



SUGAR LAND HEART CENTER

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Symposium Manual

“Interventional Cardiology--Pharmacology 2007”

Role of Aspirin, Antiplatelet agents, Heparin, LMWH, Antithrombins, Thrombolytics IV and Oral GP IIb/IIIa Inhibitors, Statins, Inotropes, Pressor agents, Conscious Sedation, and Others in the ER, Cath Lab, Intensive Care, & Out-Patient setting

Presented

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Aspirin

Action: It is a weak antiplatelet agent. It acts as a COX-2 inhibitor. In a 60,000 high-risk patients with prior cardiovascular disease, aspirin therapy resulted in a 25% reduction ($P < 0.00001$) in subsequent vascular events.

Indications: Coronary artery disease, ACS, STEMI, TIA, and high-risk patients.

Pharmacokinetics: The rapidity with which you achieve the antiplatelet activity is depended on the dose and the route of administration.

Dosage: ACS or STEMI patients should receive 160-325 mg of aspirin, preferably chewed with a sip of water. Maintenance dose: 75 to 165 mg daily.

Monitor: Rapid Platelet Function Assay [RPFA-ASA] can be used to identify aspirin resistance.

Sheath Removal: No effect on sheath removal.

Combinations: Aspirin has been used with heparin, Lovenox, GP IIb/IIIa inhibitors, and warfarin.

Advantages: When Plavix is combined with less than 100 mg of aspirin, the bleeding incidence is lower. Dual antiplatelet therapy is better than either drug administered alone.

Disadvantages: Aspirin resistance varies from 15 to 30%. It is seen more often in patients who are 60 years or older. Combined aspirin and clopidogrel resistance is seen in approximately 50% of the patients. Aspirin resistance results in a three-fold increase in adverse outcomes in patients at risk. These patients may need an increased clopidogrel dose.

Triple drug therapy with aspirin, warfarin, and clopidogrel more than doubles the risk of major bleeding (3% versus 7%).

Heparin

Action: It binds to the cofactor antithrombin and inactivates factor Xa. It affects coagulation factors in the intrinsic, extrinsic, and the common pathways of coagulation.

It cannot inhibit the thrombin bound to the clot. It fails to prevent thrombin-mediated activation of the platelets. It may cause HIT

Indications: Elective PCI. Used along with GP IIb/IIIa inhibitors. ACS with positive cardiac markers before planned PCI, along with GP IIb/IIIa inhibitors. STEMI patients going for primary PCI or those treated medically.

Dosage: It is based on weight and whether the patient is receiving IV GP IIb/IIIa inhibitors

Loading:

- 70 to 100 U/Kg IV bolus.
- Those patients on GP IIb/IIIa inhibitors, the starting dose should be 45 to 50 to U/kg IV.
- Check ACT in 5 minutes. Maintain an ACT of 200-300 in patients who are receiving other antiplatelet agents.
- If the ACT is less than 200 seconds, give an additional 2000 to 4000 U as IV bolus.
- **Infusion:** 1000 U per hour IV drip with ACT monitoring. It is for the duration of the PCI procedure. Presently, it is generally not continued in the post PCI period.

Monitor: ACT is used to monitor the therapeutic activity. ACT should be between 250-350. Minimum bleeding is seen when the ACT is between 325-350 seconds. As the ACT goes above 375, the incidence of bleeding increases. Higher incidence of ischemic events at higher ACT levels is related to heparin induced platelet activation. If the patient is on a GP IIb/IIIa inhibitor, aim for an ACT of 200 seconds

Sheath Removal: Its effect wears off in four hours after the discontinuation of the infusion. Sheath can easily be removed 4 hours later or when the ACT is less than 160 sec.

Combinations: It can be used along with intravenous GP IIb/IIIa inhibitors such as Integrilin or Aggrastat. However, the Acuity study showed that the Bivalirudin alone was better when compared to Heparin and GP IIb/IIIa inhibitors.

Advantages: Costs less, vast Knowledge base, and ease of administration

Disadvantages: Rare incidence of HIT (Heparin induced Thrombocytopenia). Patients with HIT can be treated with Argatroban that does not affect the platelet function or count.

LMWH Enoxaparin [Lovenox]

Action: A Low molecular weight Heparin is a potent inhibitor of factor Xa. It is less protein bound. It is not inactivated by platelet factor 4. It has a minimal chance of causing HIT.

Pharmacokinetics: The Plasma half-life is 4.5 to 7 hours. The therapeutic effect begins 30 to 60 minutes after a SC dose and lasts for 12 hours. It is effective within minutes after IV administration. The kidney excretes 40% of the drug, and hence, the dosage needs adjustment based on the renal function.

