

The Review Article on Parkinsons Disease

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Abstract :-

Parkinson's disease is a common movement disorder that doctors see in neurological care, but it can be hard to diagnose and treat. The diagnosis is based on the patient's symptoms and can be tricky because people with Parkinson's may have many motor and non-motor symptoms. Treating Parkinson's can be difficult because there are not many drug options available, and the main treatment is levodopa. However, a common side effect of taking levodopa is called levodopa-induced dyskinesia (LID). This side effect usually happens after a long time on the medication, but sometimes it can appear even after just a few days or months. Different types of surgeries, like unilateral pallidotomy and deep brain stimulation, have worked well for people who can't be treated effectively with medicine alone.

Key Words :- Deep brain stimulation, dopaminergic drugs, Parkinson's diseases

Introduction :-

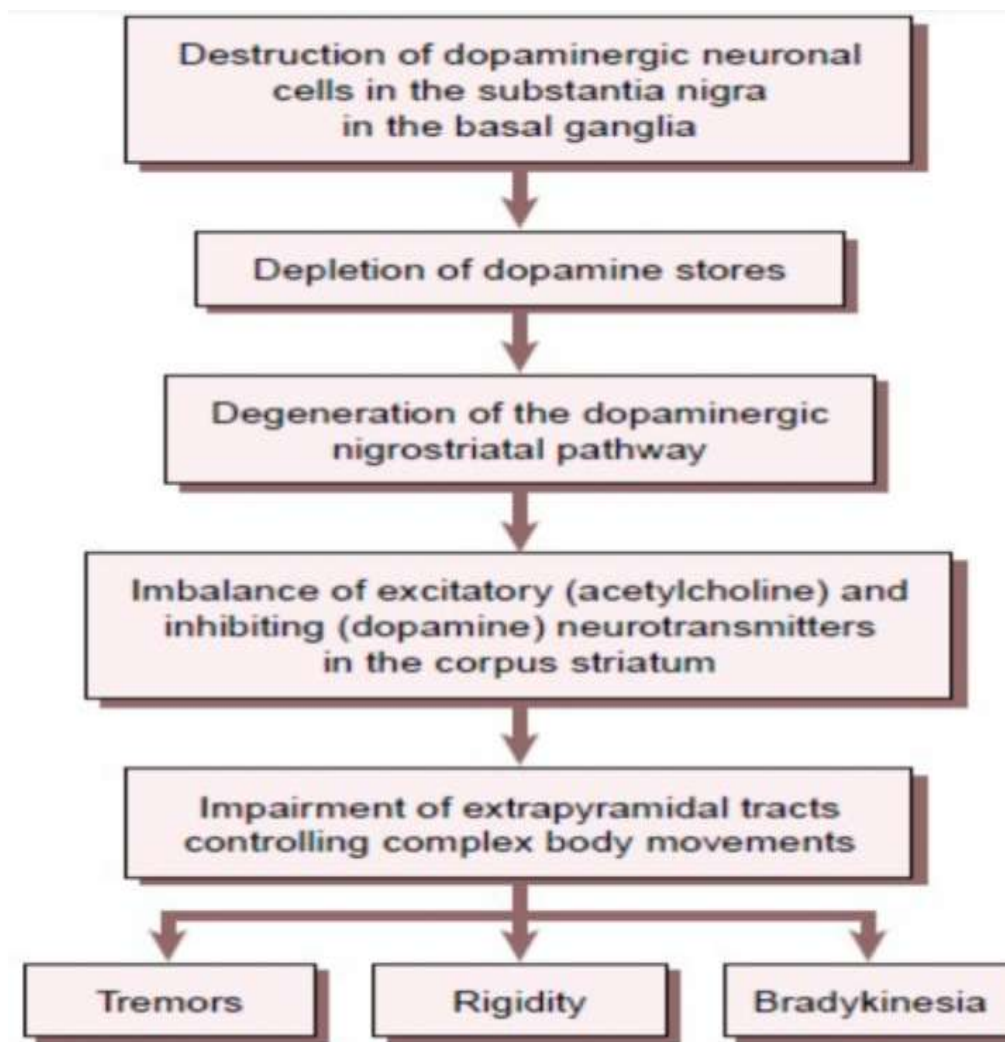
Parkinson's disease is a long-term, gradually getting worse condition that affects the nervous system. It starts with the early loss of certain brain cells called dopaminergic neurons in a part of the brain called the substantia nigra pars compacta. This loss causes a decrease in dopamine, a chemical that helps control movement. This leads to the main symptoms of Parkinson's, like slow movement, shaking, stiffness, and later, difficulty with balance. Besides the movement problems people with Parkinson's also experience non-movement symptoms, which can appear years before the movement problems get worse. These non-movement symptoms can become more serious as the disease progresses. Right now, the main way to treat Parkinson's is through medicines. However, these treatments have big limits when the disease becomes more severe. As the disease goes on, more problems appear, such as non-movement symptoms, movement issues that don't get better with dopamine, and side effects from long-term use of dopamine medicines. Even though there have been major improvements in both medical and surgical treatments for Parkinson's, there is still no treatment that can stop the disease from getting worse. But researchers are optimistic that they will find new ways to target and stop the disease's progression. In this review, we will talk about how common Parkinson's is, the signs and symptoms, what causes the disease, how it is diagnosed, and the treatments available. We won't discuss experimental treatments that have not shown much success so far.

