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REVIEW

Nutritional Management in Patients Under Warfarin Therapy: A Comprehensive Review

Warfarin Tedavisi Altındaki Hastalarda Beslenme Yönetimi: Kapsamlı Bir İnceleme

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Abstract

Warfarin is an anticoagulant drug routinely used in the treatment and prophylaxis of patients with atrial fibrillation, venous thromboembolism (deep venous thromboembolism, pulmonary embolism), and mechanical heart valves. Due to its narrow therapeutic index and its property of inhibiting vitamin K-dependent clotting factors, its pharmacological activity requires close monitoring. In the management of patients on warfarin who are followed with INR monitoring, dietary vitamin K affects INR values, which poses a risk for thromboembolic complications or bleeding. Therefore, appropriate nutritional management in patients on warfarin is vital to achieve treatment goals and ensure patient safety. This review article aims to help healthcare professionals more effectively manage the nutritional status of patients on warfarin by comprehensively evaluating recommendations for nutritional management in patients on warfarin.

Keywords: Warfarin; Nutrition; Vitamin K; Thromboembolism; Bleeding; Patient education

Warfarin is an oral anticoagulant derived from coumarin that has been used in clinical practice since the 1950s. It blocks the post-translational modification of vitamin K-dependent clotting factors (II, VII, IX, and X) in the liver by inhibiting the vitamin K epoxide reductase complex subunit 1 (VKORC1) enzyme.[1,2] These factors play a critical role in hemostasis and thrombosis formation. The primary goal of warfarin therapy is to prevent thromboembolic events by maintaining international normalized ratio (INR) values within the therapeutic range (usually 2.0–3.0) and, at the same time, to minimize the risk of bleeding.[3] The narrow therapeutic index of warfarin, interindividual pharmacokinetic and pharmacodynamic variability, and numerous drug and nutrient interactions complicate its management.

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Vitamin K is a fat-soluble vitamin found in various foods, including green leafy vegetables, some fruits, and vegetable oils. Vitamin K is a cofactor in the γ-carboxylation of clotting factors. It is required for the ability of these factors to bind calcium ions and function in the coagulation cascade.[4] Fluctuations in vitamin K intake during warfarin therapy can cause significant changes in INR values, which can lead to adverse bleeding or thrombotic events.[5]

This comprehensive review addresses the multifaceted aspects of nutritional management in patients on warfarin therapy. It examines the latest evidence in the literature and clinical guidelines, focusing on food groups with varying vitamin K content, dietary modification strategies, INR monitoring, patient education, and pharmacogenetic interactions. This review is intended to provide healthcare professionals with up-to-date and comprehensive guidance on providing evidence-based nutritional counseling to patients on warfarin and to help patients achieve optimal health outcomes during warfarin therapy.

This review consolidates insights from a broad spectrum of clinical studies, meta-analyses, and guideline documents to present an evidence-based approach to the nutritional management of patients on warfarin. Studies were selected based on their focus on vitamin K interactions, dietary management, and patient education in warfarin therapy. The findings were synthesized to provide healthcare professionals with a comprehensive guide to improving patient outcomes through optimized dietary strategies and education.

Methodology

This review article was prepared to compile the current literature on nutritional management in patients on warfarin treatment. A literature search was conducted in the PubMed, Scopus, and Web of Science databases covering the years 2010–2023. Keywords such as "Warfarin," "Vitamin K," "Nutritional Management," "INR Monitoring," and "Thromboembolic Complications" were used during the search. The articles obtained from the search were evaluated at the title, abstract, and full-text levels.

The criteria for inclusion in the review were determined as the article being a human study, having full-text access, being published in English, and being directly related to the subject. In addition, articles with low methodological quality were excluded.

Vitamin K and Warfarin Interaction

Vitamin K has two primary forms: phytomenadione (K1) and menaquinones (K2). Vitamin K1 is abundant in green leafy vegetables, while vitamin K2 is found in fermented foods and animal products. Both forms can affect the anticoagulant effect of warfarin, but the effect of vitamin K1 is more pronounced and rapid.[6–8] Warfarin inhibits the VKORC1 enzyme, preventing the reduction of vitamin K epoxide to vitamin K. This disrupts the carboxylation of vitamin K-dependent clotting factors and accumulates dysfunctional clotting factors.[9] As a result, clotting time is prolonged, and the INR value increases.

