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Review Article

A Brief Review on Parkinson's Disease

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Abstract

Parkinson's disease is a progressive neurodegenerative condition which developed in human brain due to the death of the dopamine containing cells of the substantia nigra. After Alzheimer's disease it is second most common neurological degenerative disorder. It is difficult to differentiate Parkinson's disease from many degenerative disorders which shows similar symptoms as that of Parkinson's disease. It is belong to motor system disorder. Hypokinesia, bradykinesia, rigidity and rest tremor are symptoms of Parkinson's disease which called as Parkinsonism. At present there is no complete cure for Parkinson's disease but many medicinal drugs, surgical treatment are available for treatment of Parkinson's disease.

Keywords: *Parkinson's Disease; Hypokinesia; Anti-Parkinson's; Bradykinesia*

Abbreviations

PD: Parkinson's Disease; CDC: Centers for Disease Control and Prevention

Introduction

A progressive neurological disorder associated with a loss of dopamine-generating cells in the brain that results in a complex array of symptoms is called as Parkinson's disease (PD) but it is primarily associated with progressive loss of motor control. Major cause of disability among the elder is Parkinson's disease. After Alzheimer's disease, currently the second most common neurological degenerative disorder affecting worldwide is Parkinson's disease. Parkinson's disease is more common in males and is twice as likely to affect whites and Hispanics as blacks and Asians. Young-onset Parkinson's disease is a condition where an individual under 40 years of age may develop PD. Healthcare professionals are encourages to consider PD in every patient, regardless the age, presenting with motor and non-motor symptoms of the disease. It is difficult to diagnose PD. Common diagnostic criteria generally require the initiation of antiparkinson's medication before the diagnosis can be confirmed. This ambiguity can be confusing for primary care physicians, especially when the disease presents without the characteristic tremor. Some- times PD condition in which no tremors occur may be mistaken for a musculoskeletal condition and may lead to false diagnosis and wrong treatment. Parkinson's disease is often manageable in primary care [1].

Parkinson's disease is a condition whose main features are:

- Slowed movement
- Tremor
- Gait or balance problems

More than 1 million people in the United States have Parkinson's disease. Although it more commonly develops in people in their 60s or older, it can occur as early as age 20 [2].

History

Parkinson's disease (PD) is named after the London general practitioner (GP), James Parkinson, who vividly described many of the clinical features of the condition in his Essay on the shaking palsy (1817). In this work, Parkinson refers to the condition by its earlier name of paralysis agitans a term that captures a peculiar characteristic of the disease, namely the combination of movement loss (i.e. hypokiesia) with movement gain (i.e. tremor at rest) which characterizes the condition. Shaking palsy was named 'maladie de Parkinson' in 1888 by the French neurologist Jean-Martin Charcot. Charcot admired Parkinson's clinical acumen and powers of description; l criticized him for omitting mention of rigidity, which Charcot believed to be a typical feature of the condition [3].

Modern definition

Death of the dopamine containing cells of the substantia nigra resulting into a progressive neurodegenerative condition is PD. PD cannot be differentiated from other conditions that have similar clinical presentations as there is no consistently reliable test. The diagnosis is mainly clinical and based on the history and examination. People with PD classically present with the symptoms and signs associated with Parkinsonism, namely hypokinesia (i.e. poverty of movement), bradykinesia (i.e. slowness of movement), rigidity and rest tremor.

Parkinsonism can also be caused by drugs and less common conditions such as: multiple cerebral infarction, and degenerative conditions such as progressive supra nuclear palsy (PSP) and multiple system atrophy (MSA).Although PD is predominantly a movement disorder, other impairments frequently develop, including psychiatric problems such as depression and dementia. Autonomic disturbances and pain may later ensue, and the condition progresses to cause significant disability and handicap with impaired quality of life for the affected person. Family and careers may also be affected indirectly.

One of the most complexes of the neurological disorder may be Parkinson's disease. Factors that lead to PD is still unknown, however there is lot of active research being reported with new findings.

James Parkinson, first described Parkinson's disease in 1817 as "the shaking palsy" and reported the major symptoms of the disease that was later on known after his name. Scientists further tried to find the causes and treatment of the disease for more than a century. The loss of brain cells that produce a chemical dopamine that helps direct muscle activity is a hallmark of the disease is identified by researchers as fundamental brain defect in 1960s.This discovery pointed to the first successful treatment for Parkinson's disease and suggested ways of devising new and even more effective therapies [4].

What is parkinson's disease?

Parkinson's disease (PD) is a progressive neurological disorder, which is associated with a loss of cells that generate dopamine in the brain which results in numerous complex symptoms, and results in progressive loss of motor control (Figure 1) [5].

