Guidelines Responsible, Safe, and Effective Use of Antithrombotics and Anticoagulants in Patients Undergoing Interventional Techniques: American Society of Interventional Pain Physicians Guidelines

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DISCLOSURE

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Common Agents that Modulate the Coagulation Cascade

Antiplatelet

COX Inhibitors
- Aspirin
- Other NSAIDs

GPIIb/IIIa Inhibitors
- Abciximab
- Eptifibatide
- Tirofiban

P2Y12 Inhibitors
- Clopidogrel
- Prasugrel
- Ticagrelor
- Cangrelor
- Ticlopidine

Phosphodiesterase Inhibitors
- Cilostazol
- Dipyridamole

Anticoagulants

Direct Thrombin Inhibitors
- Dabigatran
- Argatroban
- Bivalirudin
- Desirudin
- Hirudin

Indirect Thrombin Inhibitors
- Heparin-Unfractionated
- Dalteparin
- Enoxaparin
- Fondaparinux

Direct Xa Inhibitors
- Rivaroxaban
- Apixaban
- Edoxaban
- Betrixaban

Vitamin K Antagonists
- Warfarin

Thrombolytics

Plasminogen Activators

- Streptokinase
- Tissue plasminogen activator
- Reteplase
- Tenecteplase

Herbal Supplements

Various Mechanisms that May Impact Coagulation

Examples:
- Garlic
- Ginkgo
- Ginseng
- Ginger
- St John's Wort
- Saw Palmetto
- Black Cohosh
- Chamomile
- Feverfew
- Fish Oil

Pharmacological Interventions to Treat Thrombosis

- **The ideal pharmacological agent would prevent pathological thrombosis and allow a normal response to vascular injury to limit bleeding**
- **At present *all* anti-thrombotic agents have *increased* bleeding risk (hemorrhage) as their main side effect.**

- **ANTIPLATELET DRUGS:** Prevent primary hemostastic plug formation
- **ANTICOAGULANT DRUGS:** Inhibit clotting cascade to ultimately prevent fibrin clot formation
- **THROMBOLYTIC DRUGS:** Dissolve an existing clot by digesting fibrin

Bleeding Risk APP's

Will tell you the amount of time to safely wait based on guidelines and best practice standards.

Typically divide into low, medium, and high-risk procedures.

Background

A subset of patients encountered in interventional pain are medicated using anticoagulant or antithrombotic drugs to mitigate thrombosis risk.

Since these drugs target the clotting system, bleeding risk is a consideration accompanying interventional procedures.

Importantly, discontinuation of anticoagulant or antithrombotic drugs exposes underlying thrombosis risk, which can lead to significant morbidity/mortality especially in those with coronary artery or cerebrovascular disease.

This presentation summarizes the literature and provides guidelines based on best evidence for patients receiving anti-clotting therapy during interventional pain procedures.

Methods

A review of the available literature published on bleeding risk during interventional pain procedures, practice patterns and perioperative management of anticoagulant and antithrombotic therapy was conducted. Data sources included relevant literature identified through searches of

EMBASE and PubMed from 1966 through August 2018 and manual searches of the bibliographies of known primary and review articles.

Results

- 1. There is good evidence for risk stratification by categorizing multiple interventional techniques into low-risk, moderate-risk, and high-risk. Also, their risk should be upgraded based on other risk factors.

Results

- 2. There is good evidence for the risk of thromboembolic events in patients who interrupt antithrombotic therapy.

Results

- 3. There is good evidence supporting discontinuation of low dose aspirin for high risk and moderate risk procedures for at least 3 days, and there is moderate evidence that these may be continued for low risk or some intermediate risk procedures.

Results

- 4. There is good evidence that discontinuation of anticoagulant therapy with warfarin, heparin, dabigatran (PradaxaR), argatroban (AcovaR), bivalirudin (AngiomaxR), lepirudin (RefludanR), desirudin (IprivaskR), hirudin, apixaban (EliquisR), rivaroxaban (XareltoR), edoxaban (SavaysaR, LixianaR), Betrixaban(BevyxxaR), fondaparinux (ArixtraR) prior to interventional techniques with individual consideration of pharmacokinetics and pharmacodynamics of the drugs and individual risk factors increases safety.

