

# The use of low dose vitamin K to stabilize INR fluctuation during warfarin therapy

## A Case Series

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### Background

Despite aggressive management, some anticoagulated patients have marked INR fluctuations with no discernable changes in lifestyle, diet, or medications. Fluctuation of the INR is concerning, as it has been associated with an increased complication rate of anticoagulation therapy.

Since we know that dramatic changes in vitamin K intake will affect anticoagulation control, we hypothesized that supplying the liver with a consistent background amount of vitamin K would lead to a controlled production of clotting factors and a more predictable warfarin response. The vitamin K might also enhance stability by dampening the magnitude of physiologic responses to changes in vitamin K dietary intake.

### Hypothesis

A consistent supplement of vitamin K at or above the normal dietary intake will dampen the fluctuations in the INR, and improve anticoagulation control.

### Methods

- The patients individually elected to try supplementation with vitamin K
- Vitamin K was obtained at the patient's own expense through a local health food store [Vitamin K 100mcg. tablets (GNC)- approximately \$4.00/100 tablets]
- Vitamin K 100 mcg./d was chosen based on the RDA of 80 mcg./d and the usual daily intake of 50-150 mcg./d in the US

- The patient implemented vitamin K 100 mcg./d in conjunction with the anticoagulation provider's plan to monitor the response
- The standard deviation before and after vitamin K supplementation were compared with statistical significance determined by Student t-test and the Wilcoxon Signed Ranks test with  $p < 0.05$  considered significant
- Number and percent of INRs in range were calculated before and after vitamin K supplementation

### Results

- Data is available for 8 patients
  - One patient discontinued in the first week because of a TIA (INR = 3.2 at time of event)
- There was an overall decrease in the standard deviation of the INR which was statistically significant by Student t-test and Wilcoxon Signed Ranks Test
- The number of INRs in range increased overall
- One patient did not respond to vitamin K in either decreasing the SD or increasing the percentage of INRs in range (MN)
- One patient had an increase in the percent of INRs in range, but did not show a decrease in the SD (DM)
  - This patient had multiple interruptions for procedures
- One patient had a decrease in the SD, but did not show an increase in the percent of INRs in range (KB)
  - The INR was intentionally left high in this patient

- Two patients did not respond to 100 mcg. vitamin K. One of these patients responded to 200 mcg. vitamin K. The other patient stabilized only after her thyroid disease was discovered and treated.

### Discussion

This was a case series that does not carry the scientific rigor of a controlled clinical study. Although the results are compelling for this small group of patients, the limitations of these data must be considered.

#### Potential Limitations

##### Patient Care Issues

- These patients were self selected
- Most of the patients had target INR ranges that were higher than usual
- Although possible reasons for INR fluctuation were excluded, we did have one patient with unstable thyroid disease (patient LF).
- Seen in a specialized clinic s

##### Data Collection Issues

- Uncontrolled Case Series
- More INR datapoints after vitamin K than before
- All datapoints were included

### Conclusion

In this series of selected anticoagulated patients, dietary supplementation with vitamin K at a dose of 100-200 mcg./d improved individual anticoagulation control as measured by variability in the INR, and percent of INRs in the designated range.

## INRs in Range

Patient	In Therapeutic Range		In Therapeutic Range +/- 0.2	
	Before Vitamin K treatment	After Vitamin K treatment	Before Vitamin K treatment	After Vitamin K treatment
GG	54%	60%	69%	77%
DB	0%	41%	33%	55%
HS	7%	53%	36%	76%
KB	9%	18%	17%	47%
DM	8%	38%	33%	46%
LF	37%	36%	37%	36%
ML	0%	100%	0%	100%
MN	27%	30%	45%	38%
<b>Overall</b>	<b>18.3%</b>	<b>41.7%</b>	<b>32.2%</b>	<b>56.8%</b>
	<b>Absolute Increase 23.4%</b>		<b>Absolute Increase 24.6%</b>	
	<b>Relative Increase 127.9%</b>		<b>Relative Increase 76.4%</b>	

● vitamin K started at 100 mcg./d

■ Vitamin K dose increased to 200 mcg./d