An increase in dietary vitamin K may increase the activity of the VKORC1 enzyme, thereby reducing the effect of warfarin and causing the INR value to decrease. Conversely, a decrease in dietary vitamin K may increase the effect of warfarin and cause the INR value to increase.[10] The interaction between warfarin, vitamin K, and dietary components remains a critical study area. Xue et al.[11] explore the intricate relationship between vitamin K, gut microbiota, and warfarin variability, particularly in cardiac surgery patients, highlighting the role of gut health in therapeutic outcomes. Furthermore, systematic reviews, such as those by Tan and Lee, underscore the significance of interactions between warfarin and various foods, herbal remedies, and dietary supplements.[12] Expanding this perspective, Attri and Farnam-Fard[13] discuss the broader implications of dietary elements beyond vitamin K, providing a comprehensive view of dietary considerations in warfarin management. These insights collectively emphasize the importance of tailored dietary advice and monitoring to optimize warfarin therapy.

Nutritional Recommendations for Patients Taking Warfarin

When managing patients on warfarin, diet plans can be recommended to ensure regular vitamin K intake without drastic alterations. In this case, the best solution is to average the restriction of vitamin K-rich foods instead. This assists in decreasing the fluctuations of INR values and maintains the consistency of the warfarin therapy (Table 1).

Vitamin K-rich foods have been categorized according to their potential to significantly or minimally affect INR values to address variability in interactions. Practical recommendations suggest a consistent daily vitamin K intake of 90–120 µg through diet or supplements tailored to individual INR stability and therapeutic goals. This approach provides balanced management of warfarin therapy while minimizing dietary restrictions.[14]

Table 1. Some food groups according to vitamin K content[15–24]

Foods high in vitamin K	Foods with moderate vitamin K	Foods low in vitamin K
Green leafy vegetables: Spinach, kale, collard greens, lettuce, arugula, chard, broccoli, Brussels sprouts	Vegetables: Carrots, cauliflower, potatoes, tomatoes	Fruits: Strawberries, raspberries, blackberries, melons, watermelons
Other vegetables: Asparagus, green beans, peas	Fruits: Banana, apple, orange, grape	Grains: White bread, rice, pasta
Fruits: Avocado, kiwi, prunes	Grains: Whole grains, whole wheat bread	Other: Sugar, honey, fats (olive oil, butter)
Vegetable oils: Soybean oil, canola oil	Meat and dairy products: Beef, chicken, fish, eggs, milk, cheese	
Beverages: Green tea		

Dietary Management Strategies and Patient Education

There are several strategies that patients on warfarin can use to manage their vitamin K intake. Keep a food diary to track the consumption of foods high in vitamin K and to maintain a constant daily intake. Portion control is also important; controlling portions of foods high in vitamin K can help prevent fluctuations in INR values. Cooking methods can also affect vitamin K content. Boiling or steaming vegetables can reduce vitamin K content. Instead of foods high in vitamin K, foods with low or moderate vitamin K content can be preferred.

Finally, patients must remember that dietary supplements such as multivitamins and herbal supplements may contain vitamin K, and they should consult their physician before using such supplements. Dietary supplements and herbal products are increasingly used, often without awareness of their potential interactions with medications. Ginseng, ginkgo biloba, and multivitamins containing vitamin K are among the most common supplements that can interfere with warfarin therapy, potentially altering INR levels and increasing the risk of adverse events. Studies such as those by Raposo et al. and Wang et al.[15,16] highlight the importance of assessing these interactions during patient counseling to ensure therapy safety and efficacy.

Effective patient education is critical to the success of warfarin therapy and patient safety.[17] Healthcare professionals should provide patients with comprehensive information about foods with different vitamin K content, dietary modification strategies, and the importance of monitoring their INR. It is important for patients to understand the potential risks and complications of warfarin therapy and to be empowered to make informed decisions about their health.