Results

- 5. There is good evidence that diagnosis of epidural hematoma is based on severe pain at the site of the injection, rapid neurological deterioration, and MRI with surgical decompression with progressive neurological dysfunction to avoid neurological sequelae.

Results

- 6. There is good evidence that if thromboembolic risk is high, low molecular weight heparin bridge therapy can be instituted during cessation of the anticoagulant, and the low molecular weight heparin can be discontinued 24 hours before the pain procedure.

Results

- 7. There is fair evidence that the risk of thromboembolic events is higher than that of epidural hematoma formation with the interruption of antiplatelet therapy preceding interventional techniques, though both risks are significant.

Results

- 8. There is fair evidence that multiple variables including anatomic pathology with spinal stenosis and ankylosing spondylitis; high risk procedures and moderate risk procedures combined with anatomic risk factors; bleeding observed during the procedure, and multiple attempts during the procedures increase the risk for bleeding complications and epidural hematoma.

Results

- 9. There is fair evidence that discontinuation of phosphodiesterase inhibitors is optional (dipyridamole [Persantine], cilostazol [Pletal]. However, there is also fair evidence to discontinue Aggrenox [dipyridamole plus aspirin]) 3 days prior to undergoing interventional techniques of moderate and high risk.

Results

- 10. There is fair evidence to make shared decision making between the patient and the treating physicians with the treating physician and to consider all the appropriate risks associated with continuation or discontinuation of antithrombotic or anticoagulant therapy.

Results

- 11. There is fair evidence that if thromboembolic risk is high antithrombotic therapy may be resumed 12 hours after the interventional procedure is performed.

Results

- 12. There is limited evidence that discontinuation of antiplatelet therapy (clopidogrel [PlavixR], ticlopidine [Ticlid R], Ticagrelor [BrilintaR] and prasugrel [EffientR]) avoids complications of significant bleeding and epidural hematomas.

Results

- 13. There is very limited evidence supporting the continuation or discontinuation of most NSAIDs, excluding aspirin, for 1 to 2 days and some 4 to 10 days, since these are utilized for pain management without cardiac or cerebral protective effect.

Table 13. *Classification of interventional techniques based on the potential risk for bleeding.*

Low-Risk Procedures	Intermediate-Risk Procedures*	High-Risk Procedures*
1. Trigger point and muscular injections (including piriformis injection) 2. Peripheral joints 3. Peripheral nerve blocks 4. Sacroiliac joint and ligament injections and nerve blocks 5. Caudal epidural injections 6. Ganglion Impar blocks	1. Facet joint interventions (intraarticular injections, nerve blocks and radiofrequency neurotomy) 2. Lumbar transforaminal epidural injections at L4, L5, S1 3. Lumbar intradiscal procedures 4. Hypogastric plexus blocks 5. Lumbar sympathetic blocks 6. Peripheral nerve stimulation trial and implant 7. Pocket revision and implantable pulse regenerator/ intrathecal pump replacement 8. Caudal percutaneous adhesiolysis 9. Lumbar percutaneous disc decompression (L4/5 or below) 10. Lumbar vertebral augmentation (below L4) 11. Intervertebral spinous prosthesis 12. Lumbar discography 13. Lumbar interlaminar epidural injections at L5-S1	1. Cervical, thoracic, and high lumbar (above L4-L5) interlaminar epidurals 2. Cervical, thoracic and lumbar above L3 transforaminal epidural injections 3. Spinal cord stimulator trial and implant 4. Percutaneous adhesiolysis with interlaminar or transforaminal approach 5. Percutaneous disc decompression (above L4/5) 6. Sympathetic blocks (stellate ganglion; thoracic splanchnic, celiac plexus) 7. Thoracic and cervical intradiscal procedures 8. Vertebral augmentation, lumbar (above L4), thoracic and cervical 9. Intrathecal catheter and pump implant 10. Interspinous prosthesis and MILD®

