Dental Management Considerations for Patients on Antithrombotic Therapy

Warfarin and Antiplatelet

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Warfarin

- First synthesized as a potent rodenticides in the 1940s
- Coumadin was introduced into clinical practice in the 1950s
- Top 20 medication
Indications:
- prophylaxis and/or treatment of:
  - venous thrombosis
  - pulmonary embolism
  - thromboembolic complications associated with:
    - atrial fibrillation
    - cardiac valve replacement.
- reduce the risk of death, recurrent MI, and thromboembolic events after MI
**Warfarin Therapy (Coumadin)**

- INR ranges for specific indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Target INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac arrhythmias (ie: atrial fibrillation)</td>
<td>1.5-2.5</td>
</tr>
<tr>
<td>Thromboembolic events (ie: DVT, TIA, CVA, PE); Prosthetic heart valves,</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Valvular heart disease; atrial fibrillation; following acute MI</td>
<td></td>
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<tr>
<td>Mechanical heart valves, recurrent systemic embolism, some MI patients</td>
<td>2.5-4.0</td>
</tr>
</tbody>
</table>
Warfarin Therapy (Coumadin)

- Patients on warfarin with INRs in therapeutic range vs. Controls - no difference in clinically significant bleeding in numerous studies
- 73% recommend withdrawal of warfarin for some dental procedures (Wahl, 1996)
- 86% recommend referral to physicians for adjustments of warfarin dosage (Lippert, 1994)
Use of INR testing device in dental practice
(Brennan et al., JADA, 2008; 139(6):697-703)

- Prospective cohort study
- N=100
- Inclusion criteria:
  - Warfarin with an INR value not available within 48 hours of the dental visit
  - History of:
    - viral hepatitis with a self-report of abnormal liver values
    - excessive bleeding after an invasive procedure
    - current heavy use of alcohol (>20 drinks/week for >2 years)
  - Clinical signs of jaundice, ascites, or encephalopathy
  - Return visits to the clinic with significant bleeding following an invasive dental procedure
Use of INR testing device in dental practice
(Brennan et al., JADA, 2008; 139(6):697-703)

- 47% had subtherapeutic INR values
  - 3 patients taken off warfarin by their physician and 1 discontinued by the patient prior to the dental procedure.

Therefore, almost half of these patients were at risk for a thromboembolic event.
Warfarin Therapy – To alter or not to alter?

- Dental literature suggests INR < 2.0 – no scientific evidence for this!
- Half-life: 36 hours
  - Need to d/c for up to 4 days to decrease INR to 1.5
  - When restarted, takes up to 3 days to reach INR of 2.0
  - 2-3 days of subtherapeutic anticoagulation post-surgery
- d/c prior to dental treatment (Wahl, 1998):
  - life-threatening thromboembolic event - 3-5X greater risk than uncontrollable postoperative bleeding that is uncontrollable by local measures
Bleeding Potential in Dental Practice
(Nematullah et. al. JCDA, Feb 2009)

- Systematic Review and Meta-analysis
- Randomized controlled trials
- Medline, Embase and Cochrane: 1990-2008
  - One arm continued and other decreased or discontinued
  - 5/207 potential publications evaluated
No Major bleeding episodes

Clinically significant non-major bleeding
- 15 of 275 (5.5%) patients who continued their regular dose of warfarin
- 25 of 278 (9.0%) patients who discontinued or altered their dose of warfarin before dental surgery.
  RR = 0.71, 95% CI 0.39–1.28; p = 0.25

Minor bleeding
- 41 of 210 (19.5%) patients who continued their regular dose of warfarin
- 40 of 212 (18.9%) patients who discontinued
  RR = 1.19, 95% CI 0.90–1.50; p = 0.22
Warfarin – Dental Management

Current models:

- Reduce warfarin dose
- Stop warfarin for 2 days
- Hospitalize → heparin → warfarin
- Local hemostatic measures
Warfarin – Extensive Surgery Management