Epidemiology :-

Parkinson's disease (PD) becomes more common as people get older. About 1% of people aged 65 and above have PD.[1] Early-onset Parkinson's disease (EOPD) happens when symptoms start before age 40. It makes up 3 to 5% of all PD cases. It is split into two types: juvenile PD, which starts before age 21, and young-onset PD (YOPD), which starts between 21 and 40 years of age.[2] Parkinson's is more common in men than women in most areas.[3,4] Female hormones may help protect women from PD. This difference could be because of genetic factors or how men and women are exposed to environmental risks.[3,4] There isn't a lot of large-scale data on PD in India. Razdan et al. found that in rural Kashmir in northern India, the overall rate of PD was 14.1 per 100,000 people among 63,645 people. The rate was higher, at 247 per 100,000, for people over 60 years old.[5] In Bangalore, in southern India, the rate was lower, at 27 per 100,000. In rural Bengal, which is in the eastern part of India, the rate was 16.1 per 100,000. [6,7] Bharucha et al. found a much higher rate of 328.3 per 100,000 among 14,010 Parsis living in colonies in Mumbai, which is in western India. [8]

Pathophysiology :-

The pathological definition of PD is loss or degeneration of the dopaminergic (dopamine- producing) neurons in the substantia nigra and improvement of Lewy our bodies in dopaminergic neurons (9). Pathologic changes might also precede apparent signs with the aid of two decades or more (10). This preferential lack of dopamine producing neurons outcomes in marked impairment of motor control. Lewy our bodies, or atypical intracellular aggregates, incorporate various proteins which include alpha-synuclein and ubiquitin that impair best neuron functioning.



Risk Factor :-

Environmental factors that can affect health are studied to understand how they might lead to certain disorders. Traditionally, this has been done through clinical research, which can be done in a cross-sectional way using clinics or networks, or through population-based studies. Many environmental risks have been linked to health issues, such as exposure to pesticides and heavy metals, living in rural areas, working in agriculture, having a head injury, a history of cancer, consuming dairy products, and having type 2 diabetes (which can be managed with medication), among other factors.

