Anti-arrhythmic drugs

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Class	Drugs/Dose	MOA	Indication	ADRs/CI
Class I Anti-arrhythmia: sodium channel blockers	**1A: Quinidine,** procainamide, ajmaline, prajmalium	☐ Moderate sodium channel block, inhibition of potassium channels (prolonged repolarization)	☐ Atrial flutter & fibrillation ☐ Ventricular tachycardia ☐ Extrasystoles ☐ Quinidine = BRUGADA'S syndrome (congenital defects)	S/E: hypotension, negative inotropic effect (HF), blood count, arrhythmia (prolongation of AP and QT-interval prolongation), overdosing = AV block C/I: bradycardia, DHF, conduction defects, 1st trimester pregnancy Quinidine S/E: in addition to above = GI (NVD), overdosing = cinchonism (headache, dizziness, tinnitus)
	1B: Lidocaine, mexiletine	☐ Mild sodium channel block, shortened repolarization ☐ LIDOCAINE: Mainly ventricular effects; decreased depolarization velocity especially in case of decreased resting potential; increase recovery time of sodium channels with high activation frequencies (USE DEPENDENCY); High first pass effect (IV) ☐ MEXILETINE: PO admin, 2-3x/day (600-1200mg/d) (neuropathy dose: 450-750mg/d)	LIDOCAINE ☐ Acute therapy of ventricular tachycardia ☐ Prevention of ventricular fibrillation after heart attack ☐ Least cardiotoxic Na blocker BUT NO PROPHYLACTIC USE MEXILETINE ☐ Ventricular arrythmia ☐ Neuropathic pain	LIDOCAINE S/E: hypotension, negative inotropic effects (HF), overdosing = seizures LIDOCAINE C/I: AV block grade II and III Mexiletine S/E: dose related, neurologic effects include tremor, blurred vision, lethargy and nausea
	1C: Flecainide, Propafenone	☐ Marked sodium channel block, no effect on repolarization (slow dissociation from sodium channels → inhibits fast sodium influx during phase 0 strongly → QRS prolongation but no QT interval or APD prolongation)	☐ Limited, supraventricular arrythmia ☐ Life threatening ventricular arrythmias ☐ Some congenital arrhythmia syndromes (type 3 LQTS and RYR2 mutations)	PROPAFENONE: CYP2D6 SUBSTRATE (SLOW METABOLIZER) S/E distinct pro-arrhythmic potential (even at normal doses), blurred vision (F), exacerbation of congestive heart failure Flecainide S/E: increased mortality for patients after myocardial infarction
Class II anti arrhythmia: sympatholytic drugs (beta blockers)	**Propranolol** **Esmolol** **Sotalol**	☐ 1st line therapy (safety and efficacy has been proven) = reduces mortality after MI ☐ Negative inotropic, chronotropic and dromotropic effects, membrane stabilizing effects (decreases heart rate, decreases intracellular calcium overload, inhibition of after-depolarization automaticity)	☐ Sinus tachycardia ☐ Supraventricular arrythmia ☐ Ventricular extrasystoles ☐ Atrial fibrillation	Negative inotropic, AV block, bronchospasm, fatigue, hypotension, aggravation of HF
Class III anti arrhytmias: prolongation of refractory period	Inhibition of potassium channels → prolongation of repolarization and APD → reverse use-dependency (= high affinity to channels in normal physiological state so sotalol is able to prevent the development of arrythmias whereas drugs like lidocaine are only effective when there is already arrythmias i.e., has to be high fire rate)			Torsades de pointes arrythmia (strong substance specificity)
	Sotalol	☐ Beta and potassium channel blocker	☐ Life threatening ventricular arrythmias ☐ Maintenance of sinus rhythm in patients with atrial fibrillation ☐ Also used in pediatrics	
	Amiodarone	☐ Multi-channel inhibitor (dirty drug) = blocks inactivated sodium channels, decreases calcium current and transient outward delayed rectifier and inward rectifier potassium currents, prolongs action potential and refractoriness, delays repolarization	☐ Serious supra and ventricular arrythmia ☐ Effective in otherwise difficult to treat arrythmia	S/E: Long t1/2 (20 – 100 d), accumulation in several tissues including skin, cornea, photodermatitis (changing eye colour, hyper or hypothyroidism, LUNG FIBROSIS (doses ≥ 400mg/d), bradycardia, AV block

