A Look at Patient Compliance to INR Testing and Therapeutic Range Management of Patients on Warfarin at Agassiz Medical Center

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Abstract
This study sought to determine the total number of patients currently doing INR testing at Agassiz Medical Centre as well as the frequency each patient attended the appropriate intervals of testing and, how well each patient maintained the therapeutic range for warfarin therapy. The charts of those patients currently doing INR testing were reviewed for the number of tests completed and value of all completed test results in the past four years. A sample of 41 patients from the total of 184 patients doing INR testing was taken. It was found that an average of 72% (median 78%) of patients attended the appropriate interval for testing and an average of 56% of the time was spent in the therapeutic range of 2-3 (median 60%).

1. Introduction
Warfarin has many clinical uses. However, the management of warfarin is difficult due to its narrow therapeutic range. As a result, prothrombin time (PT) or more frequently International Normalized Ratio (INR) is used to monitor patients on warfarin by monitoring the clotting time of blood.

Warfarin is an anticoagulation medication used to prevent thromboembolism. Its effect on anticoagulation is due to the inhibition of vitamin K dependent gamma-carboxylation of coagulation factors II, VII, IX and X. This results in biological factors that are detectable but are inactive in coagulation. The prothrombin time is a measure of the extrinsic pathway of blood coagulation and is related to factor III and VII as well as coagulation factors in the common pathway including factors V, X, prothrombin and fibrinogen (Zehnder 2014). Prothrombin time is sensitive to reduced activity of factors II, VII, and X, but is insensitive to reduced activity of factor IX (Valentine and Hull 2014).

Prothrombin time is useful in monitoring warfarin therapy. However, it is not standardized. As a result, the World Health Organization (WHO) developed an international reference thromboplastin from human brain tissue. The WHO recommended that PT be expressed as INR, which is obtained by testing a sample with the standardized WHO reference thromboplastin known as the Manchester Comparative Reagent (Valentine ad Hull 2014).

The use of INR testing is indicated for those with an increased risk of thromboembolism, an increased incidence of bleeding or those undergoing surgery. Many of the cardiovascular conditions in older adults have risks associated with thrombosis. These include valvular disease, atrial fibrillation, ischemic heart disease, venous thromboembolic disease, left ventricular dysfunction and atherosclerotic vascular disease. In order to prevent thromboembolism anticoagulation medications, such as warfarin, are often prescribed. In addition to the use of anticoagulation medications INR testing may be done if a patient is undergoing surgery, has symptoms of excess bleeding such as nose bleeds and bleeding gums or heavy menstrual periods (Lip 2013). The therapeutic INR range for patients on warfarin is between 2 and 3. Excess bleeding due to over anticoagulation of the blood is the major side effect of warfarin. (Valentine and Hull 2013).

Due to the narrow range and complications that arise outside of the therapeutic
range it is important to monitor patients closely with INR testing. Agassiz Medical Centre was interested in conducting a study to determine the total number of patients currently doing INR testing, the percentage of patients who go at the appropriate intervals for testing, and the amount of time for which the INR is in the therapeutic range.

2. Methods

In order to determine the patients undergoing INR testing at Agassiz Medical Centre, a current list of service charges for INR testing was accessed. From this list of patients a random sample of 41 patients was taken. The random sample was acquired by taking every fifth patient from each of the 14 physicians patient lists. A sample size of 41 was taken instead of 42 due to one physician’s patient list consisting of only two patients. In order to determine how frequently each patient had INR testing completed and how well the therapeutic range of 2-3 was maintained, each patient’s chart was analyzed.

At Agassiz Medical Center all patient records are electronic and can be accessed on Accuro, the electronic medical records database. Medical records were accessed and analyzed looking at INR test results from each patient’s start date on warfarin until the most recent INR test completed. If time on warfarin therapy was greater than five years data was analyzed from the most recent test result and all previous results to the year 2010. Current standing orders from patients’ family physicians were searched for in the patient charts, in order to determine the frequency each patient was required to have INR testing completed. In the cases where a standing order could not be found it was presumed that each patient should have been going for testing at least once a month as per current guidelines (Guidelines and Protocols Advisory Committee 2010). The number of tests each patient missed was determined by calculating the appropriate test number according to the physicians standing order and then counting the number or months or weeks that test results were not acquired. Based on the total number of tests completed by each patient, the percentage of test results in the therapeutic range of 2-3 was determined.

