Blood Thinners
Rationale for stopping less than 2 weeks before surgery
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Pharmacokinetics

- The ideal time-period for stopping “blood thinners” [i.e. anticoagulation or antiplatelet agents] should maximize the return of normal blood clotting and minimize the risk to the patient.
  - i.e. what is the soonest time in which the blood returns to an acceptable clotting profile

Drug half-lives

- Half-life = time period for 50% drug clearance
- Drug might be considered effectively “out of the system” after 5 half-lives
  - 100% → 50% → 25% → 12.5% → 6.25% → 3.13%
Drug half-lives

- **Warfarin** $T_{1/2} = 36$ to 42 hours
  - Typically stopped for 5 days $\rightarrow$ -12.5% residual drug activity
  - But drug level doesn’t need to be zero to be acceptable
    - INR < 1.5

- **Aspirin** ($T_{1/2} = 15$ minutes aspirin, ~3 hours salicylate)
- **Plavix** ($T_{1/2} = 8$ hours)
  - Both of these drugs are “cleared” after 2 days
  - But platelets *irreversibly* inhibited
    - $T_{1/2}$ of platelet = ~5 days (lifespan ~ 10 days)
    - Would take ~ 10 days for a full population of platelets to be regenerated

Irreversible anti-platelet agents

- **Check INR day before surgery if possible**
  - May enable oral Vit K treatment – avoid FFP transfusion

**warfarin**
Reversible anti-platelet agents

- **NSAIDS**
  - Ibuprofen $T_{1/2} = 2$ hours
  - Naproxen (Aleve) $T_{1/2} = \approx 15$ hours

- Ibuprofen out of system by 10 hours
- Naproxen out of system by 75 hours (~ 3 days)

- Platelets *reversibly* inhibited
  - i.e. once drugs cleared, platelet function returns

Drug half-lives

Pharmacologically based discontinuation times

- Warfarin: 5 days (per prescribing physician)
  - +/- oral vitamin K 1.25 to 10 mg PO
- Aspirin / Plavix: 10 days to achieve ~100% platelets
- NSAIDS: 12 hours ibuprofen, 36 hours naproxen

Kovacs et al 2004
- Prospective study 224 patients
- Warfarin held 5 days prior to surgery
- Only 6.7% had INR > 1.5

warfarin
Warfarin -- restarting

- Douketis et al, 2004
- Prospective cohort study 650 patients
- Warfarin held and bridged with LMWH

- Upon re-starting warfarin:
  - 5.1 +/- 1.1 days to reach INR > 2

Platelets

- Average platelet count = 250,000
- If aspirin stopped for 5 days (instead of 10 d)
  - 50% platelet replacement = 125,000
- Bleeding risks:
  - Prolonged bleeding if less than 50,000
  - Spontaneous bleeding if less than 20,000
- Thus, 5 days off aspirin = > 100,000 functioning platelets

Conclusion

- 5 days should be sufficient time to allow coagulation and platelet function to return to safe levels regardless of medication
Survey says…

- 92 dermatologists in UK Re: stopping blood thinners
- 61% based on “personal preference”
- 34% (only) based on evidence-based medicine

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MODE</th>
<th>MEAN</th>
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</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>7 d</td>
<td>6.5 d</td>
</tr>
<tr>
<td>Warfarin</td>
<td>2 d</td>
<td>2.63 d</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>7 d</td>
<td>5.63</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>2 d (3 d face)</td>
<td>5.2 d</td>
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</tbody>
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**clopidogrel**

- Passemard et al 2012
- 206 eyes undergoing vitreoretinal surgery with peribulbar anesthesia
- 3 Groups
  - No anticoag / antiplatelet agents
  - Anticoag agents (e.g. warfarin)
  - Antiplatelet agents (aspirin, clopidogrel, or both)
- 3 / 206 site-threatening bleeding complications
- ALL IN PATIENTS TAKING CLOPIDOGREL
  - Sub-retinal hemorrhage X 2, vitreous hemorrhage

**Heparin vs. Aspirin / Warfarin**

- Cheng et al – Anticoagulation risk in spine surgery
- Systemic review of literature
- Spine patients receiving DVT prophylaxis perioperatively
- Re: post-operative bleeding / epidural hematoma
  - 1% to 3.5% incidence with various heparin preparations
  - Zero incidence aspirin, ketorolac, warfarin
Risk factors for perioperative bleeding