Even though these links are based on some biological plausibility, many of the observations can't be consistently reproduced. A recent meta-analysis that looked at both quantitative and qualitative studies on different environmental exposures found that some of these connections are not very consistent anymore (including things like living in rural areas, drinking well water, farming, and pesticide exposure). (11) While other meta-analyses confirmed a strong link with pesticide exposure, (12) others found no support for a connection with traumatic head injury. (13) Because of

various challenges and natural limitations, it's not surprising that these kinds of studies sometimes give different results. Age is the biggest risk factor for Parkinson's, with the average age of onset around 70. Parkinson's can happen to younger adults, but that's quite rare. Genetics also play a role—having a parent or sibling with Parkinson's increases your risk, but it's uncommon for the disease to be passed down in this way. Environmental exposure, like being around insecticides, herbicides, and other pollutants, can also raise your chances. People who live near industrial areas may also be at greater risk.

Clinical Presentation:-

The way Parkinson's disease (PD) shows up includes four main areas: motor symptoms, changes in thinking, behavior or mental health changes, and problems from the autonomic nervous system. Everyone experiences these in different ways, with some areas being more noticeable than others. Each of these areas will be explained in detail. The main motor signs of PD are tremor, slow movement (bradykinesia), stiffness (rigidity), and loss of balance (postural instability). The loss of balance often happens as the disease gets worse over time. A common way to remember the main motor symptoms is T-R-A-P, which stands for Tremors (especially at rest), Rigidity (sometimes with jerking movements), Akinesia (or slow movement), and Posture (such as a shuffling walk). Studies show that motor symptoms usually appear when about 50 to 70% of the neurons in the substantia nigra are damaged. Other conditions, like LBD, PSP, CBD, and MSA, have different symptoms compared to classic PD. These differences are covered in other references and are not discussed here. The classic tremor seen in PD starts when the body part is not moving, like when you're resting. It usually begins on one side of the body and can later affect both sides. This type of tremor is most common in over 70% of PD patients. Bradykinesia, or slow movement, is often described as feeling tired or weak. It can be seen in difficulty with fine motor skills, shuffling steps, or getting up from a chair. People often have trouble opening packages or containers. Stiffness is a common symptom in nearly all PD patients.

It may start on one side but can spread to the other. During a physical exam, this stiffness is often described as "cogwheel" rigidity, similar to a gear's pattern. As the disease progresses, patients may develop postural instability, which increases the risk of falling. If someone falls early in the disease, it might suggest another condition like PSP. Another possible symptom is "festination," where the person takes smaller, faster steps, almost like running. Postural instability is one of the hardest symptoms to treat with dopamine-based medicines. Also, there may be non-motor symptoms that appear years before the motor symptoms. These can include constipation, a reduced sense of smell, problems with dreaming during sleep, low blood pressure when standing, depression, urgency to urinate, and issues with sexual function. Because there are no clear biological markers for PD, treatments that could protect neurons (if they existed) couldn't be used to stop the disease from getting worse.

Motor Symptoms:-

Parkinson's disease is linked with resting tremor, which usually starts on one side of the body, slow movement (bradykinesia), stiffness in the muscles, a shuffling walk, and trouble with balance. The beginning of the disease is slow and people might think the symptoms are just part of getting older. The symptoms get worse over time, but how quickly they progress varies a lot from person to person. There are different types of Parkinson's disease where one symptom, like tremor, stiffness, or balance issues, may be more noticeable. In addition to the usual motor symptoms, there are other movement-related problems. These include a blank facial expression (hypomimia), slower blinking, blurred vision, difficulty looking upward, muscle spasms (dystonia), sagging posture, trouble turning over in bed, curved spine (kyphosis), sideways curve of the spine (scoliosis), shuffling walk, freezing (when you can't move), and speech problems like speaking very softly (hypophonia) or repeating words or phrases (palilalia).

