**Parkinson Disease**

Parkinson disease is a condition that is progressive and leads to the loss of nerve cells in the brain. However, the main cause of PD is not known. Most of the explanations given of symptoms of people suffering from PD are by cells being lost that has the neurotransmitter known as dopamine. This is a chemical that nerve cells release in order to communicate with other nerve cells. It has a number of functions in the brain that are important like playing roles that are important in behavior, movement that is voluntary, cognition, learning and working memory. This paper will look at the pathophysiology and pharmacology of Parkinson disease.

**Pathophysiology of Parkinson disease**

Tremors, movements that are slow (bradykinesia), rigidity of the muscle, abnormalities in postures, speech that is unclear or difficult (dysarthria), difficulty in swallowing (dysphagia), and cognitive abnormalities are symptoms that manifest PD. As a result, there is a part of the brain known as substantia nigra that starts to degrade. The degradation leads the loose of neurons by substantia nigra that produce dopamine which is a neurotransmitter that is inhibitory that is needed for muscle movements that happen normally (Magrinelli, Picelli, Tocco, Federico, Roncari, Smania & Tamburin, 2 016). As the neurons that produce dopamine degrade, excitatory (cholinergic) neurotransmitters will have more room of being active and lead to tremors, rigidity in the muscles and other dysfunctions of the muscles that are related to Parkinson disease (Huether & McCance, 2012). This is why Mr. Drew felt rigidity in his wrists, limitations in seeing, and tremor in his right arm.

The hallmark that is pathological of Parkinson disease is of neurons known as dopaminergic that are degenerated in the substantia nigra pars compacta that results in striatal dopamine depletion. The inhibitory and excitatory outflow is regulated by the transmitter of the basal ganglia.

Some neurons that are surviving contain Lewy bodies or eosinophilic intracytoplasmic inclusions that are in part made of many proteins. The accumulation of proteins is speculated by some to play a function that is prominent in the pathogenesis of both sporadic PD and familial. Also, the way that proteins appear in the Lewy bodies tends to give support to the notions. Lewy bodies appear as a representation of the aftermath of the underlying pathology. There is evidence that the inclusions that are intracytoplasmic do not appear to cells and at times can be cytoprotective (Weintraub, Comella & Horn, 2008). Neurodegeneration of the nigra pars compacta can be present in the absence of neurodegeneration. However, the presence of Lewy bodies is needed for confirmation that is pathologic of a diagnosis that is clinical of iPD.

The process of neurodegenerative in PD is not limited to the nigra pars compacta, the loss of neurons with Lewy body formation also takes place in other regions of the brain. This can account for features that are both motor and nonmotor of the disease.

**Pharmacology of Parkinson disease**

1. L-dopa

In the brain, degeneration in the basal ganglia of Parkinson disease mostly has effects on dopaminergic neurons in the substantia nigra and leads to a deficiency of dopamine. L-dopa that is exogenous replacing deficient neurotransmitter that is endogenous. Dopaminergic neurons take up L-dopa that are remaining where it goes through the terminal being decarboxylation that is presynaptic to form dopamine (Lindgren et al., 2010).

Normally L-dopa is combined with carbidopa or benserazide. The two are not able to cross the barrier of the blood in the brain but inhibits the L-dopa conversion to dopamine peripherally through aromatic acid decarboxylase enzyme being blocked that leads to the reaction being catalyzed. This leads to the adverse effects of dopaminergic being reduced, the amplification of central delivery and reduction of the dosage of L-dopa. L-dopa is a drug that is effective in treating Parkinson disease. This is because the drug is tolerated in a good manner and the side effects especially the symptoms that are psychiatric, orthostatic hypotension and nausea are limited. Some of the side effects of L-dopa include dizziness or an onset of sleep that is sudden, activation of malignant melanoma, hepatotoxicity and hemolytic anemia (Vallerand et al., 2013). L-dopa increases the levels of brain noradrenaline which in return reduces vigilance and impairment in sleep.

1. Dopamine agonists

   The drugs that belong to this class are able to act in a direct way on dopamine receptors and their classification is into ergot derivates and non-ergolines. The ergot derivates include lisuride, bromocriptine, cabergoline, and pergolide while the non-ergolines include ropinirole, apomorphine and pramipexole (Borovac, 2016).

