

تفريغ فارما 1

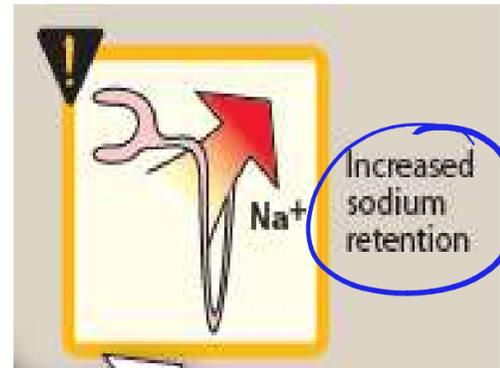
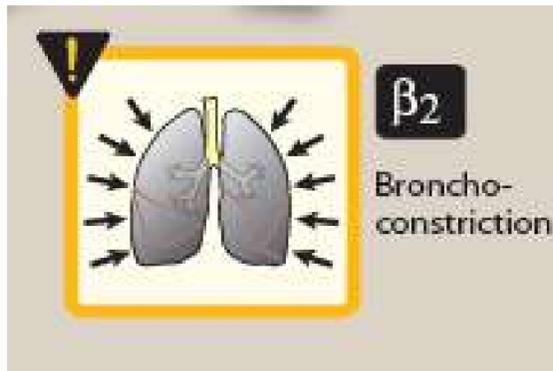
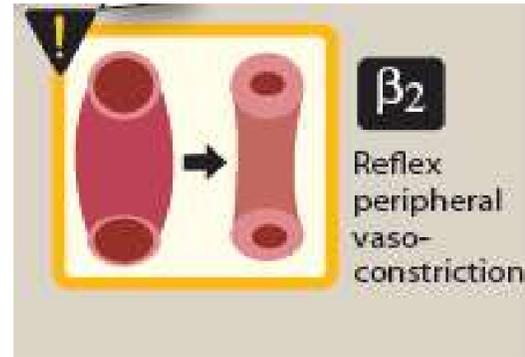
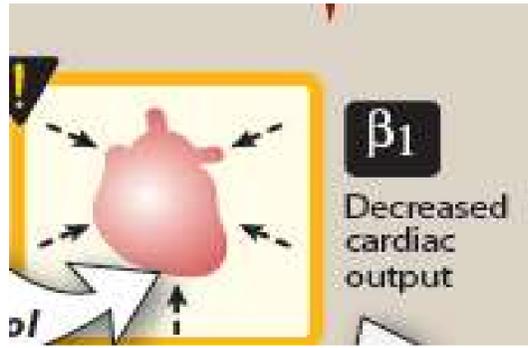
اسم الموضوع: *Lec 11 / B-adrenergic blockers*

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β -ADRENERGIC BLOCKING AGENTS

β-ADRENERGIC BLOCKING AGENTS



* الضيق الطبيعي لمفرزة
إنزيم رينين
فيقل الـ angiotensin فيقل
المصريوم، ولكن فاي
reflex mechanism
or
indirect action.
لأنه من عندى bradycardia
فقول الـ blood flow لـ kidney
عشان هيك انبج β-blockers
diuretics.

β-ADRENERGIC BLOCKING AGENTS

Competitive ←

- Nonselective β- blockers act at both β₁ and β₂ receptors.
- whereas cardio selective β antagonists primarily block β₁ receptors
- They do not induce postural hypotension → لا يها ما يتسفل
α ع
- Clinically important class with various therapeutic uses.

↳ there is no β₂ selective blockers
دواء انتقائية β₂ لا يوجد

دواء تضيق الأوعية أو تضيق الشعب الهوائية
← vasoconstriction or bronchoconstriction
! تجنب α

β-ADRENERGIC BLOCKING AGENTS

I. HTN → hypertension

II. Angina

III. MI → myocardial Infarction

IV. CHF → congestive heart failure

V. Cardiac Arrhythmias

VI. Glaucoma

VII. Migraine prophylaxis

imbalance
in O₂ ←
demand
and O₂
supply

السفة

Propranolol (Inderal)



- A nonselective β antagonist
- The prototype β -adrenergic antagonist and blocks both β_1 and β_2 receptors with equal affinity
- SR allowed once daily dosing
↳ *sustained release.*

Effects : of Propranolol

- **Cardiovascular :**

β_1 inhibition leads to :

