Purpose of the Guideline

The purpose of this guideline is to give both junior and senior medical staff succinct information on which anti-coagulant and anti-platelet agents need to be stopped prior to elective surgery. The drugs to be discussed are

1. Warfarin
2. Unfractionated Heparin
3. Low molecular weight heparin (LMWH)
4. Aspirin and other NSAIDs
5. Dipyridamole
6. Clopidogrel
7. The platelet GP IIIb/ III a receptor antagonists

Warfarin

Most authorities would suggest stopping warfarin 4 days prior to elective surgery and checking the anticoagulation profile on the morning of surgery. If the patient’s anti-coagulation can not be safely stopped eg presence of a prosthetic valve, it is recommended to replace the warfarin with either an unfractionated heparin infusion or a LMWH, unless the patient has been informed that they can safely stop anti-coagulation. If the patient is having major surgery or a central neuroaxial blockade is anticipated the patient should be commenced on an unfractionated heparin infusion rather than ‘treatment’ doses of LMWH aiming for a APTT ratio of 2.5-3.0. Unfractionated heparin has a shorter half-life, is easier to monitor, and is fully reversible and thus is preferred.

For minor surgical procedures a target INR of 2 is acceptable. For major surgical procedures or if block is planned a target INR of less than 1.2 is required, and this must be checked on the morning of surgery. Post major surgery the patient should be recommenced on the heparin infusion, and not the warfarin. This is to allow both safe removal of the epidural, and also allow quick and safe reversal of the anticoagulation if there are surgical complications.

If a patient presents for emergency surgery whilst anti-coagulated specialist haematological advice should be sought.

For more information see: CG10142: Guidelines for Reversal of Oral Anticoagulants including Warfarin and Phenindione
Unfractionated Heparin

This infusion should be stopped 6 hours prior to surgery and the APTT and the platelet count should be checked prior to surgery especially if central neuroaxial blockade is planned. It is imperative to check the platelet count to insure there is no heparin-induced thrombocytopaenia, which may occur after as little as 48 hours of heparin treatment. The heparin infusion may be recommenced after one hour after the surgery is completed or after at least two hours after instigation of central neuroaxial blockade.

For emergency surgery the APTT can be normalized with the administration of protamine, but specialist haematological advice can be sought.

Low Molecular Weight Heparins (LMWHs)

Eg Enoxaparin (clexane); Tinzaparin (innohep)

For thromboprophylactic doses an interval of 12 hours should elapse between the last dose and surgery or epidural insertion and removal. The first postoperative dose of LMWH should not be given within 2 hours of central neuro-axial blockade. This is why at the West Suffolk Hospital the normal time to administer LMWHs is 18:00.

Patients receiving higher treatment doses of LMWH require longer delays (minimum 24 hours) prior to surgery.

If urgent reversal of LMWH is required, protamine sulphate can be used, but it will not fully reverse the LMWH.

The Anti-Platelet Agents

Clopidogrel

Clopidogrel inhibits ADP-mediated platelet aggregation. It has been shown to be highly effective in reducing the mortality from acute coronary syndromes.

It is frequently co-administered with aspirin especially after angioplasty, stent insertion, post myocardial infarction, and post acute coronary syndrome for a period of up to twelve months. (Table 2). During this period it should ideally not be stopped, and evidence does suggest higher risk of re-infarction if surgery is performed in this period.

Table 2. Recommendation for duration of treatment with Clopidogrel

<table>
<thead>
<tr>
<th>Type of Procedure</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST-segment elevation myocardial infarction (STEMI) Unlicensed use</td>
<td>to be discontinued on discharge or after 1 month, whichever is sooner</td>
</tr>
<tr>
<td>Bare metal stent (BMS)</td>
<td>1 month</td>
</tr>
<tr>
<td>Drug eluting stent (DES)</td>
<td>9 months</td>
</tr>
<tr>
<td>Non-ST elevation myocardial infarction (NSTEMI), acute coronary syndrome (ACS) – moderate to high risk patients only</td>
<td>12 months</td>
</tr>
</tbody>
</table>
Occasionally, patients are truly aspirin intolerant and are then commenced on Clopidogrel indefinitely.

Thus it can be seen that there are 2 groups of patients on Clopidogrel, those on a course of treatment for a fixed period, and those on lifelong treatment.

**Peri-Operative Recommendations.**

Clopidogrel should be stopped 7 days prior to elective surgery. If the patient is on a treatment course of clopidogrel for post procedure or post an acute coronary syndrome, the risks of prematurely stopping the clopidogrel need to be balanced against the benefits of the elective surgery. The cardiologists and anaesthetists would argue in favour of postponing elective surgery until the treatment course is finished.

If the patient is on lifelong clopidogrel due to aspirin intolerance, the patient and the surgeon need to discuss the benefit of the surgery against the increased risk of a post-operative cardiac event if the clopidogrel is stopped, or against post operative hemorrhage if it decided not to stop the Clopidogrel.

