

Amiodarone Prescribing and Monitoring: Back to the Future

Subha L. Varahan, MD, FHRS, CCDS

Electrophysiologist

Oklahoma Heart Hospital

Oklahoma City, OK

Friday, February, 8th, 2019





Introduction

- Iodinated benzofuran derivative that was synthesized and tested as an antianginal agent but discovered to have antiarrhythmic properties
- Management of both supraventricular and ventricular





Pharmacokinetics

- Oral amiodarone is markedly lipophilic, resulting in a very large volume of distribution and a prolonged time to reach stable plasma levels
- Intravenous (IV) amiodarone begins to act within one hour, with rapid onset of action within minutes following an IV bolus.
- Long-term oral therapy, amiodarone has a half-life between 60-142 days



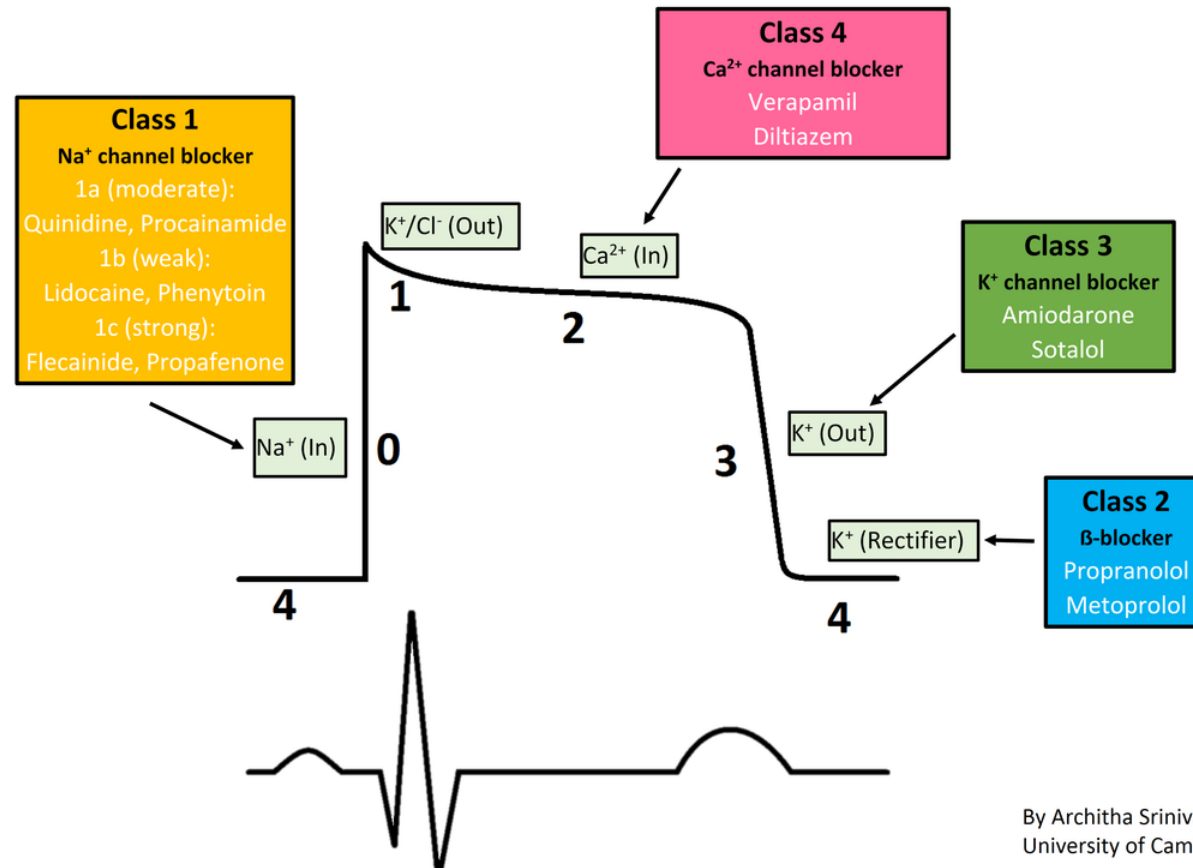
Electrophysiologic Properties

- Classified as a Vaughan-Williams class III antiarrhythmic
 - Due to its inhibition of outward potassium channels; the drug also has class I sodium channel blocking effects, class II antiadrenergic effects, and class IV calcium channel blocking effects
- Oral vs. I.V.