1. Decrease in Cardiac output & Work

2. Decrease in O₂ consumption *low heart rate*

low contractility → **Decrease cardiac output (negative chronotropic & inotropic effects)

- Supress SA & AV node

- Bradycardia

- In HTN the TPR returns to normal → with time
Total peripheral resistance
- No Postural Hypotension

❖ Bronchoconstriction**:

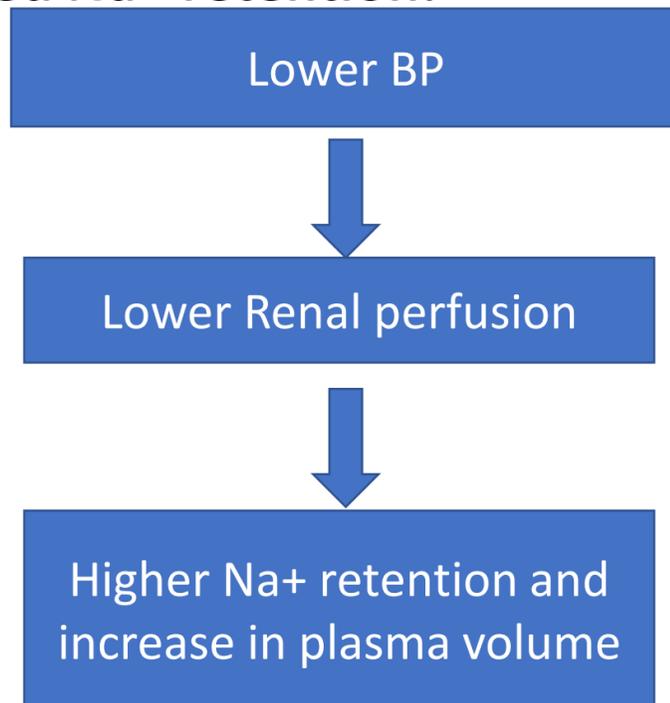
- Blocking β_2 receptors in the lungs of susceptible patients causes contraction of the bronchiolar smooth muscle.

تقلص عضلات الشعب الهوائية
Caution on COPD & Asthma patients.

- Instead use selective β_1 blockers.

