends the INR be checked at least 4 times during the first week of therapy and then less frequently, depending on the stability of the INR.[10]

In the aforementioned patient's case, the INR was drawn on day 3 and 7 of Warfarin initiation. It returned sub-therapeutic on day 3 and supra-therapeutic on day 7. More frequent testing (for instance, 3-4 times during the first week) may have prevented the INR from becoming supra-therapeutic.

When INR response is stable, the frequency of testing can be reduced to intervals as long as every 4 to 6 weeks depending on the stability of the patient's INR.[1] Optimal frequency of long-term INR monitoring is affected by modifiable factors such as patient adherence, fluctuations in severity of co-morbid conditions, dietary changes, addition or discontinuation of other meds,[1] level of physical activity,[11] weight, and smoking status.[1] Non-modifiable factors include age, sex, genetic variation, and ethnicity.[1,4]

Coordination of Initiation of Warfarin with Home Health Agencies

In this case, the results of the prothrombin time were delayed because they were drawn by a home health agency. Although the frequency of such delays has not been formally studied in clinical practice, home health labs may not be reported until 2-3 days after they are drawn. If time-sensitive lab results are needed, then it is best to have the patient go to a laboratory. If a patient is unable to go to the laboratory (e.g., impaired mobility or lack of transportation) and if home health services must be utilized, it may be best to have the labs drawn on a weekday (preferably Monday-Thursday, avoid Fridays) and early in the morning, so results are available on the same day. Some home health agencies have point-of-care INR monitors, which may expedite reporting of results. Of note, if INR is drawn by a home health agency during the weekend, the agency should report results to the on-call physician because many anticoagulation management programs are open only on weekdays and on-call physicians should be alerted to expect the results.

Although initiation of anticoagulation can be accomplished safely as an outpatient, it requires close monitoring and coordination across different providers and health care organizations.

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