Electrophysiologic Properties

Drugs Affecting the Cardiac Action Potential



By Architha Srinivasan
University of Cambridge



Effects on the ECG

- Sinus bradycardia
- Prolong the PR interval and AVN refractory period
- Widening of the QRS complex (typically less than 10 percent)
- Prolongation of the QT interval (typically less than 10 percent)

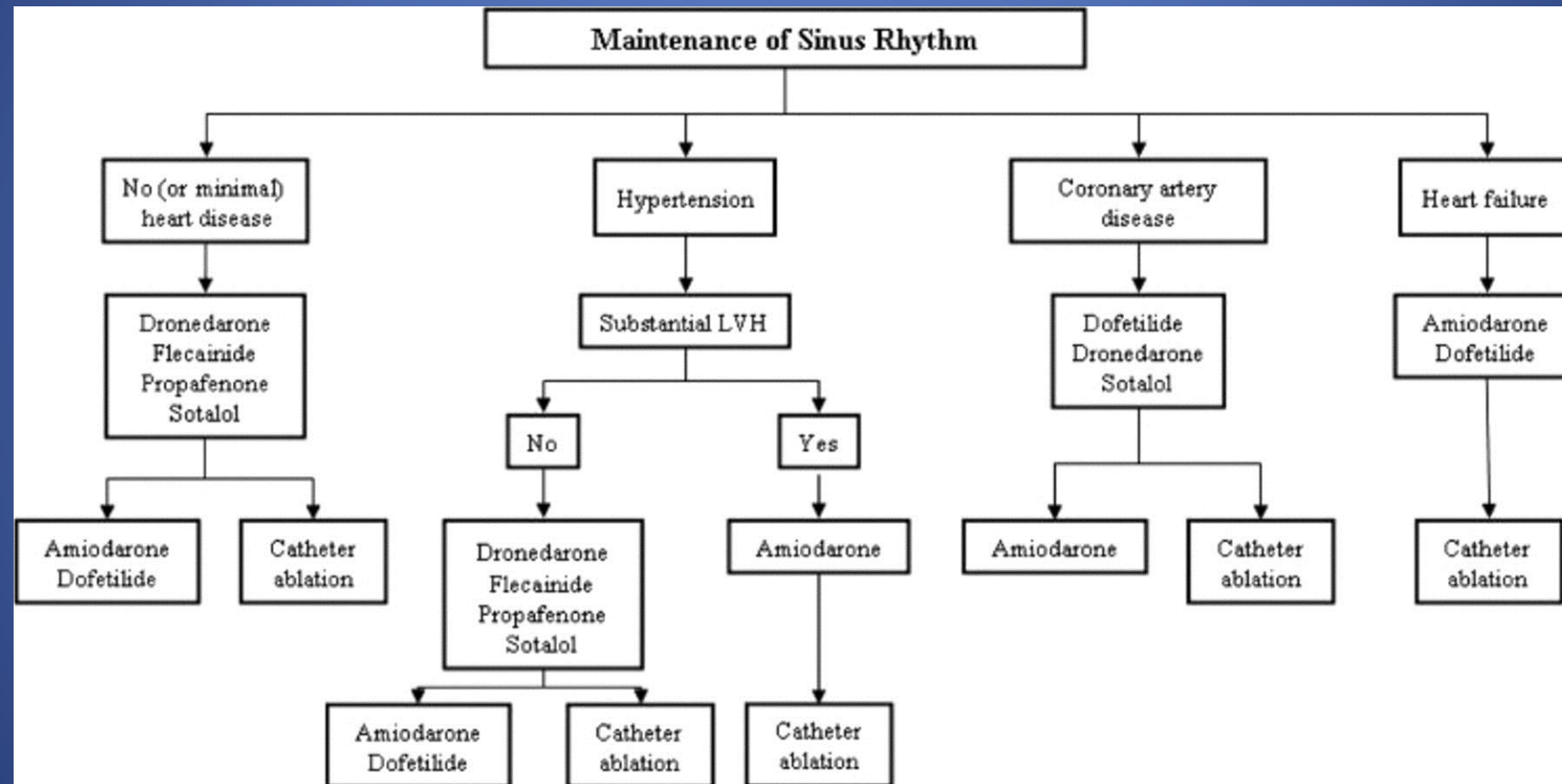


Audience Question

- Amiodarone is FDA approved for the treatment of atrial fibrillation.
 - A. True
 - B. False



Antiarrhythmic Drug (AAD) Therapy





Treatment of Atrial Arrhythmias

- Most effective medical therapy for maintaining sinus rhythm
- Low risk of ventricular pro-arrhythmia based on the electrophysiologic properties
- Does not increase mortality in heart failure patients
- Therapy can be easily initiated on an outpatient basis



Treatment of Atrial Arrhythmias

- **Paroxysmal or persistent AF**
 - Oral amiodarone load can result in conversion to NSR in about 25% of patients
 - Patients should be properly AC prior to prevent thromboembolic events
 - Can load patients that have failed cardioversion alone prior to repeat cardioversion



Treatment of Atrial Arrhythmias

- Patients with persistent AF undergoing catheter ablation
 - AMIO-CAT trial
 - 212 patients undergoing AF ablation randomized to Amiodarone vs. Placebo
 - Nonsignificant trend toward fewer recurrences of AF in the amiodarone group (39 versus 48%)
 - Significantly fewer patients required hospitalization or cardioversion for recurrent AF



