社區藥局用藥諮詢站訓練課程
冠心症的臨床治療指引

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Background

- Ischemic heart disease characterized by myocardial death or necrosis due to severe or prolonged ischemia
  - Acute reduction of blood supply to a portion of the myocardium
  - Critical imbalance between the oxygen supply and demand of the myocardium
- Plaque rupture with thrombus formation in a coronary vessel

Epidemiology

- Approximately 500,000 STEMI events per year in the U.S
  - 20-30% of the p't die before reaching a hospital as a result of ventricular fibrillation
  - Prompt recognition and treatment have dramatically reduced the mortality over the past two decades
- Cost of CAD in USA：$101 billion in 2001

American Heart Association. Heart Disease and Stroke Statistics. Accessed November 15, 2003.

Pathophysiology-1

- Narrowing of the epicardial blood vessels
  - Thrombus formation overlying a lipid-rich atheromatous plaque
  - Plaque rupture with subsequent exposure of the basement membrane results in platelet aggregation, thrombus formation, fibrin accumulation, hemorrhage into the plaque, and varying degrees of vasospasm

Pathophysiology-2

- Atheromatous plaque rupture
  - Result in partial or complete occlusion of the vessel and subsequent myocardial ischemia
  - Total occlusion of the vessel for more than 4-6 hours results in irreversible myocardial necrosis
    - Reperfusion within this period can salvage the myocardium and reduce morbidity and mortality

Non-Atherosclerotic Causes of MI

- Coronary vasospasm
  - Variant angina (by Dr. Prinzmetal in 1959)
  - Cocaine and amphetamine abuse
  - More often show ST elevation than ST depression
  - Responds to nitrates and calcium channel blockers
- Coronary emboli
  - Sources such as an infected heart valve
- Occlusion of the coronaries due to vasculitis
- Mismatch of oxygen supply and demand
  - Such as acute anemia from GI bleeding
- Severe chest trauma

Type of Infarction

- Acute coronary syndrome (ACS)
  - Unstable angina (NA)
  - Non-ST-elevation MI (NSTEMI, non-Q-wave)
  - ST-elevation MI (STEMI, Q-wave, transmural)
- Related to therapeutic decisions

	cardiac enzyme	ST elevation
NA	X	X
NSTEMI	∨	X
STEMI	∨	∨

Type of Infarction

- Unstable angina
- Non-ST-elevation MI
  - Involve only the subendocardial myocardium
  - Smaller and less extensive
- ST-elevation MI
  - Injury that transects the entire thickness of myocardial wall (Q-wave on the ECG)
  - Thrombus formation in more than 90%
  - Fibrinolytic therapy

Clinical Presentation

- Clinical presentation
  - Silent (20%)：in the elderly or p't with DM
  - Prolong substernal chest pain、pressure、shortness of breath、nausea、vomiting 、diaphoresis、fever
  - Chest pain
    - Atypical in nature as well as location
      - Confuse with indigestion or GI complaints
    - Stabbing or knife-like
    - Occur in the arms, shoulder, neck, jaw, back

Diagnosis

- History and clinical presentation
- 12-lead electrocardiogram (ECG)
  - Identify STEMI from others
    - A significant high-risk indicator for mortality
    - Benefit of thrombolytic therapy in STEMI
  - Location of an infarct

Diagnosis

- Cardiac enzyme
  - Presence or absence of myocardial necrosis
  - Check levels within 15 to 20 minutes after presentation
- Creatine kinase (CK) and CK-MB
  - Appear within 3-6h and peak in 12-24h
  - Determined at admission and repeated after 12h
  - Related to the size of the infarct, but maybe miss if admission is delayed
- Myoglobin
  - Low-molecular-weight heme protein found in cardiac and skeletal muscle
  - Released (2h) more rapidly than troponin and CK-MB

Diagnosis

- Troponin I
  - At high risk for ischemic complications
    - Independent predictor with 12-lead ECG
  - Greater benefit from treatment with
    - Platelet glycoprotein (GP) IIb/IIIa inhibitors, low-molecular-weight heparin, and early percutaneous coronary intervention
  - Raised within 3-12h after MI and remains elevated for 14d
  - More sensitive and specific for minor damage
- Lactate dehydrogenase (LDH_1)
  - Appear 24-48h, peak in 3-6 days , and returns to the baseline within 8-12 days

Pharmacologic Therapy

- Unstable angina
- Non-ST-elevation MI
  - Anti-ischemic therapy
    - Anti-platelet、anti-coagulation
    - Morphine、Oxygen、NTG (MONA)
    - Beta-blocker、ACEI/ARB、CCB
    - Anti-arrhythmia agent
- ST-elevation MI
  - Reperfusion therapy
    - Thrombolysis or primary PCI
  - A door-to-drug time of within 30 minutes and a door-to-balloon time of within 90 minutes

Anti-Platelet Drugs

- Oral Anti-platelet drugs
  - Aspirin
  - Thienopyridines
    - Ticlopidine
    - Clopidogrel
- IV Anti-platelet
  - Abciximab (monoclonal antibody)
  - Eptifibatide (peptide inhibitor)
  - Tirofiban (non-peptides)

