DEMENTIA and BPSD in PARKINSON'S DISEASE.

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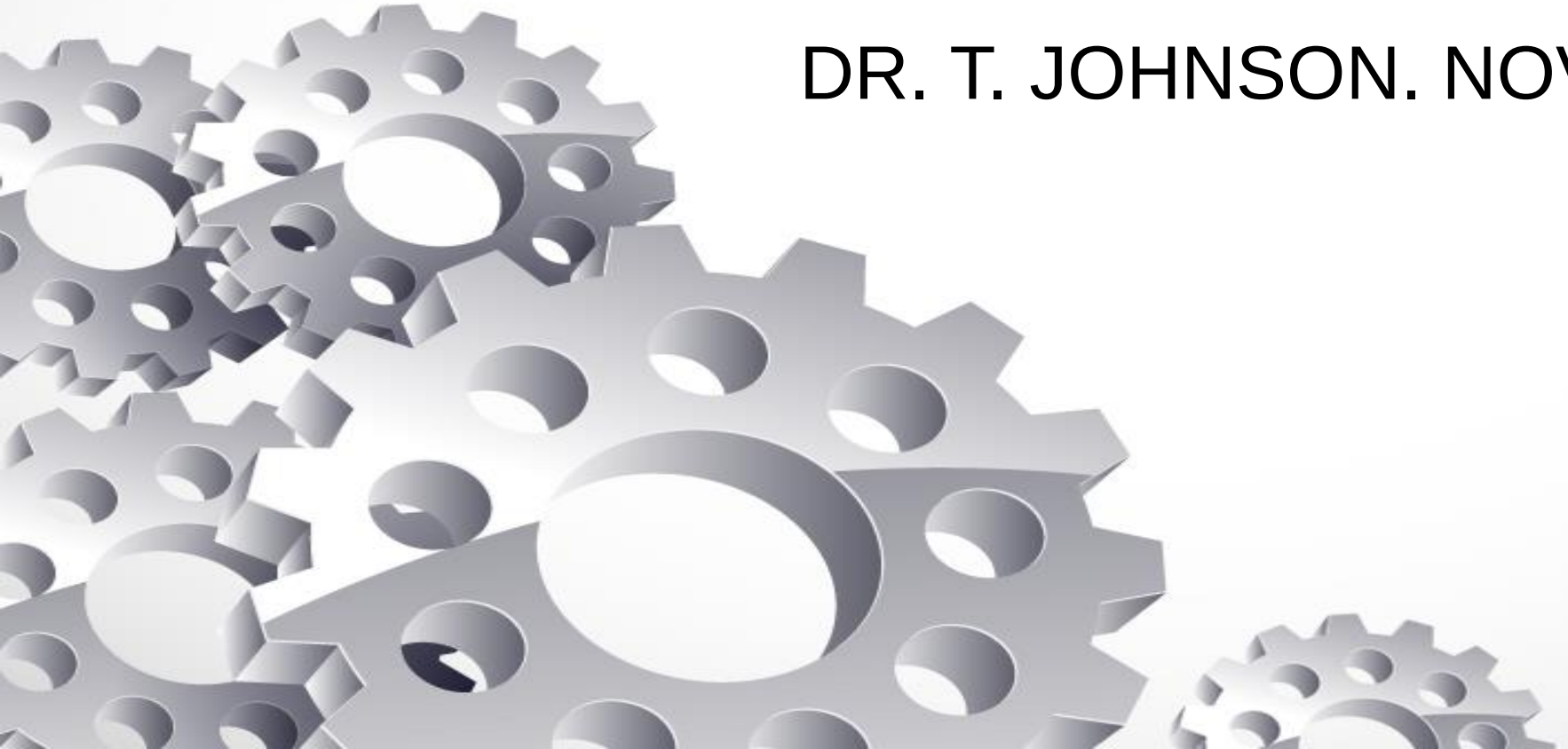

Introduction.

- Parkinson's disease (PD) has been considered largely as a motor disorder.

- It has been increasingly recognized that PD is often associated with cognitive deficits.

- Dementia develops in a substantial number of patients.
- Many of these also demonstrate Behavioural and Psychological Symptoms (BPSD),

Typical features of Parkinson's disease.

- At rest, hands, arms, or legs shake; these tremors often reduce as the individual engages in purposeful movement.
- Early signs of muscle rigidity include decreased arm swing while walking with fatigue.
- As the disorder progresses, throat and facial muscles weaken, causing choking, drooling, and difficulty swallowing.
- Rigidity in throat and facial muscles limits the range of vocal and facial expressions, resulting in a soft, monotonous voice and a vacant, mask-like facial expression.
- Cognitive functions are characteristically affected, with difficulty in memory, impairment in planning and making sound judgment

Other motor abnormalities include;

Stooped posture.

Difficulty turning.

Small, shuffling steps.

DSM -lV Diagnostic Criteria for Dementia Due to Parkinson's Disease.