- High risk of thromboembolism
  - Bridging with therapeutic-dose SC LMWH or IV UFH
- Moderate risk of thromboembolism
  - Bridging with therapeutic or low-dose dose SC LMWH, therapeutic-dose IV UFH
- Low risk of thromboembolism
  - Bridging with low-dose SC LMWH or no bridging

Hirsch J. CHEST 2008; 133:71S–105S
Antiplatelet medications – Indications

- Prophylaxis of:
  - Angina
  - Acute MI
  - Transient ischemic attack
  - Stroke
  - Atrial Fibrillation

- Prevention of clot formation around prosthetic heart valves
Aspirin

- Weak antiplatelet activity
  - Acetylates and inactivates COX
  - Irreversible
  - Platelet inhibition effects 1 hr after ingestion
  - Lasts for lifetime of affected platelets (7-10 days)
- Major hemorrhage <1.0%
- Dose and duration issues:
  - No difference based on dose and duration on antiplatelet activity (80 mg sufficient)
ASA and Single Tooth Extraction Study-
Brennan, Valerin, Noll, Napeñas et al. (J Dent Res. 2008;87(8):740-4)

- Double-blind RCT prospective pilot study
- N=36
- ASA (325 mg/day) vs. placebo
- Three days prior to extraction
- Outcome measures:
  - Cutaneous BT
  - Oral BT
  - Pre-op Platelet Aggregometry
  - Post-op complications
36 patients enrolled:
  - 17 – ASA
  - 19 – placebo

No differences in baseline information (age, sex, tobacco, EtOH, oral disease)

No differences in extraction time, site, difficulty, patient compliance
ASA and Single Tooth Extraction Study-
Brennan, Valerin, Noll, Napeñas et al. (J Dent Res. 2008;87(8):740-4)

- **Parameters (ASA vs. Placebo):**
  - Platelet aggregometry – Difference (p<0.004)
  - Cutaneous BT – No difference (p=0.07)
  - Oral BT – No difference (p=0.51)
    - ASA – 8.1 min (SD – 5.9)
    - Placebo – 6.2 min (SD – 3.4)
  - Post-op complications – No difference
ASA and Single Tooth Extraction Study—Brennan, Valerin, Noll, Napeñas et al. (J Dent Res. 2008;87(8):740-4)

- This is the first randomized placebo-controlled study concerning ASA use for patients requiring dental procedures.
- No differences in bleeding outcomes in patients on ASA vs. placebo.
- **Conclusion:** No indication to discontinue use of ASA in patients requiring single tooth extraction.
Clopidrogrel

Indications
- recent stroke
- recent MI*
- established peripheral artery disease

Incidence GI hemorrhage
- Alone- 2.0% (hosp. 0.7%)
- With ASA - 2.7% (hosp. 1.1%)

*may be in combination with ASA
Clopidrogrel

- Little JW (2002) –
  - Patients taking clopidogrel alone should not have the dose altered prior to invasive dental procedures
- No evidence for dual or multi antiplatelet therapy and dentistry
Bleeding Potential – Antiplatelet Therapy

