Introduction

Neuraxial procedures include lumbar puncture, subarachnoid block (spinal), intrathecal catheter, epidural catheter, epidural steroid injection, among others. The primary concern for neuraxial procedures and antithrombotics is the risk for epidural hematoma. The consequences of this complication includes paralysis and permanent bowel/bladder dysfunction. The historic approximate risk of this complication is estimated to be 1 in 150,000 for epiduals and 1 in 220,000 for subarachnoid blocks (Bonica's Management of Pain, 4th ed.) although recent evidence supports that the incidence may be as high as 1/9,000 for perioperative epiduals (MPOG- 2013). Thus, we have a very rare, high consequence complication associated with an elective procedure. The risks vs benefit ratio must be assessed in each situation.

The data collected for clinically relevant epidural hematoma is retrospective, and risk factors have been stratified based on case reports and case series. Beyond antithrombotic pharmacologics, the interplay between patient factors and the trauma associated with placement can lead to epidural hematoma formation.

The following table is a collection of expert recommendations from UCSF, American Society of Regional Anesthesia (ASRA), European Society of Regional Anaesthesia (ESRA), and the Scandinavian Society of Anaesthesiology using retrospective data on several agents. The newer target-specific agents do not yet have substantial data, and therefore, their times have been calculated taking their plasma half-life and stating arbitrarily that reduction by 96.9% (5 maximum half-lives) is acceptable. These examples to date include dabigatran (Pradaxa), apixaban (Elquis), and rivaroxaban (Xarelto). These numbers may be deemed as conservative. The purpose of this table is to provide recommendations-- they do not replace an individual’s judgment in specific situations.

Risks of Ceasing Antithrombotic Therapy & The Role of Bridging

There are situations where antithrombotic therapy should not be discontinued due to the risk of acute life-threatening thrombosis. In these situations, stopping the concerning antithrombotic and bridging with an anticoagulant can be done. One example is warfarin therapy for a prosthetic valve bridged with low-molecular weight heparin until 24 hours before procedure.

Peripheral Regional Anesthesia & Antithrombotics

Depending on the type of block, the risk of hematoma for peripheral regional anesthesia has presumably less severe consequences than for neuraxial anesthesia. However, there are no guidelines or studies to base recommendations for specific peripheral regional techniques. This must be based on a case by case basis.

A standardized set of recommendations for all peripheral regional anesthetics cannot be made at this time. For example, hematoma in the lumbar plexus carries greater consequence than in the transversus abdominis plane.

Hepatic & Renal Impairment

These values are valid for patients with in tact hepatic and renal function. Impairments can alter the metabolism and excretion, and evaluation of risks versus benefits must be made on a case by case basis. If unclear about the pharmacokinetics in impaired metabolism and excretion, refer to the package insert of a medication.

Cytochrome P450 Metabolism

Many of these drugs are metabolized through the CYP450 metabolism pathway. Be aware of interactions with other substances (grapefruit juice, herbas, drugs). If unclear, please refer to the package insert of a medication.

Combinations of Factors

This table does not identify the risk associated with combinations of antithrombotic etiologies. Therefore, when a patient has multiple factors, this must be assessed on a case by case basis. Examples include combinations of drugs with herbal supplements, von Willebrand disease, etc.

Traumatic or “Bloody” Tap

Inform the Acute Pain Service (APS) if there is traumatic placement of a neuraxial regional anesthetic. There is a ~10-fold increased risk of epidural hematoma with traumatic placement.

If uncertain about the risks associated with an antithrombotic and procedure, please consult the Acute Pain Service at your hospital.

References


Version 3.a. Authored by Dr. Margaret Fang, Steven Kayser PharmD, Dr. Ramana Naidu. (May 2015) Approved by UCSF Antithrombotic Subcommittee and P&T Committee, June 8, 2015 SF VA P&T Approval June 2014. Dr. Tracy Minichiello, Dr. Alain Lartigue, Dr. Daryl Wong
SF GH P&T Approval September 2014. Dr. Andrew Gray, Dr. Oliver Radke, Christina S. Wang, PharmD
### Guidelines for the Use of Antithrombotic Agents in the Setting of Neuraxial Procedures