The development of multiple cognitive deficits manifested by both;

- 1. Memory impairment.

- 2. One (or more) of :

Aphasia, Apraxia, Agnosia, Disturbance in executive functioning.

DSM lV Criteria.

The cognitive deficits in Criteria 1 and 2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.

- There is evidence that the disturbance is the direct physiological consequences of PD.

- The deficits do not occur exclusively during the course of a delirium.

DSM-V Diagnostic Criteria.

- The criteria are met for major or mild neurocognitive disorder.

  and
- The disturbance occurs in the setting of established PD.

  and
- There is insidious onset and gradual progression of impairment.

  and
- The neurocognitive disorder is not attributable to another medical condition and is not better explained by another mental disorder.

Diagnostic criteria.

- 1.There is no evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline).
- 2.The PD clearly precedes the onset of the neurocognitive disorder.

If 1 and 2 are present, Major or mild neurocognitive disorder **probably** due to PD should be diagnosed.

If 1 **OR** 2 is present,Major or mild neurocognitive disorder **possibly** due to PD should be diagnosed.

Epidemiology and Demographics

PD affects 1 -2 per 1000 of the population at any one time

The prevalence of major or mild neurocognitive disorder due to PD is:

75,000 per 100,000 (75%) with major neurocognitive disorder.

25,000 per 100,000 (25%) with mild neurocognitive disorder.

Epidemiology and Demographics.

- The prevalence of PD increases with age, from about 0.5% between ages 65 and 69, to 3% at 85 years of older.

- The disease is more common in males than in females (1.5:1).

- 75% of individuals affected will eventually develop serious cognitive problems.

Differential diagnosis.

- Lewy Body Dementia (LBD) overlaps clinically with Alzheimer's and PD but is more associated with the latter. LBD is often misdiagnosed in its early years.
- Loss of cholinergic (acetylcholine-producing) neurons accounts for degeneration of cognitive function similar to Alzheimer's.
- Death of dopaminergic (dopamine-producing) neurons accounts for degeneration of motor control similar to PD.
- Thus, LBD resembles both diseases and an accurate differential diagnosis can be difficult.
- LBD is often confused in its early stages with Alzheimer's disease and/or vascular dementia (multi-infarct dementia).However, Alzheimer’s disease usually begins gradually whilst LBD often has a rapid or acute onset, with especially rapid decline in the first few months.

DIFFERENTIAL DIAGNOSIS (cont).

- LBD progresses more quickly than Alzheimer’s disease.
- LBD is distinguished from the dementia that sometimes occurs in PD by the time frame in which dementia symptoms appear relative to Parkinson symptoms.
- PD with dementia (PDD) would be the diagnosis when dementia onset is more than a year after the onset of PD.
- LBD is diagnosed when cognitive symptoms begin at the same time or within a year of Parkinson symptoms.

BPSD.

- Diagnosis may include With or Without Behavioral Disturbances such as psychosis, agitation or apathy.

- Cognitive problems are Mild where difficulty is limited to instrumental activities of daily living, such as managing finances,
- Moderate where difficulty affects basic activities of daily living, such as feeding and dressing,
- Severe where the person is fully dependent.

DEPRESSION.

- 50% experience comorbid depression. which can exacerbate symptoms.
- Depression does not always follow PD.
- In some individuals, depression may precede other symptoms of the disorder.
- Individuals taking antidepressants are twice as likely to develop PD as individuals who do not.
- This is not seen as evidence that antidepressant use causes PD, but rather that Depression is an early symptom of the disease in some cases.

Parkinson’s disease and psychosis.

- Psychosis in Parkinson’s disease generally comes in two forms: hallucinations or delusions.
- Hallucinations are visual, usually non-threatening,seeing small people, animals, or loved ones who have already died, not interacting with them. common.
- Auditory hallucinations are rare in Parkinson’s disease and if they do occur, they are usually accompanied by visual hallucinations.

Delusions.

- Delusions are often of spousal infidelity.
- Other themes may be that people are out to steal from them or to harm or place poison on their food.
- It is not uncommon that patients actually call emergency services to report a burglary or a plot to hurt them.

Psychosis (cont).

- Psychosis occurs in up to 40% of Parkinson's disease patients.

- In the early stages, the patient often retains their insight, but this tends to worsen over time.

- At later stages, patients may be confused and be unable to distinguish personal, subjective experiences from the reality of the external world.

Management of psychosis in PD.

- If the hallucinations are mild and benign, and insight is retained, it is best that the Parkinson regimen be kept as is.

- If a patient is experiencing more threatening paranoid delusions, then pharmacological intervention treatment is warranted

Management of psychosis

Rule out possible reversible causes such as infections, metabolic and electrolyte imbalances or sleep disorders.

Decrease or discontinue adjunctive antiparkinsonian drugs (with cautious monitoring of motor function).

