Antiarrhythmic Drugs II

Drug	MOA	Uses	Effects	Side Effects	Notes
Class IA: Na^+ Channel Blockers					
Quinidine	-Inhibits α and muscarinic receptors BUT its **antiarrhythmic** activity is related to **inhibition** of Na channels	-Use nowadays **restricted** to patients with **normal** hearts with **no histopathologic abnormalities** (no failure, ischemia, hypertrophy) but **have** atrial or ventricular tachycardia	-**Slows** upstroke and conduction -**Prolongs** action potential duration, QRS duration and QT interval (prolongation of QT interval is **dangerous** and is related to side effects)	-Nausea & diarrhea -Headache, dizziness, and tinnitus = Cinchonism -Hypersensitivity, fever, rash, and angioedema -Thrombocytopenia -Excessive prolongation of QT interval, slowed conduction -Hypotension -↑Serum Digoxin levels (due to drug interaction) -↑ Warfarin effects -Sudden death (limited use)	-Prototype, related to quinine -Derived from the Cinchona tree, which was discovered to have antipyretic, antimalarial (Quinine), and antiarrhythmic activity (Quinidine)
Procainamide	-Inhibition of Na channels			-Causes **Lupus Erythematosus** in 30% of patients with treatment over 6 months	-**Oral**, but has short t½ -It is acetylated into the metabolite NAPA (n-acetyl procainamide), which has Class III action (no longer class 1A)
Disopyramide	-Related to quinidine (More anticholinergic effects)		-More anticholinergic effects than quinidine	-Causes less diarrhea than quinidine	
Class IB: Na^+ Channel Blockers					
Lidocaine (Lignocaine, or Xylocaine)	-A local **anesthetic** that also has antiarrhythmic activity -Has high affinity for binding to activated and inactivated Na+ channels with rapid kinetics	-**Ventricular** arrhythmias (Not effective in atrial arrhythmias) -It was routinely given to all MI patients to **prevent** ventricular arrhythmias	-Acts selectively in ischemic ventricular tissue to promote conduction & block re-entry -Its selectivity makes it an effective drug in ischemia and MI -More effective with ↑ K+	-Least cardiotoxic of the class except for **hypotension** with high doses **due to depression** of the myocardium -Most important side effects are related to the **CNS:** paresthesia, tremor, nausea, slurred speech & convulsions	-Well absorbed orally but **ineffective** due to first pass so given through **IV** -Well distributed, including the **brain**
Tocainide	-Analog of lidocaine	-Not a successful replacement of lidocaine due to side effects		-CNS and GI side effects and blood dyscrasia	-**Oral** analog of lidocaine
Mexiletine	-Analog of lidocaine			-Neurologic side effect	-**Oral** analog of lidocaine

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Phenytoin	-An **antiepileptic** drug that also has antiarrhythmic activity	-**Digitalis- induced** arrhythmias -Arrhythmias after **congenital heart surgery** -Congenital **prolonged QT** interval			-Not related to lidocaine
Class IC: Na^+ Channel Blockers					
Flecainide	-Potent blocker of Na + and K+ channels	-Effective in **supraventricular** tachycardia in patients with **normal** heart	-Negative inotropic effect -Proarrhythmic effect	-**Proarrhythmic** effect causes ventricular arrhythmia -CNS effects -Sudden death	
Propafenone	-Blocks Na+ channels but also has beta blocking activity (class II) and Ca^{+2} blocking activity (class IV)	-Used for **supraventricular arrhythmias**	- No effect on QT interval	-Metallic taste Constipation -Arrhythmias	
Class II: β -Blockers					
Propranolol (Prototype)	-Blocks beta channels	-To treat hypertension -IHD (reduces myocardial O2 requirement) -Documented to **reduce mortality** after acute myocardial infarction by **reducing** arrhythmias	-Effective antiarrhythmic activity -Membrane stabilizing activity -Intrinsic sympathomimetic activities		-Very effective, well tolerated
Esmolol & Acebutolol	-β1 selective drugs	-Used in **intraoperative** and **acute** arrhythmias (short acting)			
Class III: K^+ Channel Blockers					
Amiodarone	-**Main** action: blocks K+ channels and markedly prolongs AP duration -Other actions: Class I actions (blocks Na+ channels), blocks α and β receptors, & Ca^{+2} channels ***Effect is due to alteration of lipid membrane**	- Reserved for **life-threatening** atrial and ventricular arrhythmias (broad spectrum)	-Slows heart rate and AV conduction -Low incidence of TdP despite significant QT prolongation -Peripheral vasodilator (only with IV)	▫Toxicity: mainly **extracardiac** & **dose related**: -Lung fibrosis -CNS, GI and liver -Thyroid (hypo and hyper) -Corneal deposits -Skin: photodermatitis and discoloration (**blue-man syndrome**) *reversible -**Drug-drug** interactions	-A pure antiarrhythmic drug -Given **IV** (Loading dose 10gm) and **orally** -**Slow kinetics** (t½ :25-110 days) -Metabolized by **CYP3A4** enzymes (Drug-drug interactions) → **elevates digoxin & anticoagulants**

