DRUGS IN ADVANCED CARDIAC LIFE SUPPORT

Therapeutic Modalities

Class I : definitely helpful

Class IIa : acceptable, probably helpful

Class IIb : acceptable, possibly helpful

Class III : not indicated, may be harmful

Objectives

- State the role of drugs in ACLS
- Describe the use of drugs to optimize cardiac function

2 Key Questions

- What is/are the 1 or 2 primary disease processes that must be identified and treated?
- Which drugs, if any, are useful in treating the primary problem(s)?

Remember: Without treating the primary disease processes, trying to treat the secondary effects may be futile or even harmful

Principles in Delivering Drugs

Drugs that have potent effect on blood pressure and heart rate:

- Should not be given as rapid bolus except in cardiac arrest patient i.e. should be given as slow bolus or infusion
- Should be tapered / tailed down gradually under ECG and BP monitoring
- The lowest dose that achieves the desired effect is the optimal dose

IO route kinetics is similar to IV delivery in general

Note : The international guidelines no longer recommends endotracheal drug delivery

2 Scenarios

In **cardiac arrest**, drugs are used

- To help start the heart
- To preserve coronary and cerebral circulation

When **pulse is present**, drugs are used

- To optimize cardiac output by optimizing
  - Volume
  - Pump
  - Rate
- To optimize coronary circulation
- To optimize the environment for cardiac function

Cardiac Arrest Drugs

- VF / Pulseless VT
  - Adrenaline, lignocaine, amiodarone, magnesium, others
- Pulseless Electrical Activity
  - Adrenaline, others
- Asystole
  - Adrenaline

Adrenaline

Endogenous Catecholamine

Important Role in Cardiac Arrest, though little evidence to show improved outcome in humans

α - Adrenergic Agonist Activity

β - Adrenergic Agonist Activity

Primary Beneficial Effect :

1. Peripheral Vasoconstriction $\longrightarrow$ Improve Cerebral & Coronary Blood Flow
2. Makes VF more Susceptible to DC

Adrenergic Effects

Receptor	Vascular	Inotropic	Chronotropic
A_1	Constriction	+ ve	- ve
A_2	Dilatation		
β_1		+ ve	+ ve
β_2	Dilatation (Bronchial, GIT, Uterus]		

Adrenaline

Indications :
Cardiac Arrest from VF, Pulseless VT Unresponsive to Initial Counter Shock, Asystole, Pulseless Electrical Activity, or Profoundly Symptomatic Bradycardia

Dose :
IV 1 mg (10 ml of 1:10,000) followed by 20 ml Flush, At Intervals of 3 - 5 min
** High dose" (5mg) no longer recommended*

Infusion :
1 mg (1 ml of 1:1000 Solution) added to 500 ml N/S or 5% D/W, run at 2 – 10 mcg/min. Titrate to 2 - 10 mcg/min

Adrenaline

Precaution :
Adrenaline should not be added to infusions that contain alkaline solution

Can exacerbate Ischemia, induce Ventricular Ectopy

High-dose Adrenaline

- Not recommended for initial use since no improved long-term survival and neurological outcome has been demonstrated
- May rarely be considered if standard 1 mg doses fail

Sympathomimetic Amines

	Dosage	α	β
Adrenaline	0.5 - 1.0 mg	+	++
	1 - 20 mcg / min	++	+++
Noradrenaline	2 - 80 mcg / min	+++	++
Vasopressin	40 units IV bolus	+++	0
Dopamine	1 - 2 mcg/kg/min	+	+
	2 - 10 mcg/kg/min	++	++
	10 - 30 mcg/kg/min	+++	++
Dobutamine	2 - 30 mcg/kg/min	+	+++
Isoprenalin	2 - 10 mcg/kg/min	+	+++

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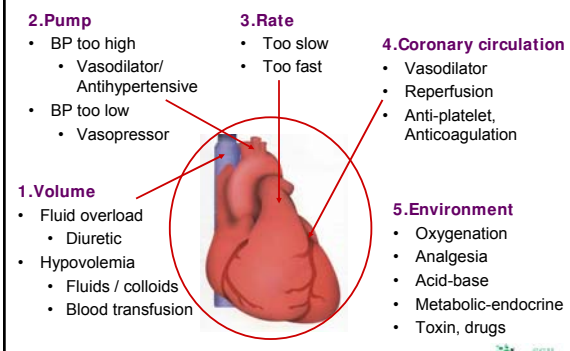
Optimization Drugs