Non-Motor Symptoms :-

Parkinson's disease is connected with a resting tremor, which usually begins on one side of the body. It also causes slow movement, called bradykinesia, muscle stiffness, a shuffling walk, and balance problems. The disease starts slowly, and people might think the symptoms are just a part of aging. Over time, the symptoms get worse, but how fast they progress can be different for each person. There are different types of Parkinson's disease, where one symptom, like tremor, stiffness, or balance issues, might be more noticeable. Besides the main movement problems, there are other movement-

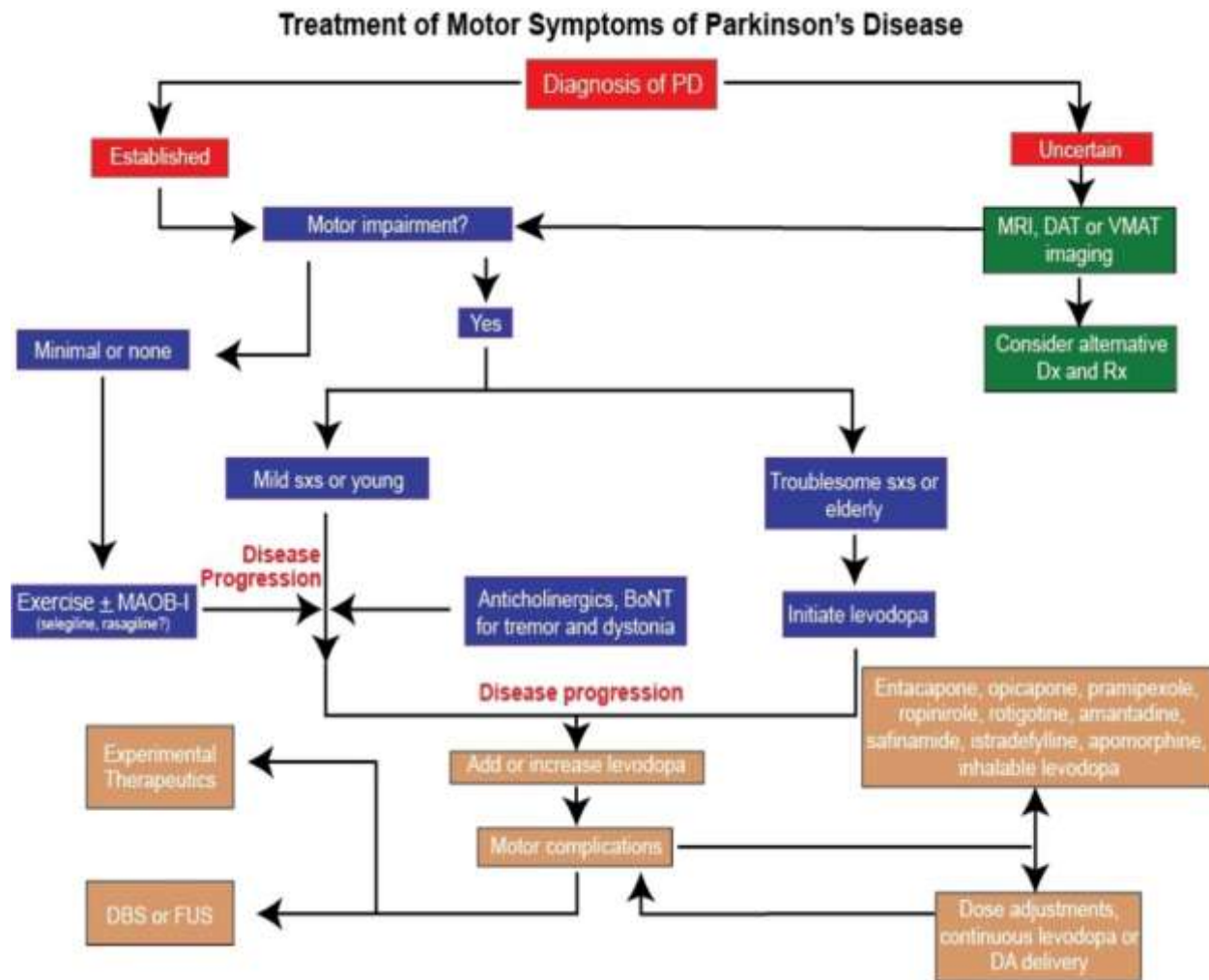
related issues. These include a blank or expressionless face, slower blinking, blurry vision, trouble looking up, muscle spasms, a slouched posture, difficulty turning over in bed, a curved spine, a sideways curve of the spine, shuffling walk, freezing when you can't move, and speech problems like speaking very softly or repeating words and phrases.