For emergency surgery, animal studies have shown that high dose corticosteroids and aprotinin can partially reverse the effects of clopidogrel, however there is no confirmatory effect in humans. Central Neuroaxial blockade should not be undertaken in this period due to the risk of epidural haematomas formation.

Clopidogrel can be recommenced 2 days post surgery.

**Dipyridamole**

Dipyridamole is an agent that inhibits platelet aggregation by increasing levels of cyclic adenosine monophospate. It is often used in the secondary prevention of strokes along with aspirin.

**Peri-Operative Recommendations.**

There is no clinical evidence to suggest that this agent should be stopped peri-operatively. However, if central neuroaxial blockade is contemplated good practice would suggest that it is insured that the patient is on no other agents that would interfere with platelet function or the coagulation cascade.
Aspirin and other NSAIDs

There used to be concern that NSAIDs would lead to increased post-operative bleeding, and increased rates of epidural haematomas following central neuroaxial blockade. Recent evidence suggests that these agents do not lead to increased post-operative bleeding or the need for transfusion, even in higher risk surgery.

If excessive bleeding is anticipated it is wise to ensure that the patient is only on 75mg od aspirin.

As in dipyridamole, good practice would dictate that if central neuroaxial blockade is contemplated, the patient should be on no other agents that interfere with platelet function or the coagulation cascade.

If it is felt that NSAIDs are contributing to excessive blood loss there is evidence that desmopressin or high dose aprotinin will inhibit bleeding. There is little evidence to suggest the use of tranexamic acid in this situation.

Platelet glycoprotein receptor (GPIIb/IIIa) antagonists

(Abciximab, Eptifibatide, Tirofiban)

These agents are potent inhibitors of platelet aggregation. They are administered intravenously in the treatment of acute coronary syndromes. Elective surgery should not be contemplated whilst on these drugs. For emergency surgery administration of platelets appears to be the only intervention likely to be of benefit, and even then a bleeding diathesis can be anticipated. Central Neuroaxial blockade should not be considered.

References:


Clarification of recommendation 1.3. National Institute for Clinical Excellence, website accessed Feb 2006

Clopidogrel Guidelines Working Group for the Anglia Cardiac Network: Guideline for the use of clopidogrel in combination with aspirin in Coronary Heart Disease.


CG10142: Surgery and Anti-Coagulation Agents
Development of the guideline

Statement of clinical evidence

This is a review of the clinical evidence from the literature. It is based on expert and consensus opinion, case reports and reviews. Due to the rarity of epidural haematoma there will be never be randomized control studies in this field.

Stopping clopidogrel is a contentious issue. NICE guidelines suggest that most patients should be on a course of clopidogrel that will stop after a finite time. However, more and more patients are being commenced on lifelong clopidogrel for criteria that do not meet NICE guidelines. The advice of this document is to postpone elective surgery until the patient finishes their course. If the patient is on clopidogrel for reasons that fall outside NICE guidelines, it is felt that the clopidogrel can be stopped 10 days prior to surgery and then re commenced 2 days later. These recommendations may change if and when NICE reviews the use of clopidogrel.

See reference section for further information.

Contributors and peer review

These guidelines were discussed at the audit meetings of the anaesthetic division, orthopaedic and surgical departments and all feedback was discussed and queries resolved.

Distribution list/dissemination method

These guideline are primarily intended to aid the decision process in pre-surgical assessment clinics and also on the surgical wards. All consultant surgeons and anaesthetists need to be aware of this document. This document will be emailed to all relevant stakeholders and be available for reference via the pink book.

Distribution list

- Consultant Surgeons
- Consultant Anaesthetists
- Surgical Clinical Ward Managers
- Junior surgical staff
- Pre-Assessment clinics

Document configuration information

<table>
<thead>
<tr>
<th>Author(s):</th>
<th>Dr N Levy Consultant Anaesthetist, Dr D Chitnavis Consultant Haematologist and Dr E Lee Consultant cardiologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other contributors:</td>
<td></td>
</tr>
<tr>
<td>Approved by:</td>
<td>Anaesthetic Division; Surgical department; and Orthopaedic department</td>
</tr>
<tr>
<td>Issue no:</td>
<td>2</td>
</tr>
<tr>
<td>File name:</td>
<td></td>
</tr>
<tr>
<td>Supercedes:</td>
<td>Issue 1</td>
</tr>
</tbody>
</table>
| Additional Information: | Modified to refer to CG10142  
In this version (issued Sept 2008), on page 3, section Peri-Operative Recommendations, 10 days has been changed to 7 days |
| Keywords:        | Surgery, anaesthetics, anti-coagulation agents, warfarin, heparin, low molecular weight heparin, aspirin, NSAIDs, dipydamole, clopidogrel GPIIIb |