Indications: ACS with or without positive cardiac markers. It is used in place of heparin in conjunction with GP IIb/IIIa inhibitors before planned PCI. It is not routinely used in STEMI patients and in patients going for primary PCI.

Dosage:

- ACS: 1 mg/kg SQ every 12 H.
- PCI: if the patient had not received Enoxaparin before or if the last dose was more than 12 hours ago then give 1 mg/kg IV bolus.
- If the patient is going to receive a GP IIb/IIIa inhibitor, then reduce the dose to 0.7 mg/Kg IV bolus.
- If the patient had the last Lovenox 8-12 hour before, then reduce the dose to 0.3mg/Kg IV bolus.
- If the last dose was given less than 8 hours before the procedure, then there is no need for additional doses.
- Renal adjustments: 0.75 mg/Kg IV for CC of 30 to 60 mL. 1 mg/Kg q 24 h if the CC is less than 30 mL.

Monitor: ACT is used to monitor the therapeutic activity. The ACT should be around 200 if the patient is receiving a GP IIb/IIIa inhibitor. You can also monitor RapidPoint Enox time that should be between 200 and 250 seconds.

Sheath Removal: Sheath can safely be removed 3-4 hours later, when the RapidPoint Enox time is less than 200 seconds.

Combinations: It can be used along with intravenous GP IIb/IIIa inhibitors such as Integrilin or Aggrastat.

Advantages: knowledge base, less cost, and ease of administration

ESSENCE: (2003) NSTEMI 7081PTS. Enoxaparin v. heparin. Lower 1 year MACE rate
SYNERGY: 9978 NSTEMI pts. Changing the antithrombin drugs during the hospitalization resulted in increased bleeding risk.
INTERACT: 746 Pts with ACS. Integrilin+Lovenox v. integrilin +heparin. 30 day MACE 5% v. 9%. Minor bleeding was higher.
STEEPLE: 0.5 mg/kg v. 0.75 mg/Kg Enoxaparin in PCI pts. Major and minor bleeding 6% v. 6.6% 30 days MACE-no difference.

Theinopyridines-- Clopidogrel [Plavix]

Action: Clopidogrel (Plavix) is an inhibitor of ADP-induced platelet aggregation. It inhibits the binding of adenosine diphosphate (ADP) to its receptor and thus the ADP-mediated activation of the glycoprotein GP IIb/IIIa complex in the final pathway to the platelet aggregation. Its effect lasts for the duration of the platelet's life-time.

Indications: Used as an antiplatelet agent in patients going for PCI, in ACS, and in patients with high-risk cardiovascular problems.

Dosage:

- A loading dose of 300 mg orally, is given in the cath lab after the PCI or in the emergency care centers for a patient with ACS with positive cardiac biomarkers.
- Recent data suggests that 600 mg clopidogrel provides better platelet inhibition much quicker when compared to that with 300 mg dose.
- The daily maintenance dose is 75 mg orally. However, if the patient is resistant to clopidogrel, increasing the dose to 75 mg twice daily has been shown to provide better platelet inhibition.
- The duration of antiplatelet treatment is up to one year for patients with DES.
- There are no studies at present beyond one year to suggest if the drug needs to be continued for longer duration.
- In high-risk cardiac patients, clopidogrel has been shown to be beneficial.

Monitor: Platelet inhibition using ADP can be readily performed in the cath lab that can provide quick results regarding platelet inhibition. Several portable machines (VerifyNow) that are available now and should be more routinely used in a PCI setting to assure that we have adequate platelet inhibition at the end of the PCI procedure. If the platelet inhibition is less than 50%, then we may consider a 600 mg dose or add an intravenous GP IIb/IIIa inhibitor for a few hours until the oral antiplatelet agent takes full effect which may vary from 4 to 24 hours depending on the dose. This may be very pertinent in patients with less than ideal platelet inhibition results or in patients with residual problems or hazy results. In a steady state, the platelet aggregation ranges from 40% to 60%.

Sheath Removal: clopidogrel administration has no effect on the timing of the sheath removal.

Combinations: Clopidogrel has been used in combination with aspirin. A Combination of aspirin and clopidogrel has a synergistic effect in term of reducing major cardiovascular events in patients. Occasionally, people have been treated with aspirin, clopidogrel, and coumadin at the same time without significant increase in serious bleeding.