Anti-coagulation

- Unfractionated heparin (UFH)
  - Inactivation of activated Factor X and inhibition of prothrombin's conversion to thrombin (variable)
  - Treat ACS with antiplatelet agents (IA)
  - Monitor
    - Activated partial thromboplastin time (aPTT)
    - 1.5-2 times normal (50-70 seconds)
- Enoxaparin
  - Low-molecular-weight heparin (LMWH)
  - Prefer over UFH unless CABG is planned within 24H (IIaA)
  - NO using in ＞75y/o or renal dysfunction
    - Scr＞2.5mg/dl in men or Scr＞2mg/dl in womem

Nitrate

- Nitroglycerin (NTG)
  - Small but statistically significant benefit in reducing mortality (IC)
  - Sublingual NTG every 5min as needed for chest pain
  - IV NTG is recommended for routine use during the first 24-48H
    - Particularly with large anterior wall infarctions

ACE inhibitor

- An ACE inhibitor should be administered orally within the first 24h of STEMI
  - Anterior infarction、tachycardia、heart failure、LV dysfunction (LVEF＜0.4)、ACS and DM
  - Without hypotension (SBP＜100 mmHg or 30 mmHg below baseline) or known contraindications to that class of medications
  - Level of Evidence：A

Others

- Beta-blocker
  - Decrease myocardial oxygen consumption and some complications of MI (ventricular fibrillation)
  - Decrease infarct-associated morbidity and mortality (IB)
- Non-Dihydropyridine
  - Verapamil and Diltiazem
  - Recure ischemia when beta-blockers are contraindicated
    - There is NO LV dysfunction

CASE DISCUSSION

from "Drugs in Use: Clinical Case Studies for Pharmacists 3th"

Case Discussion-D1 Admission

- Mr. Wang 52 y/o, bodyweight >100kg
- Presented to casualty *via* ambulance following onset of chest pain for 2H
  - Tried several doses of NTG SC, but no resolved
- Post Hx：angina
- Drug Hx：Nefedipine、Isosorbide mononitrate
- BP：150/110 mmHg
  HR：112 beats/min

Case Discussion-D1 Admission

- Initially one dose of：
  - Morphine 10mg
  - Aspirin 300mg orally
  - Metoclopramide 10mg IV

Case Discussion-D1

- ECG showed STEMI
- Laboratory data：
  - CK result not yet available
  - Troponin negative
  - Na 138 mmol/L(135~145)
  - K 3.8 mmol/L (3.5~5)
  - Creatinine 104 mmol/L (45~120) = 1.2 mg/dl
  - Urea 6 mmol/L (3.3~6.7)
  - BS 18 mmol/L (3~7.8) = 327 mg/dl
  - HB 14.2 g (14~18) RBC $6.4x10^{12}$/L (4~11)
  - Plat $167x10^{9}$/L (150~400)

Case Discussion-D1

- Bolus dose of Tenecteplase 50mg was administered
- Heparin IV
- Sliding-Scale Insulin infusion
- r/o STEMI !?

Case Discussion-D3

- Mr. Wang was transferred to ward
  - Repeat ECG at 90mins post-thrombolysis showed resolution of ST segment
  - Furosemide 80mg over 20mins
  - Morphine 5mg IV PRN
    Metoclopramide 10mg TID PRN
    NTG 400μg SC PRN
    Aspirin 75mg QD
    RI 50u/500ml to run over 24H
    Humidified oxygen at 4L/min

Case Discussion-D3

- BP：94/63 mmHg　　HR：88 beat/min
- Sodium：143 mmol/L (135-145)
- Potassium：3.1 mmol/L (3.5-5.0)
- BS：4.8 mmol/L (87 mg/dL) (3-7.8)
- Urea：5 mmol/L (3.3-6.7)
- Creatinine 110 mcgmol/L (45-120)
- HB：13.2 g/dL(14-18)　RBC：$5.2x10^{12}$/L(4.5-6.5)
- WBC：$6x10^{12}$ /L(4-11) Plate：$172x10^{9}$/L(150-400)
- Chole：5.6 mmol/L(<5.0)　　TG：4.2 mmol/L(<1.8)

What could we do for Mr. Wang?

- What routine test should be carried out to confirm a diagnosis of AMI ?
- What actions of morphine are particularly useful in the acute phase of AMI ?
- Why is Metoclopramide necessary ?
- Why should IM injections generally be avoided in patients suffering with AMI ?
- What is the rationale for Aspirin administration during an AMI ?
- What other therapy should be considered at this stage ?

What could we do for Mr. Wang?

- What is the rationale for thrombolysis in the management of AMI ?
- When should thrombolysis be administered to gain maximal benefit ?
- What are the contraindication to thrombolysis ?
- What pharmaceutical issues should be considered when choosing a thrombolytic ?
- What monitoring should be undertaken for patients prescribed and administered thrombolytic therapy ?

What could we do for Mr. Wang?

- What alternative strategies could be employed when thrombolysis is contraindicated ?
- Is intravenous Heparin indicated in this patient ?
- What other therapies might be considered at this stage ?
- Outline a pharmaceutical care plan for Mr. Wang.
- Why are his potassium levels a cause for concern ? What other electrolytes should be monitored closely ?

What could we do for Mr. Wang?

- Comment in the drugs Mr. BY was taking prior to admission ?
- What is the rationale for ACEI post-MI ? How should ACEI therapy be initiated ?
- Should beta-blocker therapy be considered at this stage ?
- What advice would you give about the initiation of a beta-blocker ?
- Comment on Mr. BY's cholesterol.
- How should Mr. Wang's cholesterol level be managed ?
- A subcutaneous insulin regimen should be initiated on cessation of his sliding-scale IV insulin ?

Thank You for Your Attention!!