Treatment of Atrial Arrhythmias

- SPECULATE trial
 - 112 patients with long-standing persistent AF were randomized to discontinuation of chronic amiodarone four months prior to ablation or continuation of therapy and then followed for ~32 months
 - Successful termination of AF at the time of ablation (79 versus 57 percent)

Mohanty *et al.* Heart Rhythm. 2015 Mar;12(3):477-



Treatment of Atrial Arrhythmias

- Can be used to treat other atrial arrhythmias such as atrial flutter or atrial tachycardia
 - Availability of other antiarrhythmic drugs with lower toxicity rates
 - High success rates of ablative approaches to atrial flutter or atrial tachycardia
- Lowers the incidence of postoperative AF in patients undergoing cardiac surgery



Treatment of Ventricular Arrhythmias

- Suppresses VPBs and episodes of non-sustained VT
 - CAMIAT trial
 - CHF-STAT trial
- Does not increase mortality when given to patients with moderate to severe LV dysfunction

Cairns *et al.* Lancet. 1997;349(9053):675.

Singh *et al.* N Engl J Med.

1995;333(2):77.



Treatment of Ventricular Arrhythmias

- Primary prevention of sudden cardiac death
- Secondary prevention of sudden cardiac death
- Prevention of ventricular arrhythmias in patients with ICDs
 - OPTIC trial
 - Amiodarone + BB vs. BB alone vs. sotalol alone
 - **Amiodarone plus beta blocker** significantly reduced the risk of shock compared with beta blocker alone or sotalol alone

Connolly *et al.* JAMA. 2006;295(2):165.



Which patients should get Amiodarone?

