The Sheet Team

Title of Lecture: Pharmacology

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Written by: Iumana Kussad

a-adrenergic antagonists

Also known as a-blockers. They are divided chemically into 3 groups (Haloalkylamins, Imidazolines, Quinazoline)
* its not required to know each a-blocker belongs to which group
Another classification of alpha blockers can be due to history of production (1st generation, 2nd generation..etc)

*Remember: Alpha-1 receptors mediate vasoconstriction and elevation of blood pressure. Alpha-2 receptors are inhibitory to norepinephrine (prevent its release). Therefore a-2 blockers would result in elevation of norepinephrine levels.

Thinking of it thoroughly, a non-selective a-blocker (like phenoxybenzamine and phentolamine) must result in no total effect on B.P since a-1 decreases B.P by blocking the mediated actions through a-1 receptors .. AND a-2 increases B.P by elevating norepinephrine levels.
YET this isn't the case, since the effect of a-blocker is more on a-1 receptor than a-2 receptor which would result in a net decrease in B.P.

These two non-selective alpha blockers are used in management of hypertension associated with phenochromocytoma. Phenochromocytoma is a tumor affecting the adrenal medulla, resulting in increase of release of epinephrine and

norepinephrine, and causing a severe increase in blood pressure.
The alpha blockers are given parentrally.

Selective alpha-1-receptors (like quinazoline) replaced non-selective a-blockers in the management of hypertension and proved to be more effective than the non-selective.
YET, due to the presence of a mild a-2-blocking activity, even the selective a-blockers are not as efficient as diuretics , Calcium channel blockers, or ACE inhibitors in relieving or protecting the individual from harmful effects of hypertension.
Therefore these drugs won't be effective in the administration of severe hypertension alone, they will be combined with other anti-hypertensive drugs to give a better effect.

*Major mechanism of action in treating hypertension is of course through blocking of a1-receptor activity by acting as a competitive inhibitor.

Therapeutic dose of a-1-blockers is enough to decrease blood pressure, yet it was found that at larger doses of a-1-blockers, blockade of a-2-receptors occur (which would lead to increase in NE).
>this effect is least seen in Prazosin, therefore it's the choice of cardiologists, it's also preferred since it leads to direct vasodilatation effect by blocking phosphodiesterase enzyme and has no effect on blood glucose levels or uric acid. (this is the advantage of an alpha-blocker over B-blocker)

 # a-1-blockers clinical uses:
1. MILD hypertension
2. treating benign hyperplasia of the prostate (in old men)
by causing the relaxation of the smooth muscles of the prostate leading to decrease in its size

 # side effects of a-1-blockers:
1. First dose effect (severe drop in B.P only on the first dose)
>happens in 90% of patients
2. orthostatic hypotension
Normally, when changing position specially (sitting to standing), there's an elevation of blood pressure to compensate for the low blood pressure during sitting to prevent dizziness.
People who are on a-blockers undergo orthostatic hypotension, due to the absence of this compensatory mechanism (the increase in B.P), therefore when a person changes his

position a drop in blood pressure occurs and person might undergo dizziness and headaches.
>therefore, patients are advised to take these drugs at bedtime or while sitting.

*Another advantage of selective a-1-blockers is that they have a good effect on blood lipid levels (decrease cholesterol and triglycerides and increase HDL) compared to other anti-hypertensive drugs.

Combined alpha & Beta antagonists

Labetalol and Carvidolol
They are used in hypertensive crisis and Labetalol is the main drug used in management of hypertension in pregnancy.
They have alpha and Beta antagonistic activity (but mainly Beta).
> in oral adminstration the Beta:alpha blocking activity is 3:1
> in parentral adminstration (IV) it increases to 7:1
Therefore they are considered B-blockers with some a-blocker activity, and even with chronic usage of the drug, the a-blocker activity may disappear

*They have 1/10 potency of phentolamine with respect to the a-blocking activity and 1/3 potency of propranolol with respect to the B-blocking activity.

Their clinical uses:
1. HTN
2. Ischemic Heart disease
3. Hypertensive emergencies
4. hypertension in pregnancy

Side effects:
1. orthostatic hypotension (side effect of a-antagonistic activity)
2.liver damage
3. tremors
4. Lupus like syndrome (a form of arthritis- auto immune disease)
5. positive antinuclear antibody test (antibodies in blood against wbc) due to autoimmune disease
6. reflex tachycardia

Parasympathetic NS

Acetylcholine is a neurotransmitter at
1. parasympathetic nerve terminals
2. sympathetic and parasympathetic ganglia
3. major substance of contraction of voluntary muscles (motor nerves)
4. sympathetic terminals of sweat glands and to adrenal gland

Acetylcholine is broken down very fast after its release in synapse.
After high muscle stimulation, excessive Ach in synapse would eventually lead to relaxation of muscle
Also antagonists of Ach cause relaxation of muscles.

We have directly acting and indirecty acting parasympathomimetic agents.
Indirectly acting are inhibitors of Acetylcholinestrase. They can be either reversible inhibitors (like quaternary ammonium agents and Carbamates) or irreversible inhibitors (like organophosphates) which are toxic.
* Sarin is an organophosphate nerve gas used in wars, it causes spasm of all volunatry muscles (due to accumilation of ACh) including respiratory muscles > death.

Done by: Jumana Kussad
GOOD LUCK ^_^

"إننا نعيش لأنفسنا حياة مضاعفة حينما نعيش للاخرين.. وبقدر ما نضاعف إحساسنا بالاخرين.. نضاعف إحساسنا بحياتنا.. ونضاعف هذه الحياة ذاتها في النهاية"
- سيد قطب