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IMPACT OF GREEN LEAFY VEGETABLES ON WARFARIN THERAPY: A REVIEW OF DIETARY VITAMIN K INTERACTIONS

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ABSTRACT

A widely used anticoagulant Warfarin is commonly prescribed for prevention and treatment of thromboembolic disorders. The mechanism works by inhibiting the vitamin K epoxide reductase complex, thereby reducing the synthesis of clotting factors II, VII, IX, and X. A common belief is that dietary vitamin K intake could counteract the anticoagulant effect of vitamin K antagonists. Hence, patients have been discouraged from consuming vitamin-K-rich foods, such as green leafy vegetables. Since green leafy vegetables—such as spinach, kale, and broccoli—are rich sources of vitamin K, there has been a long-standing concern that their consumption may counteract warfarin's anticoagulant effects by lowering INR levels. However, emerging evidence suggests that the primary concern is not the intake of vitamin K-rich foods itself, but rather inconsistencies in dietary vitamin K consumption. Studies indicate that maintaining a stable intake of vitamin K supports INR stability and improves anti-coagulation control. The findings suggest patients with highly variable vitamin K intake may experience more significant fluctuations in INR, whereas those with consistent intake demonstrate improved anti-coagulation stability. In clinical practice, a balanced and informed approach to diet is essential for patients on warfarin therapy. Complete avoidance of green leafy vegetables is unnecessary; instead, a consistent and moderate intake of vitamin K is recommended to maintain stable INR levels.

KEYWORDS: *Warfarin, vitamin K, dietary interactions, green leafy vegetables, anticoagulation, INR.*

INTRODUCTION

Anticoagulation therapy plays a vital role in preventing thromboembolic complications in patients with conditions such as atrial fibrillation (AF), prosthetic heart valves, venous thromboembolism (VTE), and coronary artery disease (CAD).[1] For more than 6 decades, the mainstay of oral anticoagulant treatment has been vitamin K antagonist. However, its narrow therapeutic index, complex dosing requirements, and significant drug-diet interactions pose clinical challenges that increased the need for ongoing education and cautious management.[1,2]

Green leafy vegetables, such as spinach, kale, and broccoli, are among the richest dietary sources of vitamin K, which plays a fundamental role in blood coagulation. Because warfarin's mechanism of action directly opposes vitamin K's role in clotting factor synthesis, there is a long-standing concern that consuming vitamin K-rich foods could interfere with warfarin's anticoagulant effects. The common belief is that a high intake of these vegetables may antagonize warfarin's therapeutic effects, leading to reduced INR levels and increasing the risk of clot formation.[3] However, emerging evidence suggests that it is not the consumption of vitamin K-rich foods per se that poses a challenge, but rather fluctuations in dietary vitamin K intake. Studies indicate that maintaining a consistent level of vitamin K intake may stabilize INR values, thereby optimizing anticoagulation control.[4-6]

The relationship between warfarin and dietary vitamin K has been widely debated, with studies showing inconsistent results regarding whether green leafy vegetables significantly reduce warfarin's effectiveness. Some studies report a clear inverse relationship between vitamin K intake and INR values, while others suggest that moderate and stable vitamin K consumption has minimal or even beneficial effects on anticoagulation stability.[7-9] Given the conflicting data, there is a need to clarify whether green leafy vegetables genuinely impair warfarin's anticoagulant effect or if they can be safely incorporated into a controlled diet without increasing the risk of thrombosis. This review aims to provide clarity on this subject by analysing existing research and offering dietary recommendations for patients on warfarin therapy.

OBJECTIVE

This review aims to evaluate the impact of dietary vitamin K and other food interactions on warfarin therapy. The study seeks to clarify misconceptions regarding green leafy vegetables

and provide evidence-based dietary recommendations to improve INR stability in patients undergoing warfarin therapy.

METHODOLOGY

A literature review was conducted using keywords "vitamin K", "warfarin", "food interactions", "anti-coagulation". Only studies published in peer-reviewed journals between 2000 and 2023 were included. Systematic reviews, randomized controlled trials (RCTs), and observational studies were considered.

