GHNHSFT GUIDELINES FOR STARTING WARFARIN

- ensure no contraindications to anticoagulation
- consider discontinuation of anti-platelet drugs (aspirin, dipyridamole, clopidogrel and NSAIDs)
- measure baseline full blood count, liver function, INR and APTT
- educate patient following 'yellow book advice' including the action to take if bleeding occurs
- advise patient to take warfarin at the same time in the early evening
- does the patient require rapid anticoagulation?

No: For patients who do not require rapid anticoagulation a slow-loading regimen is safe and achieves therapeutic anticoagulation in the majority of patients within 3–4 weeks (grade B, level IIb) [1]. This may avoid over-anticoagulation associated with rapid loading and the development of a hypercoagulable state (caused by precipitous decreases in levels of protein C) during the first 36-48 hours of warfarin therapy. Example regimen includes:

Warfarin 3mg/d -check INR on day 5 and day 8

Yes: For patients requiring rapid initiation of oral anticoagulation (usually patients receiving LMWH for acute venous thromboembolic disease) follow the standard dosing algorithm opposite [4]. Dose adjustment is guided by daily INR measurement from the second day of treatment. Consider prescribing a lower initial warfarin dose in the elderly (>60 years of age) and patients with liver disease or cardiac failure and others at high risk of bleeding (grade B, level IIb) [1, 5].

Day	INR @ 9AM	Warfarin Dose (mg) @ 6PM
1	<1.4	10
2	<1.8	10
	1.8	1
	>1.8	0.5
3	<2.0	10
	2.0 -2.1	5
	2.2 -2.3	4.5
	2.4 -2.5	4
	2.6 -2.7	3.5
	2.8 -2.9	3
	3.0 -3.1	2.5
	3.2 -3.3	2
	3.4	1.5
	3.5	1
	3.6 -4.0	0.5
	>4.0	0
4 (predicted maintenance dose)	<1.4	>8
	1.4	8
	1.5	7.5
	1.6 -1.7	7
	1.8	6.5
	1.9	6
	2.0 -2.1	5.5
	2.2 -2.3	5
	2.4 -2.6	4.5
	2.7 -3.0	4
	3.1 -3.5	3.5
	3.6 -4.0	3
	4.1 -4.5	Omit next dose then 2mg
	>4.5	Omit next two doses then 1mg

1. T. P. Baglin, D. M. Keeling and H. G. Watson. Guidelines on oral anticoagulation (warfarin): third edition -2005 update. British Journal of Haematology 132 (3) 2006: 277 -285.
2. R. C. and A. Sefick. A warfarin induction regimen for out-patient anticoagulation in patients with atrial fibrillation. British Journal of Haematology 101 (3) 1998: 450 -454.
3. A. Oates, P. R. Jackson, C. A. Austin and K. S. Channer. A new regimen for starting warfarin therapy in out-patients. British Journal of Clinical Pharmacology 46 (2) 1998: 157 -161.
4. A. Fennerty, J. Dolben, P. Thomas, G. Backhouse, D.P. Bentley, I.A. Campbell and P.A. Routledge. Flexible induction dose regimen for warfarin and prediction of maintenance dose. British Medical Journal 288 (6426) 1984: 1268 -70.
5. G.W. Roberts, T. Druskeit, L.E. Jorgensen, L.M. Wing, A.S. Gallus, C. Miller, D. Cosh and V.S. Eaton. Comparison of an age adjusted warfarin loading protocol with empirical dosing and Fennerty's protocol. Australian and New Zealand Journal of Medicine 29 (5) 1999: 731 -736.

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October 2007

1. Baglin TP, Keeling DM, Watson HG; British Committee for Standards in Haematology.

Br J Haematol. 2006 Feb 132(3): 277-85.

Guidelines on oral anticoagulation (warfarin): third edition -2005 update.

No Abstract

2. Tait RC, Sefcick A.

Br J Haematol. 1998 Jun 101(3): 450-4.

A warfarin induction regimen for out-patient anticoagulation in patients with atrial fibrillation.

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Currently available protocols for induction of warfarin anticoagulation employ initial doses of 10 mg and are best suited to in-patient use. However, with the increasing number of elderly patients with atrial fibrillation requiring anticoagulation, there is a need for a less intense regimen which could be used for out-patients. We have established such a regimen and report on its prospective evaluation in 3 7 patients referred for out-patient initiation of warfarin, and a non-randomized comparison with 37 in-patients, with similar diagnoses, commenced on a traditional warfarin protocol. After exclusion of five patients on amiodarone, all of whom experienced supratherapeutic International Normalized Ratio (INR) results, the new out-patient regimen, employing an initial 5 mg dose, resulted in a lower maximum INR during the first 21 d therapy (median 2.9 v 4.0; P = 0.0001) and fewer INRs >4.5 (2/36 v 9/33) compared to the traditional 10 mg regimen. Time to reach stable anticoagulation was similar with each regimen; however, the 5 mg regimen gave a more accurate prediction of maintenance dose (correlation coefficient for predicted versus actual maintenance dose, r = 0.985). In comparison to a traditional 10 mg protocol, the proposed 5 mg warfarin induction regimen proved both safer and more reliable for initiation of prophylactic anticoagulation in patients with atrial fibrillation.

