

Inotropes

increase contractility of a cardiac myocyte independent of preload or afterload

common ultimate cellular mechanism of action of these agents involves an influence on the release, utilisation or sequestration of intracellular calcium.

two main groups based on cAMP involvement in increasing intracellular Ca

cAMP Dependent Inotropes	cAMP Independent Inotropes
Catecholamines	Calcium Sensitisers
Natural	Levosemindan
Adrenaline	Other
Noradrenaline	Digoxin
Dopamine	Calcium
Synthetic	Thyroid hormone
Dobutamine	
Isoprenaline	
Non catecholamine sympanomimetics	
phenylephrine	
metaraminol	
Phosphodiesterase inhibitors	
Milrinone	
Other	
Glucagon	

Catecholamines

act on beta1, 2 and alpha1,2 adrenergic receptors (beta1 mostly responsible for iontropy)

beta1 receptors are numerous in the heart, they are Gs protien coupled receptors

activation - alpha subunit swaps GTP for GDP - adenylyl cyclase activated - increased cAMP

increased cAMP causes increased intracellular calcium leads to increased contractility

beta effects predominate at lower doses, adrenaline has a greater beta affinity than norad

noradrenaline and adrenaline are given at doses similar to that naturally released in shocked states

dopamine is given at higher doses, many effects may relate to a subsequent conversion to norad

dobutamine binds to beta1 vrs beta2 3:1. It is a potent iontrope which increases MVO2 ++

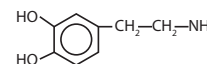
isoprenaline is a potent non selective beta agonist, iontropy benefits are = to drop in SVR

Non catecholamine sympanomimetics

do not have two OH on their benzene rings

phenylephrine is a potent alpha agonist with minimal beta activity

metaraminol is a synethetic amine with both direct and indirect actions, main beta 1



Dopamine

Phospdiesterase inhibitors

Milnorone - decreased the breakdown of cAMP by phosphodiesterase leading to increased Ca

Calcium Sensitisers

Levosemindan increases myofilament calcium sensitivity by binding troponin C, increasing iontropy

Other Glucagon increases the action of adenylyl cyclase which increases cAMP and Ca (but needs high doses)

Digoxin blocks Na.K.ATPase which decreases Na-Ca pump action increasing intracellular Ca

infusion of calcium leads to a 10-20 minute intense +ve iontropic effect (admin at end of bypass surg)

thyroxine mediates increases in Ca.ATPase activity increasing Ca release from the SR