The effect of alpha 2 - mimetics

Alpha 2 mimetics 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 side effects are not dependent on body position (there is no tendency to hypotension when changing position from horizontal to vertical). Hypotension is more likely in patients with fluid depletion.

Side effects

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

Representatives

α-metyldopa

α-methyldopa (false precursor and prodrug) turns into alpha-methylnoradrenaline (false mediator) in the nerve endings. Alpha-methylnoradrenaline then selectively stimulates **α 2 - receptors** in the brain and on the presynaptic membrane of peripheral endings, thus reducing noradrenaline release. The effect is mainly manifested by a reduction in peripheral vascular resistance. Minute output and heart rate remain constant.

Side effects

The side effects are caused by the already mentioned effect on the CNS. These include the sedative effect, fatigue and drowsiness, reduced reactivity and the ability to concentrate on mental work. Common side effects are depression, dizziness and extrapyramidal syndrome.

Clonidine

Clonidine is a prototype substance for a 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 the nasal mucosa. However, in the case of systemic application, it was found that after a short-term increase in blood pressure, it causes a long-term decrease. The pressor response is explained here by direct stimulation of peripheral α-receptors. Subsequent long-term reduction in blood pressure (evident mainly during repeated administration) is then attributed to the stimulation of **postsynaptic α 2** (it has up to 10 times higher affinity for them than for α 1) **and I 1receptors in the medulla oblongata**. At the periphery, it stimulates presynaptic α 2 receptors and thus reduces the release of norepinephrine. The decrease in blood pressure is mainly attributed to a reduction in cardiac output due to a slowing of the heart rate (much more noticeable than after methyldopa), dilatation of capacitive vessels and a decrease in peripheral vascular resistance. The advantage is a decrease in renal vascular resistance while maintaining perfusion.

Indication

- Antihypertensive.
- Stimulation of α 2 receptors in the CNS leads, among other things, to an **analgesic, central muscle relaxant and alleviation of the withdrawal syndrome** after abrupt withdrawal of opiates.
- In the form of eye drops, it is used to **treat glaucoma**.

Side effects

Side effects affect the CNS. Sedation, dry mouth (probably due to α 2 receptors) and depression are most commonly observed.

Moxonidine, Rilmenidine

Moxonidine and Rilmenidine belong to the antihypertensives acting mainly on **I 1 receptor**s, to which they have up to 30 times higher affinity than **α 2 receptor**s (for clonidine this ratio is 4: 1). Their advantage over clonidine is their lower sedative effect and lesser tendency to cause dry mouth. They do not cause rebound hypertension.

Clonidine, Moxonidine and Rilmenidine are contraindicated in children, during pregnancy and lactation (due to lack of experience)

Guanfacin

Guanfacin has similar properties to clonidine but only affects α 2 -receptors.

Links

References

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