SYMPATHOLYTIC AGENTS USED IN HYPERTENSION

BY:

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SYMPATHOLYTICS :

- A sympathetic (or sympathoplegic) drug is a medication which inhibits the postganglionic functioning of the sympathetic nervous system.

- They can block at 3 different levels:
  - **Peripheral sympatholytic drugs** (α & β receptor antagonists) block the action of NA at the effector organ (heart or blood vessel).
  - **Ganglionic blockers** that block impulse transmission at the sympathetic ganglia.
  - **Centrally acting sympatholytic drugs** that block sympathetic activity within the brain.
CLASSIFICATION OF SYMPATHOLYTIC AGENTS

- β-Blockers
- α-Blockers
- β+α-Blockers
- Ganglion blockers
- Neuronal blockers
- Centrally acting sympatholytics
β-Blockers

Non-selective (β1 + β2)
- Propanolol
- Pindolol
- Timolol
- Sotalol

Cardioselective (β1)
- Metoprolol
- Atenolol
- Acebutolol
- Esmolol
Mechanism of action

1. Beta Blockers
   - Slow heart rate and lower blood pressure

   - Blocks adrenaline & noradrenaline

   - Affects receptors in the heart and blood vessels

   - Dilated artery - lower blood pressure

   - Slow heart rate allows left ventricle to fill completely and lowers the heart workload

Blockade of the Beta₁ Receptor

- Force
- Rate
- Renin Secretion

Blockade of the Beta₂ Receptor

- Airway Resistance
- Vascular Resistance
Uses:

- In mild hypertensive patients (stage I, SBP-(140-159) & DBP-(90-99))
- Hypotensive response develops over 1-3 weeks and is maintained over 24 hrs.

Other uses:

- **Angina** - decrease frequency of attack and increase exercise tolerance.
- **Congestive heart failure** - antagonizes deleterious reflex of sympathetic system.
- **As a secondary prophylaxis in MI** - By preventing reinfarction and ventricular fibrillation.
Cardiac arrhythmias - By suppressing extrasystoles & bradycardia.
Supraventricular tachycardias are reduced due to prolonged systoles. (esmolol)

**Adverse effects:**
- Rebound hypertension on sudden withdrawal.
- Bradycardia in patients of sick sinus
- Bronchoconstriction
- GIT upset,
- Night mares, forgetfulness
<table>
<thead>
<tr>
<th>Pharmacological actions</th>
<th>Non-selective (β₁+β₂)</th>
<th>Cardio selective (β₁)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Decrease renal blood flow which ultimately decrease GFR.</td>
<td>• Minimal effect on renal blood flow &amp; GFR.</td>
</tr>
<tr>
<td></td>
<td>• Plasma LDL/HDL ratio is increased.</td>
<td>• Little/no deleterious effect on blood lipids.</td>
</tr>
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<td></td>
<td>• Most of them are lipid soluble.</td>
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</tr>
<tr>
<td></td>
<td>• Carbohydrate tolerance is impaired in prediabetes. (inhibits glycogenolysis due to decrease in adrenaline levels)</td>
<td></td>
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<tr>
<td>Adverse effects</td>
<td>• Fatigue, unconsciousness, subtle cognitive effects, loss of libido.</td>
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<td>-----------------------------------------------------</td>
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<tr>
<td></td>
<td>• Cold hands and feet syndrome.</td>
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<td></td>
<td>• C/I in partial and complete heart block (propanalol)</td>
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<td></td>
<td>• Accenuates MI.</td>
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**Esmolol**: Short lasting fall in B.P when given by i.v infusion (Rapid onset)
$\alpha$ -Blockers

