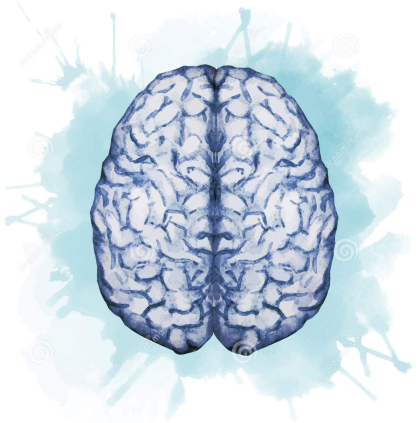
MEDICINE
KING SAUD UNIVERSITY

436 team pharmacology



MCQs | SAQs | summary

Drugs used in Parkinsonism

قادة فريق علم الأدوية :

لين التميمي & عبدالرحمن ذكري

الشكر موصول لأعضاء الفريق المتميزين :

جومانة القحطاني

ندى الصومالي

روان سعد القحطاني

pharma436@outlook.com @pharma436

Your feedback: https://docs.google.com/forms/d/1sxDqHtpP3bUaOhQmYw96IE7mX-DlrklT5dlZUA2teSI/edit

Kindly check the editing file before studying this document
https://docs.google.com/presentation/d/1_-g1vol4eBWPet5xVCkuTGFvvnhFF3PJmU0tWtEEw_o/edit?usp=sharing

Summary

Levodopa (L-dopa)

Pharmacokinetic	• a precursor of dopamine • Is converted into dopamine via dopa decarboxylase (DC) peripherally and centrally. • Dopamine formed peripherally is metabolized by MAO & COMT enzymes. • 99% L-dopa is decarboxylated to give dopamine by decarboxylase enzyme. • 1% crosses BBB to form dopamine centrally. • Given orally . • Absorbed from the small intestine and taken up to CNS by **active transport system** .(take it with empty stomach) • Short duration of action lead **to fluctuation of plasma concentration.**
Limitation	• **Dyskinesia**. (**The dyskinesia can be reduced by lowering the dosage.)** **Due to fluctuation of plasma concentration.** • **Wearing-off effect .** (duration of "on" states becomes shorter with time) • **On-off phenomenon .** (On= improved mobility & Off=Akinesia or hypomobility) Due to progression of the disease and the loss of striatal dopamine nerve terminals.
P.D	• Dopamine acts on dopaminergic receptors D1-D5 . • D1, D5 →Excitatory. - D2, D3, D4 →Inhibitory.
prescription	• **L-dopa is usually combined with carbidopa** or beserazide . • Benefit of L-dopa + carbidopa combination: 1) Lowers the effective levodopa dose. 2) Increase availability of L-dopa to CNS. 3) Reduce side effects of L-dopa.
Uses	• **1st line treatment.** • The best results of levodopa are obtained in the first few years of treatment. • L-dopa ameliorates all signs of parkinsonism **bradykinesia** & rigidity but does not cure the disease . • **Should not be used in parkinsonism associated with antipsychotic drug therapy.**
interaction	• **High proteins meals .** • **Pyridoxine (Vitamin B6).** • **Non selective MAO inhibitors .**
ADRs	• Anorexia, nausea, vomiting . • Cardiac arrhythmias. • Mydriasis. • orthostatic (postural) hypotension . • depression, delusions, confusion, insomnia, hallucinations.
C.I	• Psychotic patient . • Glaucoma . • Patients with history of melanoma.

DA receptor agonists

Overview	• Have longer duration of action than L-dopa . • less likely to cause **dyskinesias** than levodopa .
Clinical use	• As monotherapy . • can only be used as initial therapy **for early stages** . • In advanced stages, dopamine agonists are used as an adjunct to levodopa.

	Bromocriptine	**Pramipexole**
action	• D2 agonist • T½ = 6-8 h • Longer than Levodopa (t½ =2 h)	• D3 agonist • Used alone as initial therapy or in combination with Ldopa.
Rout of admin.	orally	orally, excreted unchanged in urine.
Indications	Used for the treatment of: 1. Parkinson's disease 2. **Hyperprolactinemia (galactorrhea)** . 3. Infertility in women.	Has the advantage of being free radicals scavenger .
ADRs	Similar to L-dopa: • Nausea, vomiting, • postural hypotension • Cardiac arrhythmias • Confusion, hallucinations, delusions • **Dyskinesias (less prominent) .**	
Contra-indications	• Psychosis • **Peripheral vascular disease** • Recent myocardial infarction.	

Amantadine

action	• **Increases dopamine release.** • Acts as an antagonist at muscarinic receptors . • Antagonist at NMDA receptors (N-methyl-D-aspartate) .
Efficacy	• Less efficacious than L-dopa . • Tolerance develops to its therapeutic effect after 6-8 months. • Its benefits last only for short period and **only used for L-dopa resistance.** • Amantadine and the anticholinergics may exert additive effects on mental functioning.
Indi-cations	• Useful in the early stages of parkinsonism or as an adjunct to levodopa therapy
ADRs	• Nausea, anxiety, insomnia, confusion, hallucinations . • Dry mouth, urinary retention (anticholinergic effects). • Restlessness and hallucinations . • Ankle edema, and livedo reticularis.