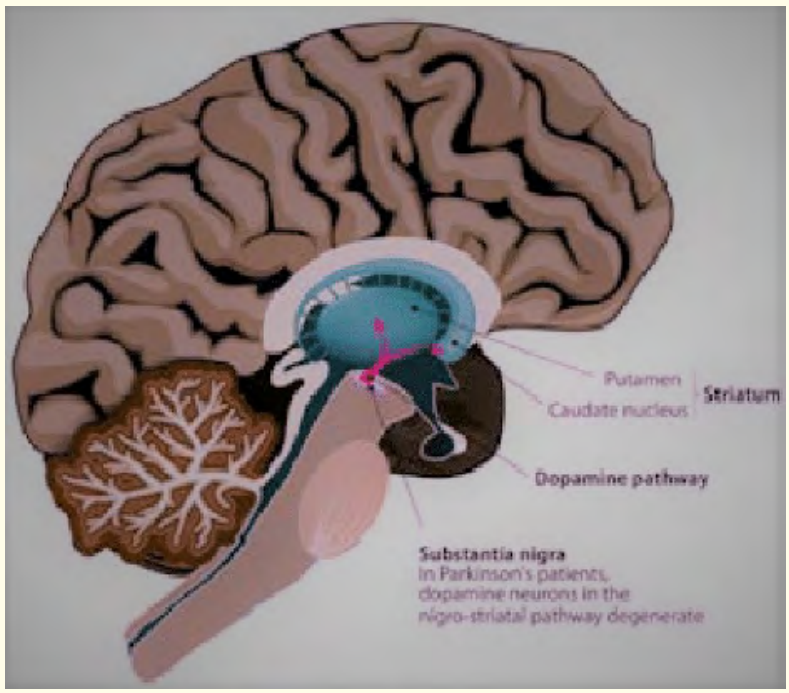


Figure 1: *Parkinson's disease.*

Parkinson's disease belongs to motor system disorders. The main symptoms are:

- There may be tremor or trembling in body parts such as hands, arms, legs, jaw, and face;
- There occurs rigidity or stiffness of the limbs and trunk;
- Patient may suffer from bradykinesia or slowness of movement;
- Patient may experience postural instability or impaired balance and coordination.

Patients experience difficulty in walking, talking, or completing other simple tasks as the mentioned symptoms become more pronounced. The disease is chronic and progressive, it persists over a long period of time and its symptoms grow worse over time. PD is not contagious nor is it usually inherited that is, it does not pass directly from one family member or generation to the next [5].

The most common form of Parkinsonism is PD. The result of the loss of dopamine-producing brain cells is primary symptoms mentioned above. PD is called as primary Parkinsonism or idiopathic Parkinson's disease. A term mentioning a disorder for which there is no cause has been found is described condition idiopathic. The cause of PD is known or suspected in other form of PD. PD is a neurodegenerative brain disorder which progresses very slowly in many people in worldwide [5].

A production of neurotransmitter called dopamine is stop by person's brain. Therefore insufficient amount of dopamine present in brain. Due to the less amount of dopamine present in brain, person loss ability to regulate the body movements, body and emotions. There are serious complications from the disease. The complications from PD are rated as the 14th top cause of death in the United States by Centers for Disease Control and Prevention (CDC).The condition when dopamine production decreases in brain is PD (Figure 2) [5].

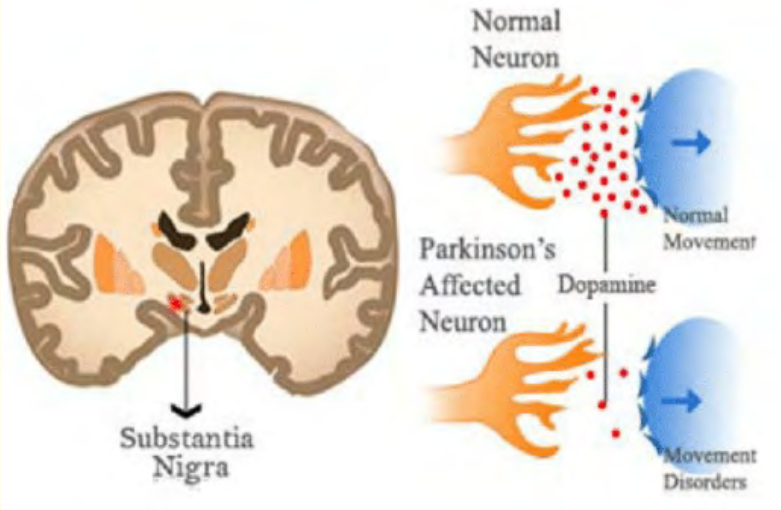


Figure 2: *Dopamine level in parkinson's disease.*

No total cure is there for PD. Dopamine is normally produced by brain cells known as neurons in the human brain. Substantia nigra is particular area of the brain where these neurons are concentrating. Dopamine is a chemical that relays messages between the substantia nigra and other parts of the brain to control movements of the human body (Figure 3). The smooth, coordinated muscle movements in human body are due to dopamine. The motor symptoms of Parkinson's disease appear when approximately 60 to 80% of the dopamine-producing cells are damaged, and do not produce enough dopamine,. This process of impairment of brain cells is called neuro degeneration.

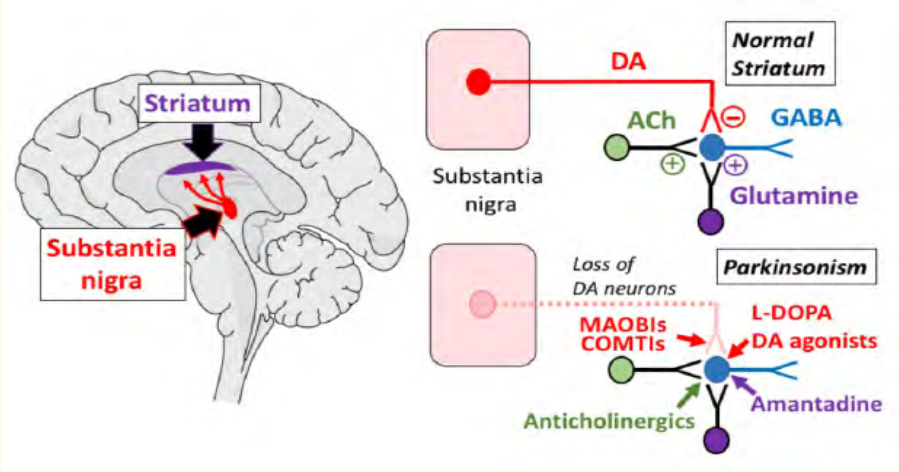


Figure 3: *Dopamine production in substantia nigra.*

The enteric nervous system, the medulla and in particular, the olfactory bulb, which controls your sense of smell involves earliest signs of Parkinson's, which is current theory called as Braak's hypothesis. The theory explains that over the years PD only to the substantia nigra and cortex. For classify the degree of pathology in Parkinson's disease and Alzheimer's disease Braak staging refers to two methods. By performing an autopsy of the brain clinical diagnosis of these diseases obtained. For detection of PD as early as possible researchers are mainly worked on these "non-motor" symptoms.