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1. Pump Optimization Drugs: Vasodilator / Antihypertensive

- **GTN**
  - **Venous** and arterial dilator
  - Reduces preload, reduces LV filling pressure
  - Drug of choice in acute heart failure/APO + IHD/ACS
  - Interaction with Viagra (Sildenafil)
- **Na nitroprusside**
  - **Arterial** and venous dilator
  - Drug of choice in hypertensive emergencies
  - Potential to induce myocardial ischemia
- **ß blockers**: e.g. propranolol, atenolol
  - Reduces heart rate, myocardial contractility
  - Caution in asthma/COLD, congestive heart failure

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1. Pump Optimization Drugs: Vasopressor

- **Catecholamine**: e.g. noradrenaline
  - Common effects: increases BP, heart rate, myocardial contractility
  - Exclude hypovolemia before using vasopressor to increase pump action / increase BP

Arrhythmogenic

May worsen ischemia

  - **Adrenaline**
    - Improves coronary and cerebral perfusion pressure*
    - Rapid bolus only in cardiac arrest*, infusion for symptomatic bradycardia
  - **Noradrenaline**
    - Preferred vasopressor for septic and neurogenic shock

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1.Pump Optimization Drugs: Vasopressor

- **Catecholamine**:
  - **Dopamine**
    - Low dose 1-2µg/kg/min: may not change heart rate or BP
    - Medium dose 2-10µg/kg/min: increases heart rate and BP
    - High dose 10-20µg/kg/min: increases heart rate and BP
    - Vasopressor for hypotension from (a) bradycardia, (b) after return of spontaneous circulation
  - **Dobutamine**
    - 2-20µg/kg/min: increases BP, less tachycardia than dopamine and noradrenaline
    - Vasopressor for hypotension with (a) pulmonary congestion, (b) left ventricular dysfunction

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2. Rate Optimization Drugs for Tachycardia with Wide QRS

- Common effects: reduces heart rate, reduces BP
- **Lignocaine***
  - Use for VF, VT, wide complex tachycardia of unknown origin
  - Numbness of mouth and digits is a sign of toxicity
- **Amiodarone***
  - Use for VF, VT, SVT, atrial fibrillation-flutter
  - Reduces clearance of warfarin, digoxin
- **Magnesium***
  - Drug of choice for Torsades de Pointes
- *Rapid bolus only in cardiac arrest, otherwise give as infusion for tachycardia

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Lignocaine

Reduces Automaticity, elevates VF Threshold

Indications :

- Haemodynamically stable VT (Class IIb)
- Refractory VF / pulseless VT (Class indeterminate)
- Control of haemodynamically compromising PVCs (Class indeterminate)

Note : Lignocaine is now a second choice behind other alternative agents in many of these circumstances

Lignocaine

Evidence no longer supports the use of lignocaine as a diagnostic discriminator between perfusing VT and wide-complex tachycardia of uncertain origin

Lignocaine is NOT recommended for ventricular escape rhythm

Lignocaine is no longer indicated to prophylactically suppress ventricular dysrhythmias associated with acute myocardial infarction and ischaemia (causes higher mortality)

Lignocaine

Dosage : In Cardiac Arrest

- 50 – 100 mg (Given as bolus IV because of poor blood flow & prolonged circulatory times)
- May add a second bolus of 0.5 mg/kg

- After restoration of spontaneous circulation, Lignocaine IV Infusion 1 - 4 mg/min

- If dysrhythmia reappears during infusion of lignocaine :

- give small IV bolus of 0.5 mg/kg
- increase infusion rate in incremental doses to max rate of 4 mg/min

Lignocaine

Toxicity (Dose should not > 3 mg/kg bolus)

Neurological Changes

Drowsiness, Disorientation, Decreased Hearing Ability, Paresthesia, Muscle Twitching, Agitated, Fits

