The effect of vitamin K supplementation on anticoagulant therapy

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Until recently, the view that dietary vitamin K interferes with oral anticoagulant therapy was based on case reports and a few small experimental studies with extremely high vitamin K intake. In two recent studies the effect of dietary vitamin K on oral anticoagulation was systematically investigated. These studies showed that even in patients on an average diet changes in vitamin K intake affect anticoagulation. When patients decreased their vitamin K intake the response on the International Normalized Ratio (INR) was more pronounced than when vitamin K intake was increased. Because changes are proportionally larger in people with a low average vitamin K intake, it is likely that the INR is more sensitive to a varying vitamin K intake in those individuals. Sconce et al. established that daily intake of vitamin K was indeed lower in patients with unstable anticoagulation than in stably anticoagulated patients. Daily supplementation of low doses of vitamin K might thus be beneficial.

To safely start vitamin K supplementation in patients receiving oral anticoagulants, it is important to know the effect of low doses of vitamin K on the INR and on the dose of the anticoagulant drug. The dose-response relationship of vitamin K supplementation on the INR in healthy subjects that received a fixed dose of oral anticoagulants was established by Schurgers et al. They concluded that 100 µg of vitamin K daily did not significantly interfere with oral anticoagulant therapy. Consequently, Oldenburg suggested 100 µg vitamin K as a recommended supplementation dose in his editorial. However, Kurnik et al. found that in patients with a low vitamin K status even daily supplement doses as low as 25 µg led to an important reduction of the INR.

We performed a pilot study to determine the effect of escalating daily doses of vitamin K on the required dose of the anticoagulant drug phenprocoumon. We included patients from the Leiden Anticoagulation Clinic that took part in a program for self-management of anticoagulant treatment. The total study period was 9 weeks, in which the INR was measured at least 3 times a week with a CoaguCheck S coagulometer (Roche Diagnostics, Almere, Netherlands). Patients received vitamin K for 3 weeks. The first and last 3 weeks served as control periods. Five patients received 50 µg and 10 patients 100 µg of oil-based vitamin K. (250 µg/g).
The primary endpoint was the percentage change in phenprocoumon dose during and after vitamin K needed to keep the INR within therapeutic limits.

Supplementation of 50 µg vitamin K had little effect on the INR and therefore only slight dose-adjustments were made (mean dose increase after starting vitamin K 3% (95% confidence interval (95%CI): -4% to 10%). Supplementation of 100 µg resulted in a mean dose increase of 9% (95%CI: 0% to 19%, figure 1). There was considerable inter-individual variability in response with dose-adjustments ranging from -7% to 37%. In the three weeks follow-up after the vitamin K was discontinued phenprocoumon doses were lowered to pre-substitution values (mean change of -7%, 95%CI: -15% to 0%).

Our results show that daily supplementation up to 100 µg can be given without a relevant decrease in the INR, on the condition of frequent monitoring during and after the supplementation to allow timely dose adjustments.

Figure 1: Effect of vitamin K supplementation on the mean International Normalized Ratio (INR) (●) and the mean phenprocoumon dose (□) in 10 patients receiving 100 µg vitamin K daily.
References


