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QUALIFICATION WORK

on the topic: «**CLINICAL AND PHARMACOLOGICAL ASPECTS OF THE USE OF ANTIPARKINSONIAN DRUGS »**

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АНОТАЦІЯ

Переважна більшість пацієнтів, яка звертається до аптеки – це пацієнти, що використовують для лікування комбінацію леводопи та карбидопі. Під впливом лікування першим зменшується тремор. Виявлено дуже погану інформованість пацієнтів щодо ліків та їх побічних ефектів.

Робота складається зі вступу, огляду літератури, опису матеріалів та методів досліджень, висновку та використаних джерел. Загальний обсяг скаладє 71 сторінка друкованого тексту, ілюстрована 14 рисунками та 7 таблицями, список використаних джерел містить 95 найменувань.

Ключові слова: хвороба Паркінсона, леводопа, карбідопа, тремор, побічна дія

ANNOTATION

The greater number of patients is important, as they go to the pharmacy - all patients who win the combination of levodopi and carbidop for the jubilation. Under the splash of glee, the tremor changes first. It was revealed even more filthy awareness of patients about the symptoms of those side effects.

The work is put together with a start, a look at the literature, a description of the materials and methods of research, a vysnovka and vikoristanih dzherel. A wild collection of texts 71 pagesof an elaborate text, illustrated with 14 drawings and 7 tables, a list of references included 95 names.

Key words: Parkinson's disease, levodopa, carbidopa, tremor, side effects

LIST OF CONTENTS

ABBREVIATION LIST

API is an active pharmaceutical ingredient

WHO is the World Health Organization

PD – Parkinson disease

SR is a side reaction

SE is a side effect

FDA - Food and Drug Agency

PREFACE

Relevance of the topic. Parkinson's disease (PD) is a progressive multi-system neurodegenerative disease affecting people mainly in later years of life. It is the second most common neurodegenerative disease worldwide with incidence and prevalence on the rise along with changing population demographics [1]. The prevalence of PD in industrialised countries is generally estimated at 0.3% of the entire population and about 1% in people over 60 years of age [2]. The prevalence increases with advancing age both for men and women with no decreases at higher ages [3]. In Europe, the prevalence at ages 85–89 has been reported as 3.5% [4].

It is estimated that up to 80% of dopaminergic cells in the nigro-striatal system are lost before the cardinal motor features of PD start to appear [5]. The disease is usually diagnosed by the first motor symptoms. The diagnosis is based on defined criteria from the UK PD Brain bank [6]. Slowness of initiation of voluntary movements with progressive reduction in speed and amplitude of repetitive actions (bradykinesia) with one additional symptom, i.e., muscular rigidity, resting tremor or postural instability, are a prerequisite for the diagnosis [7].

The aim of the study.. The purpose of the study was to develop approaches to rationalize the treatment of Parkinson's disease in a pharmacy to optimize the formation of adherence to treatment in patients with Parkinson's disease.

The objectives of the study To achieve the set goal, it was necessary to solve the following tasks:

1. Conduct a literature review on the problem of Parkinson's disease, its treatment and prevention.

2. To analyze pharmaceutical market of medicinal products for the treatment of Parkinson's disease.

3. Conduct a survey of pharmacy visitors with Parkinson's disease.

4. Develop practical recommendations for patients regarding non-pharmacological methods of treating Parkinson's disease.

5. Develop practical recommendations for patients regarding the rationality of using drugs for the treatment and control of Parkinson's disease.

The object of the study: Parkinson's disease and its pharmacocorrection.

The subject of the study: pharmaceutical care when dispensing drugs for the treatment of Parkinson's disease, adherence to treatment, effectiveness and safety of treatment.

Research methods. Questionnaires of pharmacy visitors with complaints about Parkinson's disease, statistical (Statistica 6.0 program was used, Student's t-test).

Practical value of the obtained results. The research carried out in the work is the basis for further clinical and pharmaceutical study, development and implementation of the principles of optimizing the treatment of Parkinson's disease with the help of drugs in the conditions of a pharmacy. Implementation of these principles and provisions in practical medicine and pharmacy will contribute to increasing the effectiveness and safety of treatment of Parkinson's disease. Based on the results of research, approaches to the rational use of drugs for the treatment of Parkinson's disease have been developed. In the work, for the first time, a survey of pharmacy visitors was conducted on the rational use of drugs for the treatment of Parkinson's disease and elements of pharmaceutical patient care. It has been shown that patients are very reluctant to modify their lifestyle and do not want to change it much, even if they are aware of the risks of such a decision. A widespread practice is the simultaneous use of antiparkinsonic drugs. Among drugs, the leading place belongs to combined means with levodopa and carbidopa. But the most important finding of our study can be considered the facts about patients' information about drugs and their SR/SE, which turned out to be extremely insufficient.

Structure and volume. The work consists of an introduction, a literature review, a description of research materials and methods, one section of own research, conclusions and a list of used sources. The total volume of work is 72 pages of printed text. The work is illustrated with 7 tables and 16 figures. The list of used sources contains 94 names, all in Latin

CHAPTER 1
CURRENT PARKINSON DISEASE DATA AND TREATMENT (LITERATURE REVIEW)

1.1 Parkinson's disease: definition, epidemiology, etiopathogenesis, manifestations

Parkinson's disease (PD) is a progressive multi-system neurodegenerative disease affecting people mainly in later years of life. It is the second most common neurodegenerative disease worldwide with incidence and prevalence on the rise along with changing population demographics [1]. The prevalence of PD in industrialised countries is generally estimated at 0.3% of the entire population and about 1% in people over 60 years of age [2]. The prevalence increases with advancing age both for men and women with no decreases at higher ages [3]. In Europe, the prevalence at ages 85–89 has been reported as 3.5% [4].

The disease has distinctive neuropathological brain changes. There is formation of abnormal proteinaceous spherical bodies called Lewy bodies (Fig. 1), and a spindle- or thread-like and, in part, branching Lewy neurites in the somata of the involved nerve cells, beginning at defined induction sites and advancing in a topographically predictable sequence within the nervous system [5]. Braak *et al*. have mapped PD into six neuropathological disease stages. In the pre-symptomatic stages of the disease (stages 1–2), the inclusion bodies are confined to the medulla oblongata/pontine tegmentum and olfactory bulb/anterior olfactory nucleus. With progression of the disease, substantia nigra and other nuclei of the midbrain and forebrain become affected (stages 3–4). It has been suggested that patients develop clinical symptoms of the disease at this stage. In the end stage (stage 5–6), the process enters the neocortex with a wide variety of clinical manifestations [6]. The degeneration of dopaminergic nigrostriatal neurons with Lewy bodies is regarded as the primary neuropathological correlate of motor impairment in Parkinson's disease, but glutamatergic, cholinergic, GABA-ergic, tryptaminergic, noradrenergic and adrenergic nerve cells may show similar damage in their cytoskeleton [7]. The

clinical symptoms of PD are usually defined by the motor disturbances, but there may be disturbances in several other functions of the nervous system. The symptoms are generally categorized into motor and non-motor symptoms, and some of the symptoms may be provoked or aggravated by the dopaminergic treatment (see below).

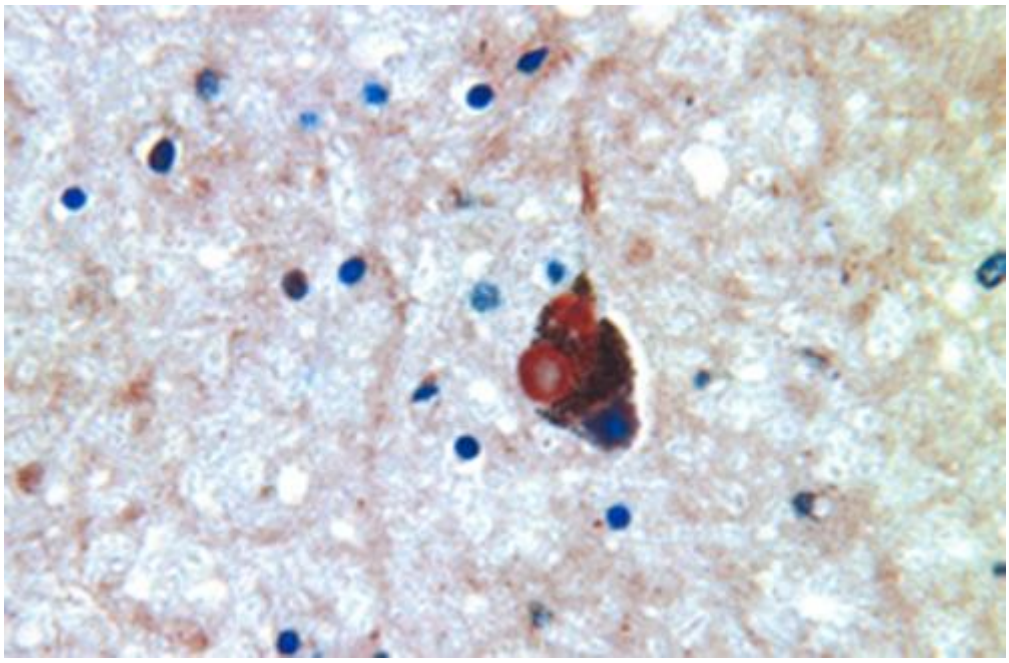

Fig. 1.1 Lewy bodies in a degenerating neuron. Synuclein staining.