Myocardial Depression

Circulatory Depression

Amiodarone

- A complex antidysrhythmic agent:
  - effects on Na^+, K^+, and Ca^{++} channels
  - alpha-and beta-adrenergic blocking properties

- Also alters conduction through accessory pathways

Amiodarone

Indications :

- pharmacological conversion of atrial fibrillation (Class IIa)
- persistent VT or VF after defibrillation and adrenalin/vasopressin (Class IIb)
- haemodynamically stable VT (Class IIb)
- haemodynamically stable polymorphic VT (Class IIb)
- haemodynamically stable wide-complex tachycardia of uncertain origin (Class IIb)

Amiodarone

Indications:

- control of rapid ventricular rate in preexcitation supraventricular dysrhythmias due to accessory pathway conduction (Class IIb)
- as an adjunt to electrical cardioversion of refractory PSVTs/atrial tachycardias (Class IIb)
- control of ventricular rate in SVTs with severely impaired LV function when digitalis has proved ineffective (Class IIb)

Amiodarone

Adverse Effects:

Hypotension and Bradycardia

- slow the rate of infusion
- IV fluid challenge
- pressors or positive chonotropic agents
- temporary pacing

Amiodarone

Dosage:

- in VF / pulseless VT - administer bolus of 300 mg. Subsequent dose at 150 mg
- In stable ventricular and supraventricular dysrhythmias - administer IV 150 mg over 10 - 15 minutes (not to exceed 30 mg/min), followed by an infusion of 1 mg/min x 6 hours, then 0.5 mg/min

Note: infusions > 2 hours must be administered in glass or polyolefin bottles due to amiodarone precipitating in plastic tubing

Magnesium

- A cofactor in numerous enzymatic reactions
- Essential for function of Na-K ATPase Pump
- Mg deficiency associated with cardiac arrhythmia, sudden death, precipitates VF, hinders replenishment of intracellular K^+

Magnesium

Indications :

Proven hypomagnesaemia with or without dysrhythmias

Note :

The routine prophylactic use of magnesium in patients with AMI is no longer recommended

Magnesium

Dosage :

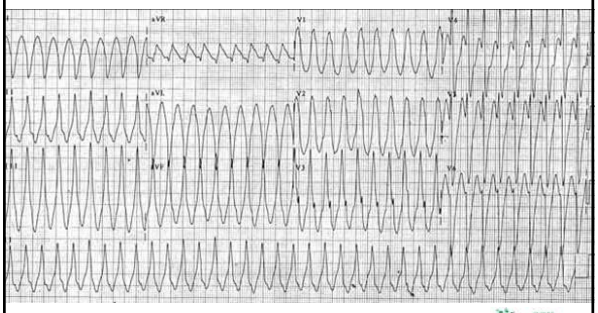
- 1 - 2 g magnesium sulfate (2 - 4 ml of 50% soln)
- Diluted in 100 ml of 5% D/W over 1 - 2 min, may give up to 5 - 10 G
- Monitor BP

Magnesium

Side Effects :

- Flushing, Sweating, Mild Bradycardia, Hypotension, Asystole
- Hypermagnesemia may produce Depressed reflexes, Flaccid paralysis, Circulatory collapse, Resp paralysis, Diarrhoea
- Rapid administration of magnesium may cause clinically significant hypotension or asystole

Tachycardia with Wide QRS: Lignocaine, Amiodarone



2. Rate Optimization Drugs for Tachycardia with Narrow QRS

- Common effects: reduces heart rate, reduces BP
- Adenosine
  - Half-life < 6 seconds: super rapid bolus needed
  - Side effects: bronchospasm, angina-like chest pain, flushing, transient hypotension
- Verapamil, Diltiazem
  - Ca-channel blockers
  - Vasodilates coronary arteries
  - Do not use in Wolf-Parkinson-White syndrome
  - Avoid concomitant use with ß blockers
- ß blockers
- Amiodarone

Verapamil / Diltiazem

Calcium Channel Blockers

Potent Direct Negative Chronotropic & Negative Inotropic Effects

Primary Beneficial Effect :