Advantages: It is an effective antiplatelet agent in reducing major cardiovascular events in patients going for PCI and in patients with ACS with positive cardiac biomarkers. Following PCI, bleeding in the groin or in the retroperitoneal area needs prompt attention. CNS bleeding can be serious. The drug must be withdrawn five days before surgery or a procedure. Non-steroidal anti-inflammatory use can enhance the clopidogrel antiplatelet activity and increase the bleeding tendency.

Disadvantages: The antiplatelet effect last for almost a week after discontinuation. Hence, if the patient needs surgery, then it would be reasonable to postpone the surgery. If the patient needs urgent surgery, fresh platelet transfusion may minimize the bleeding though not completely eliminate the risk. Rare cases of TTP has been reported. Clopidogrel resistance is common and should be suspected in patients with recurrent chest symptoms or those with a recent coronary thrombosis.

References:

CAPRIE, 19,185-patient, double blind, 75 mg Plavix v. 325 mg aspirin daily. MI 2.9% v. 3.5%. Death 2.4% v. 2.4% (NS)
CURE, 12,562 ASC pts. 75 mg Plavix v. 325 mg aspirin daily for 12 months. MACE 16.5% v. 18.8%. Death 5.1 v. 5.5 (NS)

GP IIb/IIIa Inhibitors-- Abciximab [Reopro]

Action: Abciximab [Reopro], a GP IIb/IIIa inhibitor, blocks the GP IIb/IIIa receptor and interaction of fibrinogen with the receptor, in the final common pathway to platelet aggregation.

Pharmacokinetics: A bolus dose of Abciximab blocks more than 80% of GP IIb/IIIa receptors on the platelets. Platelet aggregation is reduced to less than 20% in most patients in 10 minutes after bolus administration. It has a biphasic plasma half-life—an initial half-life of less than 10 minutes and a second phase half-life of about 30 minutes. Abciximab also has a biologic half-life of 12-24 hours because of its high affinity for the receptor. Low levels of platelet inhibition may be seen even 10 days after the initial infusion. It is largely cleared by the reticuloendothelial system and not affected by the kidney function.

Indications: Abciximab is indicated as an antiplatelet agent for patients undergoing PCI and in patients with unstable angina not responding to conventional medical therapy when PCI is planned within 24 hours. It has also been used in the cath lab as an antiplatelet agent during primary PCI in STEMI patients (ACC/AHA. Level of evidence B). It is contraindicated in patients with a history of stroke within two years or when the platelet counts is less than 100,000.

Dosage:

- Patients undergoing PCI should receive the drug as an IV bolus dose of 0.25 mg/Kg 10 to 60 minutes before the PCI.
- An infusion at 0.125 µg/kg/min (maximum of 10 µg/min) for 12 hours should be continued.

Monitor: Platelet counts should be done within 2 hours after the initiation of the drug as some patients may experience severe thrombocytopenia.

Sheath Removal: Arterial sheath can be removed safely while the patient is receiving the intravenous Abciximab, when the ACT is less than 160 seconds, if the patient is also receiving heparin.

Combinations: It has been safely used in combination with low dose heparin. Reduced doses of abciximab have also been used in patients who had already received fibrinolytic agents.

Advantages: It has been shown to reduce the major cardiovascular adverse effects (MACE) in patients with ACS and in STEMI patients undergoing PCI when compared to a placebo. However, the earlier studies compared the drug to a placebo when powerful oral or other IV GP IIb/IIIa or antithrombin agents were not available. Hence, it is not clear if we would expect similar results when compared to other newer agents in combination with antithrombins, statins, ACE inhibitors etc.

Disadvantages: Abciximab carries a risk of 1.9% incidence of major bleeding along with standard dose heparin and 7.6% incidence of minor bleeding. Lower dose heparin has been shown to reduce the risk of major and minor bleeding to 0.8% and 3.2 % respectively. Thrombocytopenia with platelet counts of less than 100,000 were noted in 2.3% of the patients. Rarely, some patients may also form a human anti-chimeric antibody that could cause an allergic or an anaphylactic reaction.

References:

- EPIC** (1994) 708pts. Abciximab v. placebo. 30 MACE 8.3% v. 12.8% (P=0.008)
EPILOG (1997) 939 pts. Abciximab+heparin v. placebo+heparin. 30 MACE 5.4% v. 11.7%. (P=<0.001)
CAPTURE (1997) 630 pts. Abciximab v. placebo. 30 days MACE 11.3% v. 15.9%. (P=0.01)
EPISTENT (1998) 809 PTS STENT+ DRUG V. STENT+PLACEBO. 30 days MACE 5.3% v. 10.8%. (P=<0.01)
TARGET: (2001) 2411 pts. Abciximab v. Tirofiban. 30 days MACE 6% v. 7.6% (P=0.038)
ISAR REACT 2: 2022 ACS PTS. 600 mg Clopidogrel+aspirin+heparin+abciximab v. 600 mg Clopidogrel+aspirin+heparin+placebo. 30-day death, MI, and TVR was 8.3% v 13.1% in troponin positive pts. (P=0.02)
RAPPORT (1997) 483 Pts. ISAR 2 (2000) 401 Pts, ADMIRAL (2002) 300 Pts, CADILLAC (2002) 2082 Pts. ACE (2003) 400 Pts