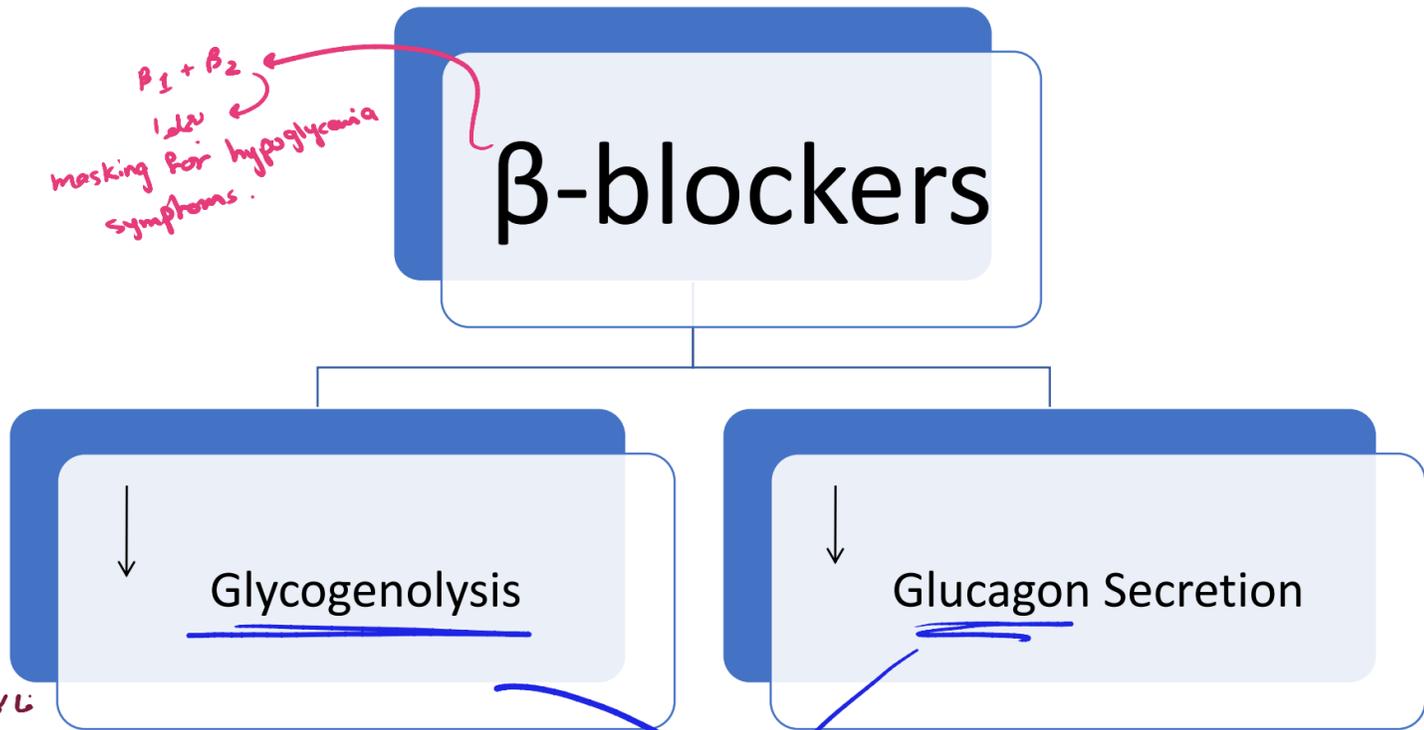
Other effects of Propranolol

❖ Increased Na⁺ retention:



Many Beta blockers are administered with diuretics to prevent Na⁺ retention

Disturbances in glucose metabolism associated with Propranolol



$\beta_1 + \beta_2$
 masking for hypoglycemia symptoms.

selective β_2 ...
 symptoms masking
 hypoglycemia

* For diabetes diagnosis:
 3Ps polyuria (urination)
 polydipsia (العطش)
 polyphagia (الاجوع)

* Symptoms for hypoglycemia?
 fatigue, tremor, dizziness,
 x palpitation, sweating.

contraindicated with diabetic patients with insulin treatment.

+ hypoglycemia ⇒ 😊

فإذا أقيمت رفعت
 hypoglycemia
 (β-blocker)
 ! palpitation, sweating
 symptoms will be masked
 sweating will be masked
 المعنى إذا تأخر في
 المعنى!

Pharmacokinetics

- ✓ Propranolol is completely absorbed orally
- ✓ 25% of the dose is BA (high 1st pass effect)
- ✓ Cross BBB, high V_d

كافية
جدا تعطيل
effect

highly lipophilic, high partition coefficient.



Therapeutic effects

✓ HTN :

-ve inotropic & -ve chronotropic

- via ↓ CO (mainly) & ↓ Renin production

direct effect

indirect → Na⁺ retention

✓ Migraine : ^{السَّيِّئَة}

- ↓ Both incidence ^{حدوث} & Severity ^{شدة} of attacks

O₂ consumption

✓ Angina pectoris and MI

الذبح الصدرى

✓ Hyperthyroidism

arrhythmia associated
tachycardia

دائماً بخافه منا

عندهم ال metabolism على

مستويين دائماً

يعمل كثير ، خفيف ، مابينهم ، HR على

β-blocker يعطاه

عشان اوقف ال palpitation

Adverse effects of Propranolol (Inderal)

- I. Bronchospasm
- II. Arrhythmias
- III. Sexual impairment
- IV. Metabolic disturbances
- V. Depression, dizziness, lethargy, fatigue, weakness, visual disturbances, hallucinations

* طب كلف ليجل arrhythmia وهو لعالجها ؟

لكنه β -blockers حيا لادوية الاليزم نعالجها
(tapering down) رما نوقفها فجأة ، لأنه
بالتوقف فجأة رجع ليعبر عندي rebound HTN
وليشغل ال PB في السما .

