

DIETARY INFLUENCE ON INR LEVELS IN ANTICOAGULATED PATIENTS

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ABSTRACT:

Objective: The international normalized ratio (INR) is the primary test for anticoagulation patients. It can also be used to evaluate the patients' coagulation state or bleeding risk. The international normalized ratio (INR) values and, consequently, the dose of warfarin are influenced by a number of variables, including vitamin K intake in diet, medication and herb interactions, disease conditions, and alcohol consumption. The aim of this study is to identify how dietary intake affects changes in INR.

Method: A 6 month prospective observational study was conducted at a tertiary care hospital, using patient data from medical records, interviews, and patient forms.

Results: The study involved 108 subjects with a mean age of 46 ± 15.7 years, with 68 males and 40 females. The majority were hypertensive, with 39 having diabetes, 21 having liver disease, 11 having renal disease, 10 having bleeding disorder, and 9 having other comorbidities. Factors contributing to increased INR levels included diet, concomitant medications, smoking, non-compliance, and comorbidities. Diet was the most common cause of fluctuations, followed by smoking, non-compliance, and alcohol consumption.

Conclusion: Dietary changes were found to be the main cause of INR changes in this investigation. Anticoagulation therapy outcomes were similarly influenced by variations in vitamin K intake and consumption of foods high in the nutrient. In order to achieve stable INR

values in patients using anticoagulants, it is crucial to understand the critical significance of dietary intake.

Keywords: INR, INR fluctuations, diet, vitamin-k diet, concomitant medications.

INTRODUCTION:

INR plays a significant role in managing oral anticoagulant treatment patients, particularly those on vitamin K antagonists (VKAs) like warfarin. It displays, to the power of the International Sensitivity Index (ISI) for the particular thromboplastin reagent employed, the ratio of a patient's PT to a normal or control PT. This systematic method lowers the likelihood of problems and empowers clinicians to decide on dosage modifications with knowledge. [1]

For anticoagulant medication to be effective and safe, INR readings must be stable. However, because of a variety of factors, INR fluctuations are probable. Patient-specific variables such as age, genetics, comorbidities, and concurrent medications all contribute to the observed heterogeneity. [2,3] The maintenance of INR levels can also be made more difficult by external factors like diet, lifestyle, and changes in drug adherence. Changes in vitamin K consumption may have an effect on the delicate equilibrium that anticoagulant works to maintain since vitamin K is essential for the manufacture of clotting components. [4,5] As a result, optimizing anticoagulation medication requires an awareness of the connection between food and INR variations. [6,7,8]

There is continuous research and clinical interest in the effect of dietary vitamin K on INR values. The anticoagulant effects of a diet high in vitamin K-containing foods, including as leafy green vegetables (such as kale, spinach, and broccoli), may be offset, resulting in changes in the INR. Our study aims to determine the impact of diet on changes in INR so it will help doctors optimize anticoagulant therapy and control their INR levels.

MATERIALS AND METHODS:

This prospective observational study was conducted in a tertiary care hospital, Hyderabad for duration of 6 months. The source of data was patient collection forms, medical records and interviews of the patients and caretakers. The study was conducted at tertiary care A.I.G hospitals in Hyderabad with institutional ethics committee approval. Following a brief

explanation of the study, patients who meet the criteria were enrolled after signing the informed consent. All the necessary and pertinent information from the patients' case sheets, treatment plans, laboratory findings, patient or patient caretaker interviews, and any other related sources. The information was entered into an MS Excel 2016 spreadsheet and exported to IBM SPSS Software Version 22 for further analysis of results.

ETHICAL APPROVAL:

The ethical committee letter was obtained before initiation of the study, (A.I.G/IECBH&R 03/02.2020-05)

RESULTS:

The study included 108 patients. The results were analyzed based on various parameters stated below.

The mean age of the study subjects was 46 ± 15.7 subjects. More number of patients i.e. 68 (62.96%) subjects were male and 40 (37.03%) subjects were females.

Table-1: Demographics

Parameter	No of patients
Mean (SD) age in years	46±15.7
Gender	
Male	68 (62.96%)
Female	40 (37.03%)
BMI (kg/m²)	
<18.5	5 (4.62%)
18.5-29.9	84 (77.77%)
>30	19 (17.59%)
Comorbidities	
HTN	39 (36.11%)
DM	21 (19.44%)
Renal disease	11 (10.18%)
Liver disease	18 (16.66%)

Bleeding disorders	10 (9.25%)
Others	9 (8.33%)
Smoking	17 (15.74%)
Alcohol	1 (0.92%)

The BMI was also calculated and reported for subjects enrolled which revealed that 5 (4.62%) subjects had BMI of <18.5 kg/m², 74 (77.77%) subjects had BMI of 18.5-29.9 kg/m², 19 (17.59%) subjects had BMI of >30 kg/m².

Majority of subjects were hypertensive i.e. 39 (36.11%), followed by 21 (19.44%) subjects had diabetes mellitus, 18 (16.66%) subjects had liver disease, 11 (10.18%) had renal disease, 10 (9.25%) had bleeding disorder and 9 (8.33%) had other comorbidities.

The history of alcohol and smoking was reported in 1 (0.92%) subjects and 17 (15.74%) subjects respectively.

Table-2: Factors affecting INR fluctuations

Factor	No of patients
Concomitant Medications	35 (32.40%)
Salicylates	5 (14.28%)
NSAIDs	2 (5.71%)
Amiodarone	4 (11.42%)
Ciprofloxacin	1 (2.85%)
Smoking	17 (15.74%)
Alcohol consumption	1 (0.92%)
Diet (Non-balanced Vitamin-K diet)	51 (47.22%)
Non-compliance	2 (1.85%)
Comorbidities	2 (1.85%)

There were various factors that contributed to the increase in INR levels like use of concomitant medications, smoking, alcohol consumption, diet, non-compliance and comorbidities.

