

***Title of Lecture: ANS***

***Date of Lecture: 19/10/2014***

***Sheet no: 13***

***Refer to slide no. : 6***

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- β blockers are widely used in medicine because they are highly effective for example they are used in the management of hypertension, cardiac arrhythmias and even simple anxiety states.

- β blockers can act on β1 and β2 receptors.

- β1 receptors are located in all tissues but mainly found in the heart and kidneys, its stimulation will lead to an increase in heart rate, contractility, cardiac output, and on the kidneys β1receptors mainly mediate rennin release.

Renin: is an enzyme that converts angiotensinogen into angiotensin 1.

- β2 receptors are mainly present in the lung and muscles, its stimulation will result in bronchodilatation.

- We have two main categories of β blockers:

1) Those that selectively block β1known as **Cardioselective**, they are named so because β1 receptors are mainly found in heart as we said and also kidneys, when administered they'll decrease HR, contractility, cardiac output and decrease rennin release.

2) Those that block both β1& β2 known as **Nonselective.** Disadvantage it'll cause bronchoconstriction so such drugs are contraindicated in patients with bronchial asthma.Not only that but they're also contraindicated in patients with heart failure (heart failure is characterized with a decrease in contractility) so giving the patient this drug will further decrease contractility and this is a problem.

-We have two major properties of β blockers

1)Membrane stabilizing activity, this property gave the β blockers the advantage of being anti arrhythmic.

2) Intrinsic Sympathomimetic activity.

We said that β blockers are contraindicated in patients with heart failure, however they found that certain βblockers have the property of little sympathomimetic effect meaning that they'll increase contractility just a little bit so this gave the βblocker the advantage of using them in certain patients with heart failure.

DON'T confuse it with the fact that it is contraindicated however SOME were found to have this sympathomimetic action!

\*\*Go back to slides 47 and 48: you have to memorize all of the βblockers and to know which are cardioselective and which are nonselective, we don't have to know if this drug has an ISA or MSA characteristic however **Pindolol** is unique by having both MSA & ISA so you should know it.

Note: we said that β blockers are contraindicated in some cases like in heart failure however if I must use β blockers in this case I shall pick either a drug with ISA characteristic or we'll pick a drug with the shortest duration of action like **Esmolol** it's duration of action is 10 minutes(very fast acting)!

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α & β blockers: they have the property of blocking both but mainly β

Slide 50/51/52 already explained above.

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-What we mean by Pharmacokinetics is that each drug will have different t1/2, duration of action, metabolic fate, lipid solubility...

-**propranolol** is orally effective although it has an extensive first pass effect this because only little amount is needed.

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Same as slide

Slide 55

Remember that the duration of hypotensive action of β-blockers does not correlate always with their serum t1/2’s...What does this mean? A drug is said to have a short t1/2 but it acts for 24hrs conclusion active metabolites are produced from parent drug !

Some β-blockers are given once daily despite their short t1/2 e.g. **Acebutelol’s** t1/2 ≈ 4hrs but metabolized to a pharmacologically active metabolites with t1/2 ≈ 10to 20hrs.

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- We are mentioning propranolol(nonselective) and atenolol(cardioselective) more than other drugs and that's because they are the most widely used drugs.

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-concerning high solubility we have two major points, they can enter CNS so easily and this will reflect some of CNS side effects like dizziness and headaches however the second point is of an advantage since they can enter CNS then they'll be able to treat diseases concerned with CNS like migraine and essential tremors.

-Migraine is a very complex disease; β blockers are effective as well as calcium channel blockers, conventional analgesic like paracetamol are in effective in treating migraine.

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1- HTN (htpertension) alot of debates have arise on whether to use β blockers or diuretics as a starting drug but the doctor says that it depends on the situation, degree of elevated blood pressure and so on ...

2- Angina pectoris (ischemic heart disease) the mechanism here is that it decreases contractility so decreases the load on the heart.

3- Mild to moderate HF (**only by ISA ...in general they are contraindicated**) Not good for pts with HF with severe ↓ in CO and bradycardia, but good in certain pts with HF who are largely dependent on enhanced sympathetic activity to maintain sufficient CO

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4- Cardiac arrhythmias by inhibiting conduction in heart especially those associated with increased HR

5- Prevention of recurrent MI

6- Hyperthyroidism: in here we have excess thyroid hormone, thyroid hormones usually increase level of cAMP especially in the heart and as you remember we said that β adrenergic receptors are mediated through cAMP. So decreasing cAMP levels in the heart by β blockers will be of beneficial effect for patients with hyperthyroidism, infact propranolol is number one drug used in hyperthyroidism and these patients will have over activity of sympathetic system (anxiety, sweating,..) and these manifestations are controlled by propranolol.

Note: βblockers are **NOT** antithyroid drugs; because they only control the manifestations of hyperthyroidism in order for a drug to be antithyroid it must inhibit synthesis.

7- Glaucoma (**Timolol** is particularly effective; it ↓ production of eye fluid)

8- Anxiety states:

when we defined antagonist we said that if it's given alone it produces no effect however when it's given with agonist it will reverse the action of the agonist so if we give β blocker for a normal person nothing will happen but if it's given to someone with a bit of anxiety meaning this person have over activity of sympathetic system it will lead to control of sympathetic system, they're excellent drugs because they will not lead to alteration in thinking and they don't have any sedative effect unlike antianxiety drug e.g.: diazepam(valium).

9- Migraine (unkown mechanism of action)

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-β-blockers side effects:

1- High degree of atrioventricular block

2- Bradycardia

3- Acute HF(especially in patients with severe left ventricular dysfunction)

4- ED (erectile dysfunction) and this is a side effect in all anti hypertensive drugs.

5- Bronchoconstriction

6- Raynaud's phenomenon is excessively reduced blood flow in peripheries in response to cold and using β blockers will block β2 receptors so they'll further reduce blood supply to peripheries and will cause severe pain**.**

Slide 61

7-if a Patient with diabetes and hypertension is put under β blockers it's good since β blocker reduce blood sugar level along with being antihypertensive however one should be careful if the patient is already under hypoglycemic agents or insulin then we should readjust the dose because hypoglycaemia is very dangerous & could lead to death. but what is more dangerous is masking the manifestations of hypoglycemia which are sweating, trachycardia, dizziness, headaches since we always tell the patient if he face those manifestation he shall take a chocolate or smth but if these manifestations are masked byβ blockers then the patient won't know and he'll die so usually β blockers are not the first drug of choice for patients having diabetes.

8- they decrease HDL (the good cholesterol) except pindolol it increases HDL and remember this drug has both MSA and ISA characteristics, α & β blockers have no effects on blood lipids and this is an advantage to them.

9- Central effect

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Same as slide

Slide 63

There is a compensatory mechanism by the body when we give β blockers, which is the increase of β receptors, and this gives us an explanation to why we adjust the dose of β blockers with chronic administration (more receptors thus higher dose of β blocker) this is not a problem as long as the patient is taking the drug but if we want to stop the drug it must be gradual otherwise if sudden withdrawal takes place all NE and E will bind to all receptors and as we said receptors increased in number so the blood pressure will increase tremendously and lead to severe hypertensive crisis!

Please don’t forget to refer to the slides ☺