The aetiology of PD is probably multifactorial and there is no available treatment that will halt or stop progression of the disease. Treatment with dopaminergic drugs is symptomatic and aims at correcting the motor disturbances. Levodopa, a prodrug to dopamine, is standard and the most common initial therapy for patients. Early on, response is usually good. With disease progression and less capacity of the system to store dopamine, the majority of patients experience shorter duration of response to individual doses (wearing-off symptoms), alternative phases with good and poor response to medication (on-off symptoms), involuntary movements of the head, trunk or limbs (dyskinesias) and other motor complications. Other dopaminergic medications are used to manage these fluctuations. They include monoamine oxidase type B inhibitors, catechol-*O*-methyltransferase inhibitors, the NMDA receptor antagonist amantadine and dopamine receptor agonists [7]. Surgical therapy, usually with deep brain electrical stimulation, is

available for a selected proportion of patients when medical therapy fails to control the motor symptoms.

The motor symptoms of Parkinson's disease

It is estimated that up to 80% of dopaminergic cells in the nigro-striatal system are lost before the cardinal motor features of PD start to appear [8]. The disease is usually diagnosed by the first motor symptoms. The diagnosis is based on defined criteria from the UK PD Brain bank [9]. Slowness of initiation of voluntary movements with progressive reduction in speed and amplitude of repetitive actions (bradykinesia) with one additional symptom, i.e., muscular rigidity, resting tremor or postural instability, are a prerequisite for the diagnosis [10]. Step 2 in the diagnosis is to exclude symptoms that might indicate other aetiologies such as parkinsonian syndromes that have their own neuropathological changes, and Step 3 to ascertain at least three supportive criteria for PD, such as unilateral onset of symptoms, persistent asymmetry of clinical symptoms, good response to levodopa treatment and induction of dyskinesias by the dopaminergic treatment. In most cases, symptoms start in one side of the body with contralateral symptoms appearing within a few years. The body posture becomes stooped, there is axial and limb rigidity with or without cogwheel phenomenon, tendency for a shuffling gait and lack of arm swing while walking. The bradykinesia may lead to expressionless face (hypomimia) and the amplitudes of hand writing become smaller (micrographia). Around 80% have limb tremor, most commonly a resting pill-rolling type of tremor of the hands. Pill rolling relates to the tendency of the thumb and the index finger to get into contact and perform a circular movement [11]. Occasionally, the tremor involves the legs and other tremor types may occur [12]. Other gait disturbances than shuffling include blocking, hesitancy and gait festination where steps become progressively smaller and more rapid which may lead to loss of balance and falls. A quarter to 60% of patients experience freezing of movements usually after several years from onset [13].

Table 1.1

UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria

Step 1: Diagnosis of Parkinsonian syndrome

Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive action)

And at least one of the following

Muscular rigidity

4–6 Hz rest tremor

Postural instability not caused by primary visual, vestibular, cerebellar or proprioceptive dysfunction

Step 2: Exclusion criteria for Parkinson's disease

History of repeated strokes with stepwise progression of parkinsonian features

History of repeated head injury

History of definite encephalitis

Oculogyric crises

Neuroleptic treatment at onset of symptoms

More than one affected relative

Sustained remission

Strictly unilateral features after 3 years

Supra-nuclear gaze palsy

Cerebellar signs

Early severe autonomic involvement

Early severe dementia with disturbances of memory, language and praxis

Babinski sign
Presence of cerebral tumour or communicating hydrocephalus on CT scan
Negative response to large doses of levodopa (if malabsorption excluded)
MPTP exposure
Step 3: supportive prospective positive criteria for Parkinson's disease (three or more required for diagnosis of definite Parkinson's disease)
Unilateral onset
Rest tremor present
Progressive disorder
Persistent asymmetry affecting side of onset more
Excellent response (70–100%) to levodopa
Severe levodopa-induced chorea
Levodopa response for 5 years or more
Clinical course of 10 years or more

Postural stability may be affected either early or later in the disease process and this may lead to falls and injuries. Early falls are atypical for those who are younger at onset but age is an independent risk factor for falls in PD [14] and, in the elderly, the disease is sometimes first diagnosed in hospitals after a fall. A study by Wood *et al*. showed that falls occurred in 68% of 109 patients with PD with a mean age of 75 years and mean disease duration of 3 years. Another study reported falls in 62% of patients with PD [15]. Predictors of falls other than older age include duration of disease, dementia, symmetrical onset, postural and autonomic instability [16. 17].

Oral motor disorders are common. Speech disturbances such as very quiet and hurried speech occur in more than half of the patients [18], swallowing problems have been reported in 40–80% [19] and a quarter of the patients report dribbling of saliva [20].

Dystonia is another motor symptom in PD. Dystonia describes a sustained muscular contraction frequently accompanied by abnormal movements, postures or both. This may rarely be a prediagnostic symptom in PD [21], but dystonic symptoms are mostly related to treatment, both medical and surgical [22]. The typical prediagnostic dystonias include unilateral equinovarus foot position, upper arm–forearm or forearm–hand flexion, writer's cramp, oro-mandibular dystonia, torticollis or different combinations of these symptoms [23]. In the majority of cases, the PD symptoms appear within 10 years from onset of the dystonia. In young onset familial PD, dystonia typically involves the foot with cramp-like discomfort or inversion of the affected foot [24].

In medically treated PD, dystonia, along with dyskinesias, constitutes one of the main motor complications related to chronic therapy, usually occurring as an off-period phenomenon, but can present as peak dose dystonia or diphasic dystonia [25]. In reports by Poewe and colleagues, the most frequent site for off dystonia is the foot, whereas in peak dose dystonia neck and face are more commonly involved [26. 27].

Postural deformities are a frequent complication of Parkinson's disease. These deformities include abnormally flexed body posture with flexion originating in the thoracic or lumbar spine (camptocormia), forward flexion of the head and neck (antecollis) and scoliosis of the spine, i.e., a lateral curve of the spine usually combined with rotation of the vertebrae (Doherty *et al*. **2011**). The pathophysiology of these deformities may be multifactorial and probably includes rigidity, axial dystonia, myopathy and centrally impaired proprioception.

The non-motor symptoms of Parkinson's disease

Before motor symptoms appear and the diagnosis is made, patients may have a variety of pre-motor symptoms. These may start as early as 10 or more years before

the diagnosis (Schrag *et al*. 2015) and presentation with non-motor symptoms may delay the diagnosis (O'Sullivan *et al*. 2008). One study of 109 recently diagnosed patients who had not yet started treatment showed that symptoms such as a lack of emotional involvement and interest (apathy), excessive daytime sleepiness, sleep problems and constipation may occur in up to 60–70% of patients prior to the diagnosis and these symptoms were more common than in normal controls. Other pre-motor symptoms included inability to experience pleasure from activities usually found enjoyable (anhedonia) memory complaints, loss of smell and taste, mood disturbances, excessive sweating, fatigue and pain. Constipation, dream-enacting behaviour (REM behaviour sleep disorder), frequent nightmares, daytime drowsiness and postprandial fullness were often reported to occur more than 10 years before onset of motor symptoms (Pont-Sunyer *et al*. 2015). Depression and anxiety may also occur long before the diagnosis is made (Chen *et al*. 2013). The pre-motor symptoms vary from patient to patient, but they continue while other motor or non-motor symptoms of PD may appear in the clinical course. With advancing disease, the non-motor symptoms generally become more troublesome for the patients than the motor symptoms.

The non-motor symptoms are categorized here into disturbances in autonomic function, sleep disturbances, cognitive and psychiatric disturbances and sensory symptoms.

Disturbances in autonomic function

Autonomic dysfunction may present prior to the diagnosis or become apparent with disease progression or be induced by medication (Koike and Takahashi 1997). All areas of autonomic function may be affected and this has been reported to affect daily life of over 50% of patients (Jost 2003). The autonomic dysfunction is considered because of involvement of both the central and peripheral postganglionic autonomic nervous system (Jost 2003). Orthostatic hypotension affects 30–40% of patients. This is defined as a fall in systolic blood pressure of > 20 mm Hg or in diastolic blood pressure > 10 mm Hg on either standing or head-up tilt to at least 60 degrees within 3 min (Lahrmann *et al*. 2006). On assuming the upright posture,

hypotension-induced hypoperfusion of the brain can result in dizziness, visual disturbances and impaired cognition that may precede loss of consciousness. In PD, the blood pressure drop may last several minutes (Jost **2003**). Duration of PD may be unrelated to the occurrence of orthostatic hypotension (Jost and Augustis **2015**). In elderly PD patients, this may mainly occur after food intake (Iodice *et al*. **2011**).

Gastrointestinal symptoms are common. There is slowing of mobility of the gastrointestinal tract with symptoms such as postprandial fullness and gastric retention, but slow-transit constipation is by far the most common, occurring in 70–80% (Jost and Eckardt **2003**; Jost **2010**). Patients may also experience difficulties in rectal evacuation because of rectal sphincter dysfunction (Mathers *et al*. **1989**).

Urinary control disturbances include urinary frequency, urgency and incontinence (Jost **2003**). Frequent nocturia is reported by 60% of patients and is caused by detrusor overactivity (Yeo *et al*. **2012**). Erectile dysfunction is common in males (Sakakibara *et al*. **2011**).

There may also be autonomic dermatological symptoms such as excessive sweating (hyperhidrosis). This may be associated with dyskinesias or low blood concentrations of the dopaminergic drugs but does not appear to correlate with duration of the disease (Hirayama **2006**). Salivary secretion appears to be reduced in PD despite frequent problem with dribbling of saliva in advanced disease (Cersosimo *et al*. **2009**). Seborrhoeic keratosis is a dermatological facial and scalp disorder that has been reported in 18.6% of patients (Fischer *et al*. **2001**). There is increased fat in the central face often associated with scaling of the skin of the forehead. The cause of this is unclear.

