

A REVIEW ON PHARMACOLOGICAL TREATMENTS OF VARIOUS DRUGS IN PARKINSON'S DISEASE

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ABSTRACT: Parkinson's disease is generally observed in the field of neurology, but the treatment and the medication can cause. Sometimes, medication can be difficult for PD patient because the selection of drugs is restricted as well as levodopa-induced dyskinesia (LID) is frequently observed in Parkinson's patients who are treated by levodopa. Different surgical techniques that include pallidotomy, deep brain stimulation have shown effectiveness for PD patients. There is no cure for the disease, there are there are many options for the earlier treatment for PD. However, managing long-term motor complications and non-motor symptoms is difficult and could be a benefit to more studies in the field of clinical research.

Keywords: Neurology, Parkinson's, Brain disorder, Levodopa, Dopamine.

INTRODUCTION:

James Parkinson who was born on 11 April 1755, the first child of Mary and John Parkinson his description leave one doubt as to whether he examined his patients in conventional. The most complete pathologic analysis of Parkinson disease and the clear delineation of brain stem lesions was performed in 1953. This disease has taken place from ancient time. In the year 1817 he published a review with detailed about the medical essay which was titled "An Essay on The Shaking Palsy" also he reported 6 to 7 cases during his practice. Charcot, he was the first to recognize the importance of Parkinson's work and name the disease after him. During his practice Parkinson's patients were identified with the disease and later they found that there were low levels of dopamine and the degeneration of nerve cells in the part of the brain called as the "Substantia Nigra" this was effective treatment for the following disease with dopamine against a possibility. Further clinical description and the research and the changes taking place related to the Parkinson disease were successfully reported by the French neurologist Richer and Miegé in the year 1895 they provided a morphological detail about of the different stages of the Parkinson's disease disability. The first symptom gives a signal of slight weakness also trembling commonly in the hands and the arms in early of twelve months or more than that, he also mentioned that this disease usually occur in the age 50, 65, 55, 72 and further years specially in the men, it is curious to know that no women were described here, this disease was considered a syndrome of the motor cortex by his predecessors, the disease is also known as the Parkinsonism, the most affecting is the stressed which can increase the risk of the disease due to this the stress level can disturb or can harm the dopamine cells in the part of the brain this can be dangerous for the health also the research says that the it can affect the memory of the person like it can show the symptoms of the forgetfulness it may disturb with your concentration level there is record of 117,400 deaths due to this disease in the year 2015 also the disease impacted that by the year 2030 it will affect more than nine million people as per the reports it is difficult to detect or identify the symptoms of the disease, there is a constant pressure to the patients due to the delayed in the treatment and this is affecting the quality of lives of millions of old aged people or else the seniors more than age 50. Also the dangerous early treatments of Parkinson's disease involved the use of a suspension apparatus stretched the spinal cord. This also result in the family history but there are less chances to transfer in this way.



James Parkinson [1755-1824]

The disease of Parkinson's (PD) commonly referred to as Parkinson's disease is a degenerative condition in the brain, which mostly affects the motor part of the system. The signs typically appear gradually, and as the illness worsens, non-motor signs are more frequent. The most evident early signs include tremors and rigidity, slowness of movement, as well as difficulty in walking. The behavioural and cognitive issues can be present too with anxiety, depression and apathy affecting many individuals with PD. The symptoms of Parkinson's disease are common place during the later stages of this disease. People with Parkinson's may also experience problems with sleeping and sensorimotor systems. Motor symptoms associated with the disease stem from the loss of cells of the substantiating which is a region in the midbrain. This causes the loss of dopamine. The reason for this cell's death is unclear, however it is a result of the accumulation of misfolded proteins in Lewy bodies, neurons. Collectively, the most prominent motor symptoms are referred to as Parkinsonism, also known

as parkinsonian syndrome. The reason for PD is unclear, with environmental and inherited factors being believed to play a part. People with an affected family member are at a higher risk of developing the disease with certain genes believed as susceptible to inheriting risk factors. Another risk factor is people who are exposed to pesticides, and those who have had previously had head injuries. Tea drinkers, coffee drinkers, as well as tobacco smokers are less at risk.

The diagnosis of most cases is mostly determined by symptoms that are triggered by motor problems being the most frequent complaint. Neuroimaging tests (magnetic resonance or image to assess dopamine neuronal dysfunction, also known by the name of Data scan) can aid in determining if there are other illnesses. Most cases of Parkinson's disease occur for people older than 60, and around one percent sufferers. Males are more frequently affected than females, with 3:2. If it occurs among people who are not yet of 50, it is known as early-onset PD. By the year 2015, PD affected 6.2 million individuals and led to around 117,400 deaths across the globe. The life expectancy for a patient following diagnosis ranges from 7 to 15 years. There is no solution for PD is available; however, treatment is designed to minimize the impact of symptoms. The initial treatment typically involves the medication levodopa (L-DOPA) and MAO-B inhibitors or dopamine agonists. As the disease progresses the effectiveness of these drugs decreases as well as simultaneously causing an adverse effect that is characterized by uncontrollable muscle movements. In this stage, the medication can be administered together and dosages could be increased. Certain forms of diet and rehabilitation have demonstrated some efficacy in reducing symptoms. The procedure of placing microelectrodes to provide stimulating the deep part of your brain has been performed to alleviate motor symptoms in extreme instances where medications are not effective.

