Beta blockers

Types

Selective
- β_1 (e.g. atenolol, bisoprolol, metoprolol, carvedilol, timolol)
- β_2 (e.g. butoxamine) – not used therapeutically

Non-selective (e.g. propranolol)

Other classifications:
- *Lipid solubility*: propranolol>>atenolol
- *Route of elimination*: atenolol = renal, propranolol = hepatic
- *Speed of elimination*
  - Atenolol – long half-life, od dosing
  - Propranolol – short half-life, bd/tds dosing
  - Esmolol – ultra-short half-life (9 min), need to give by continuous infusion
- *Intrinsic sympathomimetic activity*
  - Acebutolol, oxprenolol, pindolol

Indications

Chronic
- Cardiovascular
  - *Angina:* first line after GTN
  - *MI:* first line after event and for secondary prophylaxis
  - *HT*: first line if concomitant IHD or angina
  - *Heart failure*: traditionally accepted as CI because of negative inotropic effect. However, recent trials have demonstrated survival benefit (CIBIS, CIBIS-II, MDC, USCHFTP) for certain agents (bisoprolol, metoprolol, carvedilol). Note: start on very low dose, very gradual dose escalation, patients may get worse before they get better and many will not tolerate even a gentle regime.
  - *Arrhythmias*: esp. rate control in AF; prophylaxis and treatment
- CNS
  - *Anxiety*: propranolol for GAD and panic disorder. Symptomatic treatment, should be supplemented with psychotherapy to address underlying problems.
  - *Migraine*: propranolol is first-line in prophylaxis, together with pizotifen, a 5-HT_2 antagonist. Treat for 3-6 months and attempt withdrawal, which often leads to prolonged remission.
  - *Tremor*: propranolol for essential tremors
- Eye
  - *Glaucoma*: topical timolol is a first-line agent in acute angle closure glaucoma.
- Endocrine
  - *Hyperthyroidism*: propranolol inhibits peripheral T_4 de-iodination and provides immediate symptomatic relief. Used in chronic hyperthyroidism to supplement anti-thyroid medication, and acutely as below.
  - *Phaeochromocytoma*: after α-blockade

Acute
- *Akathisia:* give propranolol.
- *Hyperthyroidism*: thyroid operations/crisis
- *Malignant HT*

Adverse effects and their basis

Contraindications	Adverse effects	Pharmacological basis
Asthma, COPD (even if β_1-selective/'cardioselective', or topical for glaucoma)	Bronchoconstriction	Block of bronchodilatory β_2-receptors

Heart failure (if acute, or β-blocker intolerant)	Bradycardia, hypotension: common but rarely symptomatic; heart block	Negatively chronotropic and inotropic effects
	Rebound angina	
PVD	Peripheral vasoconstriction, Raynaud's phenomenon	Block of vasodilatory β_2-receptors (no β_1-receptors in periphery)
	Hyperkalaemia	Block β-dependent K^+ transport into cells (converse for salbutamol)
Pregnancy	Stillbirth, IUGR	?
	Breastfeeding – can affect infant (atenolol and sotalol excreted in greater amounts into milk)	
Depression	Malaise, fatigue Vivid dreams, nightmares, hallucinations (esp. with lipid-soluble agents such as propranolol)	Outflow from locus coeruleus to cortex, thalamus and limbic system is important in controlling mood and motivation.
	Worsened glucose tolerance Masking of hypoglycaemia (esp. non-selective agents)	Many are sympathetically mediated.
	Increase in lipids	?

Management of beta-blocker overdose

Clinical features

CV bradycardia, heart block, hypotension, low cardiac output heart failure/cardiogenic shock
death more likely with agents with membrane stabilising activity
RS severe bronchospasm in patients with asthma
CNS loss of consciousness with lipid soluble agents

Seen 5min after administration, last approx. 6h (atenolol).

Treatment

- Atropine (to remove all vagal tone)
- If no effect: glucagon 1mg slow IV injection; can be repeated twice or followed by infusion (physiological antagonism)
- Isoprenaline infusion: 10mg/500ml, 0.5-20μg/min (high doses to overcome block)
- Cardiac pacing
- Salbutamol for bronchospasm (consider if wheeze may be cardiac)