* طب بشر التفسير ؟

β -blocker رجع انقلها تنسكر ال receptors فالتاي كنو من
new receptors (defence mechanism) رجع نتج
التاي بغيره عندي up-regulation receptors لاد

والم كيرة الودا مسكر كوال receptors وانما وقفه فجأة
انما فتحه كيرة receptors كيرة وكلمة اربط خط ال sympathetic agonist

التاي رجع ليعبر عندي rebound HTN \leftarrow palpitation / arrhythmia فجول

صنف جنسي

drug-drug interactions

D-D/I

الجرعة: \leftarrow conc. \leftarrow الارتفاع في الجرعة

تقليل \leftarrow elimination

selective serotonin reuptake inhibitor

(SSRI family)

** **Enzyme Inhibitors**: cimetidine, fluoxetine, paroxetine, and ritonavir, may potentiate its antihypertensive effects

تزيد \leftarrow metabolism \leftarrow تقل \leftarrow conc. \leftarrow تزيد الجرعة

** **Enzyme Inducers**: such as barbiturates, phenytoin, and rifampin, can decrease its effects.

treat T.B

تزيد \leftarrow elimination

Timolol and nadolol

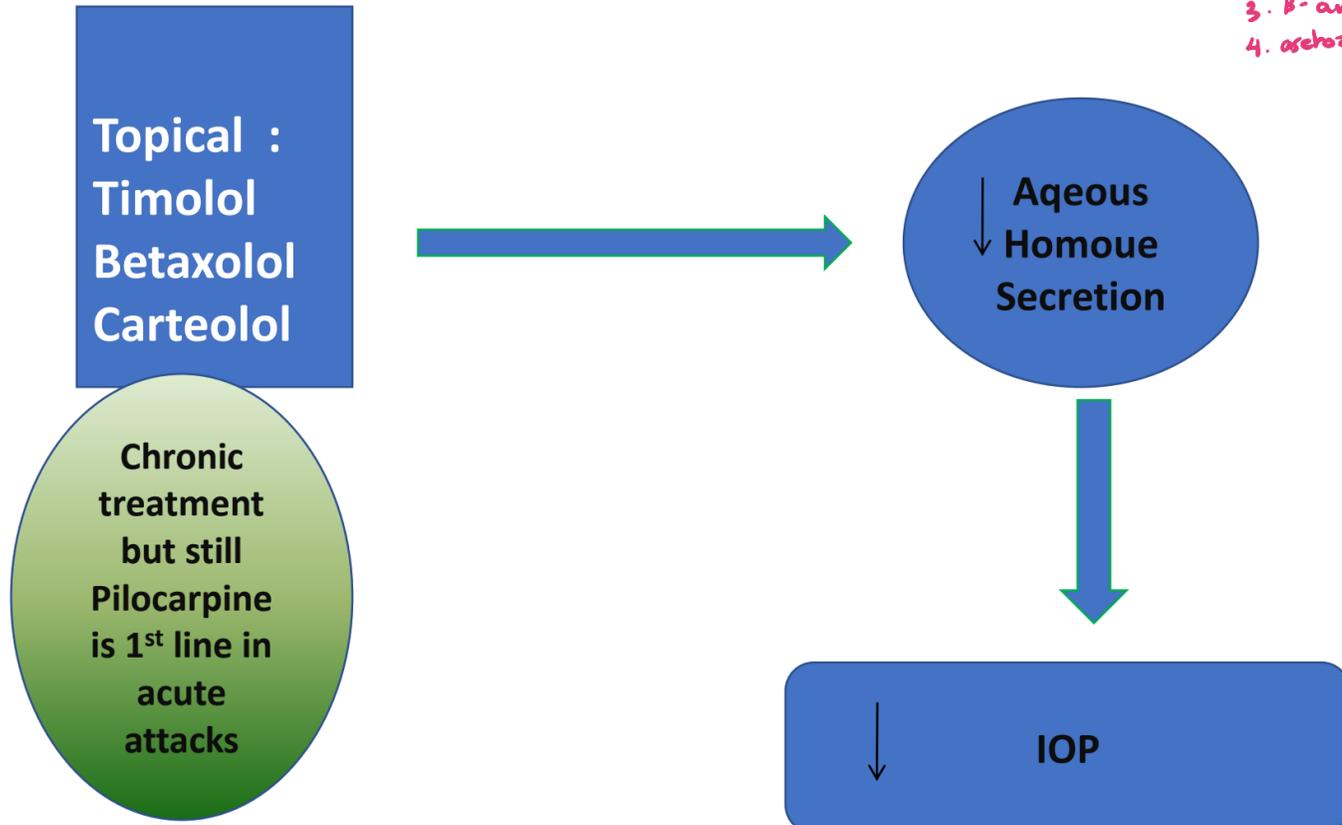
- Non-selective β -Antagonists
- Block β_1 - and β_2 - adrenoceptors and are more potent than propranolol
- Nodalol has long half life
- Timolol used in open- angle glaucoma →