- Non selective
  - Phentolamine
  - Chlorpromazine
  - Phenoxybenzamine

- $\alpha_1$ Selective
  - Prazosin
  - Terazosin
  - Doxazosin

- $\alpha_2$ Selective
  - Yohimbine
**Mechanism of action**

<table>
<thead>
<tr>
<th>Non selective</th>
<th>Selective</th>
</tr>
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<tbody>
<tr>
<td>Block both $\alpha_1$ and $\alpha_2$ receptors</td>
<td>Block selectively $\alpha_1$ receptors.</td>
</tr>
</tbody>
</table>
| Vasodilatation and fall in BP ($\alpha_1$ blockade)  
- Presynaptic $\alpha_2$ blockade releases the NA (tachycardia is prominent). | Vasodilation and fall in BP ($\alpha_1$ blockade)  
- Tachycardia is minimal. |

![Mechanism of action diagram](image-url)
Uses:

- In mild to moderate hypertensive patients (prazosin)
- Clonidine withdrawal.
- Pheochromocytoma pts: Release of CA during surgery.
- Benign hypertrophy of prostate: By decreasing the tone of prostate /bladder neck muscles and by retarding progression.
- Raynauds disease.
- Used in diabetes patients.
- Increases the HDL and lowers the LDL & TGS
Indications for $\alpha_1$-sympatholytics

- High blood pressure
- Benign prostatic hyperplasia

$\alpha_1$-blocker e.g., terazosin

Inhibition of $\alpha_1$-adrenergic stimulation of smooth muscle

Resistance arteries

Neck of bladder, prostate
Adverse effects:

- Postural hypotension. (Prazosin: first dose effect)
- Fluid retention and tolerance with monotherpy
- Head ache, drowsiness, dry mouth
- Miosis ($\alpha_1$ blockage)-blurred vision
- Nasal stuffiness
- Impotence (inhibits ejaculation)
### α + β BLOCKERS

<table>
<thead>
<tr>
<th>LABETELOL (β1 + β2 + α1)</th>
<th>CARVEDILOL (β1 + β2 + weak α1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall in BP (Decrease in peripheral resistance)</td>
<td>Fall in BP (Vasodilation)</td>
</tr>
<tr>
<td><strong>Uses:</strong></td>
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</tr>
<tr>
<td>- Essential hypertension (absence of β blocker action)</td>
<td>- Anti-oxidation property</td>
</tr>
<tr>
<td>- Pheochromocytoma</td>
<td>- Hypertension.</td>
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<tr>
<td>- Clonidine withdrawal.</td>
<td>- Cardioprotective in CHF</td>
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<td><strong>ADR:</strong></td>
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<tr>
<td>- Postural hypertension</td>
<td>- Failure of ejaculation.</td>
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<tr>
<td>- Failure of ejaculation.</td>
<td>- Rashes</td>
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<td>- Liver damage</td>
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</table>
GANGLION BLOCKERS

- **Quaternary ammonium compounds**: Hexamethonium, Pentolinium.
- **Monosulfonium compounds**: Trimethaphan, Camforsulfonate

**ACTION:**

- Ganglionic blockers *inhibit autonomic activity* by interfering with neurotransmission within autonomic ganglia.
- This *reduces sympathetic outflow to the heart* thereby decreasing CO by decreasing HR and contractility.
- Reduced sympathetic output to the *vasculature decreases sympathetic vascular tone, which causes vasodilation & fall in B.P*
**Uses:**

Trimethaphan- Used in hypertensive emergencies (aortic surgeries).

**Adverse effects:**

- excessive hypotension and impotence due to its sympatholytic effect.
- constipation, urinary retention, dry mouth due to its parasympatholytic effect
- Cannot be used in chronic HTN.
**Neuronal blockers**

- **Reserpine**: Popular antihypertensive in 1950
  - It inhibits the VMAT 2 (stores monoamines) at the neurons of intraneuronal vesicles
  - Monoamines get degraded by MAO.
  - Effects are long lasting as the CA stores are restored gradually

**Adverse effects:**
- At higher doses cause sedation, mental depression (deplete CA in brain)
Guanithidine

- Polar guanidine compound
- Taken into adrenergic nerve endings by active amine transporter.

**Actions:**

- Engages & blocks NA uptake mechanism.
- Displaces NA in vesicles.
- Inhibits nerve impulse.
- Not used now because of side effects.
THANK YOU