Perioperative Medication Management

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Disclosure

- None
Objectives

- Review general principles to continue or stop medications in the perioperative setting.
- Discuss evidence and controversies around perioperative medication management.
- Outline a practical guide for perioperative medication management.

General Principles

- **Continue**
  - rebound or withdrawal potential
- **Discontinue:**
  - Increase surgical risk
  - Non-essential for quality of life
- Use clinical reasoning

Case 1

70 y/o man with cecal mass. PMH HTN, CAD s/p BMS 3 mo ago. On Atenolol 25 mg/d; Clopidogrel 70 mg/d and ASA 81 mg/d. Scheduled for robotic hemicolecotomy.

What is your recommendation for perioperative management of antiplatelets?

a) Continue clopidogrel and ASA
b) Hold both clopidogrel and ASA on day of surgery
c) Stop clopidogrel 5 days before surgery and continue ASA
d) Stop both clopidogrel and ASA 7 days before surgery
e) Stop ASA 7 days before surgery and continue clopidogrel
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ASA

- Irreversible cyclooxygenase (COX) inhibition
- 7-10 days for platelet regeneration
- Perioperative use associated with ↓ CV morbidity
- Stop for > 5 days → ↑ stroke and ACS risk
- Decision of continue vs. hold → related to hemorrhagic risk vs. perioperative CV morbidity.
  - E.g. Neurosurgery; prostate; etc.
  - Resume 24h after surgery (ACCP 2012)

Other antiplatelets

- Thienopyridines - irreversible inhibition of ADP-induced platelet aggregation (P2Y<sub>12</sub> receptor)
- Discontinue:
  - Clopidogrel – 5 days
  - Prasugrel – 7 days
  - Ticlopidine – 10-14 days
- Resume ASAP.
- Continue ASA in patients with stents
- Unclear data on perioperative safety of dipyridamole
Cilostazol

- Phosphodiesterase-3 enzyme inhibitor
- Half-life ~ 21 hours
- Discontinue 5 days (manufacturer)

Novel antiplatelets

- **Ticagrelor**
  - Reversible
  - Short half-life (6 - 13 h)
  - DES - discontinue 1 day before surgery
- **Cangrelor**
  - Intravenous
  - Short half life (3 minutes)
NSAIDS

• Reversible inhibition of COX-1 $\rightarrow$ ↓ TXA$_2$ $\rightarrow$ ↓ platelet adhesion
  - Nephrotoxicity
  - ↑ bleeding risk x 1.5-2
• COX-2 (celecoxib) – minimal effect of platelet fx
  - Nephrotoxicity
  - Adverse cardiovascular effects
  - ↓ postoperative opioid requirements
• Non-acetylated NSAIDS (salsalate) – not antiplatelet
Case 2

80 y/o woman with PAD and AFib. Meds: warfarin 5 mg/d; ASA 325 mg/d; diltiazem ER 180 mg/d. Scheduled for cataract surgery.

What is your recommendation for perioperative management of warfarin and ASA in cataract surgery?

a) Continue both warfarin and ASA
b) Stop ASA 7d prior and warfarin 5 d prior
c) Bridge warfarin to LMWH
d) Cancel surgery given patient's age
e) Stop warfarin 5 d prior and continue ASA
2012 ACCP Guidelines

- **Continue vitamin K antagonists**
  - Dental procedures – use of local hemostatic agents (epsilon-aminocaproic acid) or stopping VKA 2-d earlier
    - Dental hygiene, uncomplicated extractions, prosthesis, restorations, endodontics, periodontal therapy
  - Minor dermatologic procedures
    - Mohs; simple excisions
  - Cataract surgery; trabeculectomy
  - EGD, C-scope w/o biopsy; EUS
  - Arthrocentesis

Case 3

65 y/o man, hyperlipidemia, HTN, diverticulosis.
Meds: rosuvastatin, chlorthalidone.
Scheduled for left hemicolectomy in 2 wk.
Patient is able to climb 2 flight of stairs.
What is your recommendation?