The highest numbers of subjects were reported fluctuations due to diet i.e. 51 (47.22%) subjects had been on a non-balanced vitamin K diet. Use of concomitant medications was found in 35 (32.40%) subjects that included 5 (14.28%) subjects using salicylates, 2 (5.71%) subjects using NSAIDs, 4 (11.42%) subjects using amiodarone and 1 (2.85%) subjects using ciprofloxacin.

Smoking was another factor in 17 (15.74%) subjects, followed by non-compliance and comorbidities in 2 (1.85%) subjects each and alcohol consumption in 1 (0.92%) subjects.

DISCUSSIONS:

The effect of nutrition on INR stability has been highlighted by numerous researches. According to research by Booth et al, patients taking warfarin have higher INR readings when they consume more green leafy vegetables since these foods are high in vitamin K. This highlights the significance of understanding the subtleties of dietary influences on anticoagulation control. In addition to vitamin K, dietary habits and nutritional counseling are also crucial. [9] A study by Ansell et al highlights the multidimensional nature of INR regulation and contends that genetic and patient variability also play a role in the complexity of dietary effect. [10]

A study by Kim KH et al found that the stability of the anticoagulation effect of warfarin is more stable in patients who take more than a certain amount of dietary vitamin K. The study divided 66 patients into three groups based on their vitamin K intake and compared the CV of prothrombin time and warfarin doses. The results suggest that the long-term anticoagulation effect of warfarin is more stable in patients with higher vitamin K intake. [11]

Diet and INR stability have a complex relationship. The difficulties in diet counseling are highlighted in a study Bansal A et al which cites the absence of standardized recommendations for healthcare professionals. Dietary management in anticoagulant therapy is further complicated by confounding factors including individual variability in vitamin K response. To ensure adherence to nutritional advice, patient education is essential. [12] Study by Ansell J, Hirsh J et al highlight the significance of providing patients with the information and abilities required to make knowledgeable food decisions. Improving patient comprehension can help them adhere to dietary limitations better, which will help keep their INR stable. [13]

A study conducted at the Massachusetts General Hospital found that changes in daily vitamin K intake can lead to significant variations in the International Normalized Ratio (INR) coagulation index in patients receiving oral warfarin anticoagulant therapy. [14,15] The study found that a weekly change of 714 mug dietary vitamin K significantly altered weekly INR by 1 unit, and a weekly change of 14.5 mg warfarin significantly altered weekly INR by 1 unit after adjustment for age, sex, weight, height, and concomitant use of medications known to interact with warfarin. Patients taking warfarin and consuming markedly changing amounts of vitamin K may have a variable weekly INR with potentially unstable anticoagulant outcomes. [16,17]

For clinical practice, it is crucial to comprehend the complex link between nutrition and INR variations. According to Garcia et al, the development of individualized dietary regimens can improve INR control while enabling patients to keep a healthy diet. But for this balance to be achieved, patients and healthcare professionals must work together. [18]

Diet and herbal supplements accounted for 31.9% of non-TINR over the study period, according to a study by Al-Momany NH et al. Despite the thorough instructional session and the printed booklet that emphasizes the need to take a consistent amount of vitamin K daily and lists the daily permissible amount of food rich in vitamin K in serving size, non-balanced dietary vitamin K intake correlated to 16.88% of non-TINR. The spring season in Jordan (primarily the end of March and April) saw a significant increase in the changes in INR (low) that are related to increased intake of vitamin K-rich foods. This is because more seasonal leafy vegetables, such as spinach, hibiscus, hedge mustard, and parsley, are available during this time. [19,20]

The study by Wittkowsky AK et al evaluated 12,897 international normalized ratios (INRs), with 6642 (51.5%) within range and 8525 (66.1%) within 0.2 INR units. Under anticoagulation was most common in 2881 out-of-range INRs below 2.0, with other common causes being drug changes, medical conditions, dietary vitamin K intake, alcohol use, and activity level. Over anticoagulation was most common in 603 out-of-range INRs above 4.0. [21]

Significant emphasis has been paid in recent years to the interaction between genetic variables and INR response. An individual's response to the medication is influenced by polymorphisms in the genes that encode warfarin-metabolizing enzymes like cytochrome P450 2C9 (CYP2C9) and vitamin K epoxide reductase complex subunit 1 (VKORC1). In order to forecast and manage

INR swings and develop individualized anticoagulation treatments, it is essential to understand these genetic variances.

Healthcare professionals face difficulties managing INR variations. Successful anticoagulation therapy requires patients to follow prescribed medication schedules, adhere to dietary restrictions, and alter their lifestyles. However, establishing this delicate balance is frequently challenging and need for constant observation, patient education, and prompt interventions to address the causes of INR fluctuation.

Our research contributes valuable insights to the broader context of anticoagulation management, reinforcing the idea that a holistic approach that includes a nuanced understanding of dietary influences is essential. As we move forward, further research and educational initiatives are warranted to empower both healthcare providers and patients in making informed decisions about diet and its impact on INR levels, ultimately enhancing the safety and efficacy of anticoagulation therapy.

CONCLUSIONS:

The study reveals that diet significantly influences fluctuations in International Normalized Ratio (INR) levels among individuals undergoing anticoagulation therapy. Diet is the most common cause of INR instability, despite other factors like medication adherence and comorbidities. This highlights the importance of dietary counseling in the overall management plan for individuals on anticoagulation therapy. The study also emphasizes the need for personalized dietary guidance, as patient diets are diverse and multifaceted, making tailoring recommendations to individual needs crucial for optimizing anticoagulation control.

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