

# Calcium channel blockers

## Types/mechanism

Block voltage-gated L-type (for large/long-lasting) calcium channel of smooth and cardiac muscle, reducing calcium availability for muscle contraction. Note that an inhibitor of the T-type (transient) cardiac calcium channel, namely mibefradil, has recently been terminated due to unacceptable drug interactions.

DHP (esp. vascular)

- *Long-acting*: amlodipine, nifedipine MR
- *Short-acting*: nifedipine, nicardipine

↓afterload

Dilatation of coronary arteries

↓inotropic (only CCB exception is amlodipine, which can be given safely in LVF)

Non-DHP (esp. cardiac)

- *Phenylalkylamine*: verapamil
- *Benzothiazepine*: diltiazem

Above actions, plus

More markedly ↓inotropic

↓chronotropic

NMDA blockers (different mechanism)

## Indications

Cardiovascular

- *IHD*: β-blockers are more effective and thus used first. If CI, non-DHP CCBs can achieve rate control, too. Esp. useful if coronary vasospasm.
- *HT*: DHP CCBs for elderly ISH, non-DHP CCBs if concomitant IHD
- *Arrhythmias*: non-DHP CCBs (class IV)
- *Heart failure*: avoid non-DHP CCBs (amlodipine is not negatively inotropic – PRAISE study)
- *PVD* (esp. Raynaud's)

CNS

- *Neuroprotection* in SAH (nimodipine – British Aneurysm Nimodipine Trial) and stroke (experimental)

## Adverse effects and their basis

| Contraindications           | Adverse effects          | Pharmacological basis  |
|-----------------------------|--------------------------|--|
|                             | Headache, flushing       | Vasodilatation (DHPs)  |
|                             | Ankle swelling           | Raised intracapillary pressure due to selective dilatation of precapillary arterioles (DHPs) – not relieved by diuretics, disappears with lying flat |
|                             | Palpitations             | Reflex sympathetic response (DHPs)   |
|                             | Rebound angina           |  |
|                             | Constipation             | Esp. verapamil   |
| β-blockers and non-DHP CCBs | Bradycardia, heart block | But avoid reflex sympathetic response! (non-DHPs)  |
| Pregnancy, breastfeeding    |                          |  |
|                             | Gynaecomastia, jaundice  |  |
|                             | Gum hypertrophy          |  |
|                             | Rashes                   |  |

|  |                  |            |
|--|------------------|------------|
|  | Aplastic anaemia | Nifedipine |
|--|------------------|------------|

Avoid short-acting formulations – more vasomotor SEs

Non-DHPs also have same SEs as DHPs, but less severe.

**Notes**

Amlodipine is the odd one out

- Little first pass metabolism cf. other CCBs → very long half-life of 40h → less reflex sympathetic activation → compliance protection
- No ↓inotropic effect (PRAISE study) – can use in LVF