Centrally acting alpha 2-mimetic

They penetrate the CNS and reduce the sympathomimetic activity of the vasomotor center while maintaining or even increasing its sensitivity to signals coming from baroreceptors. This means that both the **antihypertensive effect** and the adverse effects are not dependent on body position (there is no tendency to hypotension when changing the position from horizontal to vertical). Hypotension is more likely to occur in patients with fluid depletion.

They are only used when treatment options with the basic range of antihypertensives have been exhausted or for advantageous additional properties (e.g. alpha blockers in benign prostatic hyperplasia).

Mechanism of action

It acts on **adrenergic'**, **imizadole'** or **serotonin** receptors, affinity for multiple types of receptors is common. Alpha receptors can affect on several levels. By *stimulating alpha-2 receptors* in the area of the vasomotor center of the CNS/peripherally on presynaptic neurons, they lead to *vasodilation*, the same effect as blockade of alpha-1 receptors.

If they act on alpha-2 receptors in the CNS, we refer to them as ``centrally acting drugs*, if they also act on peripheral alpha-2 receptors, we name them as ``centrally and peripherally acting*. Medicines causing alpha-1 blockade are referred to as alpha blockers.

Side effects

Adverse effects often result from a **decrease *in the concentration of catecholamines (*dopamine' *and* noradrenaline*) at synapses in the CNS and the resulting** *predominance of the parasympathetic* - the effect sedatives, sleep disorders, depression, parkinsonism etc.

Representatives

α-methyldopa

α-Methyldopa (a false precursor and at the same time a prodrug) is transformed in the nerve ending into alpha-methylnoradrenaline (a false mediator) - this selectively stimulates *α_2-receptors''* in the brain and on the presynaptic membrane peripheral endings, thereby reducing the release of noradrenaline. The effect is manifested primarily by a reduction in peripheral vascular resistance. Minute output and heart rate remain constant.

Side effects

Adverse effects are caused by the already mentioned effect on the CNS. These include a sedative effect, fatigue and drowsiness, reduced reactivity and the ability to concentrate on mental work. Depression, dizziness and extrapyramidal syndrome are common.

Clonidine

Clonidine is the prototype substance for the group of drugs - "imidazole receptor agonists" (I_1 and I_2 subtypes of these receptors have been described so far). It was originally developed as a topical decongestant for application to nasal mucosa. With systemic application i.v. however, it was found that after a short-term increase in pressure, it causes a long-term decrease. The pressor response is explained here by direct stimulation of peripheral α-receptors. The subsequent long-term reduction of blood pressure (noticeable mainly during repeated administration) is then attributed to the stimulation of **postsynaptic α_2'** ***(it has up to 10 times higher affinity to them than to α_1) and*** *I_1 receptors in the medulla oblongata*. In the periphery, it stimulates presynaptic α_2 receptors and thus reduces the release of noradrenaline. The decrease in blood pressure after clonidine is mainly attributed to a reduction in cardiac output due to a slowing of the heart rate (much more pronounced than after methyldopa), dilation of capacitive vessels, and a decrease in peripheral vascular resistance. The advantage is a decrease in the resistance of the renal vessels while maintaining perfusion.

Indication

- Antihypertensive drug.
- Stimulation of α_2 receptors in the CNS leads, among other things, to the effect of ``analgesic*, ``central myorelaxant* and ``alleviation of withdrawal syndrome *after sudden withdrawal of opiates.*
- In the form of eye drops, it is used to *treat glaucoma*.

Side effects

Adverse effects are manifested by an effect on the CNS. Sedation, dry mouth (probably due to α_2 receptors) and depression are most often observed.

Moxonidine, Rilmenidine

It belongs to the antihypertensives acting primarily on the "I_1 receptors", to which they have up to 30x higher affinity than to the "α_2 receptors" (for clonidine this ratio is 4:1). Their advantage over clonidine is a lower sedative effect and less tendency to cause dry mouth. They do not cause rebound hypertension. They are contraindicated (including clonidine) in children, pregnancy and lactation (due to lack of experience) (Prichard 2000).

Guanfacine

It has similar properties to clonidine, but affects only α_2-receptors.

Links

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