Sleep disturbances

The neuropathology of PD is known to affect anatomical structures and central neurotransmitters that are involved in the modulation of the physiological sleep cycle. Polysomnographic findings have shown changes in the architecture of sleep waves compared with healthy controls, but the medical treatment for different symptoms related to PD may also disrupt night-time sleep (Larsen and

Tandberg 2001; Monderer and Thorpy 2009). A variety of sleep disorders may appear with approximately two third of patients affected (Mehta *et al*. 2008).

Fractionated sleep is most common (Porter *et al*. 2008). Sleep studies have shown that patients have more shallow sleep and tendency to frequent awakenings in the night (Yong *et al*. 2011). Other PD symptoms such as difficulties with turning around in bed, frequent nocturia, nocturnal tremor and depression may also lead to fractionated sleep (Lees *et al*. 1988).

Excessive daytime sleepiness has been estimated to occur in up to 50% (Monderer and Thorpy 2009) and may be partly induced by the dopaminergic drugs (Knie *et al*. 2011). Sleep syndromes are also more common in PD than in controls. They include REM behaviour sleep disorder where patients act out their dreams, thrash and kick around in the night while dreaming. The frequency in clinically manifested PD has been reported as 27–32% (Monderer and Thorpy 2009), but symptoms may appear years or decades before the motor symptoms appear (Hickey *et al*. 2007). The syndrome of restless legs with or without periodic leg movements of sleep is more common among patients than controls (Monderer and Thorpy 2008). Restless legs syndrome is an urge to move the legs while sitting or lying down that is relieved by walking about, while periodic leg movements of sleep consist of rhythmic jerking of lower limbs during sleep, usually observed by the partner.

Although obstructive sleep apnoea, where breathing stops intermittently during sleep, is well known in PD (Monderer and Thorpy 2008), not all studies have shown increased prevalence among patients (Zeng *et al*. 2013). Sudden sleep attacks occurring without normal drowsiness as induction to sleep have been reported in patients on dopaminergic treatment. It seems that nearly all available dopaminergic drugs may induce sleep attacks (Larsen and Tandberg 2001) and the dopaminergic treatment load may be implicated (Brodsky *et al*. 2003).

Neuropsychiatric symptoms and dementia

Visual hallucinations and illusions are common in PD and reportedly occur in a third to 40% of patients (Onofrj *et al*. 2007). Although virtually all anti-

parkinsonian medications have been reported to induce hallucinations and psychosis, visual hallucinations have also been reported to occur prior to drug treatment (Pagonabarraga *et al*. 2016). Neuropathological changes in the amygdala and hippocampus caused by the disease process seem to be implicated in the aetiology (Williams-Gray *et al*. 2006). Frequently, images of people, small animals or objects are conceived or the hallucinations may have multiple content. The images may be familiar or not. They last from seconds to minutes, and may recur over the day (Holroyd *et al*. 2001). Usually, non-demented patients retain insight and the hallucinations are usually not threatening. Less commonly, the hallucinations are olfactory (McAuley and Gregory 2012), auditory (Inzelberg *et al*. 1998) and tactile (Fenelon *et al*. 2002). One study showed that visual component was lacking in 10% of cases (Papapetropoulos and Heather Katzen 2008). Minor visual phenomena such as sense of presence and visual illusions affect 17–72% of patients and delusions about 5% (Fenelon and Alves 2010). Higher load of dopaminergic treatment may be related to the hallucinations, but disease severity, cognitive impairment, depression, older age and worse visual acuity may also be important (Holroyd *et al*. 2001; Fenelon and Alves 2010).

With advancing disease patients may develop paranoid illusions often with persecutory ideas or suspicions towards the spouse (Williams-Gray *et al*. 2006). If psychosis occurs it is usually late in the disease process in patients on high doses of drugs or may be associated with old age, cognitive impairment and history of depression (Thanvi *et al*. 2005).

The dopaminergic treatment may also induce behavioural abnormalities such as euphoria/hypomania, poor organisational skills, hypersexuality, abnormal hoarding or punting and risk taking behaviour (O'Sullivan *et al*. 2009). Risk taking behaviour may be reflected in gambling, driving at speed or excessive spending. These symptoms that together have been called dopamine dysregulation syndrome or impulse control disorders are increasingly recognized (Evans and Lees 2004). They appear to be related to the dopaminergic treatment load and possibly more to dopamine receptor agonist drugs than others (O'Sullivan *et al*. 2009;

Ceravolo *et al*. 2010). Dopamine dysregulation syndrome is most common in men with relatively young onset disease (Ceravolo *et al*. 2010).

Cognitive deterioration and dementia is common in PD and may occur early or late (Williams-Gray *et al*. 2006, 2007). The earliest symptoms include problems with executive function, i.e., planning and organizing goal-directed behaviour, but visuospatial dysfunction, impaired speech fluency and memory impairment are also observed (Williams-Gray *et al*. 2006). Progression of the dementia shows a correlation with spread of the neuropathological changes to cortical brain structures (Irwin *et al*. 2012). Mild cognitive impairment has been reported to be twice as common in PD as in people not affected by the disease (Aarsland *et al*. 2009). Age itself rather than age at onset of PD has been associated with incident dementia in PD (Aarsland *et al*. 2007) and disease severity has been reported as the strongest predictor of dementia risk (Riedel *et al*. 2008). A 6-year longitudinal study of 141 PD patient with average disease duration of 5 years and a mean age of 69 years showed a cumulative risk of dementia increasing from 8.5% at 1 year to nearly 50% by year 6 (Pigott *et al*. 2015).

Depression and anxiety are other common symptoms in PD. A meta-analysis reported that one third of patients have clinically significant depression, while a major depressive disorder was reported in 17% (Reijnders *et al*. 2008). Depression and anxiety may relate to several factors, including advancing disease severity (Schrag *et al*. 2001). Anxiety and depression may disappear with dopaminergic treatment, but may be persistent or recur in the long clinical course of the disease.

Sensory symptoms

Sensory symptoms are common in PD. Reduced or lost sense of smell is found in at least 80% of patients and this often appears long before the motor symptoms (Doty *et al*. 1988). Vague abnormal sensations in body parts may be perceived and these sensations may fluctuate in relation to treatment (Bayulkemand and Lopez 2011). Pain is reported by 40–85% of patients (Broen *et al*. 2012). Limb pain may be the presenting symptom and misdiagnosed as a frozen shoulder or degenerative spine disease (Williams and Lees 2009). Limb pain is most common,

but oral, thoracal, abdominal and genital pain may also occur (Waseem and Gwinn-Hardy 2001). Five different types of pain have been defined, i.e., musculoskeletal, radicular–neuropathic, dystonic, central neuropathic pain and pain-associated restlessness (akathisia) (Ford 2010). Musculoskeletal pain is reported by almost half of the patients, but such pain is common in this age group and may not always be related to the PD. Dystonic, radicular and central neuropathic pain are less common (Broen *et al*. 2012).

The clinical course of PD

There is a great variability between patients in progression of symptoms (Poewe 2006). Early in the course of the disease, symptoms are usually unilateral and mild and the response to treatment is fair or excellent with no variability in motor function over the day. Although symptoms progress and motor symptoms appear in the contralateral side, drug response is usually reliable and patients are functioning well. This is often called the honeymoon period. With progression of the disease, treatment becomes heavier and drug response less reliable and the anti-parkinsonian drugs induce potentially disabling dyskinesias. Gait and balance disturbances and speech and swallowing difficulties may appear that are poorly responding to treatment. After prolonged disease duration of 10 or more years, a majority of patients will also have developed some non-motor symptoms for which there are currently limited available treatments. These include cognitive dysfunction, dementia and psychosis, autonomic failure, sleep–wake cycle dysregulation, depression, pain and sensory symptoms (Poewe 2006). The disease increasingly affects the quality of life and leads to dependency regarding activities of daily living. Patients with PD have greater and earlier need for nursing home placements (Parashos *et al*. 2002), higher rates of emergency hospital admissions, longer admissions and higher in-hospital mortality than comparable general population (Low *et al*. 2015). Relative risk of death compared with matched control populations has been reported 1.6–3.0 (Clarke and Moore 2007). Different studies show that the mean duration until death ranges from 6.9 to 14.3 years with increased age and the

presence of dementia as the highest predictors of increased mortality (Macleod *et al*. **2014**).

The clinical treatment of PD with levodopa in the 1960s revolutionized the treatment of the motor complications of the disease. This revolution was portrayed in the film Awakenings. However, as I review, PD is a much more complex disease than just the motor manifestations. It remains a debilitating disorder for which no effective disease modification therapies have yet been identified.

There is no cure for PD, but research is ongoing and medications or surgery can often provide substantial improvement with motor symptoms.

The four primary symptoms of PD are:

Tremor—Tremor (shaking) often begins in a hand, although sometimes a foot or the jaw is affected first. The tremor associated with PD has a characteristic rhythmic back-and-forth motion that may involve the thumb and forefinger and appear as a “pill rolling.” It is most obvious when the hand is at rest or when a person is under stress. This tremor usually disappears during sleep or improves with a purposeful, intended movement.

