DUAL ANTIPLATELET THERAPY (DAPT)

BHAVI SHAH, DNP, APRN, ANP-C
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
DEPARTMENT OF MEDICINE
CARDIOLOGY SECTION

WHAT REALLY HAPPENS

- Normal endothelium regulates blood flow
- Tissue Injury
  - Vasoconstriction
  - Release of von Willebrand Factor (vWF)
- Platelet adhesion
  - GP Ib IX/V and GP IIb/IIIa
  - vWF binds with GP Ib IX/V
WHAT REALLY HAPPENS...

- Platelet Activation
  - Degranulation
    - Release of
      - Fibrinogen and vWF
      - Serotonin
      - ADP activates other platelets
      - Calcium - Secondary hemostasis
    - ADP receptors – P2Y1, P2Y12 (important)
  - Formation of Thromboxane A2 (TXA2) using Cyclooxygenase (COX-
    1)
  - TXA2 promotes
    - Degranulation of platelets
    - Increases fibrinogen receptors &
    - Stimulates platelet aggregation
WHAT REALLY HAPPENS...

- Platelet aggregation
  - TXA2 and ADP
  - Activate/express the GPIIb/IIIa receptors on the platelets
  - GPIIb/IIIa binds with fibrinogen
    - Binds with receptors on other platelets
  - Platelet mesh with GPIIb/IIIa – Fibrinogen bond
- GPIIb/IIIa – Fibrinogen – important target for antiplatelet medications

ANTIPLATELET MEDICATIONS

COX-1 INHIBITOR
- ASPIRIN

THIENOPYRIDINE
- PLAVIX (CLOPIDOGREL)
- EFFIENT (PRASUGREL)
- TICLOPIDINE (TICLID)

P2Y12 RECEPTOR BLOCKER
- BRILLINTA (TICAGRELOR)

DUAL ANTIPLATELET MEDICATIONS
COX-1 INHIBITOR + THIENOPYRIDINES/P2Y12 RECEPTOR BLOCKER
ASPIRIN

• Irreversibly inactivates COX-1, which decreases the synthesis of TXA2 and PG12
• Decrease in platelet activation
• Analgesic, Anti-inflammatory and Antipyretic effect

DOSE
Antiplatelet maintenance dose – 81mg
Acute Coronary Syndrome/PCI loading – 160mg – 325mg

DURATION
Maintenance dose - Indefinite

ASPIRIN...

ADVERSE EFFECTS

<table>
<thead>
<tr>
<th>COMMON</th>
<th>SERIOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Bleeding</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Bronchoconstriction</td>
</tr>
<tr>
<td>N/V/Abd pain</td>
<td>G.I Ulcers</td>
</tr>
<tr>
<td>Headache</td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>Aplastic anemia</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Agranulocytosis</td>
</tr>
<tr>
<td>Constipation</td>
<td>DIC</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>Pancytopenia</td>
</tr>
<tr>
<td></td>
<td>Nephrototoxicity</td>
</tr>
<tr>
<td></td>
<td>Hepatotoxicity</td>
</tr>
<tr>
<td></td>
<td>Salicylism</td>
</tr>
<tr>
<td></td>
<td>Reye Syndrome</td>
</tr>
</tbody>
</table>

ASPIRIN....

• Half life – 15-20 min (parent drug) 2-12h (active metabolite)
• Onset – Non EC - 30 – 60 min
• Onset – EC - 3-4 hours
• Post D/C – 1-4 days
• Metabolism – Gut CYP450 system
• Excretion – Urine
• Pregnancy – Risks not observed with low dose
• Ask for any existing bleeding disorders
• Ask for any episodes of GI bleeding, hematuria
PATIENT EDUCATION

- Take the medication with food to avoid GI side effects
- Inform healthcare provider in case of shortness of breath
- Avoid concomitant use of NSAIDs with Aspirin

PLAVIX (CLOPIDOGREL)

- Prodrug
- Irreversibly binds to P2Y12 ADP receptor
  - Inhibits Platelet aggregation in response to ADP

