Sept 2011
QUESTION 14

Compare and contrast the pharmacology of dobutamine and milrinone

	Dobutamine	Milrinone
Intro	Is a synthetic catecholamine derivative of isoprenaline, used for acute heart failure and stress testing	Is a selective phosphodiesterase inhibitor used in severe refractory heart failure and for short periods post cardiac surgery
Pharmaceutical	Is a racemic mixture. Presented as a white powder for reconstitution. Should not be mixed with alkaline solutions (HCO3)	is a yellow solution, stored at room temperature, should not be given with HCO3 or frusemide
Pharmacodynamics		
mechanism	the + enantiomer is a potent α1 antagonist and β1 agonist, the -ve enantiomer has opposite effects on α1 causing agonism and is less potent (10%) β1 agonist.	Via selective PDE3 inhibition which causes decreased cAMP breakdown intracellularly and hence increased Ca
effects	are a composite of the α and β actions causing a mostly β1 effect increased inotropy, chronotropy and MVO2. There are mild β2 effects as well.	the increased Ca leads to increased inotropy and lusitroppy, with associated decrease in vascular tone causing equal arterial and venodilation.
side effects	may be proarrhythmic, pts may develop tolerance, may worsen ischaemia due to increased MVO2.	may be proarryhtmogenic causing SVT and VT. Have been shown to worsen outcomes in acute on chronic heart failure
Parmacokinetics		
absorption	IV, dose starts at 5mcg/kg/min uptitrate to effect, max 40mcg/kg/min	IV
distribution	small vd 0.2L/kg	small vd 0.4L/kg
metabolism	via COMT then gluruonidation hepatically	minimally hepatic
excretion	half life is two minutes excretion is in urine as inactive metabolites	half life is 2 hours excretion is in the urine, mostly as unchanged drug, requires dose adjustment in renal failure