Acute care management of SUPRAtherapeutic INRs without bleeding following WARfarin use: An evaluation of vitamin K administration (SUPRA-WAR-K)

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Background

- Supratherapeutic international normalized ratios (INRs) due to warfarin can be reversed through vitamin K administration.
- The ACCP 2012 guidelines state that supratherapeutic INRs of 4.5-10.0 without bleeding should not be treated with vitamin K due to lack of evidence of benefit for patient-important outcomes, such as rates of major bleed, thromboembolism, and all-cause mortality. These recommendations are based upon evidence from the outpatient setting.
- At St. Paul's Hospital (SPH), it has been observed that acute care patients with INRs ≥4.5 and no evidence of bleeding are often prescribed vitamin K.

Objectives

Primary objective:

- To characterize vitamin K prescribing practices in acute care patients with supratherapeutic INRs and no evidence of bleeding.

Secondary objective:

- To compare the safety and efficacy of vitamin K administration to withholding warfarin alone for the acute care reversal of supratherapeutic INRs without bleeding by examining change in INR within 24 hours, time to INR <3.0, length of stay, and rates of major bleed, thromboembolism, and mortality.

Methods

- **Design:** Single-center retrospective chart review
- **Inclusion criteria**:
  - ≥18 years of age
  - Admitted to SPH Internal Medicine Service between January 1, 2010 and December 31, 2015
  - Received warfarin therapy with INR target of 2.0-3.0 prior to and/or during the admission
  - Had ≥1 supratherapeutic INR reading between 4.5-8.9 with no evidence of bleeding
  - Received management for the supratherapeutic INR
- **Exclusion criteria**:
  - Received fresh frozen plasma, prothrombin complex concentrate, and/or recombinant factor VIIa
  - Received >1 dose of vitamin K
  - No INR information available after supratherapeutic INR management
  - Transferred to a critical care unit
  - Received surgery
  - Documented severe liver disease and/or bleeding disorder
- **Analysis:**
  - Descriptive statistics
  - Student's *t*-test for continuous data
  - Fisher's exact test for categorical data

Results

Table 1: Baseline characteristics (n=146)

Male, %	57
Age (years), mean ± SD	76 ± 14
Primary warfarin indication, %	
Atrial fibrillation	82
Recurrent VTE	10
Aortic valve replacement	4
Left ventricular thrombus	2
Other	2
Daily warfarin dose (mg), mean ± SD	4.2 ± 2.3
Supratherapeutic INR, mean ± SD	5.4 ± 0.9

Table 2: Secondary outcomes – Safety and efficacy of interventions for supratherapeutic INR management

	Warfarin Held Only (n=87)	Received Vitamin K (n=59)	P value
Change in INR 24h after intervention, mean ± SD	-0.9 ± 1.0	-3.2 ± 1.9	<0.01
Time to INR <3.0 (days), mean ± SD	2.6 ± 1.4	1.9 ± 1.0	<0.01
Length of stay (days), mean ± SD	17.1 ± 14.2	17.5 ± 13.6	0.85
Major bleed, n (%)	1 (1)	1 (2)	1.00
Thromboembolism, n (%)	0 (0)	0 (0)	-
Mortality, n (%)	8 (9)	6 (10)	1.00

Figure 1: Primary outcome – Prescribed methods of supratherapeutic INR management

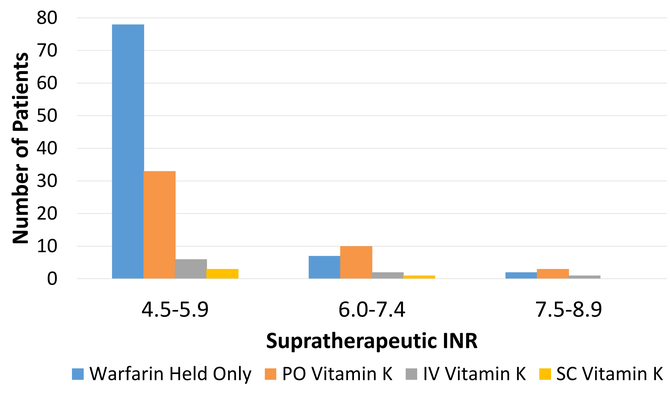


Figure 2: Primary outcome – Prescribed vitamin K dose

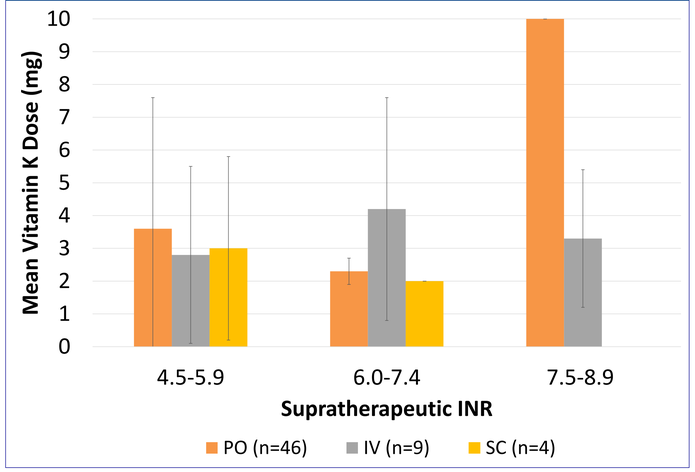
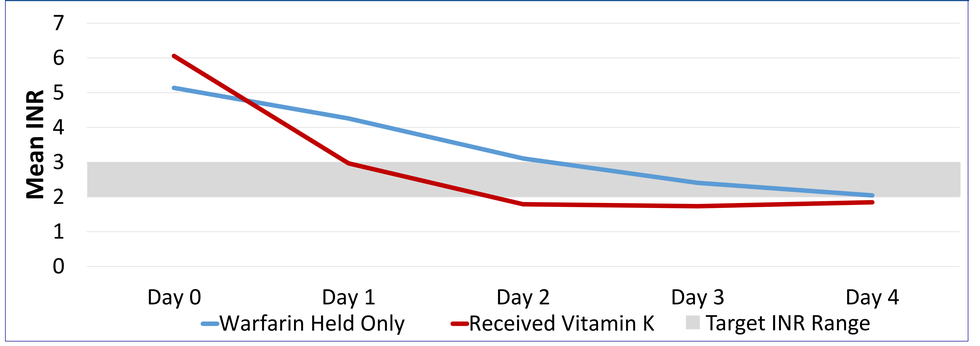


Figure 3: Change in INR after intervention



Limitations

- Single-center, retrospective design
- Small sample size
- Maximum quantifiable INR at SPH is 8.9; unable to evaluate INRs ≥9.0

Conclusions

- Vitamin K was prescribed to 40% of included patients:
  - Doses ranged from 1-10mg via oral, subcutaneous and intravenous routes.
  - The most common route of administration was oral.
  - A greater proportion of patients with INRs ≥6.0 received vitamin K compared to those with lower supratherapeutic INRs.
- Compared to simply withholding warfarin, the safety and efficacy of vitamin K in the acute care setting was found to be similar to that demonstrated in existing outpatient data.
  - Administration of vitamin K was associated with a greater decrease in INR within 24 hours and a decreased time to INR <3.0.
  - No statistically significant differences were found in length of stay or in rates of major bleed, thromboembolism, or mortality.
- Larger prospective studies are required to validate these results and to provide further guidance for vitamin K prescribing practices in the acute care setting.