a) Stop chlorthalidone on day of surgery
b) Stop both medications on day of surgery
c) Continue both medications
d) Start atenolol now – adjust dose to HR ~ 60-70x’
Diuretics

- It is recommended to **stop on day of surgery**
  - Hypovolemia
  - Electrolyte derangement
    - Hypokalemia
    - Hyponatremia
    - Hypo/Hypercalcemia
- Individualize in patients with CHF

RAAS Inhibitors

ACEI
ARB
Aldosterone antagonists
  - Eplerenone, spironolactone
Direct renin blocker
  - Aliskiren

Inhibition of Ang II vasoconstrictor effect
↓ Aldosterone
↑ Vasodilatory agents (Bradykinin, NO, prostacyclin)
↓ Venous blood “Pooling”
↓ Cardiac output
↑ **post-induction hypotension**
↑ vasoconstrictor use (adrenergic agonists, vasopressin)

RAAS Inhibitors - Recommendations

- Stop ACEI – one dose
  - CHF or severe HTN – may continue (AHA/ACC 2014 Guidelines)
- Stop ARB – 24 h
- Aliskiren – half life ~ 24 h → ~ 3 days?
- Spironolactone – one dose
- Eplerenone – one dose

Clonidine in Patients Undergoing Noncardiac Surgery

P.J. Devereaux, D.I. Sessler, K. Leslie, A. Kurz, M. Mrkobrada, P. Alonso-Coello,

Low-dose clonidine in noncardiac surgery
- did not reduce the rate of the composite outcome of death or nonfatal myocardial infarction
- increase the risk of clinically important hypotension and nonfatal cardiac arrest.
Other cardiovascular medications

- α-blockers
  - BPH (Tamsulosin, alfuzosin, terazosin, doxazosin) –
    - Floppy iris syndrome in cataract surgery
  - Notify Ophthalmologist

- Calcium channel blockers, anti-angina; antiarrhythmics, clonidine, statins, betablockers (already on it)
  - Continue

References:
Abdel-Aziz S. Curr Opin Ophthalm. 2009; 20:37–41
Wallace AW. Anesthesiology. 2004;101:284-293.

Case 4

20 y/o female with DM1, CHF (EF 30%), ESRD. Scheduled for renal transplant. Meds: insulin pump, atorvastatin, metoprolol, lisinopril.

How would you manage his insulin preoperatively?

a) Stop pump and convert to long acting insulin
b) Continue basal infusion of insulin
c) Start iv insulin and glucose (glucose clamp)
d) Stop pump and start ISS
Case 4

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Objectives of glycemic control

• Avoid hypo- and hyperglycemia
• Maintain stable electrolyte balance
• Prevent ketoacidosis
• Maintain strict glycemic control
  - ICU: > 110 mg/dL < 180 mg/dL
  - Non-ICU: > 100 mg/dL < 140 mg/dL

Standards of Care in DM. Diabetes Care 2017;40(Suppl. 1):S120–S127
Pre-operative DM management

- Stop OHA in AM of surgery
  - Chlorpropamide (~2 days before)
  - Metformin \(\rightarrow\) continue the previous day
  - Thiazolidinediones (pioglitazone)
  - GLP-1 agonists (exenatide)
  - DPP-4 inhibitors (sitagliptine)


Pre-operative DM management

- Insulin
  - Day before \(\rightarrow\) same regime
  - Day of surgery:
    - Do not use short acting insulin
    - Long acting insulin: 50% dose
    - Insulin pump \(\rightarrow\) continue basal rate

Pre-operative DM management

• 70/30 Insulin
  - Long acting insulin (NPH): 50%
  - 50 u → 70% = 35 u
  - → Administer 50% ~ 17 u

Case 5

80 y/o woman with PMR admitted for cholecystectomy. Meds: Prednisone 5 mg/d.
What is your recommendation for perioperative management of steroids?