3. Oates A, Jackson PR, Austin CA, Channer KS.

Br J Clin Pharmacol. 1998 Aug 46(2): 157-61.

A new regimen for starting warfarin therapy in out-patients.

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AIMS: Oral anticoagulation is increasingly used in elderly patients with atrial fibrillation to prevent embolic phenomena. The use of anticoagulants in this population is prophylactic rather than therapeutic and so there is no urgency to establish anticoagulation within the desired therapeutic range. The aim of the study was to develop an out-patient regimen for initiation of oral anticoagulation with warfarin which requires only weekly monitoring of the International Normalized Ratio (INR). METHODS: The study was undertaken in two phases. In the first phase, factors which predict the final maintenance dosage of warfarin were defined and used to build a decision tree and dosage algorithm. In the second study the algorithm was tested. Patients were given 2 mg warfarin daily for 2 weeks and the INR at this time was used to predict the maintenance dose. Patients then attended for weekly measurements of the INR until steady state had been reached. Dosage adjustments were not made unless the INR was >4.0 or <1.5 for 2 consecutive weeks. The accuracy of the prediction was measured by calculating the mean INR of weeks 6-8 and the number of patients in the target range 2.0-3.0 was determined. RESULTS: One hundred and seven consecutive out-patients (mean age 70 years range 64-86) completed the first study. The age, sex, height, weight, alcohol intake, number of cigarettes smoked, concomitant medication, clinical evidence of right heart failure, liver failure, abnormalities in liver enzyme estimations, baseline INR and INR after 2 weeks of 2 mg warfarin daily were used in a polytomous logistic regression analysis with stepwise inclusion of factors to determine which factors influenced the eventual maintenance dosage of warfarin. The INR after 2 weeks of 2 mg warfarin therapy predicted 70% of the variability of the maintenance dose. Of other factors only the sex of the patient had a large enough effect to be included in the prediction algorithm. One hundred and six patients (mean age 71 years range 50-85 years) completed the second study. Only one patient needed a dose adjustment in the first 2 weeks of warfarin 2 mg daily (INR 4.4). Overall, 60% patients were in the narrow target range (INR 2.0-3.0) at steady state. In five patients the INR was >4.0 at any visit after the second week and needed dosage adjustment. In four patients the INR was <1.5 at steady state. CONCLUSIONS: We have developed a method of predicting the maintenance dose of warfarin in an elderly population based on the INR after 2 weeks of warfarin 2 mg daily, and the sex of the patient. This is a safe and convenient way of initiating warfarin therapy as an out-patient which requires only weekly INR checks.

4. Fennerty A, Dolben J, Thomas P, Backhouse G, Bentley DP, Campbell IA, Routledge PA.

Br Med J. 1984 Apr 28 288(6426): 1268-70.

Flexible induction dose regimen for warfarin and prediction of maintenance dose.

Fifty patients with venous thromboembolic disease being treated by heparin infusion received a three day warfarin induction regimen tailored according to the prothrombin time (British comparative ratio) measured on days 2 and 3. A prediction of the final maintenance dose of warfarin was made on the basis of a prothrombin time measured on day 4. All patients were safely anticoagulated by day 6, and the prediction was accurate to within 1 mg in 46 patients. Predicted and actual maintenance doses were closely related (r = 0.867; n = 50; p less than 0.001). This scheme should prove helpful in the control of anticoagulation, particularly in patients likely to be sensitive to warfarin, and should shorten hospital stay.

5. Roberts GW, Druskeit T, Jorgensen LE, Wing LM, Gallus AS, Miller C, Cosh D, Eaton VS.

Aust N Z J Med. 1999 Oct 29(5): 731-6.

Comparison of an age adjusted warfarin loading protocol with empirical dosing and Fennerty's protocol.

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AIM: A warfarin loading protocol adjusting doses for age was compared to both Fennerty's protocol (Fenn) and empirical dosing (Emp). METHODS: Patients beginning warfarin were randomised to receive doses according to either the age adjusted (Age) protocol or Fenn. Data were retrospectively collected for patients who had begun warfarin in the previous six months to represent empirical dosing. The study was performed on inpatients being commenced on warfarin for the first time at two teaching hospitals. MAIN OUTCOME MEASURES: Endpoints were time to reach a stable, therapeutic International Normalised Ratio (INR) between 2-3, the number of patients experiencing an INR > or =4 in the first week and the number of patients who had a dose held in the first week. RESULTS: Thirty-five patients were assessed in the Age group, 28 in the Fenn group, and 123 patients for the Emp group. Patients using the Age protocol achieved a stable, therapeutic INR more rapidly than either the Fenn ($p=0.003$, log rank test) or Emp ($p<0.001$) group. The Age group had a lower proportion of patients experiencing an INR > or =4 in the first week ($p<0.05$) as well as a lower proportion having doses held in the first week ($p<0.01$). There were no differences between Emp and Fenn for any of the endpoints. CONCLUSION: Adjustment of warfarin loading doses for age exhibits clear superiority over the use of Fenn or Emp. This becomes increasingly important as the average age of patients being warfarinised increases, with the recognition that atrial fibrillation requires anticoagulation. Fenn consistently overdosed elderly patients, especially those aged 80 years and older.