Person might hear his doctor refer to his Hoehn and Yahr stage. This scale, first introduced in 1967, is a simple rating tool used by clinicians as a means to generally describe how motor symptoms progress in Parkinson's. It takes into account factors other than motor symptoms, including mental functioning, mood and social interaction.

While symptoms are unique to each person, and the progression of symptoms varies from person to person, knowing the typical stages of Parkinson's can help you cope with changes as they occur. In some people, it could take 20 years to go through these stages. In others, the disease progresses more quickly [5].

How many people are affected by parkinson's disease?

The 100 - 180 per 100,000 of the population (6 - 11 people per 6,000 of the general population in the UK) and has an annual incidence of 4 - 20 per 100,000 affected by PD. There is a rising prevalence with age and a higher prevalence and incidence of PD in males [6].

PD can lead to extensive disability, which affects both the individual with the disease as well as indirectly family and careers. The economic impact of the disease includes:

- Direct cost to the National Health Service (NHS)
- Indirect cost to society
- Personal impact of PD on individuals with the condition and their family and carers.

Each year, 60000 Americans get affected by PD and 7 - 10 million people gets affected by PD through worldwide The chances of occurring PD is more in males than females [7].

Synonym of parkinson's disease

Parkinson disease, idiopathic or primary parkinsonism, hypo kinetic rigid syndrome, paralysis agitans [8].

Stages of Parkinson's Diseases

Stage one

The person has mild symptoms that commonly do not interfere with daily activities are observed in stage one. On the one side of body only, tremor and other movement symptoms may occur. The other person may observe changes in walking, posture and facial expression of patient [9].

Stage two

The symptoms are getting worst in stage two. On the both side of body, tremor, rigidity and other movement symptoms may occur. In this stage there is difficulty for patient in completing day to day tasks. Walking problems and poor posture may become apparent [9].

Stage three

Mild stage in progression of PD is stage three. Main symptoms of this stage are loss of balance and slowness of movements. Patient is still fully independent in third stage. Symptoms significantly impair activities of daily living such as dressing and eating [9].

Stage four

Symptoms are severe and limited in this stage. Patient can stand without assistance but walker is required foe standing. For completing daily living activities, person needs help [9].

Stage five

Most advanced stage of PD is stage five. IT is impossible to stand and walk because of Stiffness in the legs. Wheelchair, around-the-clock nursing care is required for patients care. Hallucination and delusion may observe in patient [9].

Causes of parkinson's disease

Genetic factor and environmental factor are considered as cause of PD. The risk of causing PD is more in persons whose family member is suffer from OD or person who gets more contact with pesticide, toxins. The head injuries also lead to causing PD.

Parkinson's disease is caused by a loss of nerve cells in a specific part of the brain called the substantia nigra. Dopamine which is important chemical for brain is produced by these neurons. Cells in the substantia nigra communicate with other movement control centers in the brain by secreting dopamine and other neurotransmitters. Secretion of dopamine gets stop when substantia cell are die and movement of other control centers become unregulated. This disturbance in the movement control centers of the brain cause the main symptoms of Parkinson's disease [10].

Environmental toxins that may cause Parkinsonism include

- Manganese
- Carbon monoxide
- Organic solvents
- Certain pesticides [11].

The cause of this disease is due to combination of four mechanisms which are as follows:

- Oxidative damage,
- Environmental toxins,
- Genetic predisposition,
- Accelerated aging [12].

Sign and symptoms of parkinson's disease

- Tremors or shaking in hands, arms, legs, jaw, and face
- Rigidity or stiffness of limbs and trunk
- Slowness of movement
- Difficulties with balance, speech, and coordination

There are also non-motor symptoms which may develop years before the onset of motor problems. These may include:

- Poor sense of smell Constipation
- Depression
- Cognitive impairment
- Fatigue, cramped handwriting or other writing changes
- Tremor, especially in finger, hand or foot
- Uncontrollable movements during sleep
- Limb stiffness or slow movement (bradykinesia), voice changes
- Rigid facial expression or masking
- Stooped posture
- Muscular: Difficulty standing, difficulty with bodily movements, involuntary movements, muscle rigidity, problems with coordination, rhythmic muscle contractions, slow bodily movement, stiff muscles, or slow shuffling gait
- Tremor: Can occur at rest, in the hands, limbs, or can be postural
- Whole body: Dizziness, fatigue, poor balance, or restlessness
- Cognitive: Amnesia, confusion in the evening hours, dementia, or difficulty thinking and understanding
- Sleep: Early awakening, nightmares, or restless sleep
- Speech: Impaired voice, soft speech, or voice box spasms
- Mood: Anxiety or apathy
- Nasal: Distorted sense of smell or loss of smell
- Urinary: Dribbling of urine or leaking of urine
- Facial: jaw stiffness or reduced facial expression
- Also common: blank stare, constipation, daytime sleepiness, depression, difficulty swallowing, drooling, falling, fear of falling, limping, loss in contrast sensitivity, neck tightness, small handwriting, trembling, unintentional writhing, or weight loss [13].