Rigidity—Rigidity (muscle stiffness), or a resistance to movement, affects most people with PD. The muscles remain constantly tense and contracted so that the person aches or feels stiff. The rigidity becomes obvious when another person tries to move the individual's arm, which will move only in short, jerky movements known as “cogwheel” rigidity.

Bradykinesia—This is a slowing down of spontaneous and automatic movement that can be particularly frustrating because it may make simple tasks difficult. Activities once performed quickly and easily—such as washing or dressing—may take much longer. There is often a decrease in facial expressions (also known as "masked face").

Postural instability—Impaired balance and changes in posture can increase the risk of falls.

PD does not affect everyone the same way. The rate of progression and the particular symptoms differ among individuals. PD symptoms typically begin on one

side of the body. However, the disease eventually affects both sides, although symptoms are often less severe on one side than on the other.

People with PD often develop a so-called parkinsonian gait that includes a tendency to lean forward, taking small quick steps as if hurrying (called festination), and reduced swinging in one or both arms. They may have trouble initiating movement (start hesitation), and they may stop suddenly as they walk (freezing).

Other problems may accompany PD, such as:

Depression—Some people lose their motivation and become dependent on family members.

Emotional changes—Some people with PD become fearful and insecure, while others may become irritable or uncharacteristically pessimistic.

Difficulty with swallowing and chewing—Problems with swallowing and chewing may occur in later stages of the disease. Food and saliva may collect in the mouth and back of the throat, which can result in choking or drooling. Getting adequate nutrition may be difficult.

Speech changes—About half of all individuals with PD have speech difficulties that may be characterized as speaking too softly or in a monotone. Some may hesitate before speaking, slur, or speak too fast.

Urinary problems or constipation—Bladder and bowel problems can occur due to the improper functioning of the autonomic nervous system, which is responsible for regulating smooth muscle activity.

Skin problems—The skin on the face may become oily, particularly on the forehead and at the sides of the nose. The scalp may become oily too, resulting in dandruff. In other cases, the skin can become very dry.

Sleep problems—Common sleep problems in PD include difficulty staying asleep at night, restless sleep, nightmares and emotional dreams, and drowsiness or sudden sleep onset during the day. Another common problem is “REM behavior disorder,” in which people act out their dreams, potentially resulting in injury to themselves or their bed partners. The medications used to treat PD may contribute to some sleep issues. Many of these problems respond to specific therapies.

Dementia or other cognitive problems—Some people with PD develop memory problems and slow thinking. Cognitive problems become more severe in the late stages of PD, and some people are diagnosed with Parkinson's disease dementia (PDD). Memory, social judgment, language, reasoning, or other mental skills may be affected.

Orthostatic hypotension—Orthostatic hypotension is a sudden drop in blood pressure when a person stands up from a lying down or seated position. This may cause dizziness, lightheadedness, and, in extreme cases, loss of balance or fainting. Studies have suggested that, in PD, this problem results from a loss of nerve endings in the sympathetic nervous system, which controls heart rate, blood pressure, and other automatic functions in the body. The medications used to treat PD may also contribute.

Muscle cramps and dystonia—The rigidity and lack of normal movement associated with PD often causes muscle cramps, especially in the legs and toes. PD can also be associated with dystonia—sustained muscle contractions that cause forced or twisted positions. Dystonia in PD is often caused by fluctuations in the body's level of dopamine (a chemical in the brain that helps nerve cells communicate and is involved with movement).

Pain—Muscles and joints may ache because of the rigidity and abnormal postures often associated with the disease.

Fatigue and loss of energy—Many people with PD often have fatigue, especially late in the day. Fatigue may be associated with depression or sleep disorders, but it may also result from muscle stress or from overdoing activity when the person feels well. Fatigue may also result from akinesia, which is trouble initiating or carrying out movement.

Sexual dysfunction—Because of its effects on nerve signals from the brain, PD may cause sexual dysfunction. PD-related depression or use of certain medications may also cause decreased sex drive and other problems.

Hallucinations, delusions, and other psychotic symptoms can be caused by the drugs prescribed for PD.

Diseases and conditions that resemble PD

PD is the most common form of parkinsonism, which describes disorders of other causes that produce features and symptoms that closely resemble Parkinson's disease. Many disorders can cause symptoms similar to those of PD, including:

Multiple system atrophy (MSA) refers to a set of slowly progressive disorders that affect the central and autonomic nervous systems. The protein alpha-synuclein forms harmful filament-like aggregates in the supporting cells in the brain called oligodendroglia. MSA may have symptoms that resemble PD. It may also take a form that primarily produces poor coordination and slurred speech, or it may involve a combination of these symptoms. MSA with parkinsonian symptoms is sometimes referred to as MSA-P (or striatonigral degeneration).

Lewy body dementia is associated with the same abnormal protein deposits (Lewy bodies) found in Parkinson's disease but appears in areas throughout the brain. Symptoms may range from primary parkinsonian symptoms such as bradykinesia, rigidity, tremor, and shuffling walk, to symptoms similar to those of Alzheimer's disease (memory loss, poor judgment, and confusion). These symptoms may fluctuate (vary) dramatically. Other symptoms may include visual hallucinations, psychiatric disturbances such as delusions and depression, and problems with cognition.

Progressive supranuclear palsy (PSP) is a rare, progressive brain disorder caused by a gradual deterioration of cells in the brain stem. Symptoms may include problems with control of gait and balance (people often tend to fall early in the course of PSP), an inability to move the eyes, and alterations of mood and behavior, including depression and apathy as well as mild dementia. PSP is characterized by clumps of a protein called tau.

Corticobasal degeneration (CBD) results from atrophy of multiple areas of the brain, including the cerebral cortex and the basal ganglia. Initial symptoms may first appear on one side of the body, but eventually affect both sides. Symptoms include rigidity, impaired balance, and problems with coordination. Other symptoms may include dystonia that affects one side of the body, cognitive and visual-spatial

impairments, apraxia (loss of the ability to make familiar, purposeful movements), hesitant and halting speech, myoclonus (muscular jerks), and dysphagia (difficulty swallowing). CBD also is characterized by deposits of the tau protein.

Several diseases, including MSA, CBD, and PSP, are sometimes referred to as “Parkinson's-plus” diseases because they have the symptoms of PD plus additional features.

In very rare cases, parkinsonian symptoms may appear in people before the age of 20. This condition is called juvenile parkinsonism. It often begins with dystonia and bradykinesia, and the symptoms often improve with levodopa medication.

Diagnosing PD

There are currently no specific tests that diagnose PD. The diagnosis is based on:

Medical history and a neurological examination

Blood and laboratory tests to rule out other disorders that may be causing the symptoms

Brain scans to rule out other disorders. However, computed tomography (CT) and magnetic resonance imaging (MRI) brain scans of people with PD usually appear "normal" or "unremarkable"

In rare cases, where people have a clearly inherited form of PD, researchers can test for known gene mutations as a way of determining an individual's risk of developing the disease. However, this genetic testing can have far-reaching implications and people should carefully consider whether they want to know the results of such tests.

1.2 Treating PD

Currently, there is no cure for PD, but medications or surgery can often provide improvement in the motor symptoms.

Drug Therapy

Medications for PD fall into three categories:

Drugs that increase the level of dopamine in the brain. The most common drugs for PD are dopamine precursors—substances like levodopa that cross the blood-brain barrier and are then changed into dopamine. Other drugs mimic dopamine or prevent or slow its breakdown.

Drugs that affect other neurotransmitters in the body to ease some of the symptoms of the disease. For example, anticholinergic drugs interfere with production or uptake of the neurotransmitter acetylcholine. These can be effective in reducing tremors.

Medications that help control the non-motor symptoms of the disease, or the symptoms that don't affect movement. For example, people with PD-related depression may be prescribed antidepressants.

Symptoms may significantly improve at first with medication but can reappear over time as PD worsens and drugs become less effective.

Levodopa-Carbidopa—The cornerstone of PD therapy is the drug levodopa (also known as L-dopa). Nerve cells can use levodopa to make dopamine and replenish the brain's reduced supply. People cannot simply take dopamine pills because dopamine does not easily pass through the blood-brain barrier, which is a protective lining of cells inside blood vessels that regulate the transport of oxygen, glucose, and other substances in the brain.

People are given levodopa combined with another substance called carbidopa. When added to levodopa, carbidopa prevents the conversion of levodopa into dopamine except for in the brain; this stops or diminishes the side effects due to dopamine in the bloodstream. Levodopa-carbidopa is often very successful at reducing or eliminating the tremors and other motor symptoms of PD during the early stages of the disease. People may need to increase their dose of levidopa gradually for maximum benefit. Levodopa can reduce the symptoms of PD but it does not replace lost nerve cells or stop its progression.

Initial side effects of levodopa-carbidopa may include:

Nausea

Low blood pressure

Restlessness

Drowsiness or sudden sleep

Side effects of long-term or extended use of levodopa may include:

Hallucinations and psychosis

Dyskinesia, or involuntary movements such as mild to severe twisting and writhing

Later in the course of the disease, people with PD may begin to notice more pronounced symptoms before their first dose of medication in the morning and between doses as the period of effectiveness after each dose begins to shorten, called the wearing-off effect. People experience sudden, unpredictable “off periods,” where the medications do not seem to be working. One approach to alleviating this is to take levodopa more often and in smaller amounts. People with PD should never stop taking levodopa without their physician's input, because rapidly withdrawing the drug can have potentially serious side effects.