GP IIb/IIIa Inhibitors-- Eptifibatide [Integrilin]

Action: Eptifibatide reversibly inhibits binding of fibrinogen, von Willebrand factor, and other adhesive ligands to GP IIb/IIIa, thus preventing GP IIb/IIIa activation and platelet aggregation. It has a dose dependent platelet aggregation inhibition after intravenous administration. The platelet inhibition reverses six to eight hours after the drug cessation.

Pharmacokinetics: Greater than 85% platelet inhibition occurs within 15 minutes of IV administration of 180 µg/Kg Eptifibatide bolus. The plasma half-life is 2.5 hours

Indications: When used in patients with ASC with NSTEMI and in patients going for PCI, the drug has been shown to reduce combined endpoint of death and MI, or need for urgent intervention.

Dosage:

- Single bolus of 180 µg/kg, or a double bolus of 180 µg/kg IV given ten minutes apart. The bolus dose maintains a steady state for 4-6 hours.
- The maintenance dose is 2.0 µg/kg/min infusion for 72 hours or for 12-24 hours after a PCI.
- The dosage needs to be adjusted based on the patient's weight. In patients with a creatinine clearance <50 mL/min, the eptifibatide clearance is reduced by approximately 50% and the steady-state plasma levels approximately double,
- While patients are on Eptifibatide, the heparin dose should be adjusted so that the ACT is between 200-300 instead of 300-375. Recently, some physicians are using a heparin dose of 45- 50 units/Kg to minimize the bleeding complications.

Monitor: With the modern bedside platelet function test monitors, now we can monitor platelet aggregation.

Sheath Removal: If the patient is on concomitant heparin, sheath can easily be removed 3-4 hours later, when the ACT is less than 160 sec.

Combinations: It has been safely used in combination with heparin, Lovenox, or other antiplatelet agents. However, close attention to creatinine clearance may guide us with dosage adjustments to minimize the bleeding risk.

Advantages: Immediate platelet inhibition achievable in situations such as acute coronary intervention.

Disadvantages: Major bleeding had been seen at the catheter site, GI, and the urinary tracts. It has not been tested in STEMI patients. However, in the study groups, a small percentage of patients had received fibrinolytics in addition with a slight increase in bleeding complications. The incidence of stroke is 0.5%.

Studies:

PERSUIT: ASC-NSTEMI 10,948 pts. At 30 days, death or MI 14.2% (drug) v. 15.7% (P= 0.04)

ESPRIT: 2064 PCI-stent pts. 30 days MACE 6.8% (drug) v. 10.4% (P<0.003) at 1yr Death and MI 8% V. 12.4% (P= 0.001)

IMPACT II: 4010 PCI-balloon pts. 30 day MACE 9.1% (drug) v. 11.6% (P= 0.02)

Direct Thrombin Inhibitor--Bivalirudin [Angiomax]

Action: Bivalirudin is a direct thrombin inhibitor. Thrombin has one active site and two exosites. The bivalirudin reversibly binds to the active site on the thrombin molecule. It also binds to the exosite-1. It also acts on the thrombin within a clot.

Pharmacokinetics: Its effect is immediate following intravenous administration exhibiting a dose response relationship. The half-life is 25 minutes in patients with normal renal function, 34 minutes in patients with moderate renal impairment, 57 minutes in patients with severe renal impairment, and 210 minutes in patients on dialysis. Anticoagulant effect returns to baseline within two hours after the drug discontinuation.

Indications: It is used as a single agent without the need for heparin or GP IIb/IIIa inhibitors in elective PCI patients. It has also been used in ACS patients with positive cardiac markers before planned PCI, in place of heparin and GP IIb/IIIa inhibitors. Bivalirudin has not been studied in STEMI patients who are treated medically or those going for primary PCI. It can be started in the emergency center.

Dosage:

- Loading: 0.75 mg/Kg IV (range 0.5 to 0.75 mg/Kg). Check ACT in 5 minutes. If the ACT is less than 225 seconds, give an additional 0.3mg/Kg IV bolus.
- Infusion: 1.75 mg/Kg/h IV drip, (range 0.25 to 1.75 mg/Kg/h).
- Duration: For the duration of the PCI procedure.
- Reduce the infusion rate by 20% in patients with moderate renal impairment and by 60% in patients with severe renal impairment.