Early symptoms

Early symptoms of PD involve tiredness in patient or notice a general malaise, patient have little shaky or have difficulty getting out of a chair, speak too softly or that their handwriting looks cramped and spidery, lose track of a word or thought, or they may feel irritable or depressed for no apparent reason, person's face lacks expression and animation or that the person remains in a certain position for a long time or does not move an arm or leg normally, person seems stiff, unsteady, and unusually slow, may begin to interfere with daily activities, shaking makes reading a newspaper difficult [14].

Major symptoms

The major symptoms observed in PD patient are generally tremor, rigidity, bradykinesia, postural instability which is observed in higher stages of PD patient.

Tremor

PD have tremor with characteristic appearance. Pill rolling is term when tremor takes form of rhythmic back and forth motion of the thumb and forefinger at three beats per second. Tremor is normally begun in hand; foot or jaw. In many patients during the early stage of the PD tremors may affect only one side of the body. It is disappear during sleep, rarely disabling and improve with intentional movement [15].

Rigidity

A major principle of body movement is that all muscles have an opposite muscle. Rigidity is comes out in PD patient he delicate balance of opposing muscle is disrupted in response to signal from the brain. When other person tries to do movement of arm or leg of PD patient then rigidity becomes obvious [15].

Bradykinesia

Bradykinesia is a condition when there a difficulty in next movement for patient after doing one movement which also noted as allowing down in spontaneous movement and loss of automatic movement. The patient cannot rapidly perform routine movements [15].

Postural instability

Impaired balance and coordination or postural instability causes patient to fall easily. It is occurs at higher stage of Parkinsonism disease. There is more problem for patient for performing different activities [15].

Other form of parkinson's disease

Post-encephalitic Parkinsonism

Post-encephalitic Parkinsonism is neurological disorder or severe form of movement disorder including various form of catatonia. Other infections which show symptoms of PD are viral infections, western equine encephalomyelitis, eastern equine encephalomyelitis, and Japanese B encephalitis [16].

Drug-induced Parkinsonism

Drugs which are prescribed for patients with psychiatric disorders such as chlorpromazine and haloperidol, Metoclopramide for stomach disorders, Reserpine for high blood pressure may induce PD [16].

Striatonigral degeneration

In patient with primary PD the substantia nigra is mildly affected whereas sever damage in the other brain areas. This type of PD progresses more rapidly than other and show more rigidity [16].

Arteriosclerotic Parkinsonism

Due to the multiple small strokes damage to brain vessel is occurs which lead to PD. This type of PD is called as Pseudo Parkinsonism or arteriosclerotic Parkinsonism. In this type of PD tremor is rare but loss of mental skill and ability in dementia is common [16].

Parkinsonism accompanying other conditions

Other condition or neurological disorder in PD patient is as follows:

- Shy-Drager syndrome (sometimes called multiple system atrophy),
- Progressive supra nuclear palsy,
- Wilson's disease, Huntington's disease,
- Hallervorden-Spatz syndrome,
- Alzheimer's disease,
- Creutzfeldt-Jakob disease,
- Olivoponto cerebellar atrophy [17].

Treatment and drugs

For the treatment of PD there are many medicine are available which provide some relief from symptoms of PD but not complete cure of PD. In some later cases, surgery may be advised.

Medication

Carbidopa-Levodopa

Levodopa is a natural chemical that passes into human brain and then converted into dopamine which is very effective medication for PD. Carbidopa when combined with levodopa, which protect levodopa form conversion into dopamine outside brain and minimize side effects such as nausea or light-headedness. As disease progresses after years the benefit form levodopa may become less stable. After taking higher dose of Levodopa, person may experience dyskinesia (involuntary movements) [2].

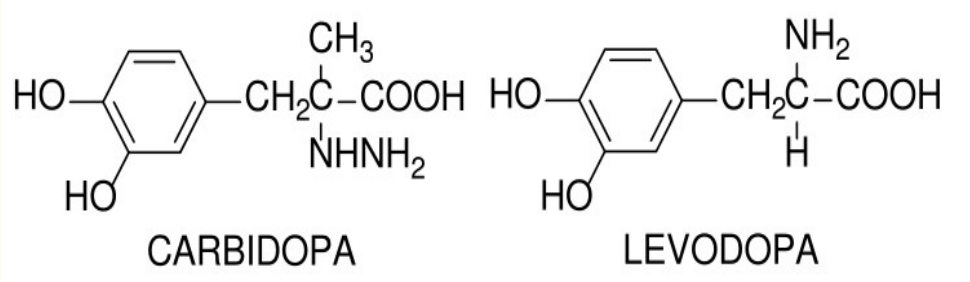


Figure 4

Dopamine agonists

Dopamine antagonist cannot convert into dopamine but they mimic dopamine effects in brain and they are not more effective but can control symptoms of disease. They can be used with Levodopa to smooth the off-and-on effects of Levodopa. Dopamine agonists include pramipexole, ropinirole and rotigotine. Some of the side effects of dopamine include hallucinations, sleepiness and compulsive behaviors such as hyper sexuality, gambling and eating [18].

