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

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<th>Adverse effects</th>
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<td>Vasodilatation (DHPs)</td>
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<td>Ankle swelling</td>
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<td>Raised intracapillary pressure due to selective dilatation of precapillary arterioles (DHPs) – not relieved by diuretics, disappears with lying flat</td>
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<td>Palpitations</td>
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<td>Reflex sympathetic response (DHPs)</td>
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<td>Rebound angina</td>
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<td>Constipation</td>
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<td>Esp. verapamil</td>
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<td>β-blockers and non-DHP CCBs</td>
<td>Bradycardia, heart block</td>
<td>But avoid reflex sympathetic response! (non-DHPs)</td>
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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