DOSE

Loading dose - Revascularization – 300mg-600mg
Maintenance dose – 75mg PO daily

DURATION

Varies according to the cardiac event and type of stent

PLAVIX (CLOPIDOGREL) ADVERSE EFFECTS

<table>
<thead>
<tr>
<th>COMMON</th>
<th>SERIOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Bleeding – Hemorrhage</td>
</tr>
<tr>
<td>Pruritis</td>
<td>TTP</td>
</tr>
<tr>
<td></td>
<td>Agranulocytosis</td>
</tr>
<tr>
<td></td>
<td>Pancytopenia</td>
</tr>
<tr>
<td></td>
<td>Aplastic Anemia</td>
</tr>
<tr>
<td></td>
<td>Exfoliative dermatitis</td>
</tr>
<tr>
<td></td>
<td>Stevens-Johnsons syndrome</td>
</tr>
<tr>
<td></td>
<td>Erythema multiforme</td>
</tr>
<tr>
<td></td>
<td>Toxic epidermal necrolysis</td>
</tr>
<tr>
<td></td>
<td>Exanthematos pustulosis</td>
</tr>
<tr>
<td></td>
<td>Pneumonia</td>
</tr>
</tbody>
</table>
PLAVIX (CLOPIDOGREL)...

- Half life – 8 hours
- Onset – 24-48 hours. Max Effect – 4-6 days
- Post D/C – 4-10 days
- Metabolism – Liver, CYP450 (CYP2C19 – primary)
- Excretion – Urine (50%) Feces (46%)
- Pregnancy – Benefits outweigh Risks
- D/C medication at least 5 days prior to any elective surgical procedure
- Consult prescribing provider prior to modification in regimen

PATIENT EDUCATION

- Take uninterrupted at about the same time daily
- Take with food to avoid GI complications
- Talk to your provider prior to scheduling any elective surgeries/dental procedures
- Seek emergency attention in case of unexplained/ prolonged bleeding
- Avoid concomitant use of Omeprazole with Plavix

EFFIENT (PRASUGREL)

- Prodrug
- Irreversible binding to P2Y12 ADP receptors
- Inhibits platelet activation and aggregation

DOSE

Loading dose – Revascularization - 60mg
Maintenance dose – 10mg PO daily

DURATION

Varies according to the cardiac event and type of stent
### EFFIENT (PRASUGREL)... ADVERSE EFFECTS

<table>
<thead>
<tr>
<th>COMMON</th>
<th>SERIOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Bleeding, Hemorrhage</td>
</tr>
<tr>
<td>Headache/backpain/extremity pain</td>
<td>TTP</td>
</tr>
<tr>
<td>HTN, hypotension</td>
<td>Severe thrombocytopenia</td>
</tr>
<tr>
<td>HLD</td>
<td>Anemia</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Leukopenia</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Fever, rash</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>Pericardial effusion</td>
</tr>
<tr>
<td>Nausea, diarrhea</td>
<td>Pericardial effusion</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>Leukopenia</td>
</tr>
</tbody>
</table>

### EFFIENT (PRASUGREL)... 

- Half life – 7 hours
- Metabolism – Liver, CYP450: 2B6
- Excretion – Urine (68%) Feces (27%)
- Pregnancy – Benefits outweigh Risks
- D/C medication at least 7 days prior to any elective surgical procedure
- Consult prescribing provider prior to modification in regimen
- Not recommended for patients >75 yrs
- Increased bleeding risk in patient <60 kg
- In case of bleeding – manage without D/C medication due to high risk of cardiovascular events especially in first few weeks after ACS

### PATIENT EDUCATION

- Take medication regularly
- Seek emergency attention in case of unexplained prolonged bleeding.
- Contact provider before starting any new medications
- Talk to your provider prior to scheduling any elective surgeries/dental procedures
BRILLINTA (TICAGRELOR)

- Orally active P2Y12 receptor blocker
- Reversibly binds to the P2Y12 ADP receptor
  - Inhibits platelet activation and aggregation
- Not a Prodrug
  - Rapid onset of action

DOSE
Loading dose during revascularization – 180mg
Maintenance dose – 90mg PO BID

DURATION
Varies according to the cardiac event and type of stent

BRILLINTA (TICAGRELOR)
ADVERSE EFFECTS

<table>
<thead>
<tr>
<th>COMMON</th>
<th>SERIOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Bleeding</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Syncope</td>
</tr>
<tr>
<td>Gt Elevation</td>
<td>AV Block</td>
</tr>
<tr>
<td>Headache</td>
<td>Brady-arrhythmias</td>
</tr>
<tr>
<td>HTN, hypotension</td>
<td>Hypersensitivity</td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
</tr>
<tr>
<td>Nausea, diarrhea</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td></td>
</tr>
</tbody>
</table>

BRILLINTA (TICAGRELOR)

- Half life – 7 hours
- Metabolism – Liver CYP450: 3A4 (primary)
- Excretion – Urine (26%) Feces (58%)
- Pregnancy – Benefits outweigh Risks
- D/C medication at least 5 days prior to any elective surgical procedure
- Consult prescribing provider prior to modification in regimen
- Do not start on patients undergoing urgent CABG
- Contraindicated in case of severe liver disease
- In case of bleeding – manage without D/C medication due to high risk of cardiovascular events
PATIENT EDUCATION