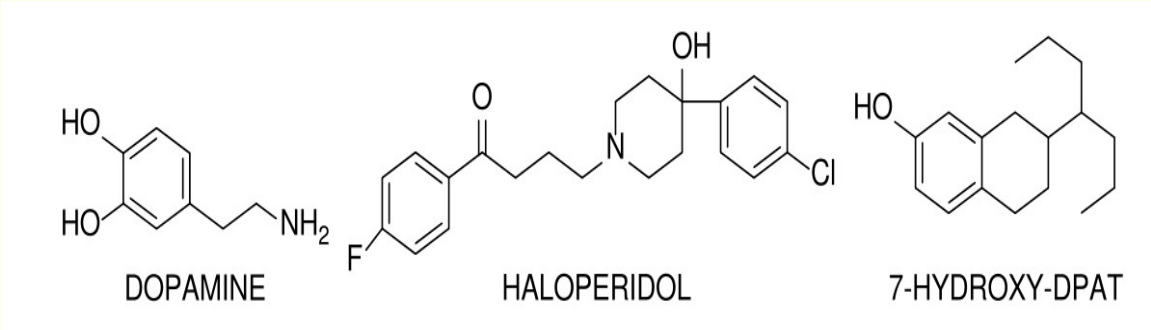
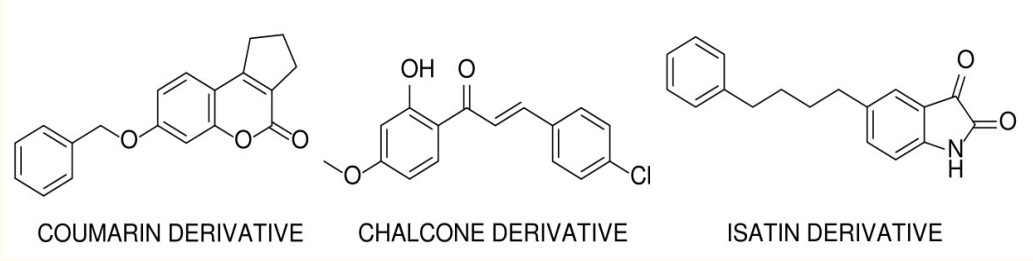


Figure 5

MAO-B Inhibitors

Selegilie and Rasagiline are MAO_B inhibitors which prevent the breakdown of dopamine in brain by inhibiting the monoamine oxidase B which is brain enzyme which metabolized brain dopamine. Nausea and insomnia are side effects of these drugs. The risk of hallucination may increase when it given with carbidopa-levodopa [18].



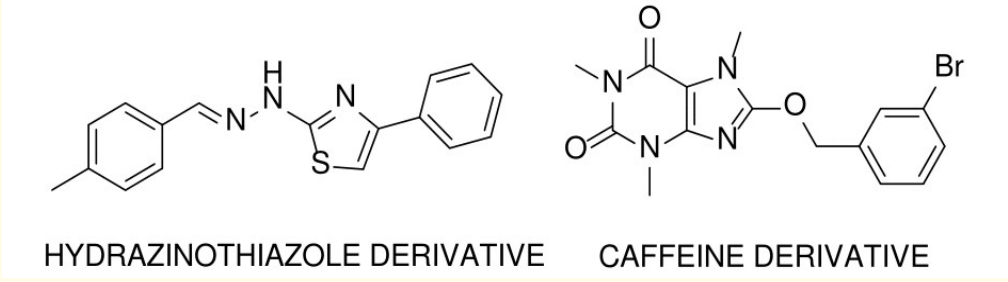


Figure 6

Catechol-O-methyltransferase (COMT) inhibitors

Primary medication of this class is Entacapone. The effect of levodopa therapy mildly prolongs due to use of this medication by blocking an enzyme which breakdown dopamine. Increased risk of involuntary movements, diarrhea are side effects. Another drug of this class which is rarely prescribed due to the risk of serious liver damage and liver failure is Tolcapone [18].

Anticholinergic

To control the tremor associated with PD this drugs are used from many years. Benztropine or trihexyphenidyl are available medication. Impaired memory, confusion, hallucination, constipation, dry mouth and impaired urination are side effects [18].

Amantadine

To provide short term relief from symptoms of PD this drug is used. It may give along with Carbidopa-Levodopa therapy at later stages of PD which results in control involuntary movements induced by Carbidopa-Levodopa. A purple mottling of skin, ankle swelling and hallucination are side effects of drug [18].

There are different drugs are used for the treatment of PD. The mechanism of action of all drugs which are used to treat PD is as shown in figure 7.