***Patients with high risk of bleeding (e.g., old age, history of bleeding tendency, concurrent uses of other anticoagulants/antiplatelets, liver cirrhosis or advanced liver disease, and advanced renal disease) undergoing low or intermediate-risk procedures should be treated as intermediate or high risk, respectively.**

Table 18. *Guidelines for antithrombotic medication management and spinal procedures (risk stratification described in Table 13).*

Medication	Time to Wait After Last Dose of Medication Before Low Risk Interventional Techniques Are Performed		Time to Wait After Last Dose of Medication Before Moderate Risk Interventional Techniques Are Performed		Time to Wait After Last Dose of Medication Before High Risk Interventional Techniques Are Performed		Timing of Therapy restoration or Restarting	
	ASIPP	**ASRA (40)**	**ASIPP**	**ASRA (40)**	**ASIPP**	**ASRA (40)**	**ASIPP**	**ASRA (40)**
NSAIDS (COX 1) (COX 2)	May continue or stop 1-10 days due to lack of protective effect	Stop 1-10 days due to lack of protective effect	May continue or stop 1-10 days due to lack of protective effect	Stop 1-10 days due to lack of protective effect	May continue or stop 1-10 days due to lack of protective effect	Stop 1-10 days due to lack of protective effect	24 hours	24 hours
Aspirin								
Low-Dose Aspirin	Continue or may stop for 3 days	Stop for 4 days	Continue or may stop for 3 days	Stop for 4 days	Stop for 5 days	Stop for 6 days	24 hours	24 hours
High Dose Aspirin	Continue or may stop for 3 days	Stop for 4 days	Continue or may stop for 3 days	Stop for 4 days	Stop for 5 days	Stop for 6 days	24 hours	24 hours
Antiplatelet Agents (Phosphodiesterase Inhibitors)								
Dipyridamole (Persantine)	May continue	May continue	May continue	May continue	May continue or stop for 2 days	Stop for 2 days	12 hours	12 hours
Cilostazol (Pletal)	May continue	May continue	May continue	May continue	May continue or stop for 2 days	Stop for 2 days	12 hours	12 hours
Aggrenox (dipyridamole plus aspirin)	May continue	Stop for 4 days	May continue	Stop for 4 days	Stop for 5 days	Stop for 6 days	24 hours	24 hours
Platelet Aggregation Inhibitors								
Clopidogrel (Plavix)	May continue	May continue	May continue or stop for 3 days	Stop for 7 days	Stop for 5 days	Stop for 7 days	12 hours	12 hours
Prasugrel (Effient)	May continue	May continue	May continue or stop for 6 days	Stop for 7-10 days	Stop for 6 days	Stop for 7-10 days	24 hours	24 hours
Ticlopidine (Ticlid)	May continue	NA	May continue or stop for 7 days	NA	Stop for 7-10 days	NA	24 hours	24 hours
Ticagrelor (Brilinta)	May continue	Continue	May continue or stop for 3 days	NA	Stop for 3-5 days	Stop for 5-10 days	24 hours	24 hours
Vitamin K Antagonists								
Warfarin	May stop for 2 days INR ≤ 3.0	INR < 3.0	Stop for 2-5 days INR ≤ 1.5	Stop for 5 days INR normalize	Stop for 2-5 days INR ≤ 1.5	Stop for 5 days INR normalize	24 hours	24 hours
Thrombin Inhibitors								
Dabigatran (Pradaxa)	May continue or stop for 2 days	May continue or stop for 2 days	Stop for 4-5 days 6 days - renal	Stop for 4-5 days 6 days - renal	Stop for 4-5 days 6 days - renal	Stop for 4-5 days 6 days - renal	24 hours	24 hours

Table 18 (cont.). *Guidelines for antithrombotic medication management and spinal procedures (risk stratification described in Table 13).*

