Drug for Parkinson's disease

Drug	Uses	Pharmacokinetics	Side effect	Drug interaction	Contraindication
Levodopa (L-dopa)	1-Precursor of dopamine 2-First line treatment 3-used combined with carbidopa (Peripheral dopa decarboxylase inhibitor): *To inhibit peripheral conversion of L-dopa to dopamine *To decrease metabolism of L-dopa in GIT and peripheral tissues, Thus,increasing t1/2. *To increase availability of levodopa. *To reduce dose of levodopa and side effects. *Do not cross BBB. -Note: L-Dopa Ameliorates the signs of Parkinsonism particularly bradykinesia But does not cure the disease.	1-absorbed from the small intestine by active transport. 2-Ingestion of meal especially high protein meal interferes with absorption and transport into CNS (taken on empty stomach). 3- Short duration of action t½= 1-2 h (fluctuation of plasma concentration).	1-On-off phenomenon (Off= akinesia or hypomobility) phenomenon (Rx MAOI-B & low protein diet). 2-Wearing-off effect (duration of "on" states becomes shorter). 3-Dyskinesia (involuntary movements occurs in 40 to 90% of patients) due to fluctuating plasma levels of levodopa and the presence of hypersensitive dopamine receptors. 4-Peripheral effects: *Anorexia, nausea, and vomiting (due to stimulation of emetic center). *Mydriasis, orthostatic hypotension, cardiac arrhythmias. 5-CNS effects: (Psychological disorders) mainly psychosis, delusions, hallucinations, confusion, sleep disturbances and depression.	1-Proteins ingested with meals. 2-Pyridoxine (Vitamin B6) bez it diminished the effect of the drug due to increased peripheral metabolism. 3-Nonselective MAO inhibitors (phenelzine) it will cause hypertensive crisis due to increased catecholamines (NE).	1-Psychotic patient. 2-Closed angle glaucoma (due to mydriatic effect). 3-Patients with history of melanoma Why? Bez L-dopa is a precursor of melanin.

Amantadine	1-originally introduced as an antiviral. 2- Amantadine increases dopamine release. 3-Acts as an antagonist at muscarinic and NMDA *(N-methyl-D-aspartate)* receptors. 4- modestly effective in treating symptoms of parkinsonism but last only for short period (few weeks) and only used for L-Dopa resistance.	1-given orally with short half life. 2-most of the drug being excreted unchanged in the urine.	1-Nausea, anxiety, insomnia, confusion, hallucinations (dopamine like side effects). 2-Dry mouth, urinary retention (anticholinergic effects). 3-Restlessness and hallucinations (NMDA antagonist).		
Dopamine receptor agonists	➢ Ergot derivatives Bromocriptine ➢ Non ergot derivatives Pramipexole 1-Dopamine agonists are used in advanced Parkinson's disease with fluctuation and dyskinesia. **Bromocriptine** 1-Bromocriptine, an ergot derivative, is an agonist at D2-receptors. 2-Rx of hyperprolactinemia *(galactorrhea)* 3-Rx of infertility in women. **Pramipexole** 1-Non Ergot dopamine agonist 2-Used alone or in combination with L-Dopa. 3-Has the advantage of being free radicals scavenger.	1-Have longer duration of action than L-dopa *(less likely to cause dyskinesias than levodopa)* **Bromocriptine** 1-Is given orally, short t1/2.	**Bromocriptine** 1-Nausea, vomiting, postural hypotension 2-Confusion, hallucinations, delusions 3-Dyskinesias (*less prominent*). 4-To minimize adverse effects, the dose is built up slowly over 2 or 3 months. **Pramipexole** 1-similar to L-Dopa, but less dyskinesias.		**Bromocriptine** 1-Psychosis 2-Peripheral vascular disease 3-Recent myocardial infarction

Selegiline	**1-Selegiline is an irreversible inhibitor of MAO-B.** **2-It inhibits dopamine degradation by MAO-B in CNS.** **3-It increases dopamine available for its receptors.** **4-It slows the disease progression by reducing the formation of toxic *free radicals* produced during dopamine metabolism (*antioxidant*).** **5-Selegiline is metabolized to desmethylselegiline, *Which is (antiapoptotic).*** **6-As monotherapy, may be effective in the newly diagnosed patient with parkinsonism.** **7- Combined with levodopa / carbidopa in later-stage parkinsonism to:** ***reduce the required dose of levodopa** ***delay the onset of dyskinesias and motor fluctuations that usually accompany** **long-term treatment with levodopa.**		**1-At high doses, selegiline may inhibit MAO-A *(hypertensive crises).*** **2-May cause insomnia when taken later during the day**		**1-Selegiline should not be co-administered with tricyclic antidepressants, or selective serotonin reuptake inhibitors *(may cause hyperpyrexia, agitation, delirium, coma).***

COMT Inhibitors (Catechol-O-methyl transferase) Inhibitors Entacapone	1-Acts peripherally and centrally to inhibit COMT enzyme required for dopamine degradation. 2-It is used: as adjuvant to L-Dopa to: – Decrease fluctuations – Improve response – Prolonged the ON-Time.		1-L-Dopa side effects. 2-Orange discoloration of urine.		
Anticholinergic Drugs Benztropine	1-muscarinic antagonist. 1-Has modest anti- parkinsonian actions. 3-used during the early stages of the disease or as an adjunct to levodopa therapy. 4-Provide benefit in drug-induced parkinsonism (antipsychotics).		1-Cycloplegia, dry mouth, urinary retention, and constipation. 2-Confusion, delirium, and hallucinations may occur at higher doses.		1-Prostatic hypertrophy 2-Glaucoma 3-Intestinal obstruction

Done by: Sara ALShehri