Pharmacogenetic Interactions

Warfarin's narrow therapeutic index and potential for interactions with multiple drugs complicate management. These interactions may potentiate the effect of warfarin, increasing the risk of bleeding, or reduce its effect, increasing the risk of thrombosis. Genetic variations in the CYP2C9 and VKORC1 genes significantly influence warfarin metabolism and dose requirements, affecting therapeutic outcomes and bleeding risks. Pharmacogenomic assessments can help optimize warfarin therapy by enabling personalized dose adjustments based on genetic profiles. Recent comprehensive evaluations, such as those by Ndadza, further highlight critical genomic factors influencing warfarin response, emphasizing the importance of integrating genetic testing into clinical practice.[18]

Drugs that Increase the Effect of Warfarin and May Increase the Risk of Bleeding

- Non-steroidal anti-inflammatory drugs (NSAIDs): Commonly used analgesics and anti-inflammatories such as aspirin, ibuprofen, and naproxen may increase the risk of bleeding by increasing the effect of warfarin. These drugs inhibit platelet function and increase the risk of ulceration in the gastrointestinal tract.[19]
- Antibiotics: Some antibiotics may increase the effect of warfarin by affecting the bacteria that produce vitamin K in the intestines. This group contains macrolides (erythromycin, clarithromycin), metronidazole, and some cephalosporins.[20]
- Antifungal drugs: Some antifungal drugs, such as fluconazole and itraconazole, may increase plasma concentrations and the risk of bleeding by inhibiting warfarin metabolism.[21]
- Antidepressants: Some antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), may increase the risk of bleeding by affecting platelet function and inhibiting warfarin metabolism.[22]
- Amiodarone: This antiarrhythmic drug can significantly increase INR values and increase the risk of bleeding by inhibiting warfarin metabolism.[16]

Drugs that May Reduce the Effect of Warfarin and Increase the Risk of Thrombosis

- Enzyme inducers: Drugs such as rifampicin, carbamazepine, and phenytoin accelerate warfarin metabolism by inducing drug metabolism enzymes in the liver and reducing its effectiveness. This may lead to a decrease in INR values and a risk of thrombosis.[19]
- Oral contraceptives: Birth control pills containing estrogen may reduce the effectiveness of warfarin by increasing the production of clotting factors in the liver.[16]

Other Important Interactions

Excessive alcohol consumption can affect liver function, alter warfarin metabolism, and cause fluctuations in INR values.[23] Grapefruit juice can increase the effect of warfarin by inhibiting the CYP3A4 enzyme involved in warfarin metabolism and increasing the risk of bleeding.[15,24] The effect of warfarin may also increase the deficiency of certain minerals, especially magnesium.[25,26] Genetic variations in the CYP2C9 and VKORC1 genes may affect warfarin metabolism and VKORC1 enzyme activity, affecting warfarin dose requirements and bleeding risk. Pharmacogenetic testing can be used to make individual dose adjustments and reduce the risk of bleeding before initiating warfarin therapy.[27]

Conclusion

One effective means of preventing and treating thromboembolic events is warfarin, an oral anticoagulant that is easy to administer.[1,2] However, this drug has a narrow therapeutic index and can be affected by dietary constituents, necessitating the need for INR monitoring and control during therapy.[10] The anticoagulant effect of warfarin is also affected directly by the nutrient vitamin K.

In order to ensure greater success in the treatment and control of INR, those on the drug must understand the importance of maintaining a consistent level of vitamin K, preventing any sudden alterations, and seeking approval from their doctor before making drastic adjustments in their intake. Effective patient education is an essential aspect of ensuring the successful therapy of patients on warfarin. Healthcare professionals must elaborate to patients about various dietary vitamin K-modifying foods, ways to change their diet, the need to monitor INR levels, and empower patients to make informed decisions regarding warfarin medication.[28]

Genetic factors also influence individual dose tailoring and response to warfarin treatment, an area that research will address in the future. Hence, future focus should emphasize why nutritional management in the warfarin patient population is so important. Healthcare professionals should provide evidence-based nutritional recommendations, prioritize patient education, and consider pharmacogenetic interactions to ensure patients eat healthily and safely during warfarin therapy.

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