In addition to the development of non-motor symptoms of PD as a component of the disease, therapy used in PD can exacerbate or cause the symptoms. For example, psychosis, orthostatic hypotension and, sleep attacks may relate to Ldopa dosing or side effects (/). Cognitive dysfunction and dementia are common in PD, but develop over time. The dementia of PD is subcortical with altered personality, psychomotor retardation, and memory problems.



Treatment:-

Parkinson's disease is a complex brain disorder that affects both movement and other non-movement functions. Because of this, each person with the condition may need a different treatment plan. Medical studies that aim to provide reliable results should include a clear group of patients and comparison groups. They should also use the best, most accurate tools to measure how well treatments work. Even though many tools are used to check how patients respond to different treatments, the Unified Parkinson's Disease Rating Scale, or UPDRS, is most commonly used as the main way to measure outcomes in research studies. Table 1 and Figure 4 show an overview of common and surgical treatment options for people with Parkinson's disease at different stages of their condition. In addition to traditional treatments, we also provide information on evidence-based, as well as new and experimental, treatment options.



Medical Therapy:-

Medical therapy, which includes scientific treatments, is the main way to treat Parkinson's disease. These treatments can be drugs or non-drug methods like exercise, training, support groups, speech therapy, and proper nutrition. The treatment that is best for a person depends on their age, how serious their disease

is, what symptoms they are having, and how the benefits and risks of each treatment compare. People who are newly diagnosed with Parkinson's may feel worried about living with a condition that is long-term and gets worse over time, and that affects the nervous system. Teaching them about their condition slowly and focusing on managing symptoms can help reduce fear and build understanding. Learning how to manage the disease can lead to better self-care over time. Non-drug treatments include things like exercise, training, support groups, speech therapy, and good nutrition. While none of these can stop the disease from getting worse, they can help with some symptoms and deal with some of the effects the disease has on the body. Studies show that these methods should start early in the course of the disease. Regular exercise and physical therapy can help with many physical problems caused by Parkinson's, such as joint pain and a bent posture. It's important to focus on exercises that improve flexibility, strength, and balance. These activities can help patients feel more in control of some parts of their condition. Education for patients and their families or caregivers is very important, especially for a long-term condition that affects the nervous system. The key to success is finding the right balance between wanting to learn and being ready to deal with possibly upsetting information. Some programs have been made to give important information about specific neurological conditions like Parkinson's. Even with the best medical treatment, many people with moderate to severe Parkinson's disease often have a poor quality of life.

Surgical Treatment:-

Despite getting the best possible medical treatment, many people with moderate to severe Parkinson's disease still experience a poor quality of life due to fluctuating symptoms, difficult dyskinesia, or symptoms that are not well controlled by levodopa. In the past, surgeries like stereotactic destruction of certain brain areas (like thalamotomy and pallidotomy) were commonly used. But now, deep brain stimulation (DBS) is mostly used instead. DBS uses implanted devices to send electrical signals to specific brain areas. The main advantage of DBS over traditional surgery is that the stimulation can be adjusted to suit each person's needs, allowing for better symptom control. (13)(14)Thalamic DBS is often used to treat high-amplitude tremors in people with essential tremor, while the subthalamic nucleus (STN) or globus pallidus interna (GPi) are the most common targets for

