How to start warfarin therapy

Index: Anticoagulation

Original article by: Michael Tam

Warfarin is an interesting medication – it saves many lives but causes many problems including some deaths of its own. At present, it is the only oral anticoagulant available in Australia and it is a commonly used drug. Warfarin management, however, is done notoriously badly in hospital.

The key to warfarin management is patience

Warfarin works by being an antagonist to vitamin K. Vitamin K is the cofactor in the production of the (not surprisingly named) vitamin K dependent clotting factors (Factor II, VII, IX and X). However, the anticoagulant enzymes Protein C and S are also dependent on vitamin K and have shorter half-lives than the clotting factors.

Thus, when you first start warfarin, there is a paradoxical initial pro-thrombotic effect. Other forms of anticoagulation are a necessity.

Step 1: Consent

Bleeding to death is a particularly unpleasant way to go and warfarin isn’t the safest drug if used inappropriately. Documented informed consent is necessary. Even better, arrange for a clinical pharmacist (if in a hospital) to counsel the patient on warfarin.

The annual incidence of fatality due to warfarin is oft quoted at around 1% though it is more likely to be around 0.2%. About 15% of patients have at least one minor bleed a year.

Step 2: Anticoagulation with heparin

Usually, by the time a clinical decision is made to commence warfarin, the patient is already on unfractionated heparin (UFH) or low molecular weight heparin (LMWH). However, this is not always the case (for example, discovering that the cause of a stroke is paroxysmal atrial fibrillation) so always remembering to anticoagulate with UFH or LMWH first is important.

Step 3: Start warfarin

If a patient has previously taken warfarin and had been stable on a particular dose, then start
with that dose. Otherwise, check their baseline INR and start:

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warfarin 5 mg daily (nocte) for three doses
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**Step 4: Check INR on the morning of day 4 and adjust the dose**

<table>
<thead>
<tr>
<th>INR (morning of day 4)</th>
<th>Change warfarin dose to</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1.3</td>
<td>increase to 7 mg daily</td>
</tr>
<tr>
<td>1.3 - 1.7</td>
<td>continue with 5 mg daily</td>
</tr>
<tr>
<td>1.8 - 2.5</td>
<td>decrease to 3 mg daily</td>
</tr>
<tr>
<td>&gt; 2.5</td>
<td>decrease to 1 mg daily</td>
</tr>
</tbody>
</table>

**Note:** This is my personal opinion only – I do not believe in giving “loading doses” of warfarin. I believe that the dose of warfarin you should be giving is what you consider to be their “maintenance” dose in the longer term. There are other “initiation schemes” ([here](#) and [here](#)) that are designed for rapid attainment of the therapeutic level so the patient can be discharged earlier and come off other forms of anticoagulation.

Unfortunately, what commonly happens then is that the patient is discharged on much too high a dose with a high INR in 1-2 weeks time; much to the annoyance of the general practitioner, potentially risking a serious bleed in the patient, and will come back to bite you in the buttocks if they get readmitted.

**Step 5: Stop heparin when INR reaches therapeutic levels**

Some institutions would advocate daily INR tests until it reaches a therapeutic level (INR between 2.0 and 3.0). When the INR is 2.0 or above, the UFH or LMWH can be ceased and the patient discharged (if medically appropriate).

Some areas have an outpatient team that can warfarinise a patient at home. They have daily blood tests and a doctor calls them for their next dose of warfarin. A community nurse usually helps administer a LMWH like enoxaparin (Clexane) subcutaneously at home.

**Step 6: Regular INR checks**

Once the warfarin level is therapeutic, INR need only be performed every 1-2 weeks initially for
a new patient. Changes in the dosage of warfarin should be to what is estimated as the
maintenance dose. The practice of deliberate under or overdosing to more “quickly” reach the
desired level should be avoided.

Remember that most GPs would only do the INR fortnightly.

For a stable patient, the INR needs only be performed perhaps once a month.

**Step 7: Continuing warfarin education**

It is important to educate and remind patients about warfarin – usually done by the general
practitioner but it should be addressed for patients who are on warfarin and admitted to
hospital. Medication compliance, education on diet (e.g., eating consistent amounts of vitamin K
rich foods), drug interactions, avoiding unnecessary over-the-counter “vitamin” pills are all
significant issues in the longer term management of a patient on warfarin.

**Hints and tips**

- Be aware that there are two brands of warfarin in the Australian market, *Coumadin* and
*Marevan*. Unfortunately, they are not bioequivalent. The public NSW Health system only
uses *Coumadin*. Though perhaps not particularly fair on the company that makes
Marevan, I advocate using only Coumadin as it causes less confusion when the patient is
admitted to hospital.
- Many patients can’t remember their dose, but remember the colour tablets that they are
on. For Coumadin:
  - 1 mg tablet = light tan
  - 2 mg tablet = lavender
  - 5 mg tablet = green
- If the patient is on a "3 mg tablet" of warfarin, then they are on Marevan:
  - 1 mg tablet = brown
  - 3 mg tablet = blue
  - 5 mg tablet = pink
- Half milligram doses are difficult for the elderly as they may not have the manual
dexterity to break or cut a tablet in half. Consider alternate day full milligram doses
instead (e.g., rather than 4.5 milligrams daily, 4 milligrams and 5 milligrams alternate
days).
- A pill box or blister pack and help many people stay compliant on their warfarin (and
other medications as well).
- It is useful to have a good grasp on when and how to reverse warfarin when there is a
high INR result (3).

A useful resource - an estimate of the final maintenance dosage of warfarin after commencing
on 4 consecutive days of 5 mg daily dose (4):

<table>
<thead>
<tr>
<th>INR (morning of day 5)</th>
<th>Warfarin dose per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>71 mg</td>
</tr>
<tr>
<td>1.2</td>
<td>48 mg</td>
</tr>
<tr>
<td>1.4</td>
<td>39 mg</td>
</tr>
<tr>
<td>1.6</td>
<td>33 mg</td>
</tr>
</tbody>
</table>
Reference articles

(1) Coumadin (warfarin sodium), MIMS, 1 April 2006.

(2) David A Fitzmaurice, Andrew D Blann, Gregory Y H Lip. Bleeding risks of antithrombotic therapy (ABC of antithrombotic therapy). BMJ 2002;325:828-831 (12 October) [download PDF :: 258 Kb]

(3) Tam M. How to reverse warfarin [electronic article]. The Medicine Box. Last updated 23 June 2006. [Link]


Updated: Michael Tam (20 July 2006)

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