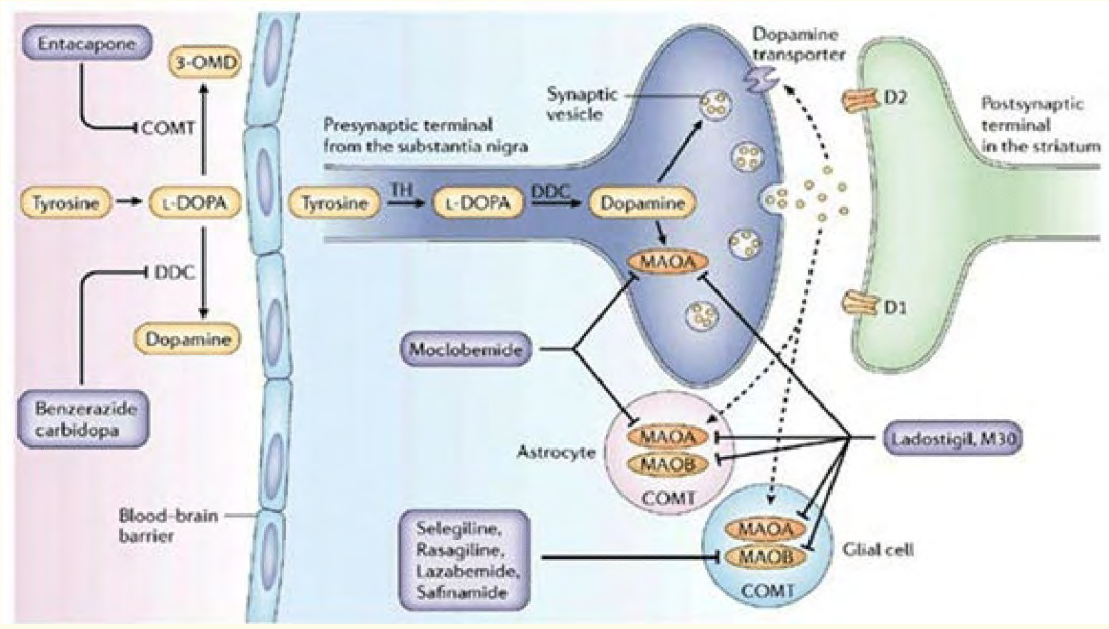


Figure 7: *Summary of the treatment of parkinson's disease.*

Surgical Treatment

Now days there are surgical treatment is available for patient of PD. Mainly deep brain stimulation surgery is used for treatment of PD patient for symptomatic relief. Good surgical candidates are the patients who are fluctuate between "on medications" and "off medication". A more complex therapy is DBS which required regular neurological follow up. The surgical treatment reduces symptoms of PD but cannot completely eliminate them [19].

Current status of research on parkinson's disease

In the last decade research has laid the groundwork for many of today's promising new clinical trials, technologies, and drug treatments. Scientists, physicians, and patients hope that today's progress means tomorrow's cure and prevention.

Parkinson's disease research focuses on many areas. Some investigators are studying the functions and anatomy of the motor system and how it regulates movement and relates to major command centers in the brain. Scientists looking for the cause of Parkinson's disease will continue to search for possible environmental factors, such as toxins that may trigger the disorder, and to study genetic factors to determine if one or many defective genes play a role. Although Parkinson's disease is not directly inherited, it is possible that some people are genetically more or less susceptible to developing it. Other scientists are working to develop new protective drugs that can delay, prevent, or reverse the disease [12].

Levodopa-carbidopa symptoms relief is increased by 60 percent when given along with the experimental drug R0 40-7592 for treatment of PD. The breakdown of dopamine is blocks by this new promising drug. For dosing of this drug scientist are still working on it so it now also in experimental stage. PD drugs which are under investigation are additional control released formulas and implantable pump which provide continuous supply of Levodopa to control the problem of fluctuation level in patient. The implementing capsule is also promising treatment which contain dopamine which are surrounded by a biological inert membrane which allows passing of drug into brain [12].

Experimental technique for treatment of disease is neural grafting or transplantation of nerve cells. The replacement of lost or damaged dopamine producing neuron with healthy fetal neurons is done by treatment which results into improve movement and good response to medication. A use of genetically engineered cells is promising approach for treatment. A genetically engineered cell is modified skin cells that do not come from the nervous system but are grown in tissue culture which have the same beneficial effects. Harvesting of skin cell is much easier and for tis patient could serve as own donor [12].

Preventive measures of parkinson's disease

Genetics

The risk of PD increases when a close relative having PD. While you can't change the genes you were born with, epi genetics research is proving that the life you live turn those genes on and off [20].

Diet

Eating a healthy diet is a key element in an anti-PD lifestyle. As with the prevention of disease and promoting maximum health, an optimum diet for reducing the risk of Parkinson's would include lots of greens, vegetables, and fruits, preferably organic, and foods high in protein, vitamins, antioxidants, minerals, and good fats [20].

Exercise

People who engage in moderate to vigorous physical activities have a significantly lower prevalence of PD. Moving your body increases the blood flow to your brain which elevates oxygen levels which triggers biochemical changes protecting the new resulting neurons by bathing them in nerve growth factor (BDNF) [20].

Stress Management

Chronic stress can upset the brain activity which causes PD. Acute stress causes alterations in the protective function of the blood brain barrier, and long-term stress is toxic to the brain. Therefore it is necessary to manage the stress [20].

Avoiding Toxins

Due to getting contact with toxins chances of occurring PD gets more. The toxins may contain air pollution, bug and weed killers, solvents, metals, PCBs, smoke, drug and radiation [20].

Preventing Head Injuries

The chance of developing PD is increases due to head injury. While it's well-known that traumatic brain injuries can lead to short-term or permanent. Due to prevention of head injuries the chances of causing PD also reduced [20].

Things used to avoid parkinson's disease

Peppers

Peppers contain small amount of Nicotine which help to protect brain from PD. The risk of PD decreases by at least 30 percent due to edible version of nicotine in peppers. Person gets the benefits if he eats them at least twice a week [21].

White tea

Green tea contains polyphenol which avoids PD, but white tea contains more quantity of polyphenols which helps more to avoid PD which protects neurons from damaging. Therefore it is better to use white tea instead of green tea to avoid PD. Due to use of white tea brain gets protected from damage and oxidative stress [21].

Vitamin B6

Due to lower level of vitamin B6 risk of PD may increases. To reduce the risk supplement of vitamin B6 should be taken which is found in Bell peppers, wild-caught salmon, eggs, and grass-fed beef are sources of vitamin B6 [21].

Healthy fats

Healthy fats actively protect your brain from Parkinson's. Proteins in brain cells must "fold" to fit and do their job. When they don't fold the right way, it may damage the cell which leads to PD. But the DHA in fish oil prevents the improper folding of these proteins which makes brain cells live longer. Avocados, fish oil supplement such as krill oil is a good source of fats which cross blood brain barrier [21].

