**Q17 Classify the calcium channel blockers and provide one example of a drug for each class (20% marks). Compare and contrast the pharmacology of nimodipine and verapamil (80% marks) (Sept 2011, Q2 March 2014))**

**Class I –** Phenylalkylamines eg, verapamil
**Class II –** Dihydropyridines.
First generation - nifedipine
Second generation - felodipine
Third generation - amlodipine
**Class III –** Benzothiazepines eg, diltiazem

| | **Nimodipine** | **Verapamil** |
|---|---|---|
| Description/indications | Nimodipine is a calcium antagonist that causes vasodilatation, it has a relatively specific effect on cerebral arterioles and it used in the management of SAH | Verapamil is a synthetic derivative of paparavine which acts as a calcium channel blocker. It is used in the management of HTN, supraventricular arrhythmias and angina. |
| Pharmaceuticals | Available in PO tablets (30mg) and IV solution200mcg/ml | Comes in immediate or sustained release tablets of varying strengths and IV solution for injection |
| Pharmacodynamics | Binds to the N binding site of the L-type calcium channels on vascular smooth muscle to reduce intracellular calcium levels. Increases cerebral blood flow without any demonstrable steal effect. | Binds to the V binding site of the L type calcium channel. Reduces conduction in atrial, ventricular and purkinje cells, reduces cardiac contractility and also causes peripheral vasodilatation. |
| Side effects | Decreases SVR and can increase CO (overall may drop BP) | Dizziness, nausea, flushing, postural hypotension. In patients without CCF can improve cardiac function by improving ischaemia. In patients with CCF can make LV function worse (because it reduces myocardial contractility). Contraindicated in patients with WPW as may cause VT/VF |
| Pharmacokinetics | | |
| - Administration | Route- PO or IV<br>Dose - 60mg Q4H PO or 20mcg/kg/hr IV<br>Bioavailability - well absorbed but high first pass metabolism so bioavailability 30% | Route - PO or IV<br>Dose - from 40mg PO or 5-10mg IV<br>Bioavailability - extensive first pass metabolism, bioavailability 25%<br>Time to onset - minutes for IV, 1-2 hours PO |
| - Distribution | Vd 1-2L/kg<br>Highly protein bound 98%<br>Highly lipid soluble | Vd - 3.8L/kg<br>Extensive protein binding 90% |
| - Metabolism | Demethylation and dehydrogenation to inactive pyridine analogue | Via hepatic enzymes. One active metabolite. |
| - Elimination | Inactive metabolites urine and faeces. Half life 2-4 hours | 70% via urine (active and inactive metabolites), remainder in faeces. Half life 3-6 hours |