Medication	Time to Wait After Last Dose of Medication Before Low Risk Interventional Techniques Are Performed		Time to Wait After Last Dose of Medication Before Moderate Risk Interventional Techniques Are Performed		Time to Wait After Last Dose of Medication Before High Risk Interventional Techniques Are Performed		Timing of Therapy restoration or Restarting	
	ASIPP	ASRA (40)	ASIPP	ASRA (40)	ASIPP	ASRA (40)	ASIPP	ASRA (40)
Anti-Xa Agents								
Apixaban (Eliquis)	May continue or stop for 2 days	May continue or stop for 2 days	Stop for 3-5 days	Stop for 3-5 days	Stop for 3-5 days	Stop for 3-5 days	24 hours	24 hours
Rivaroxaban (Xarelto)	May continue or stop for 1 day	May continue or stop for 1 day	Stop for 2 days	Stop for 3 days	Stop for 2 days	Stop for 3 days	24 hours	24 hours
Edoxaban (Savaysa, Lixiana)	May continue or stop for 1 day	NA	Stop for 3 days	NA	Stop for 3 days	NA	24 hours	24 hours
Heparins								
Heparin (treatment) - IV	Discontinue for 4 hours	Discontinue for 4 hours	Discontinue for 4 hours	Discontinue for 4 hours	Discontinue for 4 hours	Discontinue for 4 hours	24 hours	24 hours
Heparin (treatment) - SC	Discontinue for 8-10 hours	Discontinue for 8-10 hours	Discontinue for 8-10 hours	Discontinue for 8-10 hours	Discontinue for 8-10 hours	Discontinue for 8-10 hours	24 hours	24 hours
Low Molecular Weight Heparin	Discontinue for 24 hours	Discontinue for 24 hours	Discontinue for 24 hours	Discontinue for 24 hours	Discontinue for 24 hours	Discontinue for 24 hours	24 hours	24 hours
Thrombolytic Agents								
TPA, Streptokinase, Alteplase, Reteplase	May continue	May continue	Stop for 2 days	Stop for 2 days	Stop for 2 days	Stop for 2 days	24 hours	24 hours
GPIIb/IIIa Inhibitors								
Abciximab (ReoPro)	May continue	May continue	Stop for 1-2 days	Stop for 2-5 days	Stop for 1-2 days	Stop for 2-5 days	8-12 hours	8-12 hours
Eptifibatide (Integrilin)	May continue	May continue	Stop for 8 hours	Stop for 8-24 hours	Stop for 8 hours	Stop for 8-24 hours	8-12 hours	8-12 hours
Tirofiban (Aggrastat)	May continue	May continue	Stop for 8 hours	Stop for 8-24 hours	Stop for 8 hours	Stop for 8-24 hours	8-12 hours	8-12 hours
Miscellaneous								
Fondaparinux (Arixtra)	May continue	May continue	Stop for 4 days	Stop for 4 days	Stop for 4 days	Stop for 4 days	8-12 hours	8-12 hours

ASIPP = American Society of Interventional Pain Physicians; ASRA = American Society of Regional Anesthesia and Pain Medicine

Clinically Relevant Points Summary

- Be vigilant
- Detailed clinical history of patients
- Depend on your own experience
- Be familiar with the current evidence and guidelines
- Always weigh risk-benefit ratio of treatment plan
  - Individualize therapy
- Consult with cardiologist/PCP
- Bleeding directly associated with:
  - **Anticoagulation & proximity to vascular structures**
  - **Trauma of injection (multiple attempts)**
  - **Size of needle**
  - **Size of epidural space**
  - **Use of catheters or leads**
- Remember embolic events

Guidelines Conclusion

Based on the survey of current literature, and published clinical guidelines, recommendations for patients presenting with ongoing antithrombotic therapy prior to interventional techniques are variable and are based on comprehensive analysis of each patient and the risk-benefit analysis of intervention.

APP's can provide quick guidelines.

Thank You

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