DISCUSSION

Warfarin exerts its anticoagulant effect by inhibiting the cyclic interconversion of vitamin K and its epoxide form (vitamin K1 epoxide). This action reduces the synthesis of active clotting factors II, VII, IX, and X, thereby preventing thrombus formation. Warfarin interacts with numerous medications, herbal supplements, and foods, potentially leading to either an increased risk of bleeding or thrombosis.[1] Clinically significant interactions may occur with the initiation, discontinuation, or intermittent use of interacting agents. A common concern is the interaction between warfarin and dietary vitamin K, traditionally believed to significantly influence anticoagulation stability. A systematic review by **Violi *et al.*** assessed the evidence for dietary vitamin K and INR stability, concluding that rather than eliminating vitamin K-rich foods, patients should aim for a stable intake to maintain consistent anticoagulation levels.[2] Similarly, Pedersen *et al.*, demonstrated that INR instability occurred in both vitamin K-deficient and vitamin K-excessive diets, reinforcing the importance of dietary consistency rather than restriction. Small, short-term changes in dietary vitamin K had very little impact on INR levels in patients taking warfarin. It was only when higher doses of vitamin K_1 supplements—specifically 150 micrograms or more per day—were taken that a noticeable drop in INR occurred. In contrast, lower doses (100 micrograms or less) didn't seem to interfere with anticoagulant control. Interestingly, the study also pointed out that vitamin K from natural food sources like green leafy vegetables is less likely to cause issues, as it's absorbed less consistently by the body.[6]

The misconception that patients on warfarin must completely eliminate green leafy vegetables has been challenged by multiple studies. Holbrook *et al.*, found that those who entirely avoided vitamin K-rich foods had less stable INR levels than those who maintained a moderate and consistent intake. The evidence linking these foods to significant changes in INR was limited and largely based on isolated case reports.[9] Gebuis *et al.*, recommended

patient-specific dietary modifications, suggesting that warfarin users should not eliminate leafy greens but instead consume a regulated and predictable amount daily.[7]

Pengo *et al.*, emphasized the importance of comprehensive anticoagulation management programs incorporating dietary education to help patients achieve optimal INR control. Pengo and colleagues conducted a nested case–control study in a large anticoagulation clinic to explore how habitual vitamin K intake affects INR stability. They discovered that patients with consistently higher vitamin K consumption had a lower risk of sub-therapeutic INR, while those with low habitual intake were more vulnerable to INR drops—especially after occasional spikes in dietary vitamin K (for instance, consuming 164 µg/day compared to 85 µg/day among controls). They concluded that a diet rich enough in vitamin K actually buffers INR by reducing the impact of unplanned intake variations. From a clinical standpoint, they recommend that patients on vitamin K antagonists should maintain adequate and steady intake of vitamin K–containing foods to avoid destabilizing warfarin therapy.[8]

The 2003 AHA/ACC and 2010 ESC guidelines highlighted the need to monitor dietary vitamin K in patients on warfarin, more recent evidence suggests that the interaction between vitamin K intake and INR variability may not be as strong or linear as once believed. Rather than emphasizing restriction, the focus should be on encouraging patients to maintain a consistent dietary pattern that includes moderate amounts of vitamin K. This approach supports more stable anticoagulation, improves patient adherence, and aligns with the current understanding that consistency—not avoidance—is the key to optimizing warfarin therapy.[2]

Table No. 1: Dietary Recommendations for Green Leafy Vegetable Intake in Patients on Warfarin Therapy.

Vitamin K. Source	Recommended Daily Intake	Vitamin K Content (µg per 100g)	Clinical Recommendation
Spinach (cooked)	½ cup	~440 µg	Include regularly; ensure consistent daily portion size.
Broccoli (cooked)	½ cup	~110 µg	Safe in moderation; maintain weekly consistency.
Kale (cooked)	½ cup	~500 µg	Avoid sudden increases; maintain stable weekly average.
Romaine lettuce (raw)	1 cup	~50–60 µg	Suitable daily in salads; avoid frequent type changes.
Cabbage (cooked)	½ cup	~80 µg	Acceptable regularly; educate on steady portioning.
Green beans (cooked)	½ cup	~15–20 µg	Low vitamin K; considered safe in free amounts.

CONCLUSION

Warfarin remains a vital anticoagulant in clinical practice despite the advent of NOACs. Its effective management requires individualized dosing, regular INR monitoring, and careful consideration of drug and dietary interactions. While dietary vitamin K intake can influence warfarin's efficacy, the impact is often overstated, and consistent consumption is key. Ongoing education for healthcare providers and patients is critical to optimizing warfarin therapy, minimizing complications, and improving patient outcomes. Furthermore, interactions with fruits and herbal supplements must be considered in clinical practice. Future research should focus on personalized dietary plans to optimize warfarin therapy and improve patient outcomes.

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