



Assessment Of Adherence to Warfarin Anticoagulation Using the Ratio Of Vitamin K Dependent Factors



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Introduction

- Despite recent significant advances in therapeutic anticoagulation, warfarin remains the most affordable and widely used anticoagulant¹.
- Warfarin has dual anticoagulant effect (reflecting the short half-life clotting factors (CF)) and antithrombotic effect (reflecting the long half-life of CF)². A therapeutic INR may reflect the anticoagulant effect but not antithrombotic effect.
- Non-adherent patients may have a therapeutic INR but still be at risk of thrombosis³.
- We hypothesized that a potential approach to monitor adherence to warfarin therapy is to measure the INR in relation to the ratio of short half-life and long half-life of the CF.

Aim of the study

The aim of this study was to evaluate adherence to warfarin therapy by measuring the ratio of FVII to FII in patients on steady state warfarin anticoagulation

Material and methods

- This was a prospective, cross sectional study conducted in a tertiary referral teaching hospital in Johannesburg
- The study was approved by the institutional human research ethics committee and participants gave written informed consent.
- Participants were included in the study if they were ≥18 years, attendees of the anticoagulation clinic at Charlotte Maxeke Hospital and on steady state warfarin for ≥ 3 months with a therapeutic INR of 2-3.5.
- A 5ml venous blood sample was collected in trisodium citrate and analysed for FVII and FII on a STA-R coagulation analyser according to the local standard operating procedure. Data on patient demographics, concurrent medication and monthly INR results was collected using a data collection sheet

Results

- Of the 350 participants enrolled in the study on warfarin for ≥3 months,
 - 92 had a sub-therapeutic INR,
 - 45 were above therapeutic range and
 - 213 had an INR in therapeutic range.
- In the therapeutic INR group,
 - the mean age was 54 years (range 18-94 years) and
 - the mean period on warfarin was 66 months (range 3-288).
- Only 2 of the 204 patients in the therapeutic INR group had a low factor VII level and normal factor II level.
- Time in therapeutic range was assessed over a 4 month period.
 - 32% of patients had a 100% TTR, while
 - 9.3% had 25% TTR.
- Demographic subgroup analysis indicated that Caucasians spent more time in TTR whilst Asians spent the least TTR (p<0.0001; Cramer's V=0.24).
- Using the subtherapeutic INR patients as a control group (n=79),
 - sensitivity (i.e. true adherence) was calculated to be 79.8% and
 - specificity (i.e. true non-adherence was calculated to be 93.3%
 Please refer to table 1 below

Table 1. Therapeutic INR by Adherence in the analysis group

		Adherence		
		No	Yes	Total
Therapeutic INR	No	28	51	79
	Yes	2	202	204
	Total	30	253	283

Conclusion

- In our population of anticoagulation clinic attendees, non-adherence on steady state warfarin anticoagulation was very low and the ratio of vitamin K dependent factors proved to be less informative about patient adherence.
- While the INR is a good test to detect non-adherent patients, it has shown to overcall adherent patients as being non-adherent.
- This may result in the inappropriate dose increases of warfarin and thus associated increase in bleeding risks.

References

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Acknowledgement and conflict of interest declaration

- This study was funded by research grants from the University of the Witwatersrand Faculty of Health Sciences and the National health Laboratory Service
- The authors declared no relevant conflict of interest