مميزة هامة
الأدوية في علاج
ال glaucoma
ما يتقل
miosis
و كذا لا تستخدم كغداد
غضال

يستخدم أيضاً
الـ bicarpine
← The first choice

Treatment of glaucoma

- * 4 Families For glaucoma treatment:-
1. parasympathetic agonist (pilocarpine)
 2. ACE inhibitors (physostigmine)
 3. β -antagonist / β -blockers (timolol)
 4. acetazolamide (ACE)
↳ carbonic anhydrase inhibitor.



Selective β_1 antagonists

- Acebutolol
- Atenolol
- Metoprolol
- Bisoprolol
- Betaxolol
- **Nebivolol,**
- Esmolol

المسؤول عن افراز
nitric oxide
المسؤول عن
vasodilation.



- Drugs that preferentially block the β_1 receptors have been developed to eliminate the unwanted bronchoconstrictor effect (β_2 effect) of *propranolol* seen among asthma patients.
- Lower Dose is required 50-10 fold less than non-selective beta blockers

Selective β_1 antagonists

- Lower blood pressure in hypertension
- Esmolol has a very short lifetime IV
- Cardioselective β blockers are useful in diabetic hypertensive patients who are receiving insulin or oral hypoglycemic agents.
- Also safe in Asthma & COPD patients

in hospitals
في حالات الطوارئ
بسرعة

Antagonists with partial agonist activity

Pindolol (Non selective β - Antagonist)

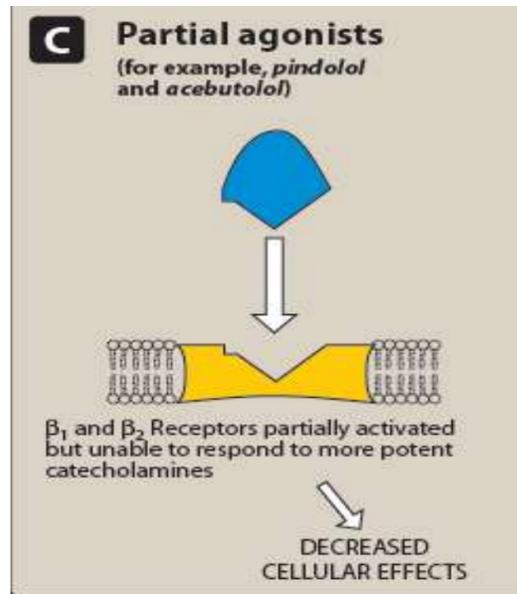
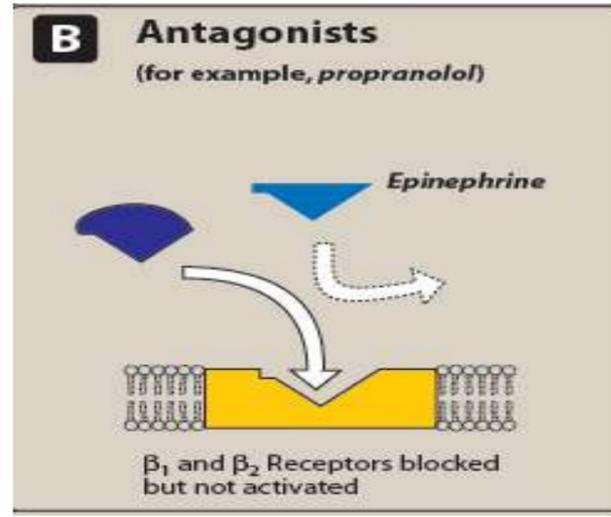
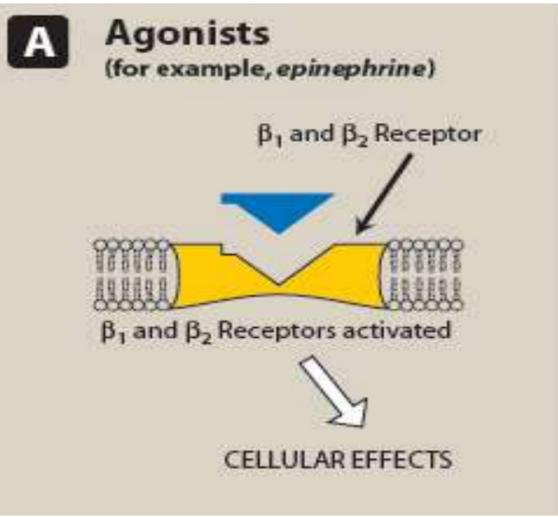
Acebutolol (Selective β_1 - Antagonist)

strong or لا يقترن
traditional Hypertensive agents
weak sympatholytic effect
لا تملك التأثير القوي على
effect