- Both slow conduction and increase refractoriness in the AV node
- Diltiazem produces less myocardial depression than verapamil, but is equipotent as a negative chonotrope

Verapamil / Diltiazem

Indications :

- Treatment of PSVT
- Slow down Ventricular response in Atrial Flutter & Fibrillation
  (But not for AF with WPW)

Verapamil / Diltiazem

Dosage of Verapamil :

- I.V 1 mg/min
- Maximum 20 mg in total dose

Dosage of Diltiazem :

- I.V 0.24 mg/kg (approx 20 mg) over 2 min
- May repeat 0.35 mg/kg 15 min later
- Infusion 5 - 15 mg/hr titrate to heart rate for control of Ventricular Response in AF

Verapamil / Diltiazem

- Transient Hypotension due to peripheral vasodilation may occur
- I.V calcium chloride 5 - 10 ml of 10% solution will restore arterial pressure, without affecting the electrophysiological properties of verapamil

Verapamil / Diltiazem

Precautions :

- May cause hypotension
- Not to use with I.V Beta Blocker
- Avoid in sick sinus syndrome, AV Block or Heart Failure
- Diltiazem IV is incompatible with simultaneous IV Frusemide

Adenosine

- An endogenous purine nucleoside that slows conduction through AV node
- Interrupts AV nodal re-entry pathways
- Restores normal sinus rhythm in PSVT (including PSVT associated with WPW)
- Short-lived pharmacologic response
- Half-life of free adenosine 5-10 sec (sequestrated by circulating RBCs)

Adenosine

Indications :

- Termination of PSVT (Re-entry type)
- Diagnosis of SVT

Dosage :

- 6 mg bolus over 1 - 3 sec, followed immediately by 20ml saline flush
- If unsuccessful, give 12 mg bolus (may be repeated once to a total dose of 30 mg)

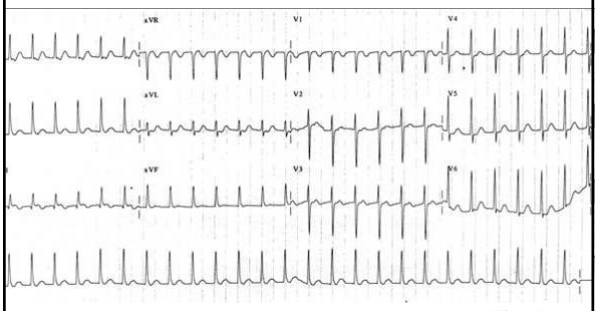
Note : preferably administer via antecubital or central IV line

Adenosine

Precaution :

- Side effects are transient: -
- Flushing, Dyspnea, Chest Pain, Transient Bradycardia, Asystole
- Drug Interaction with
- Theophylline & related xanthines - block effect of adenosine
- Dipyridamole potentiates effect of adenosine
- Relatively C/I in asthma

Tachycardia with Narrow QRS: Adenosine, Verapamil, Diltiazem



2. Rate Optimization Drugs for Bradycardia

- Atropine
  - Vagolytic i.e. inhibits parasympathetic action
  - Large doses needed for acute cholinergic poisoning (organophosphates)
  - Side effects similar to adrenaline, can also cause seizure, respiratory failure
  - Given in a dose of 0.6mg intravenously & may be repeated at 3 – 5 min intervals up to a max dose of 2.4mg
- Adrenaline infusion
- Dopamine infusion

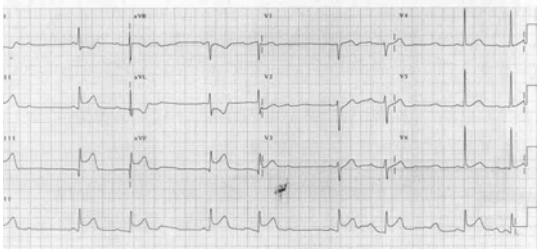
3. Coronary Circulation Optimization Drugs

- Vasodilator
  - GTN
- Reperfusion
  - Thrombolytic
  - PCI
- Antiplatelet
  - Non-specific
    - Aspirin
  - Specific
    - Clopidogrel (Plavix)
    - Glycoprotein IIb/IIIa inhibitors (GP IIa/IIIb): Risk of hemorrhage
- Anticoagulant
  - Heparin
  - Low molecular weight heparin e.g. fraxiparine