Evidence for treatment options for non-movement-related symptoms of PD including emotional and sleep problems are less convincing.

Classification: It is by far the most well-known form of Parkinsonism. It is often referred to as "Idiopathic Parkinsonism" that is, parkinsonism with no known reason. It can be described is referred to as a form of neurodegenerative disorder called synucleinopathies to an abnormal accumulation of the protein alpha-synuclein in brain. Synucleinopathies is a distinct classification from neurodegenerative illnesses like Alzheimer's disease where the brain can accumulate an additional protein called Tau protein. A significant overlap in pathology and clinical is observed among Tauopathies and synucleinopathies. Contrary to PD those with Alzheimer's are most likely to suffer from memory loss. The most prominent symptoms of PD (slowness and tremors stiffness, stiffness, and postural instability) are not typical symptoms of Alzheimer's disease.

Sign and symptoms:

The signs and symptoms of Parkinson's disease may differ for each person. Initial signs could be minimal and not be noticed. The symptoms typically appear with one part of your body, and tend to be more severe on that side even when symptoms start to take a toll on the limbs from both angles. The signs and symptoms of Parkinson's disease could include: **Tremor:** A tremor, or a rhythmic shaking, typically begins with a limb, typically the fingers or hands. It is possible to move your forefinger and thumb between your thumb and forefinger. This is referred to as an erratically rolling tremor. Your hands may shake while you are at peace. The shaking could diminish when you are doing tasks. Slowed movement (bradykinesia). As time passes, Parkinson's disease could slow down your movement and make simple tasks more demanding and demanding.

The steps you take may be shorter as you walk. It might become difficult for you to step up from your chair. It is possible to be dragging or shuffled while you walk. Muscles that are rigid. The stiffness of muscles can occur throughout your body. The muscles that are stiff can be painful and restrict your motion. A lack of balance and posture. Your posture can be slouching. You could fall, or suffer from balance issues because of Parkinson's disease. Loss of automatic movement. It is possible that you will lose the ability to do unconscious movements such as blinking, smiling, or swinging your arms while you walk. Speech changes. You might speak slowly, softly, or even slur when speaking. Your speech could seem more monotonous and not follow the normal speech patterns. Writing styles change. It might become difficult to write, and your work could appear to be tiny.

Causes:

In Parkinson's disease certain neurons (neurons) within the brain are gradually destroyed or cease to function. Most symptoms result from a reduction in the number of neurons that create the chemical messenger that is found within your brain that is known as dopamine. If dopamine levels drop this causes abnormal brain activity, which can result in diminished movement and other signs of Parkinson's disease. The root cause of Parkinson's disease is not known. However, a variety of factors are believed to play a part in the development of Parkinson's disease, such as: Genes. Researchers have identified certain genetic modifications that may trigger Parkinson's diseases. These are not common, except in rare instances with many relatives affected by the disease. Certain

gene variants are believed to enhance the chance of having Parkinson's disease, but they have a tiny risk of developing Parkinson's disease for all the genetic indicators.

Exposed to certain toxins or environmental elements can increase the chance of developing the disease later, but the risk is minimal. Researchers have also observed that there are a variety of changes within the brains of patients suffering from Parkinson's disease. However, it is not clear what causes these changes. The changes that are observed includes the presence of Lewy body. Clumps of certain substances inside the brain are microscopically visible indicators for Parkinson's diseases. These are known as Lewy bodies. Researchers believe that Lewy bodies provide a key information about the underlying cause of Parkinson's disease. Alpha-synuclein is a protein found within Lewy bodies. While many different substances can be found in Lewy bodies, researchers believe that one of the most important is a naturally occurring and widely used protein known as Alpha-synuclein (a-synuclein). It is found throughout Lewy body parts in a form that is clumped so cells are not able to degrade. This is an ongoing research area for Parkinson's disease researchers.

Risk factors: The risk causes for the diseases:

Age: Young adults are less likely to suffer from Parkinson's disease. The disease usually manifests in late or middle age and the risk for developing the disease grows with the advancing years. Most people will get the disease when they are 60 or more. If a person is young and is diagnosed with Parkinson's disease genetic counselling can help with the right family planning decisions. Social-work and the effects of medication differ in the case of an older person suffering from Parkinson's disease. They require special care.

Heredity: If you have a family member who has Parkinson's disease can increase the likelihood that you will get the condition. Males are more likely to be diagnosed with Parkinson's disease than females. Regular exposure to herbicides and pesticides could increase your risk of contracting Parkinson's disease.

