Sept 2010
QUESTION 22

Compare and contrast the pharmacology of digoxin and amiodarone

	digoxin	amiodarone
Uses	glycoside derived from foxglove leaves used in the treatment of AF/Flutter, SVT and in heart failure	benzofuran derivative contains 37% iodine by weight class III antiarrhythmic displays actions of all four classes
Pharmaceutical	oral or IV formulations	structurally resembles thyroxine
Pharmacodynamics		
Mechanism	Direct effects are the blocking of the Na.K.ATPase pump, the decoupling of the Na.Ca pump and the increase in intracellular Ca. AV node refractory period is increased but ventricle refractory period is decreased. Indirectly, increased vagal activity leads to decreased HR.	blocks potassium channels, calcium channels, sodium channels and adrenoceptors
Effects	Decreased HR, prolonged PR, ST depression, T wave flattening, QT shortening	prolongs the refractoriness of all cardiac myocytes, conduction through the AV node the action potential duration & QT interval
Side effects	Narrow therapeutic window, needs monitoring, at toxic doses arrhythmias develop Causes n+v, anorexia and fatigue	May cause respiratory fibrosis, corneal depositis, hypo or hyperthyroidism, cirrhosis, is not arrhythmogenic
Pharmacokinetics		
Absorption	bioavailabilty 60% to 80% requires loading dose	poorly absorbed, bioavailability 40-70%
Distribution	moderate Vd, alters with thyroid fn low protien binding 25%	very large volume of distribution (66L/kg) highly protein bound (96%)
Metabolism	some hydrolysis in the gut minimal hepatic metabolism	complex metabolism, hepatic via de-ethylation catalysed by CYP 2C8 active metabolite
Elimination	half life 36-48hrs excreted mostly unchanged	very long half life (weeks) via skin, faeces, urine and lachrymal glands