Dopamine agonists—These mimic the role of dopamine in the brain and can be given alone or with levodopa. They are somewhat less effective than levodopa in treating PD symptoms but work for longer periods of time. Many of the potential side effects are similar to those associated with the use of levodopa, including drowsiness, sudden sleep onset, hallucinations, confusion, dyskinesias, edema (swelling due to excess fluid in body tissues), nightmares, and vomiting. In rare cases, they can cause an uncontrollable desire to gamble, hypersexuality, or compulsive shopping. Dopamine agonist drugs include apomorphine, pramipexole, ropinirole, and rotigotine.

MAO-B inhibitors—These drugs block or reduce the activity of the enzyme monoamine oxidase B, or MAO-B, which breaks down dopamine in the brain. MAO-B inhibitors cause dopamine to accumulate in surviving nerve cells and reduce the symptoms of PD. These medications include selegiline and rasagiline. Studies supported by the NINDS have shown that selegiline (also called deprenyl) can delay the need for levodopa therapy by up to a year or more. When selegiline is

given with levodopa, it appears to enhance and prolong the response to levodopa and thus may reduce wearing-off. Selegiline is usually well-tolerated, although side effects may include nausea, orthostatic hypotension, or insomnia. The drug rasagiline is used in treating the motor symptoms of PD with or without levodopa.

COMT inhibitors—COMT stands for catechol-O-methyltransferase and is another enzyme that breaks down dopamine. The drugs entacapone, opicapone, and tolcapone prolong the effects of levodopa by preventing the breakdown of dopamine. COMT inhibitors can decrease the duration of "off periods" of one's dose of levodopa. Side effects may include diarrhea, nausea, sleep disturbances, dizziness, urine discoloration, abdominal pain, low blood pressure, or hallucinations. In a few rare cases, tolcapone has caused severe liver disease, and people taking tolcapone need regular monitoring of their liver function.

Amantadine—This antiviral drug can help reduce symptoms of PD and levodopa-induced dyskinesia. It can be prescribed alone in the early stages of the disease and can be used with an anticholinergic drug or levodopa. After several months, amantadine's effectiveness wears off in up to half of the people taking it. Amantadine's side effects may include insomnia, mottled skin, edema, agitation, or hallucinations. Researchers are not certain how amantadine works in PD, but it may increase the effects of dopamine.

Anticholinergics—These drugs, which include trihexyphenidyl, benztropine, and ethopropazine, decrease the activity of the neurotransmitter acetylcholine and can be particularly effective for tremor associated with PD. Side effects may include dry mouth, constipation, urinary retention, hallucinations, memory loss, blurred vision, and confusion.

When recommending a course of treatment, a doctor will assess how much the symptoms disrupt the person's life and then tailor therapy to the person's particular condition. Since no two people will react the same way to a given drug, it may take time and patience to get the dose right. Even then, symptoms may not be completely alleviated.

Table 1.2

Medications to treat motor symptoms of PD

Category	Generic	Brand Name
Drugs that increase brain levels of dopamine	Levodopa/carbidopa	Parcopa, Sinemet
Drugs that mimic dopamine (dopamine agonists)	Apomorphine Pramipexole Ropinirole Rotigotine	Apokyn Mirapex Requip Neupro
Drugs that inhibit dopamine breakdown (MAO-B inhibitors)	Rasagiline Selegiline (deprenyl)	Azilect Eldepryl, Zelapar
Drugs that inhibit dopamine breakdown (COMT inhibitors)	Entacapone Tolcapone	Comtan Tasmar
Drugs that decrease the action of acetylcholine (anticholinergics)	Benztropine Ethopropazine Trihexyphenidyl	Cogentin Parsidol Artane
Drugs with an unknown mechanism of action for PD	Amantadine	Symmetrek

Surgery

Before the discovery of levodopa, surgery was an option for treating PD. Studies in the past few decades have led to great improvements in surgical techniques, and surgery is again considered for people with PD for whom drug therapy is no longer sufficient.

Pallidotomy and Thalamotomy

The earliest types of surgery for PD involved selectively destroying specific parts of the brain that contribute to PD symptoms. Surgical techniques have been refined and can be very effective for the motor symptoms of PD. The most common lesion surgery is called pallidotomy. In this procedure, a surgeon selectively destroys a portion of the brain called the globus pallidus. Pallidotomy can improve symptoms

of tremor, rigidity, and bradykinesia, possibly by interrupting the connections between the globus pallidus and the striatum or thalamus. Some studies have also found that pallidotomy can improve gait and balance and reduce the amount of levodopa people require, thus reducing drug-induced dyskinesias.

Another procedure, called thalamotomy, involves surgically destroying part of the thalamus; this approach is useful primarily to reduce tremor.

Because these procedures cause permanent destruction of small amounts of brain tissue, they have largely been replaced by deep brain stimulation for treatment of PD. However, a method using focused ultrasound from outside the head is being tested because it creates lesions without the need for surgery.

Deep Brain Stimulation

Deep brain stimulation (DBS) uses an electrode surgically implanted into part of the brain, typically the subthalamic nucleus or the globus pallidus. Similar to a cardiac pacemaker, a pulse generator (battery pack) that is implanted in the chest area under the collarbone sends finely controlled electrical signals to the electrode(s) via a wire placed under the skin. When turned on using an external wand, the pulse generator and electrodes painlessly stimulate the brain in a way that helps to block signals that cause many of the motor symptoms of PD. (The signal can be turned off using the wand.) Individuals must return to the medical center frequently for several months after DBS surgery in order to have the stimulation adjusted very carefully to give the best results. DBS is approved by the U.S. Food and Drug Administration (FDA) and is widely used as a treatment for PD.

DBS is primarily used to stimulate one of three brain regions: the subthalamic nucleus, the globus pallidus interna, or the thalamus. Stimulation of either the globus pallidus or the subthalamic nucleus can reduce tremor, bradykinesia, and rigidity. Stimulation of the thalamus is useful primarily for reducing tremor.

DBS does not stop PD from progressing, and some problems may gradually return. While the motor function benefits of DBS can be substantial, it usually does not help with speech problems, “freezing,” posture, balance, anxiety, depression, or dementia.

DBS is generally appropriate for people with levodopa-responsive PD who have developed dyskinesias or other disabling “off” symptoms despite drug therapy. DBS has not been demonstrated to be of benefit for “atypical” parkinsonian syndromes such as multiple system atrophy, progressive supranuclear palsy, or post-traumatic parkinsonism, which also do not improve with Parkinson's medications.

Complementary and Supportive Therapies

A wide variety of complementary and supportive therapies may be used for PD, including:

A healthy diet—At this time there are no specific vitamins, minerals, or other nutrients that have any proven therapeutic value in PD. The National Institute of Neurological Disorders and Stroke (NINDS) and other components of the NIH are funding research to determine if caffeine, antioxidants, and other dietary factors may be beneficial for preventing or treating PD. A healthy diet can promote overall well-being for people with PD just as it would for anyone else. Eating a fiber-rich diet and drinking plenty of fluids also can help alleviate constipation. A high protein diet, however, may limit levodopa's absorption.

Exercise—Exercise can help people with PD improve their mobility, flexibility, and body strength. It also can improve well-being, balance, minimize gait problems, and strengthen certain muscles so that people can speak and swallow better. General physical activity, such as walking, gardening, swimming, calisthenics, and using exercise machines, can have other benefits. People with PD should always check with their doctors before beginning a new exercise program.

Alternative approaches that are used by some individuals with PD include:

A NINDS-funded clinical trial demonstrated the benefit of tai chi exercise compared to resistance or stretching exercises in people with PD

Massage therapy to reduce muscle tension

Yoga to increase stretching and flexibility

Hypnosis acupuncture

The Alexander Technique to optimize posture and muscle activity

Coping with PD

While PD usually progresses slowly, eventually daily routines may be affected—from socializing with friends to earning a living and taking care of a home. These changes can be difficult to accept. Support groups can help people cope with the disease's emotional impact. These groups can provide valuable information, advice, and experience to help people with PD, their families, and their caregivers deal with a wide range of issues, including locating doctors familiar with the disease and coping with physical limitations. A list of national organizations that can help people locate support groups in their communities appears at the end of this information. Individual or family counseling may also help people find ways to cope with PD.

People with PD may also benefit from being proactive and finding out as much as possible about the disease in order to alleviate fear of the unknown and to take a proactive role in maintaining their health. Many people with PD continue to work either full- or part-time, although they may need to adjust their schedule and working environment to accommodate their symptoms.

The average life expectancy of a person with PD is generally the same as for people who do not have the disease. Fortunately, there are many treatment options available for people with PD. However, in the late stages, PD may no longer respond to medications and can become associated with serious complications such as choking, pneumonia, and falls.

Because PD is a slow, progressive disorder, it is not possible to predict what course the disease will take for an individual person.

Carbidopa/Levodopa

Carbidopa/levodopa is the most common drug used to treat Parkinson’s disease and is usually started as soon as the patient becomes functionally impaired.

Mechanism of Action

Administration of dopamine is ineffective in the treatment of Parkinson’s disease because it does not cross the blood-brain barrier, but levodopa, the metabolic precursor of dopamine, does cross the blood-brain barrier and presumably is converted to dopamine in the brain. Carbidopa is combined with levodopa to help

stop the breakdown of levodopa before it is able to cross the blood-brain barrier. Additionally, the incidence of levodopa-induced nausea and vomiting is less when it is combined with carbidopa.

Indications for Use

Carbidopa/levodopa is indicated for Parkinson's disease. It is also used to treat restless leg syndrome.

Nursing Considerations Across the Lifespan

Carbidopa/Levodopa is recommended for use in patients older than age 18. It can take several weeks to see positive effects and this should be explained to patients and their caregivers.