#### Anticoagulants for Venous Thromboembolism Prophylaxis

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Minimum time between the last dose and when neuraxial shot/catheter placement can occur</th>
<th>Minimum time after catheter placement to drug start.</th>
<th>Minimum time between last dose of drug and catheter removal</th>
<th>Minimum time between neuraxial shot/catheter removal and when next dose can be given</th>
</tr>
</thead>
<tbody>
<tr>
<td>dalteparin (Fragmin) 5000 units SQ daily</td>
<td>12 hours</td>
<td>ADVISE CAUTION. May be given. Wait 6 hrs after catheter placement before next dose.</td>
<td>12 hours</td>
<td>4 hours</td>
</tr>
<tr>
<td>enoxaparin (Lovenox) 40mg SQ daily</td>
<td>12 hours</td>
<td>ADVISE CAUTION. May be given. Wait 6 hrs after catheter placement before next dose.</td>
<td>12 hours</td>
<td>4 hours</td>
</tr>
<tr>
<td>enoxaparin (Lovenox) 30mg SQ bid or 40mg SQ bid</td>
<td>12 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>4 hours</td>
<td></td>
</tr>
<tr>
<td>fondaparinux (Arixtra) ≤2.5mg SQ daily</td>
<td>48 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>4 hours</td>
<td></td>
</tr>
<tr>
<td>heparin 5000 Units SQ bid</td>
<td>May be given; No time restrictions for catheter placement or removal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>heparin 5000 Units SQ tid</td>
<td>4 hours 2 hours</td>
<td>4 hours</td>
<td>2 hours</td>
<td></td>
</tr>
<tr>
<td>rivaroxaban (Xarelto) 10mg PO daily</td>
<td>72 hours</td>
<td>6 hours</td>
<td>24 hours</td>
<td>6 hours</td>
</tr>
</tbody>
</table>

#### Anticoagulants at Therapeutic Doses

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Minimum time between the last dose and when neuraxial shot/catheter placement can occur</th>
<th>Minimum time after catheter placement to drug start.</th>
<th>Minimum time between last dose of drug and catheter removal</th>
<th>Minimum time between neuraxial shot/catheter removal and when next dose can be given</th>
</tr>
</thead>
<tbody>
<tr>
<td>apixaban (Eliquis) 2.5, 5, 10mg PO bid</td>
<td>72 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>dabigatran (Pradaxa) 75, 150mg PO bid</td>
<td>5 days &amp; TT or aPTT is normal</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>dalteparin (Fragmin) 100 units/kg SQ q12h</td>
<td>24 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>4 hours</td>
<td></td>
</tr>
<tr>
<td>dalteparin (Fragmin) 200 units/kg SQ daily</td>
<td>36 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>4 hours</td>
<td></td>
</tr>
<tr>
<td>edoxaban (Savaysa) 30, 60mg PO daily</td>
<td>72 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>enoxaparin (Lovenox) 1mg/kg SQ bid</td>
<td>24 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>4 hours</td>
<td></td>
</tr>
<tr>
<td>enoxaparin (Lovenox) 1.5mg/kg SQ daily</td>
<td>36 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>4 hours</td>
<td></td>
</tr>
<tr>
<td>fondaparinux (Arixtra) 5-10mg SQ daily</td>
<td>72 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>4 hours</td>
<td></td>
</tr>
<tr>
<td>heparin full dose IV (In emergent situations, may have to be used. Recommend neuro checks q2h)</td>
<td>when aPTT &lt; 40</td>
<td>CONTRAINDICATED while catheter in place. In emergent situation, start at least 1 hour after.</td>
<td>CONTRAINDICATED while catheter in place. In emergent situation, 4 hours and check aPTT&lt;40</td>
<td>2 hours</td>
</tr>
<tr>
<td>rivaroxaban (Xarelto) 15 mg PO daily to bid, 20mg PO daily</td>
<td>72 hours</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>warfarin (Coumadin) 5 days &amp; INR &lt; 1.5</td>
<td>5 days</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>2 hours (no consensus)</td>
<td></td>
</tr>
</tbody>
</table>

#### Oral AntiplATELET Agents

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Minimum time between the last dose and when neuraxial shot/catheter placement can occur</th>
<th>Minimum time after catheter placement to drug start.</th>
<th>Minimum time between last dose of drug and catheter removal</th>
<th>Minimum time between neuraxial shot/catheter removal and when next dose can be given</th>
</tr>
</thead>
<tbody>
<tr>
<td>aspirin/NSAIDS/COX inhibitors/dipyridamole</td>
<td>May be given; No time restrictions for catheter placement or removal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>clopidogrel (Plavix) 7 days</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>2 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>prasugrel (Effient) 9 days</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>6 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ticagrelor (Brilinta) 5 days</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>6 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ticlopidine (Ticlid) 14 days</td>
<td>CONTRAINDICATED while catheter in place</td>
<td>2 hours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**

- Thrombosis risk is increased when these anticoagulants are held. Although parenteral bridging is not generally needed for target specific oral anticoagulants (dabigatran, rivaroxaban, apixaban, edoxaban) it may be considered in some situations. Consult Anticoagulation Clinic or Hematology if additional input is desired.