Complications:

Parkinson's disease is often triggered by other problems that can be treated Problems with thinking: It is possible to suffer from cognitive impairment (dementia) along with problems in thinking. They are typically seen in the later stages of Parkinson's disease. These cognitive issues aren't usually treated with medication. Depression and emotional shifts can alter your state. There are instances when you could be depressed typically in the early stages. The treatment for depression can help in the treatment of additional issues associated from Parkinson's illness. There are also other emotions such as anxiety and fear or feeling of being unmotivated. The doctor you see might prescribe medications to help manage these symptoms. Problems swallowing: It's possible to have difficulty swallowing when your condition becomes more severe. The saliva can accumulate inside your mouth due to slowing the process of swallowing, which could result in your mouth becoming drooling. In the later stages it can affect the muscles of the mouth, making chewing more difficult. This may lead to chokes and inadequate nutrition. The sleep disorder and the sleep issues. Patients suffering from Parkinson's disease are often suffering from sleep problems, which could include frequent awakenings through the night, rising early, or staying awake throughout the daylight hours. People may also be suffering from frequent eye movements, a sleep-related disorder which involves reliving dreams. A medication regimen may help enhance sleep.

The problem with the bladder: Parkinson's disease can cause bladder problems that cause problems with bladder control. For instance, if you are unable to regulate the frequency of your urination or difficulty getting a urinate, a large number of people with Parkinson's disease suffer from constipation. It is usually caused by a slower digestion. It may also be due to blood pressure may fluctuate. You may feel dizzy or lightheaded while standing because of an abrupt reduction in your blood pressure (orthostatic hypotension). The smell of a problem: It's possible to experience problems with your sense of smell. It's possible that you cannot identify certain scents, or distinguish between various scents.

TREATMENTS:

There is no specific treatment for the Parkinson's disease but to overcome the motor and non-motor symptoms of Parkinson's disease there are some medication, surgical procedures, and physical therapies:

Medications: There are some drugs or preparations that are used to treat symptoms of disease as their problem of signalling the body by brain. As they do not have enough dopamine in their brain gives rise to problems in controlling functions and body movement. Drugs such as levodopa, rasagiline, ropinirole, pramipexole, selegiline, etc are used to treat the low levels of the dopamine in brain, stiffness, tremors, spasms and poor muscle control, rigidity, etc.

Surgical Procedures: The surgical treatments for those who have optimized and exhausted medications for Parkinson's tremor, or profound motor fluctuations. at present most favourable treatment for Parkinson's disease are known as deep brain stimulations (DBS) and Duopa.

Physical therapies: There are well-known exercises of all kinds is beneficial for the patients with Parkinson's disease. As it increases the mobility, strength, balance of body and help to remain in active state of mind. They

are Amplitude training, reciprocal pattern, balance work, stretching and flexibility, strength training and meditation i.e., yoga, etc.

DRUG CLASSIFICATION:

Motor:

Sr No	Class	Treatment	Drug Name	Side Effects
1	Dopaminergic agents	Redness tremor, Stiffness, Slow movement	Levodopa And Carbidopa	Sleep problem, Jerky muscles movement, low blood pressure
2	Monoamine Oxidate inhibitor	Prevents the breakdown of chemical dopamine	Selegiline	Nausea, headache, Confusion Severe high blood pressure
3	Dopamine agonists	Stimulate directly to dopamine receptor	Apomorphine , Retigabine	Hallucination, Swelling in limbs
4	Catechol-o-methyl transferase	Treats the motor fluctuational movements	Tolcapone, Entacapone	Dyskinesia, Diarrhoea, Orange colour urine
5	Anticholinergics	Reduces the symptoms of bothersome tremors and difficult in walking	Benztropine, Trihexyphenidyl	Blurred vision, dry mouth, rapid heat rate
6	Adamantants	Helps to reduce the dyskinesia	Amantadine	Livedo reticularis, swelling in ankles

Non-motor:

Sr NO	Class	Treatment	Drug Name	Side Effects
1	Selective serotonin uptake inhibitors	Medication to treat depression	Nortriptyline	Nightmares, constipation, weakness
2	Cholinesterase Inhibitors	Reduced difficulties in memory and thinking	Rivastigmine Donepezil	Stomach ache, loss of appetite
3	Antipsychotic	Reduced psychosis and hallucination	Quetiapine, clozapine	Dizziness, irregular periods
4	Neuroprotective	Slow down the progression of disease on CNS	Tacrolimus cyclosporine	Numbness of limbs, uncontrolled hair growth

CONCLUSION:

The verification is that to managing Parkinson's disease motor and non-motor symptoms and medicinal effect is highly moderate. And it also concluded that genetic factors and environmental factors play an important role to degenerate neurons. Now-a-days multiply therapies are in development based on currently hypothesis of disease pathogenesis.

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