• Take medication uninterrupted regularly
• Seek emergency attention in case of unexplained prolonged bleeding.
• Contact provider before starting any new medications

---

Action of Antiplatelets and Anticoagulants in Primary Hemostasis

---

• Acute Coronary Syndrome (ACS)
  — Clinical symptoms compatible with acute myocardial ischemia including unstable angina (UA), Non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI)
• Stable Ischemic Heart Disease (SIHD)
  — Pts with Hx of ACS >1 year ago who have remained free of recurrent ACS are said to have transitioned to SIHD
• Percutaneous Coronary Intervention (PCI)
  — Catheter based, non-surgical procedure to treat stenosis of coronary arteries
• Drug Eluting Stents (DES)
  — Stents with controlled local release of anti cell proliferative medication
• Bare Metal Stents (BMS)
  — Stents without any drug coating
DAPT Guidelines for SIHD
• SIHD treated with PCI

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>DES</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>ASA (75mg - 100mg) PO daily</td>
<td>ASA (75mg - 100mg) PO daily</td>
</tr>
<tr>
<td>I</td>
<td>P2Y12 Inhibitor (CLOPIDOGREL) 6 months</td>
<td>P2Y12 Inhibitor (CLOPIDOGREL) 1 month</td>
</tr>
<tr>
<td>III</td>
<td>No Benefit</td>
<td>Pts with SIHD without Hx of ACS, PCI, or recent CABG (within 12 months) =&gt; DAPT is not beneficial</td>
</tr>
</tbody>
</table>

DAPT Guidelines for ACS (NSTEMI/STEMI)
• ACS treated with PCI

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>DES</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>ASA (75mg -100mg) PO daily</td>
<td>ASA (75mg -100mg) PO daily</td>
</tr>
<tr>
<td>I</td>
<td>P2Y12 Inhibitor (CLOPIDOGREL/TICAGRELOR/PRASUGREL) 12 months</td>
<td>P2Y12 Inhibitor (CLOPIDOGREL/TICAGRELOR/PRASUGREL) 12 months</td>
</tr>
<tr>
<td>III</td>
<td>HARM</td>
<td>PRASUGREL should NOT be administered in patients with a prior history of stroke or TIA</td>
</tr>
</tbody>
</table>

DAPT Guidelines for ACS...

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>ACS =&gt; Medical therapy w/ Fibribrinolitics</th>
<th>ACS =&gt; Medical therapy w/o PCI or Fibribrinolitics</th>
<th>ASA (75mg -100mg) PO daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>DAPT (CLOPIDOGREL) minimum for 14 days and ideally for 12 months</td>
<td>DAPT (TICAGRELOR/CLOPIDOGREL) for 12 months</td>
<td></td>
</tr>
</tbody>
</table>
DAPT guidelines for Coronary Artery Bypass Graft (CABG)

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Event Description</th>
<th>Post OP Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Post PO (on DAPT) =&gt; =&gt; Subsequent CABG</td>
<td>Resume DAPT post-op to complete recommended duration</td>
</tr>
<tr>
<td>I</td>
<td>ACS (on DAPT) =&gt; CABG</td>
<td>Resume DAPT post-op to complete 12 months</td>
</tr>
<tr>
<td>I</td>
<td>ASA (75mg - 100mg) PO daily</td>
<td></td>
</tr>
</tbody>
</table>

Perioperative management – DAPT for NonCardiac Elective Surgery

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Event Description</th>
<th>Post OP Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>NonCardiac Elective surgeries =&gt; Delay for 30 days after BMS implant and ideally 6 months after DES implant</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>If unable to postpone surgery =&gt; Continue ASA 81mg perioperatively and resume P1Y12 inhibitor as soon as possible</td>
<td></td>
</tr>
<tr>
<td>III HARM</td>
<td>Elective NonCardiac surgery should NOT be performed within 30 days of BMS implant and within 3 months of DES implant</td>
<td></td>
</tr>
</tbody>
</table>

MEDICATION COMPLIANCE

- Importance of DAPT in case of coronary artery revascularization
  - Adherence is critical
  - Stent thrombosis/In stent restenosis
  - Acute Coronary Syndrome
  - BMS vs DES
PREVENTION

• Lifestyle Modification
  – Physical Activity
• Risk factor management
  – Diabetes management
  – Hypertension management
  – Smoking cessation
  – Dietary modification
• Follow-up compliance
• Medication compliance

DAPT

Questions??

References