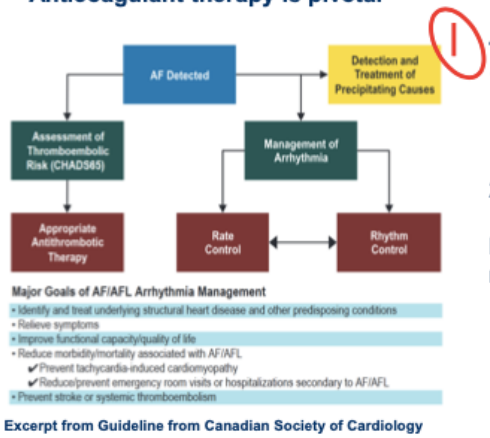
			▯ Broadly used (1st line) ▯ No increase in mortality in patients with HF or CAD	**Lots of interactions**: substrate of cyp3a4, inhibitor of cyp1a2, cyp2d6, cyp3a4, inhibition of p-GP, increased anticoagulation of coumarins
	Dronedarone	▯ Structural analog of amiodarone ▯ No iodine atoms → reduced lipophilicity → reduced t/12 (25-35h)	▯ Atrial fibrillation ▯ Atrial flutter	S/E: diarrhea, impaired sense of tasting, bradycardia, GI problems, liver toxicity, black box warning against ADHF or NYHA IV HF Less risk of accumulation and S/E (but also less effective) Less interactions with thyroid hormones, cyp3a4 substrate, cyp2d6 inhibitor
	Ibutilide	▯ IV admin only	▯ Acute conversion of atrial flutter fibrillation (within 20 minutes)	Pronounced QT interval prolongation and torsade-de-pointes (→ ECG monitoring for 4 hours after use)
Class IV: calcium channel blockers	**Verapamil, diltiazem, and bepridil**	▯ Block calcium channels in cardiac tissue and thus have anti-arrhythmic effects ▯ Verapamil: inhibition of activated and inactivated L-type calcium channels → active in very frequently firing tissue, less completely polarized tissue at rest and in SA and AV node (activation depends exclusively on calcium), prolongation of AV conduction ▯ Diltiazem similar to verapamil	▯ Verapamil: extracardiac effects (vasodilatation) ▯ Supraventricular arrhythmia (2nd choice after adenosine) ▯ Rate control in ventricular flutter or fibrillation	
Miscellaneous anti-arrythmia	**Adenosine**	▯ Increased potassium influx, decreased calcium influx ▯ Marked hyperpolarization, suppression of calcium dependent AP, shortening of AP ▯ Bolus: inhibits AV nodal conduction (less effects on SA) ▯ Very short duration of action (10s) ▯ Less effective in presence of adenosine receptor blockers (e.g. theophylline, caffeine)	▯ 1st choice for paroxysmal supraventricular tachycardia to sinus rhythm (high efficacy)	S/E: transient asystole, flushing, shortness of breath, chest burning (≥10% of patients), atrial fibrillation C/I: Grade II and III AV block, atrial fibrillation or flutter, obstructive lung disease
	Cardiac glycosides: Digoxin	▯ Reduced intracellular potassium levels → hyperpolarization → decreased conduction velocity ▯ Vagotonic actions → inhibition of calcium current in AV node ▯ Increased calcium exceeds storage capacity of endoplasmic reticulum → extrasystoles ▯ Positive inotropic ▯ Digitoxin = enterohepatic circulation (t1/2: 168-192h); digoxin = renal elimination (t1/2: 40h)	▯ Supraventricular tachycardia ▯ Atrial fibrillation and flutter ▯ Standby medication	S/E: low therapeutic index, arrhytmia, disturbances of cognitive functions, nausea, blurred vision, hyperkalemia C/I: ventricular fibrillation (NEEDS TO BE CLEAR DIAGNOSIS FOR USE)
	Magnesium	▯ 1-2g MgSO4 IV ▯ MOA unknown ▯ effective in patients with normal magnesium serm levels and low magnesium levels	▯ Prevention of recurrent episodes of torsade-de-pointes arrythmia ▯ Digitalis associated arryhtmia	S/E: flush, bradycardia, hypotension, impaired AV conduction
	Ivabradine	▯ Selective inhibitor of If channels in SA node → decreases heart rate → effect in inappropriate sinus tachycardia but is NOT YET approved		
	Vernakalant	▯ Multic-ion channel blocker, frequency and voltage dependent block of sodium current → mild QT interval prolongation ▯ Rapid termination of atrial fibrillation but NOT YET approved		

Condition	Exclude/use with caution
Heart failure	Flecainide, disopyramide
Sinus or AV node dysfunction	Digoxin, β-blockers, amiodarone, verapamil, diltiazem
History of myocardial infarction	flecainide
Prolonged QT interval	Quinidine, procainamide, sotalol, ibutilide, amiodarone
Cardiac transplant	adenosine

Guidelines for Treatment of Atrial Fibrillation

- Most common sustained arrhythmia = atrial fibrillation
- Prevalence: 0.5% ≤ 65 years; 10 % ≥ 80 years

- **Treatment goal:** relieve of symptoms, prevention of complications of thromboembolism an tachycardia-induced heart failure
- **Anticoagulant therapy is pivotal**



Excerpt from Guideline from Canadian Society of Cardiology

Treatment objectives:

1. ventricular rate control (60-80 bpm; Ca^{2+} blocker and/or β-blocker; 2nd line digoxin in case of heart failure)
2. Sinus rhythm control

Rate control has better benefit-to-risk ratio compared to rhythm control

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