a) Continue same dose of prednisone
b) Administer 15 mg of prednisone
c) Stop prednisone on day of surgery
d) Administer hydrocortisone 100 mg i.v. upon induction
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Perioperative Steroids

<table>
<thead>
<tr>
<th>Axis suppression</th>
<th>Minor surgical stress (hernia)</th>
<th>Moderate surgical stress (articular replacement)</th>
<th>Major surgical stress (CABG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PDN ≤ 5 mg/d Steroids &lt; 3wk</td>
<td>Daily dose No supplementation</td>
<td>Daily dose No supplementation</td>
<td>Daily dose No supplementation</td>
</tr>
<tr>
<td>Documented or suspicion PDN &gt; 20 mg/d &gt; 3wk Cushingoid +ve Cosyntropin</td>
<td>Daily dose No supplementation</td>
<td>Hydrocortisone 50 mg iv (induction) 25 mg iv q8h x 24-48h</td>
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</tr>
<tr>
<td>Unknown PDN 6-10 mg ≥ 3wk</td>
<td>Daily dose No supplementation</td>
<td>Cosyntropin +ve Hydrocortisone 50 mg iv (induction) 25 mg iv q8h x 24-48h</td>
<td>Hydrocortisone 100 mg iv (induction) 50 mg iv q8h x 24h 25 mg iv q8h x 24-48h</td>
</tr>
</tbody>
</table>

Shaw M. CJCJM. 2002;69(1):9-11
## Biologic Agents – Hold x 2 ½ lives

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>2 half lives (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>TNF inh</td>
<td>8.6</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>TNF inh</td>
<td>28</td>
</tr>
<tr>
<td>Infliximab</td>
<td>TNF inh</td>
<td>16-20</td>
</tr>
<tr>
<td>Golimumab</td>
<td>TNF inh</td>
<td>24</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>Pegylated Fab frag</td>
<td>28</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Chimeric CD20 mAb</td>
<td>42</td>
</tr>
<tr>
<td>Abatacept</td>
<td>T cell co-stimulator</td>
<td>26</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>IL-6 receptor mAb</td>
<td>26</td>
</tr>
</tbody>
</table>

J Rheumatol 2012;39;1583-1602
Case 7

50 y/o woman with bipolar disorder and paranoid schizophrenia. Meds: Lithium carbonate, valproic acid, olanzapine and escitalopram.
Scheduled for mastectomy secondary to breast cancer.

What are your recommendations for management of psychiatric drugs?

a) Stop all of them on day of surgery
b) Continue valproic acid and Lithium only
c) Continue olanzapine and escitalopram only
d) Stop olanzapine
e) Continue all of them
Neuropsychiatric drugs

- SSRI:
  - Potential antiplatelet effect
  - Withdrawal symptoms
  - In certain procedures (neurosurgery) its discontinuation can be considered – discuss with Psychiatry and stop gradually.
  - Continue in perioperative period.

Huyse F.J. Psychosomatics 2006; 47:8–22

Need to be cautious and don’t underestimate the potential adverse risks of these drugs.
Neuropsychiatric drugs

- **Tricyclic antidepressants:**
  - Inhibit recapture of norepinephrine and serotonin
- Theoretical ↑ risk of dysrhythmias
- Abrupt discontinuation → cholinergic effect
- Continue in perioperative period.

Huyse FJ. Psychosomatics 2006; 47:8–22

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Neuropsychiatric drugs

- **Benzodiazepines** → continue
- **Antipsychotics** → continue
  - Document ECG (QTc)
- **MAOI** → stop 2 weeks before
  - Risk of HTN with sympathetic agents
  - Serotonergic syndrome
  - Avoid meperidine, thyramine
  - Use direct sympathomimetics (phenylephrine)

Huyse FJ. Psychosomatics 2006; 47:8–22
Neuropsychiatric drugs

- **Lithium** → continue
  - Monitor electrolytes (Nephrogenic Diabetes insipidus)
- **Antiepileptics** → continue
  - Monitor serum levels
  - Consider i.v. use
- **Anti-Parkinson agents** → continue
  - Abrupt discontinuation → Malignant neuroleptic Sx
  - Neurology consult

Hoyos F.J. Psychosomatics 2006; 47:8-22.