MAO-B inhibitors (Selegiline)

Mech. of action	• It is a selective irreversible inhibitor of MAO-B . • The blockade of dopamine metabolism makes more dopamine available for stimulation Mech. of its receptors. Metabolized to desmethylselegiline**, which is anti-apoptotic.** • **may have neuroprotective effect.** • Has anti-oxidant activity .
Indi-cations	• **Adjunctive to levodopa/carbidopa in later-stage parkinsonism .** • **Reduce the required dose of levodopa .** • **Delay the onset of dyskinesia and motor fluctuations that usually accompany long-term treatment with levodopa.**
ADRs	At high doses: - It may inhibit MAO-A →(hypertensive crises) - May cause insomnia when taking later during the day.

Drug	**COMT inhibitors**		**Muscarinic receptor antagonist**	
	Entacapone	Tolecapone	Tolecapone	Trihexphenidyl
action	Acts peripherally to inhibit COMT enzyme .	Peripheral and central COMT inhibitor.	• Central muscarinic antagonist. • It has modest anti-parkinsonian action.	
Indications	Used as adjuvant to L-dopa + carbidopa to: - Decrease fluctuations . - Improve response . - Prolong the ON-TIME .		• **Improve tremor & rigidity.** • **drug-induced parkinsonism, such as in psychosis patients.** • Used during early stage of the disease • adjunct to levodopa therapy.	
ADRs	• L-dopa side effects: • Orange discoloration of urine.		Cycloplegia . Mydriasis . Dry mouth . Urinary retention . Constipation	At high doses: Confusion . Delirium . Hallucinations.

MCQs

1- 60 years old schizophrenic man comes to the hospital complaining of an abnormal walking, slow movements and an observable tremor of his hands when sitting .What is the best approach of treatment recommended for his case?

A) MAO-B inhibitors. B) muscarinic antagonist. C) DA-releaser

2- Patient with Parkinson's disease came to the dermatologist complaining of skin discoloration (livedo reticularis) what Parkinson's disease treatments could cause this reaction?

A) Pramipexole B) Amantadine C) Bromocriptine

3- 30 years women visited the OB-GYN complaining of the inability to get pregnant, her lap results showed an elevated serum prolactin levels. What is the best treatment for her?

A) Bromocriptine B) Amantadine C) Selegiline

4- What of the following should NOT be given with Amantadine?

A) Levodopa B) Bromocriptine C) Trihexyphenidyl

5- Which of the following drugs have a neuroprotective effect?

A) Selegilline B) Amantadine C) Pramipexole

6- The doctor prescribed to 65 Years old man a treatment for Parkinson's disease. After few days, the man came back to the doctor complaining of change in its urine color. What drug of the following have this side effect?

A) Entacapone B) Bromocriptine C) Amantadine

Answers:

1-B (because of schizophrenia=psychosis)
2- B
3- A
4- C (Amantadine have a negative reaction with anticholinergic drugs)
5- A
6- A

MCQs

7- Which one of the following combinations of antiparkinsonian drugs is an appropriate treatment plan?

A) Amantadine, carbidopa, and entacapone.
B) Levodopa, carbidopa, and entacapone.
C) Pramipexole, carbidopa, and selegiline.

8- Peripheral adverse effects of levodopa, including nausea, hypotension, and cardiac arrhythmias, can be diminished by including which of the following drugs in the therapy?

A) Amantadine. **B) Carbidopa.** **C) Pramipexole.**

9- Which of the following antiparkinsonian drugs may cause vasospasm and we can not use it with patient has Raynaud's disease?

A) Bromocriptine **B) Amantadine** **C) Selegiline**

10- Which of the following may delay the onset of dyskinesia and motor fluctuations that usually accompany long-term treatment with levodopa in parkinsonism patient?

A) Trihexyphenidyl **B) Selegiline.** **C) Amantadine**

Answers:
7-B
8- B
9- A
10- B

SAQs

A) 67 Years man with Bipolar disorder comes to the clinic complaining of gait abnormality, slow initiation of movement, tremor and stiff shoulders.
Given that He takes Olanzapine for his Bipolar disorder

1- What is the best treatment for his case and what is the mechanism of action?

we use anticholinergic drugs because of psychosis (Benzotropine or Trihexyphenidyl)
Mechanism of action: Central muscarinic antagonist to decrease the level of Ach.

2- If this treatment was taken in a high dose, what adverse effects it may cause?

Confusion , delirium , hallucination

3- Mention 2 contraindications of this treatment.

Prostatic hypertrophy , Glaucoma , Intestinal obstruction

B) A doctor has prescribed Selegiline + Levodopa + carbidopa to a patient after diagnosing him with Parkinson

1- What is Selegiline mechanism of action?

It is a selective MAO-B inhibitor. It inhibit the dopamine metabolism which lead to more dopamine being available for stimulation of its receptors

2- Mention 2 things that should NOT be co-administered with selegilin.

Tricyclic Antidepressant , Selective Serotonin Reuptake Inhibitors , tyramine (low tyramine diet)

3- The Adverse effects of selegiline if taken at high dose.

It may inhibit MAO-A as well wich leads to hypertensive crisis & Insomnia

4- Why we combine Levodopa with Carbidopa?

Because Carbidopa is act as a peripheral dopa decarboxylase inhibitor which prevent the conversion of levodopa into dopamine before it reaches its target, so we get these Benefits (Lowers the effective levodopa dose, Increase availability of L-dopa to CNS and Reduce side effects of L-dopa)