3. Results

The three clinical questions asked for the purpose of this study were:

a) Determine total number of patients currently doing INR testing
b) Determine the percentage of patients who go at the appropriate intervals for testing
c) Determine the amount of time the INR is in the therapeutic range

The answer to the first clinical question was determined according to the billing list for Agassiz Medical Center from July 29, 2013 to July 29, 2014. Within this one-year span of time there are 184 patients who have had INR testing. The random sample of 41 patients, taken from the 184, shows an average of 72% go at the appropriate intervals for testing,
with a median of 78%. Lastly, the therapeutic range was maintained an average of 56% of the time. The median value for time spent in the therapeutic range was 60%.

From Fig. 1 a trend is observed between how often a patient goes at the appropriate intervals for testing and how well the patient stays within the therapeutic range.

Figure 1. Correlation between patient compliance to appropriate monthly testing and percent of total tests in therapeutic range.

4. Discussion

The results from this study showed an average of 72% of patients went to the appropriate intervals of testing. The patient sample maintained INR values in the therapeutic range 56% of time. From Figure 1 there seems to be a slight correlation between the percentage of time a patient goes to the appropriate interval for testing and the percentage of time the patient is in the therapeutic range. The more often patients attended the appropriate testing interval the higher the percentage of time in therapeutic range. A correlation could relate to patients who are more compliant to their health care plan, taking other medications regularly, and following dietary guidelines. However, a direct correlation cannot be determined without further statistical analysis.
Furthermore, a systematic and meta-analysis review including forty studies and 26064 patients found that the time spent in the therapeutic range of 2-3 was 54% in the first month, 55.6% in months 1 to 3, 60% in months 2 to 3, 60% in months 1 to 6+ and 75.2% in months 4 to 12+ (Erkens, PMG et al. 2012). In this study the time spent in the therapeutic range for different time intervals was not considered. This may have skewed the results. The last four years of INR tests results were analyzed for each patient. However, if the duration of INR testing was less than four years the data was taken from the first test result until the most current. It was assumed that each patient should be going for testing monthly unless otherwise stated on a physician requisition form. For therapeutic range analysis the total number of test results were analyzed which were often larger in number than the monthly requirement. This means that if a patient went more frequently than once a month all test results accumulated were considered to calculate the time spent in therapeutic range. Due to time restraints, how well patients maintained therapeutic range at different intervals during their testing was not analyzed. Moreover, the results of patients who started warfarin therapy less than four years earlier likely had a lower percentage of time spent in therapeutic range during initial therapy. Although it may only have slightly skewed the results, to consider these initial test results among the long term test results of other patients may be of importance to note when considering the results.

In addition to patients not meeting the required time intervals, are other reasons why the therapeutic range may not be maintained. Variables must be considered that increase a patient’s sensitivity to warfarin or require the patients to need larger doses. Listed here are some of the considerations for a patient on warfarin in managing the therapeutic range:

- Drug interactions must be closely monitored and noted while managing a patient’s warfarin dose. Additions or deletions of medications may influence warfarin metabolism.
- Diet- variable dietary vitamin K intake from foods, vitamins and herbal products will alter INR results. Patients must be educated to maintain a constant dietary intake of vitamin K.
- Management setting: patients moving from inpatient to outpatient settings may affect INR results
- Other disease states

(Valentine and Hull (2013). Several of the previously mentioned reasons may be involved in why therapeutic range management was slightly lower in this study than the literature results.

Frequent INR testing and therapeutic range management is important for a patients’ health. The question was raised while analyzing the results was how monthly testing affected patients’ quality of life. The current recommendations may have an affect on a patients freedom if they are required to attend a lab for monthly testing. The question raised was would it be better to calculate averages based on a 10 time per year frequency rather than the 12? I think for patient safety the recommended monthly testing is appropriate however finding ways to allow the patients freedom to be away from their regular lab and still have testing done would be beneficial to a patients quality of life. This
could include at home monitoring or prearranging with labs in the patients destination to have tests completed and results sent back to the clinic.

It is difficult to say without further research what are the major contributing factors to the results of this study.

4. Conclusion

Warfarin therapy prevents thromboembolism. Used appropriately it can prevent the occurrence of strokes and heart attacks. Due to the narrow therapeutic range it is important to manage patients on warfarin closely. Patients complying with regular testing intervals may affect how well the therapeutic range is maintained. Attendance at regular testing intervals at Agassiz Medical Centre is fairly well maintained although from the results of this study INR results in the study sample were in the therapeutic range less frequently than expected from literature.
References