- Patients with LV dysfunction
- Patients with chronic kidney disease
- Persistent AF that are undergoing catheter ablation
- Patients with multiple ICD shocks/refractory VT/VF
- **OLDER PATIENTS!!!!**



Amiodarone monitoring and recommendations

System	Monitoring		Possible adverse effect	Recommendation
	Baseline	Follow-up		
Cardiac	ECG (at baseline and during loading dose)	Yearly	QT prolongation; torsade de pointes	Reduce amiodarone dose or discontinue use
			Symptomatic sinoatrial or conduction system impairment	
Dermatologic	Physical examination	As needed for signs/symptoms	Photosensitivity to UV light	Avoid sunlight; use sunscreen
			Blue-gray skin discoloration	Reduce amiodarone dose or discontinue use
Endocrine	Thyroid function tests	Every 6 months	Hyperthyroidism	Discontinue amiodarone; refer to endocrinologist
			Hypothyroidism	Treat with levothyroxine
Hepatic	AST or ALT	Every 6 months	AST or ALT elevation $\geq 2\times$ upper limit of reference range	Reduce amiodarone dose or discontinue use
Neurologic	Physical examination	As needed for signs/symptoms	Ataxia, dizziness, fatigue	Reduce amiodarone dose or discontinue use
Ophthalmologic	Eye examination	As needed for signs/symptoms	Corneal microdeposits	Continue amiodarone treatment
			Optic neuropathy	Discontinue treatment
Pulmonary	Pulmonary function tests	As needed for signs/symptoms	Pulmonary toxicity (cough, fever, dyspnea)	Discontinue amiodarone immediately; consider corticosteroid treatment
	Chest radiograph	Yearly		



Side Effects of Amiodarone

For side effects of amiodarone, think of **LEG PANIC!**

Liver enzyme fluctuations

Emesis

Gynecomastia

Pulmonary fibrosis

Abnormal thyroid function

Nausea

Interstitial lung disease

Corneal micro-deposits





Amiodarone Side Effects

- Extracardiac SE
 - Pulmonary toxicity may develop as early as 6 days
 - Corneal deposits develop in almost ALL patients who are treated for 6 months
 - Optic neuritis – rare but serious
 - Amiodarone-induced skin pigmentation





Amiodarone Side Effects

- Extracardiac SE (cont'd)
 - Neurologic adverse effects
 - Tremor
 - Ataxia
 - Headache
 - Endocrine adverse effects
 - Hypothyroid (6%)
 - Hyperthyroid (2%)
 - Gastrointestinal adverse effects
 - Constipation (20%)
 - Hepatocellular necrosis



Use in Pregnancy

- Hypothyroidism or hyperthyroidism in the mother or fetus because of the iodine in amiodarone
- Fetal bradycardia
- Fetal QT interval prolongation
- Premature labor
- Low birth weight



Amiodarone Drug Interactions

- Interfere with metabolism of several AAD drugs
 - ↑ Digoxin
 - ↑ Warfarin
 - Antidepressants
 - Antibiotics → QT prolongation
 - Statins
 - ↑ Phenytoin



Amiodarone

Baseline and Follow-Up Monitoring Parameters of Patients Receiving Amiodarone

Test	Baseline	3 Months	6 Months	12 Months	With Symptoms
CBC	X				
Serum CR & Electrolytes	X				
Digoxin or Other Drug	X				
levels Which May Increase*	X				
ECG	X	X	X	X	
PFT	X				X
Chest X-ray*	X				X
Thyroid Function*†	X		X	X	
Liver Enzymes (SGOT + SGPT)*	X		X	X	
Ophthalmic Exam	At Least Yearly Ophthalmic Examination, Including Fundoscopy and Slit-Lamp Examination, Is Recommended During Therapy				

* Repeat when Clinically Indicated; † Amiodarone Alters the Results of Thyroid-Function Tests, Causing an Increase in Serum T₄ and Serum Reversal T₃, and a Decline in T₃ Levels. Despite these Biochemical Changes, Most Patients Remain Euthyroid.

THANK YOU