Dopamine agonists have a duration of actions that are long that mimics the release of physiological tonic of action closely from nigral neurons that are normal and may help in the prevention or reduction of motor fluctuations. In practice that is clinical, there have been findings that dopamine agonists are efficacious in Parkinson disease. These are mostly used as therapy that is adjunctive to L-dopa after a person has hadcomplications that are connected to motor have developed but in some cases may be taken as monotherapy before the start of L-dopa especially in patients that are young (Borovac, 2016).

Nausea is a side effect that is common of dopamine agonists because of the area in the medulla, postrema, being stimulated which is a region that is not inside the barrier of the blood-brain. Also, the peripherally that is acting dopamine antagonist domperidone may increase the symptom of parkinsonian. Another side effect includes hallucination.

1. Amantadine

Amantadine is an agent that is antiviral and has been used for many years in Parkinson disease. It can lead to an increase of dopamine noradrenaline presynaptic reuptake blocker, dopamine, and synthesis and has an action that is anticholinergic that is mild. Amantadine has influences on predominantly akinesia and rigor and has an effect that is mild on rest tumor. Two-thirds of patients that have Parkinson disease have showed an improvement on monotherapy for amantadine (Smulders et al., 2016). There is a study that showed that amantadine can lead to the reduction of L-dopa dyskinesias that is induced in patients that have Parkinson disease with no alteration of the antiparkinsonian effect of L-dopa. There is caution use that is needed in renal failure considering that it is removed in the urine. The side effects of the use of amantadine are livedo reticularis, hallucinations, nightmares, oedema, and insomnia.

1. Monoamine oxidase B inhibitors

Some of these classes of drugs are selegeline. Selegeline is irreversibly and selectively inhibits both extracellular and intracellular monoamine oxidase B and thus leads to the reduction or delaying dopamine being broken down to hydrogen peroxide and dihydroxyphenylacetic acid (Riederer & Laux, 2011).  The two have been found to lead to damages of oxidative in dopaminergic neurons in the substantia nigra. In addition, it hinders the reuptake of dopamine from the synaptic cleft. The addition of selegeline to L-dopa can give room to a dose of L-dopa being reduced of about 10-15 percent. The fluctuations of responses in L-dopa that are mild can often be reduced by the addition of selegeline. The side effects of L-dopa that include problems that are psychiatric and dyskinesias are enhanced potentially by selegine. There is also a possibility of orthostatic hypotension occurring.

1. Catechol O-methyl transferase inhibitors

The conversion of dopamine from L-dopa is by a reaction that is catalyzed by an enzyme known as aromatic acid decarboxylase that is hindered by benserazide and carbidopa. The metabolism of L-dopa that is peripheral and significant is also shown by catechol-o-methyldopa. As the inhibition of acid decarboxylase that is aromatic by L-dopa preparation that are conventional takes place the metabolism that is peripheral is shunted towards reactions that are catalyzed by COMT. Adding a COMT inhibitor as a form of therapy that is adjunctive to L-dopa together with benserazide or carbidopa results to reduction of the metabolism of L-dopa peripheral, leads to the prolongation of the half-life of plasma of L-dopa and leads to an increase in the amount that is found in the brain. The addition of COMT inhibitors will not alter the peak concentration of L-dopa. Some of the side effects of using COMT inhibitors are nausea, potentiation of dyskinesia, urine being discolored to color orange, and disturbances while sleeping.

1. Anticholinergics

Stiffness and tremor are improved by anticholinergic drugs to a degree that is greater than akinesia and in effect they are mild. Because of the action that is peripheral parasympathomimetic, side effects like the mouth being dry, glaucoma, a vision that is blurred, urinary retention and constipation can occur (Dauphinot et al., 2017). This is why the drugs should be used in a cautious manner especially for the elderly.

Parkinson disease results from loss of neurons that is gradual that produce dopamine. Many people are affected by Parkinson disease in the world. There is no clear understanding of the causes of PD but there are treatment options that can be used. L-dopa is the best treatment for patients that are elderly is L-dopa especially in the early stages because it is the therapeutic window that is best when it comes to side effects that are psychiatric. Considering the view that there is a high potential of causing confusion it is advisable to avoid anticholinergics but the drugs that can be used are amantadine and dopamine agonist. Selegeline can be used but the need of L-dopa being delayed for a number of years in this age group as Mr. Drew is less meaningful.

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