Monitor: ACT is used to monitor the therapeutic activity. ACT should be between 250-350.

Sheath Removal: Its effect wears off in two hours after the discontinuation of the infusion. Sheath can easily be removed 3-4 hours later.

Combinations: It can be used along with intravenous GP IIb/IIIa inhibitors such as Integrilin or Aggrastat. However, the Acuity study showed that the results of Bivalirudin alone were better when compared to Heparin and GP IIb/IIIa inhibitors.

Advantages: It can be used as a single agent in elective PCI or PCI in NSTEMI patients. The incidence of bleeding is less when compared to that in patients receiving Heparin and IV GP IIb/IIIa inhibitors. Costs less compared to IV GP IIb/IIIa agents.

Studies:

REPLACE-1: 1034 pts. Bivalirudin v. heparin. Similar triple end point of death, MI, and revascularization. Lower bleeding rates.

REPLACE-2 (2004) 6010 elective PCI pts. Bivalirudin+ GP v. heparin +GP. Results equal with less bleeding (41% less) and 0.8% absolute increase in MI. at 6 months death and MI were 18.3% v. 17% (NS).

ACUITY: (2006) 13,800 ACS pts H or LMWH+GP, B+GP, B alone.

BAT

Factor Xa inhibitor--Fondaparinux

Action: It inhibits the factor Xa in the coagulation cascade. Inhibition of one molecule of factor Xa inhibits the generation of 50 molecules of thrombin. Thrombin is the most potent activator of platelets. Fondaparinux does not act on the existing thrombin unlike the direct thrombin inhibitors. It has no known effect on the platelets.

Pharmacokinetics: It has a rapid onset of action reaching therapeutic levels within 25 minutes. It has a long half-life of 17-21 hours, thus allowing for once-a-day dose. However, if the patient needs urgent surgery, the bleeding incidence will increase. It is excreted by the kidneys.

Indications: Several studies have shown that Fondaparinux is superior compared to enoxaparin in preventing deep venous thrombosis. It is approved for DVT prophylaxis and for PE. Presently it is not approved for ACS or for STEMI patients.

In ACS patients it has been shown to reduce death, MI, stroke, and bleeding complications when compared to those patients treated with Enoxaparin (OASIS 5).

In STEMI patients, it has been shown to reduce death and MI in patients who are treated conservatively. It also reduces the restenosis rate in STEMI patients, by improving the TIMI flow grade. Those patients who went for coronary intervention had higher rates of acute coronary thrombosis when heparin was not used. Hence, patients who receive Fondaparinux during primary PCI should also receive heparin to prevent acute thrombosis (OASIS 6).

Dosage: It is given as a single daily SC injection of 2.5 mg. The dosage should be reduced for those weighing less than 50 Kg or for those with a creatinine clearance of <30 mL/min.

Monitor: The drug clearance is decreased in patients with renal impairment and in patients older than 75 years. It is contraindicated in patients with a creatinine clearance of less than 30 mL/min.

Sheath Removal: Sheaths can easily be removed 3-4 hours later. It does not affect the ACT measurements.

Advantages: Once a day dose. Less bleeding. Reduces death and MI in ACS patients and in STEMI patients treated conservatively.

Others: Cost? Thrombocytopenia (<100,000 platelet count) occurs in 3% of the patients.

Studies:

ASPIRE,

OASIS 5 ACS patients

OASIS 6 STEMI patients

Other drugs

Drug	Dosage	Comments
Fentanyl	25-100 Mcg IV	Sedation
Midazolam (versed)	1-4 mg IV	Sedation. Respiratory depression
Narcan	0.4 to 2 mg IV Q 2 min. (max=10 mg)	For respiratory depression
Romazicon	0.2 mg IV Q1 min (max=3mg)	Benzodiazepine antagonist
Nipride	5-100 mcg/min IV infusion X 48 hours	For Hypertension Measure thiocynite levels. Rarely used in the cath lab
Dopamine	2-15 mcg/Kg/min IV infusion	Inotropic agent. Used for Hypotension. Increased myocardial oxygen demand.
Dobutamine	2-20 mcg/Kg/min IV infusion	Inotropic agent, CHF
Primacor	0.5 mg/Kg IV infusion	Inotropic agent, CHF
Norepinehprine	8-12 mcg/min IV infusion	Alpha and beta agonist For severe hypotension
Phenylephrine	100-180 mcg/min IV infusion	Alpha agonist. For severe hypotension
Aramine	100 mcg IV infusion.	Alpha agonist for hypotension.