If a patient is on several anti-parkinsonian medications, reduce one drug at a time, until the psychosis resolves or when further reduction may worsen Parkinson motor symptoms.

Management of Psychosis (continued).

Simplify the Parkinson’s disease medication regimen.

Add a new or second generation antipsychotic.

If psychosis occurs in a Parkinson’s disease patient with cognitive impairment or dementia, a cholinesterase inhibitor, such as donepezil or rivastigmine may be considered

SUMMARY.

- PD is a progressive neurological disorder.
- Symptoms include resting tremor, motor slowness, rigidity; postural instability, decreased voice volume, and mask-like facial expression.
- Up to 60 percent of PD patients will develop dementia.
- Up to 50 percent of cases will develop Depression and that in turn may exacerbate dementia
- In some individuals, depression precedes other symptoms of the disorder
- A significant percentage develop psychotic symptoms.

Medications commonly used to treat BPSD

- Antipsychotics.
- The goal of antipsychotic therapy is the improvement in a targeted behaviour, without impairment of cognition, function or quality of life.
- Antipsychotics are frequently associated with adverse effects, including parkinsonism.
- Patients with Lewy Body dementia have increased sensitivity, to typical and atypical antipsychotics, especially risperidone - this may include neuroleptic malignant syndrome.

Atypical antipsychotics

- There's a significant improvement in aggression with risperidone and olanzapine compared to placebo.
- There's a significant improvement in psychosis with risperidone.
- Risperidone and olanzapine patients have a higher incidence of serious adverse CV events and EPS (especially with risperidone doses greater than 1 milligram daily).

Conventional antipsychotics

- Conventional antipsychotics are associated with a higher adjusted risk of death than atypicals

- The greatest increases in risk occur soon after therapy begins and with higher dosages.

- Conventional antipsychotics are at least as likely as atypicals to increase the risk of death among elderly persons.

Conventional antipsychotics (continued).

- Elderly patients are sensitive to EPS, especially parkinsonism, akathisia, and TD.
- Only one third of patients with dementia show behavioral improvement with conventional antipsychotic treatment'
- The majority of patients treated with these will experience anticholinergic effects.
- The presence of EPS can lead to medication intolerance, falls and other adverse effects.
- Typical antipsychotics have serious, potentially fatal, consequences in patients with Lewy Body dementia.

Anticonvulsants.

- Anticonvulsants such as carbamazepine, valproic acid and gabapentin may be effective in the treatment of BPSD.
- Gabapentin has shown some benefit when treating aggressive behavior in patients with dementia.
- Carbamazepine has been investigated in several trials and was found to reduce agitation, restlessness and anxiety. Ataxia can occur in elderly patients treated with carbamazepine.
- Valproic acid had been reported to show some positive effects, with a benign adverse effect profile, but it does not appear to be effective for the treatment of neuropsychiatric symptoms. It also caused significantly more adverse effects than placebo, especially sedation.

Antidepressants

- Selective serotonin reuptake inhibitors (SSRI's) may have "neuroleptic" effects by reducing dopaminergic outflow, and dysregulation in serotonergic neurotransmission may play an important role in the psychotic symptoms of dementia patients.
- Citalopram is the most selective, with moderate potency and high bioavailability and may improve emotional bluntness, confusion, irritability, anxiety, fear, depressed mood, and restlessness
- Trazodone is widely used for agitation, sleep disorders, and disruptive behavior because of its sedative effect and negligible anticholinergic activity.

Cholinesterase inhibitors

- Cholinesterase inhibitors can be used for the treatment of mild to moderate dementia.
- In Lewy Body dementia, donepezil can cause improvement over time in behavioral symptoms.
- Rivastigmine may slow the progression of BPSD symptoms, including aggressiveness and activity disturbances.
- However further research is needed.

Other medications

- Medications such as memantine, buspirone, beta blockers, benzodiazepines, and thiothixene have been evaluated for their use in treating BPSD.
- Adding memantine to donepezil results in better outcomes for dementia patients on measures of cognition, agitation, ADLs, global outcome, and behaviour.
- Buspirone's benign adverse effect profile makes it a useful alternative in mild agitation.
- Low dose propranolol may reduce disruptive, aggressive behavior.
- Benzodiazepines show significantly more improvement in BPSD symptoms when compared with placebo; however, they should be

Conclusions.

- Behavioural and psychological disorders occur in most dementing conditions, usually in later stages.
- One half of these patients experience psychotic symptoms, such as delusions and hallucinations, which in turn makes them more vulnerable to severe agitation.
- Caregiver education, support and behavioural training, and environmental modifications should be the first step in approaching the dementia patient with BPSD.

Conclusions.

- Good clinical practice dictates that patients receive individualized pharmacotherapeutic dosing regimens initiated and modified relative to clinical efficacy and tolerability and targeted to specific neuropsychiatric symptoms.

- “The art of drug treatment is to use the right drug for the right symptoms at the proper stage of the disease starting low and going slow (Gauthier 2005, p 857).”