

## LETTER TO THE EDITOR

# Enteral and Parenteral Nutrition-Induced Resistance Mechanisms and Clinical Approaches to Warfarin Use

*Varfarin Kullanımında Enteral ve Parenteral Beslenme Kaynaklı Direnç Mekanizmaları ve Klinik Yaklaşımlar*

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Dear Editor,

I read with great interest the recent review published by Aslan et al.<sup>[1]</sup> titled "Nutritional Management in Patients Under Warfarin Therapy: A Comprehensive Review." This review contains vital, up-to-date information regarding nutritional management in patients under warfarin therapy.

In this review, the authors detailed nutritional and drug interactions that alter the effectiveness of warfarin therapy. In addition to oral feeding, enteral and parenteral nutrition are frequently used for both nutrition and drug administration in patients receiving warfarin who cannot swallow safely due to pulmonary embolism, deep vein thrombosis (DVT), or post-stroke mental status or neuromuscular problems.<sup>[2]</sup> Numerous publications have reported warfarin interactions during enteral and parenteral nutrition. Camilo et al.<sup>[3]</sup> reported that an intravenous lipid solution containing 154 µg of phylloquinone per 500 ml blocked the effects of warfarin. Similarly, Penrod et al.<sup>[4]</sup> reported two cases of warfarin resistance following enteral nutrition. An interaction between nutritional supplements

and warfarin has been suggested as a mechanism of resistance, but no additional evidence has been presented to support this hypothesis.

In an integrative literature review, Silva et al.<sup>[5]</sup> identified an *in vitro* study and clinical studies with warfarin that demonstrated a decrease in drug bioavailability when administered with enteral feeding. They recommended that consideration be given to potential risks in prescribing and administering the drug. In a retrospective study of six adult patients receiving enteral nutrition support during the first 10 days of warfarin therapy, Dickerson et al.<sup>[6]</sup> reported that the INR change during a 3-day observation period during which enteral feeding was interrupted for 1 hour before and after warfarin administration was statistically significantly different from the INR change during the period when warfarin was administered with continuous enteral feeding. This study demonstrated that continuous enteral feedings should be withheld 1 hour before and after warfarin administration to prevent warfarin resistance due to enteral feeding. Within the class of anticoagulants, a study with warfarin also showed a 73% decrease in INR (international normalized ratio, one of

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the parameters used to assess clotting) compared with the period when feedings were withheld for drug administration. Therefore, it has been recommended that nursing staff be informed about this issue and that management protocols that ensure effective treatment be proposed. Penrod et al.<sup>[4]</sup> evaluated the potential interactions between commonly used enteral nutrition products and warfarin. Two reported cases of clinically significant interactions prompted an *in vitro* study to support these observations. Both clinical cases and laboratory findings demonstrated that various enteral nutrition products bind to warfarin, reducing the bioavailability of the drug. Specifically, a binding mechanism was observed between warfarin and the protein components of the nutrition products. This pharmacokinetically significant interaction was reported to occur with concomitant administration of warfarin and enteral nutrition products.

In conclusion, while Aslan et al.'s<sup>[1]</sup> study provides an important contribution to the literature, future studies should consider the aforementioned issues to obtain more robust and generalizable results. Clinicians should be aware of the potential for warfarin resistance resulting from dietary supplements containing high concentrations of vitamin K and carefully select appropriate dietary supplements for patients taking warfarin, avoiding coadministration with nutrition. They should also closely monitor INR levels during enteral or parenteral nutrition or when nutrition is discontinued.

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