Bleeding Increases death and ischemia

- Reduces BP, intravascular volume, Hg, that leads to ischemia
- Ischemia leads to infarction, reduced LV function, and long term survival
- Increased transfusion and transfusion reactions.
- Hypotension leads to renal insufficiency
- Unnecessary surgery for bleeding in a patient on antiplatelet drugs increases morbidity and mortality.
- Antiplatelet drug discontinuation leads to thrombosis and more myocardial ischemia
- Prolongs the hospital stay
- Bleeding adds to the total cost of PCI

Measure creatinine clearance on all patients coming for interventions

Drug that need adjustments

- Lovenox
- GP IIb/IIIa inhibitors
- Antithrombins
- Sedatives
- Contrast agents

Patients on Warfarin:

- Avoid cardiac catheterization until the INR is <1.5 (PT <16 sec)
- Stop warfarin for 2-4 days.
- For urgent catheterization, avoid parental Vitamin K. Use fresh frozen plasma.
- Use vascular closure device when available.

Patients on metformin (Glucophage):

- Withhold metformin for 24-48 hours before and after the procedure.
- Correct hypovolemia. Hydration with NS 50-75 mL/h starting in the morning and continued for 8-12 hours after the procedure.
- Closely monitor the urine output and kidney function.
- Mucomyst 600 mg in the morning before the procedure and repeat in 12 hours.
- Use low osmolar contrast agent
- Avoid cardiac catheterization until the INR is <1.5 (PT <16 sec)
- Stop warfarin for 2-4 days.
- For urgent catheterization, avoid parental Vitamin K. Use fresh frozen plasma.
- Use vascular closure device when available.

Creatinine Clearance Measurement

- Formula:
$$\frac{[(140 - \text{age (yr)}) \times \text{weight (kg)}]}{[72 \times \text{serum Cr (mg/dL)}]}$$
-
- (multiply by 0.85 for women)
-
- **Example:**
- Weight : 70 Kg
- Age : 68 yrs
- Sex : M
- Serum Creatinine: 1.7

- $$\frac{(140-68) \times 70}{72 \times 1.7}$$

- Creatinine Clearance: 41 mL/min.
- Normal more than 60 mL/min.

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ACLS Drugs and Treatment Page-1

Name	Indications Features	Start	Frequency	Precautions
Adenosine	PVST. 6 mg premixed vial	6 mg IV bolus in 1-3 sec. Flush with 20 ml NS	12 mg second and doses in 1-2 min intervals	Flushing, CP, drop in BP, bradycardia. Doesn't convert AF, A. Flutter, or VT
Amiodarone	Cardiac arrest, VT, VF, AF, SVT, and PSVT.	Arrest: 300 mg IV 150 mg in 3-5 min Wide QRS tachycardia 150 mg IV in 10 min	Repeat 150 mg IV. Slow: 360 mg IV /6h. Maintenance: 540 mg IV/18 h.	Hypotension, prolonged QT interval, Use caution in renal failure. Negative inotropic effect
Amrinone	CHF, low CO Use NS not D5W	Loading: 0.75 mg/kg over 1-15 min	Infusion: 5-15 mcg/kg/min	Tachycardia, hypotension, thrombocytopenia
Aspirin	Antiplatelet agent 80-325 mg	One tab daily regular for acute case	Enteric coated for chronic use	Bleeding, gastric ulcers,
Atropine sulfate	Bradycardia Asystole	Asystole: 1 mg IV push Repeat every 3-5 min Max: 0.03-0.04 mg/kg	Bradycardia: 0.5 to 1 mg IV every 3-5 min. Max: 0.04 mg/kg	Increases myocardial demand, causes hypoxia. Not useful in infra-nodal AV block or CHB with wide QRS
Beta Blockers Metoprolol	PSVT, SVT, MI, BP	5 mg IV at 5 min intervals X 3	50 mg bid or 100 mg bid PO	Bradycardia, hypotension, bronchospasm, worsens CHF
Atenolol	PSVT, SVT, MI, BP	5 mg IV over 5 min Repeat 5 mg in 10 min	50 mg qd, 50 mg bid Max: 100 mg bid	Bradycardia, hypotension, bronchospasm, worsens CHF
Propranolol	PSVT, SVT, MI, BP	0.1 mg/kg IV push X 3 doses at 2-3 min interval		Bradycardia, hypotension, bronchospasm, worsens CHF
Esmolol	PSVT, SVT, MI, BP	0.5 mg/kg/ over 1 min	Infusion: 0.05 mg/kg/min max: 0.3 mg/kg/min	Bradycardia, hypotension, bronchospasm, worsens CHF
Lobetalol	Hypertension	10 mg IV over 1-2 min	Repeat same or double dose in 10 min. Max: 150 mg	Bradycardia, hypotension, bronchospasm, worsens CHF
Calcium Chloride	Hyperkalemia Hypocalcemia Routinely not used	8-16 mg/kg (5-10 ml) IV	May repeat as necessary	Do not use routinely. Do not mix with sodium bicarbonate
Cardioversion	PSVT, At. Flutter Symptomatic PSVT, atrial flutter, VF, VT	50, 100, 200, J 50, 100, 200, 300 100, 200, 300, 360 100, 200, 300,360 J	Biphasic: SVT: 30, 50, 100 VT: 150	Make sure the R waves are synchronized. Clear the patient
Defibrillation	Pulse less VT or VF	200, 300, 360 J	Biphasic: Use less energy-150 J	Clear the patient.
Digibind	Digitalis toxicity	3 to 5 vials IV		Serum digoxin level rises after digibind and is not reliable.
Digoxin	AF, A. Flutter PSVT	Loading dose: 10-15 mcg/kg lean mass (0.75 to 1 mg)	Maintenance: depends on body size & renal function	PVCs, arrhythmias.