"I suspect you’re bi-polar!"
50 y/o woman with glioblastoma multiforme.
Meds: Dexamethasone, Levetiracetam, Ginseng, Garlic Ginkgo-biloba.
Scheduled for brain tumor removal in 2 weeks.
What is your recommendation for medication management?

a) Continue all her medications
b) Stop all medications on day of surgery
c) Stop Levetiracetam on day of surgery
d) Stop Ginseng and Ginkgo-biloba on day of surgery
e) Stop now the Garlic, Ginseng y Ginkgo-biloba
Supplements and herbs

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginseng</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>Inhibit platelet aggregation (irreversible)</td>
</tr>
<tr>
<td></td>
<td>↑ PT-PTT in animals</td>
</tr>
<tr>
<td></td>
<td>↑ Anticoagulant effect of warfarin</td>
</tr>
<tr>
<td>Ephedra (ma huang)</td>
<td>AML, stroke</td>
</tr>
<tr>
<td></td>
<td>Deplete endogenous catecholamine deposits</td>
</tr>
<tr>
<td></td>
<td>→ Intraoperative hemodynamic instability</td>
</tr>
<tr>
<td></td>
<td>→ Fatal interaction with MAOIs</td>
</tr>
<tr>
<td>Garlic</td>
<td>Inhibit platelet aggregation (irreversible)</td>
</tr>
<tr>
<td></td>
<td>↑ fibrinolysis → ↑ hemorrhagic risk</td>
</tr>
<tr>
<td></td>
<td>Erratic hypotensive activity</td>
</tr>
<tr>
<td>Ginkgo-biloba</td>
<td>Inhibit PAF → ↑ hemorrhage risk</td>
</tr>
</tbody>
</table>

Kava kava          | Sedation, anxiolysis                       |
|                  | ↑ Sedative effect of anesthetic agents     |
|                  | Addictive potential → suppression          |

St. John's Wort    | Multiples pharmacologic interactions → P450 |
|                  | induction                                  |

Echinacea          | Activate cellular immunity                 |
|                  | Allergic reactions; immunosuppression      |
|                  | Potentiates barbiturates                   |

Valerian           | ↑ Sedative effect of anesthesia            |
|                  | Suppression; refractoriness to anesthesia  |

Ang-Lee NK. JAMA. 2001;286:208-216.
Supplements and herbs

- Others: Chamomile – anticoagulant effect
- Other resources:
  - www.nccam.nih.gov
  - www.fda.gov/consumer
  - www.herbmed.org

Other classes

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2 Receptor Antagonists</td>
<td>Continue</td>
<td>Concern for postop anticholinergic effect and risk for delirium</td>
</tr>
<tr>
<td>Proton Pump Inhibitors</td>
<td>Continue</td>
<td>Stress ulcer prevention</td>
</tr>
<tr>
<td>Immunomodulators</td>
<td>Stop*</td>
<td>Discuss with treating specialist or PCP</td>
</tr>
<tr>
<td>Thyroid Replacement</td>
<td>Continue</td>
<td>IV route if PO unavailable</td>
</tr>
<tr>
<td>Anti-Thyroid</td>
<td>Continue</td>
<td></td>
</tr>
<tr>
<td>HIV Medications</td>
<td>Continue</td>
<td>Stop/resume together to avoid development of resistance</td>
</tr>
<tr>
<td>Asthma Medications</td>
<td>Continue</td>
<td></td>
</tr>
</tbody>
</table>
Cleveland Clinic

Every life deserves world class care.