DBS in people with Parkinson's disease who have disabling tremors or motor complications related to levodopa. (15)(16)To find out which is better—optimal medical treatment or DBS—a study involving 55 patients from seven Veterans Affairs hospitals and six university hospitals was conducted. The study compared the results of DBS (with STN and GPi targets) and optimal medical treatment after six months of treatment. (17)(18). Patients who received DBS gained an average of 4.6 hours per day without troublesome dyskinesia, compared to zero hours for those receiving only medical treatment. (19)Additionally, 71% of DBS patients saw a five-point or greater improvement in motor function on the motor Unified Parkinson's Disease Rating Scale (UPDRS), while only 1% of those on medical treatment did. These improvements were also reflected in better quality of life and minimal decline in cognitive testing. However, the risk of experiencing a serious adverse event was 3.8 times higher in the DBS group compared to the medical treatment group. (20 -27)There has been debate about which brain area—STN or GPi—is better for DBS targeting. A study involving 199 patients looked at outcomes after 14 months of treatment and found no significant difference in motor outcomes between the two groups. Patients receiving STN DBS needed a lower dose of dopamine agonists and had greater decline in visual-motor processing speed, but they also experienced more worsening of depression. Patients receiving GPi DBS had better improvement in mood. Both groups experienced similar rates of serious adverse events. Based on these and other studies, there is growing evidence that GPi DBS is especially suitable for people with troublesome dyskinesias and mild cognitive or behavioral issues, while bilateral STN DBS is often preferred for people who are cognitively intact and where reducing levodopa dosage is the main goal. Compared to GPi, STN DBS tends to have a better impact on "off" periods but is more likely to cause side effects like impulse control disorders (ICDs). Another common question is whether DBS performed at an earlier stage of Parkinson's or at a younger age leads to similar positive outcomes. A study compared STN DBS plus medical treatment with medical treatment alone in 151 younger patients with early motor symptoms. Patients in the DBS group saw an improvement of 7.8 points in their quality of life scores, while those in the medical treatment group experienced a slight worsening. Motor disability and daily function also showed significant improvement in the DBS group. People who lived in the surgical group had better results with levodopa-related movement problems. (28 -30)When considering early deep brain stimulation (DBS), it's important to first improve clinical treatment. This includes methods to reduce motor fluctuations and dyskinesia, as well as considering the risks of surgery and other factors. Even though DBS is a proven effective treatment, its success depends on choosing the right patients and having a skilled stereotactic surgeon to maximize benefits and reduce complications. Advances in DBS technology, such as adaptive stimulation, better connectivity, directional stimulation, and exploring new targets, are expected to continue improving outcomes. (31).

Cell Replacement Therapies:-

In earlier studies using fetal tissue for transplants in Parkinson's disease, the results were all over the place. Some patients had a bit of improvement at first, but many eventually developed troublesome movement problems called dyskinesias, even when the transplanted cells survived well. Because some patients had these unwanted movement issues, there were ethical concerns, and there wasn't enough tissue available, this type of transplant wasn't widely used in medicine. However, new developments in making dopamine-producing neurons from regular human cells and better ways to create these cells have brought cell transplants back into consideration for Parkinson's treatment. Scientists can now make a lot of human embryonic stem cells and other types of cells that can turn into real midbrain dopamine-producing neurons that meet high-quality standards for medical use.

Conclusion:-

Parkinson's disease is a complicated brain condition that causes the nerves to slowly break down. The exact causes and ways the disease starts are not fully understood. While a small number of cases are linked to a single gene mutation, most people with Parkinson's likely don't have a specific genetic problem. Instead, the risk for the disease is probably caused by a mix of several genes that make someone more likely to develop it. Environmental factors might also play a role in increasing the chance of getting Parkinson's, although it's not clear exactly how things like smoking, drinking coffee, or being exposed to pesticides affect the disease. In terms of how the disease affects the brain, it happens because the cells that make dopamine are lost, especially in a part of the brain called the substantia nigra. Other areas of the brain can be involved too. A key sign of Parkinson's is the

presence of Lewy bodies, which are clumps made mostly of a protein called alpha-synuclein. It's not clear exactly how these clumps lead to the death of brain cells. Understanding these processes could help find new ways to treat the disease and, in the future, maybe even stop it from happening.

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