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ACLS Drugs and Treatment Page-2

Name	Indications Features	Start	Frequency	Precautions
Diltiazem	Rate control in AF or A. Flutter	15-20 mg IV over 2 min repeat in 15 min	Infusion: 5-15 mg/hr	Hypotension. Avoid in WPW, wide QRS tachycardia
Disopyramide	Wide QRS tachycardia	2 mg/kg over 10 min	Infusion: 0.4 mg/kg/h	Arrhythmogenic, negative inotropic effect.
Dobutamine	CHF, Low CO		2-20 mcg/kg/min	Tachycardia, headache
Dofetilide	At. Fib	8 mcg/kg over 30 min		QT prolongation Torsades-de-pointes
Dopamine	Bradycardia, Hypotension	1-5 mcg/kg/min-L 5-10mcg/kg/min-M 10-20mcg/kg/min-H		Tachycardia, increases myocardial oxygen demand
Epinephrine	Cardiac arrest, Bradycardia, Hypotension, anaphylaxis	1:1000 dilution 1:10,000 dilution 1 mg IV every 3-5 min Higher dose: 0.2 mg/kg	Infusion: 30 ml (30 mg) in 250 ml NS at 100 ml/h	Increases heart rate High doses don't improve survival or neurological outcome
Fibrinolytics Activase	Acute Q wave MI	15 mg bolus IV .75 mg/kg in 30 min .5 mg/kg in 60 min		Internal bleeding, CNS bleeding
Fibrinolytics Retavase	Acute Q wave MI	10 U IV bolus-2min	10 U IV bolus after 30 min	Internal bleeding, CNS bleeding
Fibrinolytics Streptokinase	Acute Q wave MI	1.5 million U in 1 h		Allergic reaction, bleeding
Fibrinolytics TNKase	Acute Q wave MI	30-50 mg based on weight		Internal bleeding, CNS bleeding
Flecainide	AF, A. Flutter, PSVT, VT, PVCs	2 mg/kg IV	Infusion: 10 mg/min	bradycardia, hypotension, and paresthesia. Avoid in pts with LV dysfunction
Flumazenil Respiratory depression		0.2 mg IV in 15 sec	0.3 mg IV in 30 sec 0.5 mg IV in 30 sec	Short acting
Furosemide	Pulmonary edema	0.5-1 mg/kg over 1-2 min. Double the dose if no response	Repeat every 4-6 hours	Monitor potassium, magnesium. Hypotension
Glucagan	CCB or Beta blocker toxicity	1-5 mg over 2-5 min		Vomiting, hyperglycemia
Glycoprotiens IIb IIIa Inhibitors Integrelin	Acute coronary syndrome	ACS: 180 mcg/kg/ IV bolus PCI: 135 mcg/kg IV bolus. Second bolus in 15 min	ACS: 2 mcg/kg/min PCI: 0.5mcg/kg/min	CNS bleeding, hematoma low platelet count