- Hypertension
- Abnormal renal / liver function
- Stroke history
- Bleeding history / predisposition
- Labile INR
- Elderly (> 65 y)
- Drugs / alcohol abuse

HAS-BLED

Omran et al

- Prospective 1,000 procedures
- Cardiac cath, pacemakers, etc.
- OAC (e.g. warfarin) bridged with LMWH 94%
- HAS-BLED: bleeding events < 3 vs. 3 or more

Evidence-Based Clinical Practice Guidelines:

Perioperative management of antithrombotic therapy 2012

American College of Chest Physicians
American College of Chest Physicians

• Vitamin K antagonist therapy (e.g. warfarin)
  • Recommend stopping 5 days before surgery (Grade 1B)
    • High-risk patients with mechanical heart valve, a-fib, venous thromboembolism
      • Recommend bridging therapy e.g. LMWH
    • Low-risk patients – no bridging therapy recommend

American College of Chest Physicians

• Aspirin
  • Moderate to high-risk patients
    • Ischemic heart disease, CHF, DM, renal insuff, cerebral vasc. Dz
  • Recommend continuing aspirin therapy for non-cardiac surgery

American College of Chest Physicians

• Clopidogrel / Aspirin
  • History of cardiac stent placement
    • Continue antiplatelet therapy or defer surgery:
      • > 6 weeks bare-metal stent
      • > 6 months drug-eluting stent
Shore JW, Menke AM. Hemorrhage Associated with Ophthalmic Procedures: Focus on Blepharoplasty.

www.omic.com

• History
  • Bleeding disorders
  • Medication history, supplements (ginkgo biloba), Vitamins (E)
  • Cerebral vascular disease
  • Atrial fibrillation
  • Prosthetic heart valve
  • Cardiac stents
  • Peripheral vascular disease
  • Hypertension
  • History of bleeding / bruising in patient or family member
  • Consider referral to PCP or hematologist

• Typical stoppage times (with clearance from prescriber)
  • Warfarin  5 days
  • IV Heparin  12 hours (check PTT)
  • LMWH  12 to 24 hours
  • Aspirin  7 days
  • NSAIDS  24 to 72 hours
  • Furosemide / prednisone  48 hours
  • Clopidogrel  7 days
    • Often advised to continue aspirin – surgery may not be possible

  • Verify yourself that patient has stopped medications
  • May have to re-schedule surgery
Hemorrhage Management:
- Needs timely diagnosis / evaluation / treatment
- Document time of onset of bleeding
- Active bleeding from wound
- +/- pain
- Vision, motility, pupils
- Able to open lids (spontaneously, forcefully, unable?)

Management – Orbital Compartment Syndrome:
- Open wound at bedside and evacuate clot
- No need for anesthetic injection
- Do not probe deeply → more bleeding
- May need to open upper and lower eyelid wounds if applicable
  - Release canthopexy → this may require anesthesia
  - IV corticosteroids (e.g. 8mg Decadron bolus)
  - Note: no role for IV mannitol in orbital compartment syndrome

Re-examine patient
- Opening wounds may be all that is necessary
- If orbit is still firm and/or vision still decreased
  - Canthotomy / superior & inferior cantholysis
  - Do not delay; perform at bedside
• Management – Orbital Compartment Syndrome:
  • Re-examine patient after canthotomy / cantholysis
  • Determine whether patient needs to return to OR
    • To obtain hemostasis
    • To further decompress orbit (rare if good lid release)

• Management – Orbital Compartment Syndrome:
  • No role for AC paracentesis
  • No role for IV Mannitol
  • IOP monitoring – minimally useful
    • Problem is orbital pressure on the optic nerve
      • IOP may be high or low.
  • Decision for canthotomy / cantholysis is based on:
    • orbital compliance, vision, motility, pupil response, NOT IOP

• Canthotomy / Cantholysis is rarely performed correctly / adequately
  • An alternative is to perform a full thickness cut of the eyelid at the lateral 1/3. This will release the orbital pressure and allow globe proptosis. Can be repaired secondarily once clinically appropriate (days)

Full thickness lid cut
• Blood-thinning medications should be stopped to minimize thrombotic risk to the patient while gaining maximum bleeding avoidance

• 14 days unnecessarily exceeds the pharmacologic time-frame needed to achieve normal hemostasis

• If a hemorrhage does develop that causes an orbital compartment syndrome, this must be assessed and treated immediately and completely.

Conclusions

References