Vitamin D3

Level of vitamin D3 found to be low in patient of PD. To avoid PD supplement of vitamin D should be taken. The good source of vitamin D3 is wild-caught salmon, eggs, and mushrooms [21].

Literature Review

1) Yabe I., *et al.* reported on the Efficacy of Istradefylline for treating Mild Wearing-Off in Parkinson Disease. The adenosine A2A antagonist istradefylline has been used to treat Parkinson disease (PD) with symptoms of wearing-off since 2013 in Japan. Changes in the Unified Parkinson's Disease Rating Scale part III scores in the ON state (ON-UPDRS-III) scores and daily OFF time were assessed at baseline and after 4, 8, and 12 weeks of administration of istradefylline [22].

2) Macleod AD., *et al.* reported on development and validation of prognostic survival models in newly diagnosed Parkinson's disease**.** The objective of this study was to develop valid prognostic models to predict mortality, dependency, and "death or dependency" for use in newly diagnosed PD. The models were recalibrated to the baseline risk in the Park West study and then calibrated well in this cohort. These models have validity for use for stratification of randomization, confounder adjustment, and case-mix correction, but they are inadequate for individualized prognostication [23].

3) Ford KJ., *et al*. reported on pedestrian safety in patients with Parkinson's disease: A case-control study. Patients with Parkinson's disease experience debilitating motor symptoms as well as non-motor symptoms, such as cognitive dysfunction and sleep disorders. The association of motor symptoms, daytime sleepiness, impaired vigilance, and cognitive dysfunction with pedestrian behavior in patients with Parkinson's disease and healthy older adults is investigate in this study [24].

4) Pagano G., *et al*. reported on research of Levodopa-induced dyskinesias in Parkinson's disease and positron emission tomography (PET) molecular imaging. A research of levodopa-induced dyskinesias (LIDs) in Parkinson's disease (PD) is done to check the development of PET molecular imaging in PD. In the development of LIDs in PD the level of Dopaminergic, serotonergic, glutamatergic, adenosinergic and opioid systems and phosphodiesterase levels have been shown to be implicated [25].

5) Francesco Pinnen, Ivana Cacciatore., *et al.* reported on synthesis and study of L-Dopa−Glutathione co-drugs as new anti-Parkinson agents with free radical scavenging properties. A potential antiparkinson's agent with antioxidant property includes a novel molecular combination which includes L-dopa covalently linked with glutathione via amide bond. The evaluation of this novel compound was done by performing evaluating solubility, chemical and enzymatic stabilities, apparent partition coefficient (log *P*). Tested compounds prolonged the plasma LD levels and were able to induce sustained delivery of DA in rat striatum with respect to an equimolar dose of LD [26].

6) Moussa BH., *et al.* reported on the anti-parkinson drug Rasagiline and its cholinesterase inhibitor derivatives exert neuro protection unrelated to MAO inhibition in cell culture. In PC 12 cell, examination of novel drug derived from rasagiline is done and it concludes that it is novel anti-Alzheimer cholinesterase-MAO inhibitor drug [27].

7) J Stanicova, P Miskovsky, V Sutaik reported on Amantadine: an antiviral and anti-parkinsonian agent. Unlike other drugs used to treat PD the effect of amantadine were discovered randomly. The PD symptoms such as akinesia, rigidity and tremor disappeared. After discontinuing amantadine the PD symptoms returned. This finding was verified many times, and so amantadine has become an effective antiparkinsonian agent. It has a good effect mainly atakinetic crises and in combination with the conventional preparation L-Dopa it suppresses the main symptoms of PD if L-Dopa alone is not effective [28].

8) Jennifer SAM, Reijnders MA, Uwe Ehr, MD, Wim EJ Weber reported on A Systematic Review of Prevalence Studies of Depression in Parkinson's Disease. A rate of depressive disorder ranging from 2.7% to more than 90% in PD [29].

9) F Azam, IA Ibn-Rajab, AA Alruiad reported on Adenosine A2A receptor antagonists as novel anti-Parkinson agents: a review of structure-activity relationships. An attractive target for PD is adenosine A2A receptor. The antagonists of the AA2AR may be neuroprotective which helps to reduces symptoms of PD [30].