SUGAR LAND HEART CENTER

ACLS Drugs and Treatment Page-3

Name	Indications Features	Start	Frequency	Precautions
Glycoproteins IIb IIIa Inhibitors Aggrastat	Acute coronary syndrome	ASC or PCI: 0.4 mcg/kg/min IV over 30 min	Infusion: 0.1 mcg/kg/min	CNS bleeding, hematoma, low platelet count
Glycoproteins IIb IIIa Inhibitors Reo-pro	Acute coronary syndrome	ASC: 0.25 mg/kg IV bolus PCI: 0.25 mg/kg/ IV	Infusion: 0.125 mcg/kg/min PCI: 10 mcg/min	CNS bleeding, hematoma, low platelet count
Heparin	MI, USA, ACS, DVT	MI: 60 IU/kg Bolus	Drip: 12 IU/kg/h PTT Q4-6 h	Bleeding, thrombocytopenia
LMWH: Fragmin	USA, DVT	1 mg/kg bid SC		Bleeding, thrombocytopenia
LMWH: Lovenox	ACS, DVT, USA	1 mg/kg bid SC		Bleeding, thrombocytopenia
Ibutilide	SVT, AF, A. Flutter	1 mg (10mL) IV over 10 min	Same second dose after 10 min	Ventricular arrhythmias
Isoproterenol	Symptomatic bradycardia	Infusion: 2-10 mcg/min		Increase myocardial work and ischemia
Lidocaine	PVCs, VT, VF	Cardiac arrest, VT: 1.0 to 1.5 mg/kg IV 0.5 to 0.75 mg/kg in 5-10 min	Infusion: 1-4 mg/min	Prophylactic use in MI is not recommended. Reduce dose in CHF or liver failure patients
Magnesium Sulfate	Refractory VF, Torsedes-de-pointes, Low magnesium	1-2 g in 10 ml D5W push. 1-2 g in 50 mL D5W over 5-60 min		Hypotension with rapid administration Use caution in renal failure patients
Mannitol	Reduce intracranial pressure	0.5 to 1 g/kg over 5-10 min	0.25 to 2 g/kg every 4-6 h IV	Watch fluid balance and osmolality. Use with caution in renal failure
Morphine sulfate	Chest pain, pulmonary edema	2-5 mg IV every 5-30 min		Hypotension, respiratory depression
Naloxone	Respiratory depression	0.4 to 2 mg every 2 min. Max: 10 mg		Short acting, allergic reaction
Nitroglycerine	Angina, hypertension	10-20 mcg/min	0.4 mg SL q5 min X 3	Hypotension, headache
Nitroprusside	Hypertension Onset: 30 seconds Peak: 1-2 min Duration: 3-5 min	50 mg/250 ml D5W 0.25 to 8.0 mcg/kg/min	Titrate every 5 min up to 5 mcg/kg/min	Wrap in foil. Thiocyanate toxicity, intrapulmonary shunting, hypoxia
Norepinephrine	Hypotension Onset: Immediate Peak: 1-2 min Duration: 2-5min	50 mg/250 ml D5W Infusion: 0.5 to 1 mcg/min	Titrate every 5 min up to 30 mcg/min	Increased myocardial oxygen demand, arrhythmias, tissue necrosis.

SUGAR LAND HEART CENTER

ACLS Drugs and Treatment Page-4

Name	Indications Features	Start	Frequency	Precautions
Oxygen	Hypoxia	NC1-6L/min 24-44% VM 4-8L/min 24-40%	PR: 6-10L/min 35-60% BM: 15L/min 100%	Oxygen toxicity Reduce dose in COPD
Procainamide	PSVT, VT, AF	20 mg/min IV infusion	Infusion at 1-4 mg/min	Hypotension, wide QRS, reduced dose in CHF or CRF
Propaferone	SVT, VT	1-2 mg/kg infusion at 10 mg/min		Negative inotropic effects, bradycardia, hypotension
Sodium Bicarbonate	Hyperkalemia acidosis prolonged CPR	1 mg/kg IV bolus	Repeat 0.5 mg/kg every 10 min	Good CPR is a better buffer agent. Not recommended for routine use in cardiac arrest
Sotalol	AF, A. Flutter	1-1.5 mg/kg IV	10 mg/min	Hypotension, negative inotropic effect, bradycardia, arrhythmias
Trancutaneous Pacing	Symptomatic bradycardia, arrest, or heart block	Pace at 80 beats/min Gradually increase mA from 20 to 80	Asystole: use maximum mA.	Contraindicated in severe hypothermia. Conscious patient may need sedation
Vasopressin	VF, shock	40 U IV push		Increase myocardial ischemia and angina
Verapamil	PSVT, AF, A. Flutter	2.5-5.0 mg/ IV over 2 min	Second dose: 5-10 mg IV in 15-30 min Max: 20 mg	Avoid wide QRS tachycardia. hypotension, worsen CHF and LV dysfunction

End