The drug is contraindicated for use with MAOIs. All patients should be observed carefully for the development of depression with concomitant suicidal tendencies.

Patients taking carbidopa and levodopa have reported suddenly falling asleep without prior warning of sleepiness while engaged in activities of daily living (including operation of motor vehicles). Patients should be advised to exercise caution while driving or operating machines during treatment with carbidopa and levodopa.

Sporadic cases of symptoms resembling neuroleptic malignant syndrome (NMS) have been reported in association with dose reductions or withdrawal of certain antiparkinsonian agents. Therefore, patients should be observed carefully when the dosage of levodopa is reduced abruptly or discontinued.

Periodic evaluations of hepatic, hematopoietic, cardiovascular, and renal functions are recommended during extended therapy. The most common adverse effect of carbidopa/levodopa is dyskinesia, which may require dosage reduction.

Patients should be instructed to plan their meal times around medication times to improve the ability to use their utensils and to avoid diets high in protein due to decreased absorption of the medication.

Adverse/Side Effects

Hallucinations and psychotic-like behavior have been reported with dopaminergic medications. Patients taking dopaminergic medications may experience intense gambling urges, increased sexual urges, intense urges to spend money, binge eating, and/or other intense urges, and the inability to control these urges. These urges stopped when the dosage was decreased or the medication discontinued.

A higher risk for melanoma has been reported. Occasionally, dark red, brown, or black color may appear in saliva, urine, or sweat after ingestion of carbidopa and levodopa. Although the color appears to be clinically insignificant, garments may become discolored.[2],[3],[4]

Patient Teaching & Education

Patients should take their medications at regular intervals as directed. If gastric irritation is experienced, patients may eat food shortly after taking medications but high-protein foods may impair drug action. Medications may cause increased drowsiness, dizziness, and orthostatic changes. Patients should carefully assess their skin to monitor for new lesions and any abnormality should be reported to the healthcare provider.

Now let's take a closer look at the medication grid for carbidopa-levodopa in Table 1.3.[5]

Table 1.3

Carbidopa-Levodopa Medication Grid

Class-subclass	**Prototype / Generic**	**Administration Considerations**	**Therapeutic Effects**	**Adverse/Side Effects**
Antiparkinson agent	carbidopa/levodopa	Avoid high-protein diets due to decreased absorption Monitor for sudden somnolence and increased depression Contraindicated with MAOIs	Slow progression of symptoms of Parkinson's disease (tremors,	Depression, suicidal ideation, hallucinations, and intense urges with inability to control them

		Periodically monitor hepatic, renal, and hematopoietic functions	rigidity, and mobility issues)	Somnolence and fatigue NMS symptoms with dose reductions or when discontinued Dyskinesia Discolored body fluids Hypomobility with long-term use

Selegiline

Selegiline is often used conjunction with carbidopa-levodopa when patients demonstrate a deteriorating response to this treatment. It is helpful to control symptom fluctuations.[6]

Mechanism of Action

Selegiline inhibits MAO-B, blocking the breakdown of dopamine.[7]

Indications for Use

Selegiline capsules are indicated as an adjunct in the management of Parkinsonian patients being treated with levodopa/carbidopa who exhibit deterioration in the quality of their response to this therapy. There is no evidence from controlled studies that selegiline has any beneficial effect in the absence of concurrent levodopa therapy.

Considerations Across the Lifespan

Large doses of selegiline may inhibit MAO-A that promotes metabolism of tyramine in the GI tract, which can cause a hypertensive crisis.

Adverse/Side Effects

Side effects are dose dependent, with larger doses posing a hypertensive crisis risk if there is consumption of food or beverages with tyramine.

Patient Teaching & Education

Patients should be advised to avoid foods high in tyramine. Additionally, medications may cause increased drowsiness, dizziness, and orthostatic changes. If patients experience abnormal behaviors such as hallucination, sexual urges, gambling, etc., this should be reported promptly to the healthcare provider.

Now let's take a closer look at the medication grid for selegiline in Table 1.4.

Table 1.4

Selegiline Medication Grid

Class/ Subclass	Prototype/ Generic	Administration Considerations	Therapeutic Effects	Adverse/Side Effects
Antiparkinson agent, MAO Type B Inhibitor	selegiline	Avoid food with tyramine if on a large dose (above 10mg/day)	Minimize progression of Parkinson's disease symptoms	Higher doses increase risk for hypertensive crisis

Amantadine

Amantadine is used in early stages of Parkinson's disease but can be effective in moderate or advanced stages in reducing tremor and muscle rigidity.[9]

Mechanism of Action

The exact mechanism of action is unknown. Amantadine is an antiviral drug that acts on dopamine receptors.[10]

Indications for Use

Amantadine is used for Parkinson's disease, medication-induced extrapyramidal symptoms, and influenza A.

Nursing Considerations Across the Lifespan

Use cautiously with renal impairment. This drug may cause suicidal ideation and should not be stopped abruptly or can cause Parkinsonian crisis. Neuroleptic Malignant Syndrome (NMS) has been reported in association with dose reduction or withdrawal of amantadine therapy.

Adverse/Side Effects

Suicide ideation, congestive heart failure, and peripheral edema can occur. This drug can cause intense gambling urges, increased sexual urges, intense urges to spend money uncontrollably, and other intense urges with an inability to control them. There is an increased risk of melanoma.

Adverse reactions reported most frequently are nausea, dizziness (lightheadedness), and insomnia. This drug can also cause anticholinergic side effects, impaired thinking, and orthostatic hypotension.[11]

Patient Teaching & Education

Patients should take medications as directed and ensure they do not skip or double doses. Medications may cause drowsiness, dizziness, and orthostatic blood pressure changes. Patients should avoid using this medication with OTC cold medications or alcoholic beverages. If patients, family, or caregivers note worsening depression or suicidality, this should be reported immediately to the healthcare provider.

Now let's take a closer look at the medication grid for amantadine in Table 1.5.[12]

Table 1.5

Amantadine Medication Grid

Class	Prototype/Generic	Administration Considerations	Therapeutic Effects	Adverse/Side Effects
Anti-Parkinson Agent, Antiviral	amantadine	Monitor renal function Monitor mental state Assess blood pressure	Improve Parkinson's disease symptoms	Increased suicidal ideation and urges Congestive heart failure and

				peripheral edema Neuromalignant syndrome (NMS) when dosage decreased Orthostatic hypotension Nausea, dizziness, and insomnia Anticholinergic side effects

The clinical treatment of PD with levodopa in the 1960s revolutionized the treatment of the motor complications of the disease. This revolution was portrayed in the film Awakenings. However, as I review, PD is a much more complex disease than just the motor manifestations. It remains a debilitating disorder for which no effective disease modification therapies have yet been identified.

Conclusions for chapter 1.

1. Parkinson's disease (PD) is a progressive multi-system neurodegenerative disease affecting people mainly in later years of life. It is the second most common neurodegenerative disease worldwide with incidence and prevalence on the rise along with changing population demographics [1]. The prevalence of PD in industrialised countries is generally estimated at 0.3% of the entire population and about 1% in people over 60 years of age [2]. The prevalence increases with advancing age both for men and women with no decreases at higher ages [3]. In Europe, the prevalence at ages 85–89 has been reported as 3.5% [4].

2. Currently, there is no cure for PD, but medications or surgery can often provide improvement in the motor symptoms.

3. Medications for PD fall into three categories:

Drugs that increase the level of dopamine in the brain. The most common drugs for PD are dopamine precursors—substances like levodopa that cross the blood-brain barrier and are then changed into dopamine. Other drugs mimic dopamine or prevent or slow its breakdown.

Drugs that affect other neurotransmitters in the body to ease some of the symptoms of the disease. For example, anticholinergic drugs interfere with production or uptake of the neurotransmitter acetylcholine. These can be effective in reducing tremors.

Medications that help control the non-motor symptoms of the disease, or the symptoms that don't affect movement. For example, people with PD-related depression may be prescribed antidepressants.

CHAPTER 2. MATERIALS AND METHODS

The study was conducted on the basis of a pharmacy Wassim El Khatib, Masnaa-Rachaiya Rd, Lebanon by interviewing patients in the form of filling out a questionnaire “Research on the rationality of using antiparkinsonian drugs”. This questionnaire was developed by us and distributed to pharmacy visitors when applying for the purchase of anti-Parkinsonian drugs. Given that Parkinson's disease mainly affects the elderly, on the one hand, and in itself can lead to motor and cognitive impairment, some patients needed help in filling out the questionnaire. The questionnaire is presented below. Patients provided some additional information outside the survey on their own initiative. In the analysis, only questionnaires were taken, in which answers to all questions were given.