تذكر: أهمية ال agonist
ولكن ما يبطئ ال 100% efficacy
شما زدت ال dose ويغرد ال
ال agonist في ال receptors
antagonist في ال receptors

partially agonist

- Not Pure Antagonists ,
- Also posses weak agonist activity **ISA** → Intrinsic Sympathetic Activity
- Prevent potent stimulants from acting
- Also less metabolic disturbances compared to full antagonists → blocking β_2 → activation β_2
- Effective in hypertensive patients with moderate bradycardia (specific cases)



Antagonists of both α and β adrenoceptors

→ strong hypertensive agents compared with non-selective or selective β -blockers

$\alpha_1 + \alpha_2$ antagonist ← phentolamine, phenoxybenzamine

α_1 antagonist ← terazosin

α_2 antagonist ← yohimbine

β antagonist ← olol's

selective non-selective

➤ Labetalol and Carvedilol

- Non-selective β -blockers with concurrent α_1 -blocking actions that produce peripheral vasodilation*, thereby reducing blood pressure.

Therapeutic use in hypertension and heart failure

• **Labetalol** is useful for:

- ✓ Elderly or black hypertensive patient
- ✓ Alternative to Methyldopa in pregnancy-induced HTN
- ✓ IV administration in ER, fast onset

• **Carvedilol** also used to prevent cardiovascular mortalities in patients with stable chronic heart failure

❖ **Orthostatic hypotension and dizziness are associated with α_1 blockade**

من أهم الأدوية لعلاج ال HF
 زيادة تليف القلب
 و ال wall thickening of the heart
 وبالتالي تليف ال deterioration HF

EF (ejection fraction) الطبيعي من 55% - 70%

* هو ال HF أصلاً
 هو ضعف في عضلة القلب
 ejection fraction (كفاءة لضخة) ←
 بتكون أقل من الطبيعي

thickening in ventricles wall
 ال واحد كبير بالسنة ليعرف في عندي

degrade ال HF ايها deteriorate يعني بقتل لتسوى ما بتحسن
 هو ال الأدوية ال ال بتعطي لسن بتبطل المصدر ما لتتجدد ولا بتاكله!

ليه؟ عندها كفاءه ال thickness عم بيزيد ← كمية ال blood ال بتطلع أقل ← صادر ال ال paroreceptors
 ايها تزيد ال workload مع ال heart بزيادة
 لما تعمل صيلك بطبيعة الحال أي عضلة لذي أقبضا بزيادة
 ال-م-كبير ، في حالة القلب يكون التضخم كجوا فتسبب ال hypertrophy (hypertrophy) مع صياح ال chambers .

سجانه ال!

DRUGS AFFECTING NEUROTRANSMITTER RELEASE OR UPTAKE

- Historical value, seldom use

Reserpine

old hypertensive drug
منه موجود مسالين

anti hypertensive

centrally acting

منع دخول الـ NE, dopamine
والتالي يمنع NE release

symp. effect

- A plant alkaloid
- Blocks the Mg²⁺/adenosine triphosphate-dependent transport of biogenic amines, (Norepinephrine, Dopamine, and Serotonin) from the cytoplasm into storage vesicles in the adrenergic nerves of all body tissues.
- Decreases NE release and impairment in SNS
- Slow onset of action, long duration
- Old anti HTN medication

يعني متاخر ووقت
المداخلة قليل

المفعول فيه الطويل

Guanethidine

أول ما أعطى هذا الدواء
يغير عندك BP increase
بعدها روح تنزل

- Blocks the release of stored norepinephrine as well as displaces norepinephrine from storage vesicles (thus producing a transient increase in blood pressure)
- Leads to NE depletion peripherally
- causes Orthostatic Hypotension



- End of unit II regarding ANS drugs!!!!!!