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Bretylium Tosylate	-Works on sympathetic nerve endings and causes the release of NE, then it decreases the release and reuptake of NE	-Rarely used, except for **prevention** of ventricular fibrillation **after failure** of cardioversion and lidocaine -When repeated recurrent attacks of ventricular fibrillation persist		-Hypotension -Parotid swelling	-Originally an antihypertensive, but tolerance develops
Sotalol	-A beta blocker, but has Class III actions	-Used for atrial and ventricular arrhythmias (broad spectrum)		-bradycardia -Heart failure -Prolongation of QT	-Amiodarone is a better choice due to side effects
Ibutilide & Dofetilide					-New drugs: amiodarone is a better choice
Class IV: Ca^{+2} Channel Blockers					
Verapamil & Diltiazem	- Block activated and inactivated L-type Ca++ channels	-Effective in treatment of atrial arrhythmia -Verapamil is widely used in Paroxysmal Supraventricular Tachycardia	-Effects more marked in tissues that fire frequently, less completely polarized at rest, and those dependent on Ca^{+2} (SA and AV nodes) -Vasodilators -Negative inotropic effects	- Can cause severe AV block in diseased hearts -Relatively safe: Constipation, gastric discomfort, vertigo, headache, nervousness, pruritis -↑ Digoxin levels	
Miscellaneous Drugs (Unclassified)					
Digoxin	- Direct Actions	-Restricted for very rapid atrial arrhythmias with the presence of **heart failure**	-Causes **vagotonic effects**, such as SA suppression and increased AV refractoriness, → it **blocks** conduction		-Old fashioned agent for heart failure and atrial arrhythmias
Magnesium	-Works on Na+/K+ ATPase, Na+ channels, certain K+ channels and Ca^{+2} channels	-Effective IV in refractory digitalis- induced ventricular arrhythmias **with hypo-magnesemia** -Effective in TdP patients **even** if **serum Mg^{+2} is normal**	-Magnesium counteracts the effect of calcium, so increased levels of magnesium results in reduced activity of calcium channels		
Potassium salts		-For digitalis- induced arrhythmias with **hypokalemia**	-Depress ectopic pacemakers and slow conduction		

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Adenosine	-Stimulates purinergic(P1) receptors -Activates inward rectifier K+ current and inhibits Ca^{+2} current	-90-95% effective in supraventricular tachycardia, replaced verapamil (which has 80% effectivity)	-↓ Phase 4 depolarization in SA node - ↓ AV conduction -No effect on ventricles	-Can cause transient flushing (benign and lasts for only a few seconds) -Chest tightness -AV block -Headache -Hypotension -Nausea, and paresthesia	-Naturally occurring nucleoside -Very short acting (t 1/2 10 seconds) ***Less effective** in the presence of adenosine receptor blockers, e.g. **theophylline and caffeine**

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