Questionnaire

"The use of antiparkinsonian drugs"

1. Your age
□ 50-65 years
□ 66-74 years
□ 75-84 years
□ 85+ years
2. Your gender
□ Women's
□ Men's
3. What symptoms of Parkinson disease bother you?
□ Tremor in hands, arms, legs, jaw, or head
□ Muscle stiffness, where muscle remains contracted for a long time
□ Slowness of movement
□ Impaired balance and coordination, sometimes leading to falls
□ Depression and other emotional changes
□ Difficulty swallowing, chewing, and speaking
□ Urinary problems or constipation
□ Skin problems
□ Your option _____

4. How many years you have been diagnosed with Parkinson disease?
□ less than 3 years
□ 3 – 10 years.
□ more than 10 years
□ Your option _____

5. Which antiparkinsonic drug you use now?
□ Levodopa only
□ Levodopa+carbidopa
□ Bromocriptine (cabergoline)
□ Levodopa+carbidopa+tolcapone or entacapone
□ Selegiline only
□ Levodopa+carbidopa+ selegiline
□ Benztropine mesylate or trihexyphenidyl
□ Amantadine
□ Rasagiline
□ Safinamide
□ Your option _____
6. Which of the following symptoms reduce during your treatment first?
□ Tremor in hands, arms, legs, jaw, or head
□ Muscle stiffness, where muscle remains contracted for a long time
□ Slowness of movement
□ Impaired balance and coordination, sometimes leading to falls
□ Depression and other emotional changes
□ Difficulty swallowing, chewing, and speaking
□ Urinary problems or constipation
□ Skin problems
□ Your option _____
7. Is current antiparkinsonic treatment first in you experience?
□ Yes
□ No
□ Your option _____
8. If orevious answer is no which antiparkinsonic drug you used back than?
□ Levodopa only
□ Levodopa+carbidopa
□ Bromocriptine (cabergoline)
□ Levodopa+carbidopa+tolcapone or entacapone
□ Selegiline only
□ Levodopa+carbidopa+ selegiline
□ Benztropine mesylate or trihexyphenidyl
□ Amantadine
□ Rasagiline
□ Safinamide
□ Your option _____
9. Do you have any chronic diseases or chronic conditions?
□ No
□ Diabetes mellitus
□ Heart failure
□ Bronchial asthma

□ Ischemic heart disease
□ Atherosclerosis
□ Chronic kidney disease
□ Chronic liver failure
□ Your option _____

10. When was the last time there was an exacerbation of a chronic disease before using the drug?
□ Less than a week
□ In 2-3 weeks
□ For a month
□ For 3-6 months
□ For 6-12 months
□ More than a year
□ Your option _____

11. Has the chronic disease worsened after taking the drug?
□ Yes
□ No.
□ I don't know
□ Your option _____

12. Did you know that drugs have side effects, adverse reactions?
□ Yes
□ No.

13. Do you know about side effects, adverse reactions of your drug?
□ Yes
□ No.

14. Have you had any side effects associated with taking the drug?
□ Yes
□ No.
□ I don't know

15. Which of the following symptoms did you have after taking the medicine?
□ vision changes;
□ twitching or uncontrolled muscle movements;
□ confusion, agitation, unusual thoughts or behavior;
□ hallucinations (seeing or hearing things that are not real);
□ a seizure;
□ fever, sweating, fast heart rate, overactive reflexes;
□ nausea, vomiting;
□ diarrhea;
□ increased blood pressure--severe headache, blurred vision, pounding in your neck or ears, anxiety, nosebleed
□ a light-headed feeling, like you might pass out
□ extreme drowsiness, falling asleep suddenly even after feeling alert
□ shortness of breath (even with mild exertion)
□ swelling in your hands or feet

□ painful or difficult urination
□ severe nervous system reaction - very stiff (rigid) muscles, high fever, sweating, confusion, fast or uneven heartbeats, tremors
□ uncontrolled muscle movements in your face (chewing, lip smacking, frowning, tongue movement, blinking or eye movement)
□ worsening of tremors (uncontrolled shaking)
□ posture changes you cannot control, such as involuntary bending forward of your neck, bending forward at the waist, or tilting sideways when you sit, stand, or walk
□ sleep problems (insomnia), unusual dreams
□ Your option _____

16. Who told you about the medicine and its side effects?
□ Doctor
□ Pharmacist
□ Instructions for the drug
□ Your option _____

17. Who recognized those side effects?

□ Doctor
□ Pharmacist
□ Yourself
□ Relatives/caregivers
□ Your option _____

Conclusion to chapter 2.

The collection and analysis of information obtained from studies will improve the safety and efficacy of Parkinson's disease therapy, especially given the fact that PD treatment is lifelong.

CHATER 3

RESULTS AND DISCUSSION

During the study, 37 respondents were interviewed, of which only 29 were selected for analysis. The excluded questionnaires were not completely filled out and therefore could not provide all the information necessary for the study. Among the respondents there were 9 women and 20 men (Fig. 3.1), which corresponds to the literature data on the frequency of occurrence among men and women, where it is described that men suffer from PD 2 times more often than women.

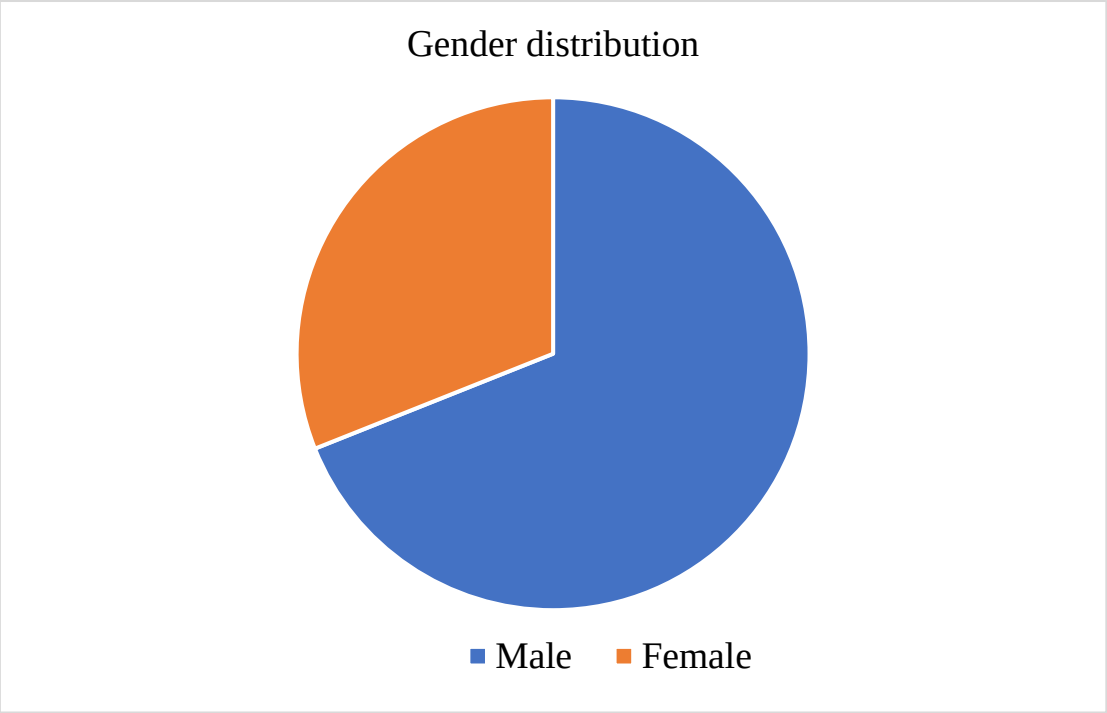

Fig. 3.1 Gender distribution

By age, they were distributed as follows: from 50 to 65 years old - 3 people, 66-74 years old - 8 people, 75-84 - 16 people, and over 85 years old - 2 people, so the majority of respondents were in the age group of 75-84 years (Fig. 3.2).

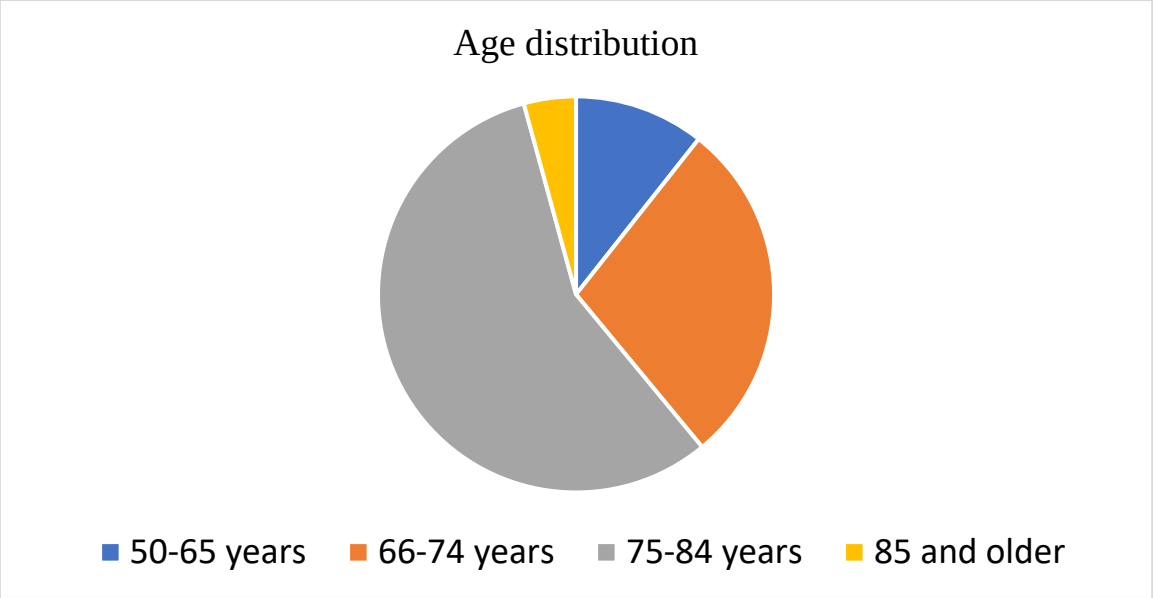

Fig. 3.2 Age distribution

The polymorphism of the clinical picture of Parkinson's disease is a certain difficulty for differentiation from other chronic diseases, however, we tried to bring the most frequent and typical of them into the questionnaire and revealed the following picture: tremor as the most common symptom of Parkinson's disease occurred in all respondents, muscle rigidity, as still very a frequent and important symptom for diagnosing PD in 97% of respondents. Also among the most frequent symptoms were: slowness of movement - 81%; impaired coordination of movements up to falls - 33%, emotional disorders and depression - 66%, difficulty in swallowing - 10%, urinary disorders and constipation - 43% (although it is impossible to attribute this symptom as typical of PD), skin rash - 12% (also non-specific for PD) (Fig. 3.3).