- There is an increased risk of thrombosis when antiplatelets are held for patients with vascular stents (e.g. cardiac, intracranial, etc.). Consult cardiology.

Version 3.0. Author: Dr. Margaret Fang, Steven Kayser PharmD, Dr. Ramana Naidu. (May 2019) Approved by UCSF Antithrombotic Subcommittee and P&T Committee, June 8, 2019
SF VA P&T Approval June 2014. Dr. Tracy Minichiello, Dr. Alain Lartigue, Dr. Daryl Wong
SFH&P T Approval September 2014. Dr. Andrew Gray, Dr. Olivar Radke, Christina S. Wang, PharmD
## GUIDELINES FOR THE USE OF ANTITHROMBOTIC AGENTS IN THE SETTING OF NEURAXIAL PROCEDURES

### DIRECT THROMBIN INHIBITORS
- **argatroban / bivalirudin (Angiomax)**
  - Minimum time between the last dose and when neuraxial shot/catheter placement can occur: When TT or aPTT is normal
  - Minimum time after catheter placement to drug start: CONTRAINDICATED while catheter in place
  - Minimum time between last dose of drug and catheter removal: 2 hours

### GP IIb/IIIa INHIBITORS
- **abciximab (Reopro)**
  - Minimum time after catheter placement to drug start: 48 hours
  - Minimum time between last dose of drug and catheter removal: CONTRAINDICATED while catheter in place
  - Minimum time between neuraxial shot/catheter removal and when next dose can be given: 2 hours (ACS)

- **eptifibatide (Integrilin) / tirofiban (Aggrastat)**
  - Minimum time after catheter placement to drug start: 8 hours
  - Minimum time between last dose of drug and catheter removal: CONTRAINDICATED while catheter in place
  - Minimum time between neuraxial shot/catheter removal and when next dose can be given: 2 hours (ACS)

### THROMBOLYTIC AGENTS
- **alteplase (TPA)**
  - Minimum time between last dose and when neuraxial shot/catheter placement can occur: 10 days
  - Minimum time after catheter placement to drug start: CONTRAINDICATED while catheter in place
  - Minimum time between last dose of drug and catheter removal: 10 days
  - Minimum time between neuraxial shot/catheter removal and when next dose can be given: May be given; No time restrictions for catheter placement or removal

### MISCELLANEOUS AGENTS
- **bevacizumab (Avastin)**
  - Minimum time between last dose and when neuraxial shot/catheter placement can occur: Caution
  - Minimum time after catheter placement to drug start: No time restrictions for catheter placement or removal
  - Minimum time between last dose of drug and catheter removal: 6 hours

- **cilostazol**
  - Minimum time between last dose and when neuraxial shot/catheter placement can occur: 5 days
  - Minimum time after catheter placement to drug start: CONTRAINDICATED while catheter in place
  - Minimum time between last dose of drug and catheter removal: 6 hours

- **sulodexide**
  - Minimum time between last dose and when neuraxial shot/catheter placement can occur: 5 days
  - Minimum time after catheter placement to drug start: CONTRAINDICATED while catheter in place
  - Minimum time between last dose of drug and catheter removal: 6 hours

### HERBALS & SUPPLEMENTS
- **Gingko**
  - May be given; No time restrictions for catheter placement or removal

- **Garlic**
  - May be given; No time restrictions for catheter placement or removal

- **Ginseng**
  - May be given; No time restrictions for catheter placement or removal

- **Omega-3 Fish Oil**
  - May be given; No time restrictions for catheter placement or removal

- **Turmeric**
  - May be given; No time restrictions for catheter placement or removal

### VITAMINS
- **Vitamin C**
  - May be given; No time restrictions for catheter placement or removal

- **Vitamin E**
  - May be given; No time restrictions for catheter placement or removal

### Antineoplastic Agents
This group of medications may have an impact on coagulation and should be evaluated on a case by case basis.

### Herbs & Supplements
This group of medications may have an impact on coagulation and should be evaluated on a case by case basis. In general, the UCSF PREPARE clinic advises that these medications be discontinued at least 1 week prior to surgery.

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The contents of these clinical practice guidelines are to be used as a guide, and not a substitute for medical judgment. Healthcare professionals should exercise sound clinical judgment and individualize patient care based upon the patient’s condition.