4. Environment Optimization Drugs

- Oxygen
- Morphine
- NaHCO3
  - Use in hyperK, tricyclic overdose, pre-existing acidosis, prolonged cardiac arrest
  - Do not mix with other drugs
- Calcium
  - Use in hyperK, hypoCa, Ca-channel blocker overdose
- HyperK treatment
  - Insulin+dextrose, calcium, NaHCO3, resonium etc

Case NN



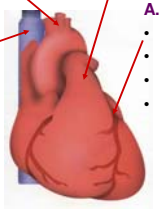
- A 53 year old man c/o chest pain
- BP 75/47, PR 45, RR 22, SaO2 97%, ECG as above
- 1° problems: Inferior, right ventricular AMI, complete heart block
- What drugs are useful?

Case NN: Optimization

B. Pump
- RV AMI: RV pump failure - BP too low
  - Dopamine

D. Rate
- Complete heart block: atropine, [pacing], (adrenaline or dopamine infusion)

C. Volume
- RV pump failure: insufficient venous return to pulmonary system – "Hypovolemia"
  - Judicious fluids



A. Coronary circulation
- Vasodilator: GTN -CAUTION!
- Reperfusion: PCI, SK, rTPA
- Anti-platelet: aspirin, Plavix
- Anticoagulation: heparin

Environment
- Oxygenation
- Analgesia: morphine

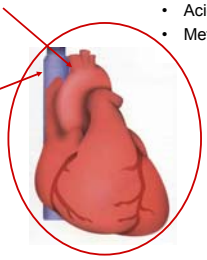
Case FEW

- 19 year old maid c/o GE symptoms x 3 days, then SOB
- GCS 3, BP 68/41, PR 100, RR 18, SaO2 95
- Blood sugar 19.8, ECG sinus
- pH 6.6, pCO2 53, HCO3 5, BE –30
- CXR acute pulmonary edema
- 1° problems: Cardiogenic shock from ?myocarditis, DKA
- What drugs are useful?

Case FEW: Optimization

A. Pump
- LV pump failure – cardiogenic shock
  - Dopamine

B. Volume
- Dehydration from GE, DKA
  - CVP monitoring
  - Judicious fluids



C. Environment
- Oxygenation: intubation
- Acid-base: NaHCO3
- Metabolic-endocrine: insulin

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Case LSW

- 72 year old man c/o non-radiating left chest pain x 45 min
- HPT, smoker
- Brought in to ED with GCS 15, SBP 42, PR 60, RR 20, SaO2 96%
- Hs1s2, lungs clear
- Right radial and carotid pulses weaker than left
- Remained comfortable in Resus Room

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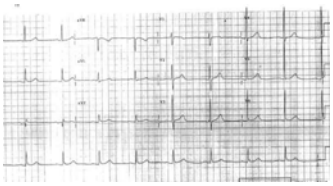
Case LSW



- ECG X 3: no change
- Chest X-ray showed widened mediastinum
- 1° problems: Thoracic aortic dissection
- What drugs are useful?

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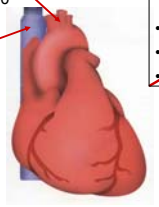
Case LSW: Optimization

B. Pump
- Maintain lowest possible myocardial contractility
  - Keep SBP 90-110

A. Volume
- Aortic dissection - relative hypovolemia
  - Judicious fluids



~~Coronary circulation~~
- ~~Vasodilator: GTN - CAUTION!~~
- ~~Reperfusion: SK, rTPA~~
- ~~Anti-platelet: aspirin~~
- ~~Anticoagulation: heparin~~

C. Environment
- Oxygenation
- Analgesia: morphine

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Summary

- In cardiac arrest, drug administration is secondary to other interventions
- When pulse is present, drugs are used
  - To optimize cardiac output by optimizing
    - Volume
    - Pump
    - Rate
  - To optimize coronary circulation
  - To optimize the environment for cardiac function
- The key to management is to identify the primary disease process(es) and use the appropriate drugs, if any, to optimize the deranged process(es)

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