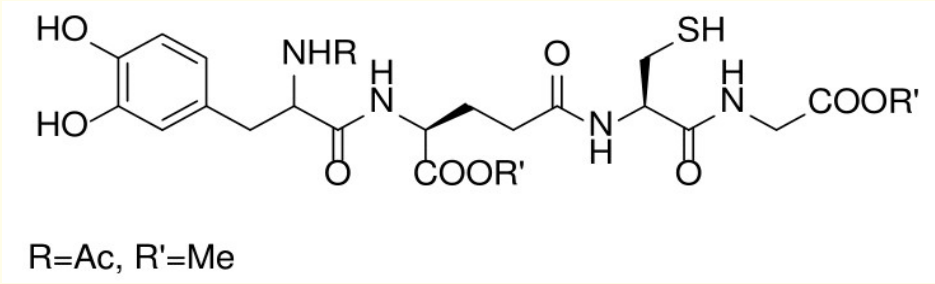


Figure 8

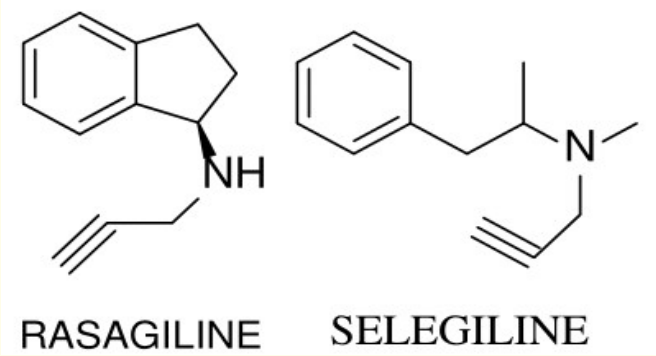


Figure 9

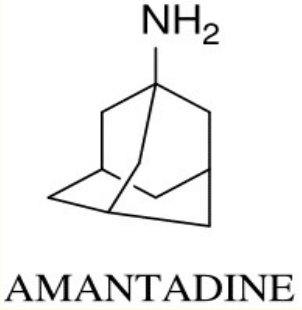


Figure 10

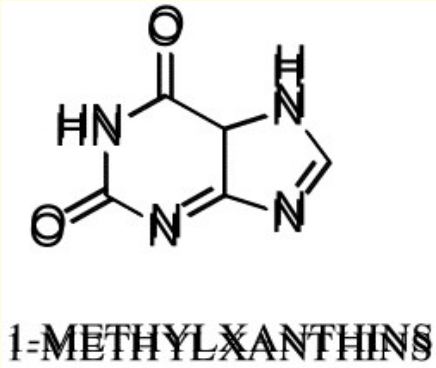


Figure 11

Current research on treatment on parkinson's disease

The MPTP primate model of treatment of Parkinson's disease

Current research into Parkinson's disease (PD) is directed at developing novel agents and strategies for improved symptomatic management. The aim of this research is to provide effective and maintained symptom control throughout the course of the disease without loss of efficacy and without priming the basal ganglia for the onset of dyskinesia. At present, the most effective experimental model of PD is the methyl phenyl tetrahydropyridine (MPTP)-treated primate. Primates treated with MPTP develop motor disturbances resembling those seen in idiopathic PD, including bradykinesia, rigidity and postural abnormalities. MPTP-treated primates are responsive to all commonly used anti-parkinsonian agents and display treatment-associated motor complications such as dyskinesia, wearing-off and on-off, which occur during the long-term treatment of the illness. The mechanisms by which MPPþ induces dopaminergic neuronal death are complex, and still the subject of much debate. MPPþ induces a variety of cytotoxic mechanisms including mitochondrial dysfunction, oxidative stress, energetic failure and activation of genetic programmes leading to apoptotic cell death. A number of dopaminergic therapies have been investigated in MPTP-treated primates and subsequently in clinical practice. So far, all of the actions of these drugs observed in MPTP-treated primates have proved to be highly predictive of drug action in man. Indeed, the MPTP primate model has significantly contributed to the development of improved therapies for idiopathic PD and to concepts of dyskinesia induction [31].

Intranasal Apomorphine: a new treatment in Parkinson's disease

Apomorphine, a directly acting dopamine agonist, has recently been used in the treatment of Parkinson's disease complicated by motor fluctuations. Benefit is seen rapidly and reliably following subcutaneous injection. We have sought alternative, more convenient routes of delivery for the drug. Effective mucosal absorption has been reported' and we now describe the use of apomorphine delivered intranasally. This preliminary study suggests that intranasal delivery may offer an effective alternative to subcutaneous injection of apomorphine. The benefits of the latter, including the speed and quality of motor response, appear to be retained in most cases with this simpler technique, prompting further evaluation of its long-term use [32].

Adenosine A2A receptor antagonists as new agents for the treatment of Parkinson's disease

The adenosine A2Areceptor, one of four cloned adenosine receptors, is a member of the seven-transmembrane, G protein-coupled receptor superfamily. It is highly concentrated in the striatum, nucleus accumbens and olfactory tubercle, as measured by autoradiography, ligand binding and the stimulation of adenylate cyclase by adenosine receptor agonists. There are few commonly available ligands showing much selectivity for the adenosine A2Areceptor, selective agonists being restricted to CGS21680 and APEC {2- [(2-aminoethylamino)

carbonylethyl-phenethylamino]-59N-ethylcarboxamidoadenosine}. The original adenosine receptor antagonists were xanthine's such as caffeine and theophylline, which show little or no selectivity for this receptor. More recently, a number of other xanthine and non-xanthine antagonists with A2A receptor selectivity have been developed, and their properties reviewed. The potential efficacy of adenosine receptor antagonists for the treatment of Parkinson's disease has been shown in humans using the nonselective adenosine receptor antagonist theophylline, which caused measurable improvements in both subjective and objective scores of the disease. It is clear that block of the striatal adenosine A2Areceptor could help restore the balance of striatal function by modulating both the striato-Gpe projection neurons and the cholinergic interneurons in hypokinetic movement disorders. Therefore, these antagonists show great potential as anti-Parkinson's disease drugs [33].

Conclusion

Parkinson's disease was found in ancient era. It was described in ancient writing. There is no exact treatment for PD but different medications are available which are used to treat PD. The treatment includes plant based treatment, medicinal drugs such as dopamine which replaces with dopamine replacement therapy, surgical treatment such as deep brain stimulation (DBS). There is no particular diagnostic test is available for PD but by observing symptoms it can be recognized. These symptoms are tested by medication with levodopa. According to researchers there is hope for development for method which not only cures PD but also help to control development of PD. The treatment is becoming more sophisticated as there are new methods are developed such as inhaled and intestinal gel. Gene therapy trials, stem cell therapy are promising but results are currently undefined. It is concluded that may be new method can be developed which help to develop PD along with cure it.

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Conflict of Interests

Declared None.

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