- Retrospective cohort study
- Examined the frequency of, and factors associated with bleeding complications following invasive dental procedures for patients on single or dual antiplatelet therapy
- N=43
- Inclusion criteria:
  - antiplatelet medications at the time of dental treatment
  - having had at least one invasive dental procedure
Primary outcome measures of post-operative bleeding (as documented in the medical and dental record):
- return visit or phone call to the dental clinic or ED for post-operative bleeding
- documented bleeding for more than 24 hrs for inpatients
- post-operative adjunctive local or systemic hemostatic measures
- post-operative blood products
<table>
<thead>
<tr>
<th></th>
<th>Combined</th>
<th>Antiplatelet therapy</th>
<th>p-value</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Single</td>
<td>Dual</td>
</tr>
<tr>
<td>Number of patients</td>
<td>43</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>Demographic data</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean age (years) ± SD</td>
<td>59.0±14.4</td>
<td>62.1±15.3</td>
<td>57.5±14.0</td>
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<tr>
<td>Male Gender</td>
<td>21</td>
<td>4</td>
<td>17</td>
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<tr>
<td>Inpatient</td>
<td>7</td>
<td>2</td>
<td>5</td>
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<tr>
<td>Medical history</td>
<td></td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>36</td>
<td>11</td>
<td>25</td>
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<tr>
<td>Coronary artery disease</td>
<td>24</td>
<td>5</td>
<td>19</td>
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<tr>
<td>Cerebrovascular accident</td>
<td>17</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Type II Diabetes</td>
<td>14</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Antiplatelet</td>
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<tr>
<td>Clopidogrel</td>
<td>39</td>
<td>13</td>
<td>26</td>
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<tr>
<td>Dipyridamole</td>
<td>2</td>
<td>0</td>
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</tr>
<tr>
<td>Ticlopidine</td>
<td>2</td>
<td>1</td>
<td>1</td>
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<tr>
<td></td>
<td>Combined</td>
<td>Antiplatelet therapy</td>
<td>p-value</td>
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<td></td>
<td></td>
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<td>Dual</td>
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<tr>
<td>Number of patients</td>
<td>43</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>Invasive visits (total # visits)</td>
<td>88</td>
<td>24</td>
<td>64</td>
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<tr>
<td>Mean per patient ± SD</td>
<td>2.0 ± 1.8</td>
<td>1.7 ± 1.2</td>
<td>2.2 ± 2.0</td>
</tr>
<tr>
<td>Extraction visits (total # visits)</td>
<td>70</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Mean per patient ± SD</td>
<td>1.6 ± 1.7</td>
<td>1.4 ± 1.3</td>
<td>1.6 ± 1.9</td>
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<tr>
<td>Visits involving surgical extractions</td>
<td>19</td>
<td>4</td>
<td>15</td>
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<td>Visits with use of hemostatic measures</td>
<td>41</td>
<td>10</td>
<td>31</td>
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<tr>
<td>Extractions (total # teeth)</td>
<td>213</td>
<td>81</td>
<td>132</td>
</tr>
<tr>
<td>Mean # of extractions per patient ± SD</td>
<td>4.7 ± 5.4</td>
<td>5.8 ± 6.2</td>
<td>4.5 ± 5.1</td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>Combined</td>
<td>Single</td>
<td>Dual</td>
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</tr>
<tr>
<td>Number of patients</td>
<td>43</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>Dental clinic</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Return visit for post-op bleeding</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Phone call for post-op bleeding</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other visit or phone call for oral bleeding</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Emergency department</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Visit for post-op bleeding</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other visit for oral bleeding</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total number of ED visits</td>
<td>72</td>
<td>48</td>
<td>24</td>
</tr>
<tr>
<td>Average num. ED visit per patient ± SD</td>
<td>1.7 ± 6.5</td>
<td>3.4 ± 11.1</td>
<td>0.8 ± 1.8</td>
</tr>
<tr>
<td>Documented oral bleeding &gt; 24 hrs</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Post-operative blood products</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Post-op adjunctive hemostatic measures</td>
<td>0</td>
<td>0</td>
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</table>
Unresolved questions:

- multiple extractions and other invasive procedures
- dual anticoagulant therapy (e.g.: LMWH and warfarin)
- new antithrombic medications (e.g.: dabigatrin)
- prospective RCTs
Patient management considerations

- Alteration of antithrombotic medication prior to an invasive dental procedure
  - Risk assessment of invasiveness of dental procedure to determine the bleeding potential
  - Risk assessment of thrombotic outcomes if discontinue
  - Risk assessment of potential severity of post-operative bleeding
Post-op Bleeding

- Usually attributed to local factors (i.e.: severe local infection, inflammation, spitting, rinsing)
- Patient instruction:
  - Moist gauze pressure
  - Tea bags
  - No spitting or rinsing 24 hours
- Post-operative contact (phone, pager)
When to get help

- INR > 3.5
- Advanced uremia
- Platelets < 30,000 – 40,000
- Pre-liver transplant
- Aplastic anemia
- High dose chemotherapy
- Multiple coagulopathies