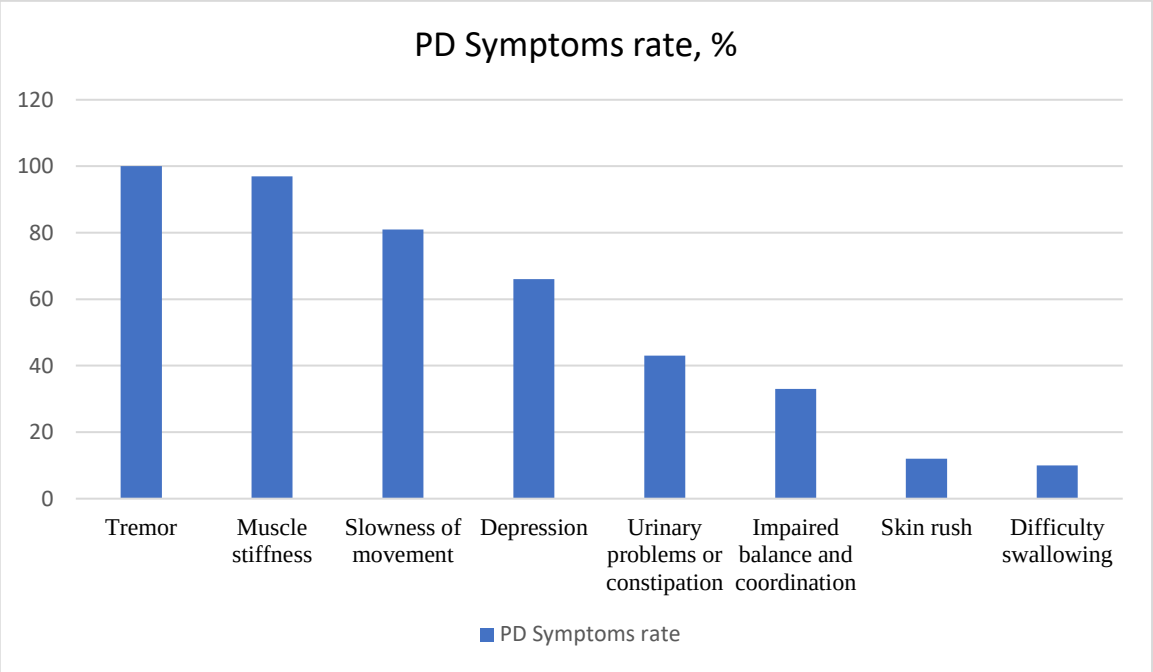

Fig.3.3 PD Symptoms rate

Patients with PD rarely have one symptom in isolation, so we found that only 1 patient had an isolated tremor, all the rest had 2-3 symptoms at the same time - 30% of the respondents and another 66% had 4-5 symptoms at the same time (Fig. 3.4).

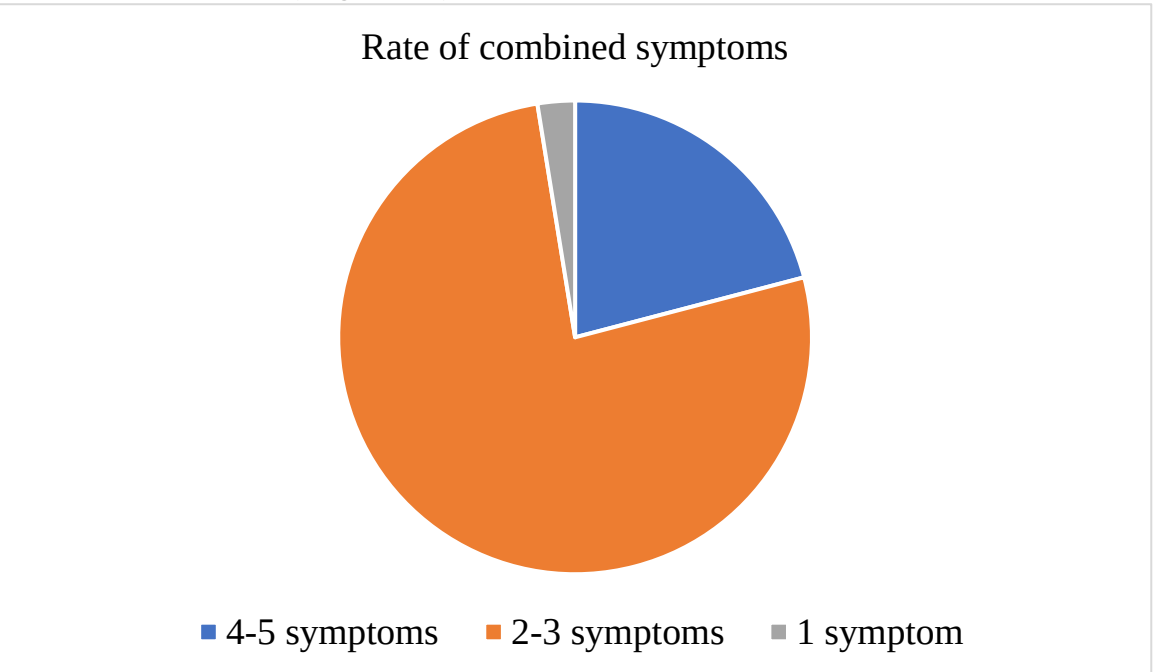

Fig. 3.4 Rate of combined symptoms.

The symptoms of PD are not static and can change over time, both in the direction of aggravation with improper treatment in its complete absence, and in the direction of weakening with the right treatment, so it was important to find out the duration of the disease in patients. The study found that 18% of patients were diagnosed with PD less than 3 years ago, 55% from 3 to 10 years ago, and 27% more than 10 years ago. It can be concluded that the majority of respondents suffer from PD for 3 to 10 years (Fig. 3.5).

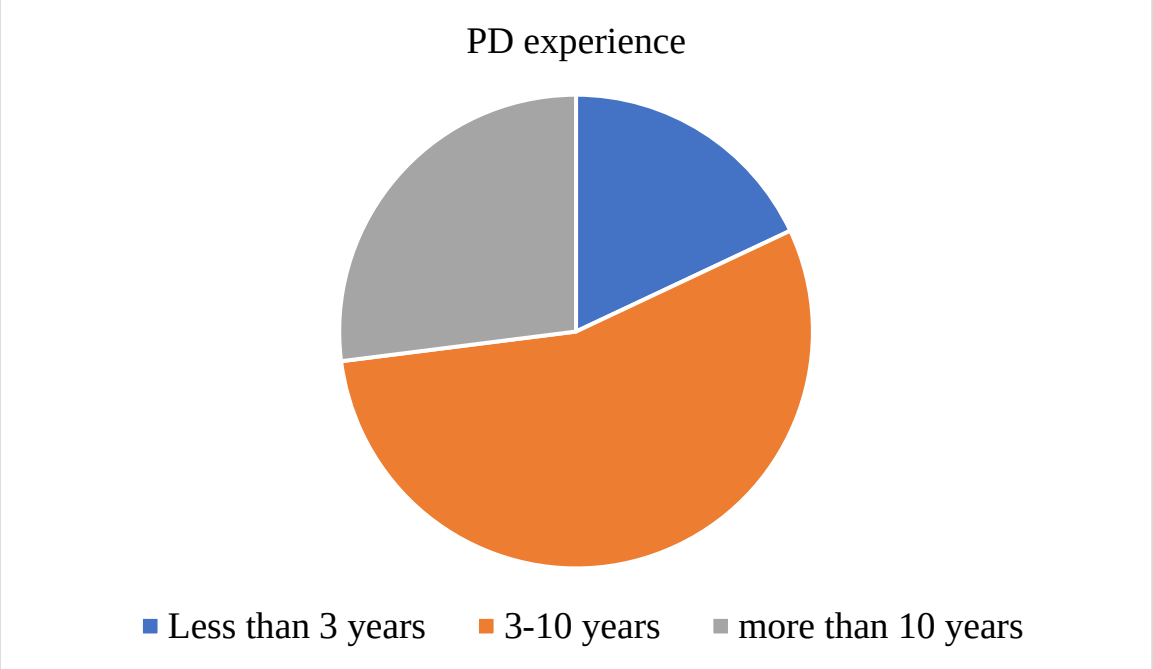

Fig. 3.5 PD experience

Without appropriate treatment, all of the above symptoms will progress and lead to a complete loss of the ability to self-care and a reduction in the patient's life expectancy. Therefore, it is critically important to choose an individually appropriate therapy for each patient with PD. We found out what drugs our respondents take: 55% receive a combination of levodopa and carbidopa, 12% rasagiline, 9% seligiline, bromocriptine and a combination of levodopa, carbidopa and entacapone, another 6% are treated with trihexyphenidyl (Fig. 3.6). Thus, the vast majority of patients receive a combination of levodopa and carbidopa as

the main drugs, which is in line with modern global trends in the treatment of PD.

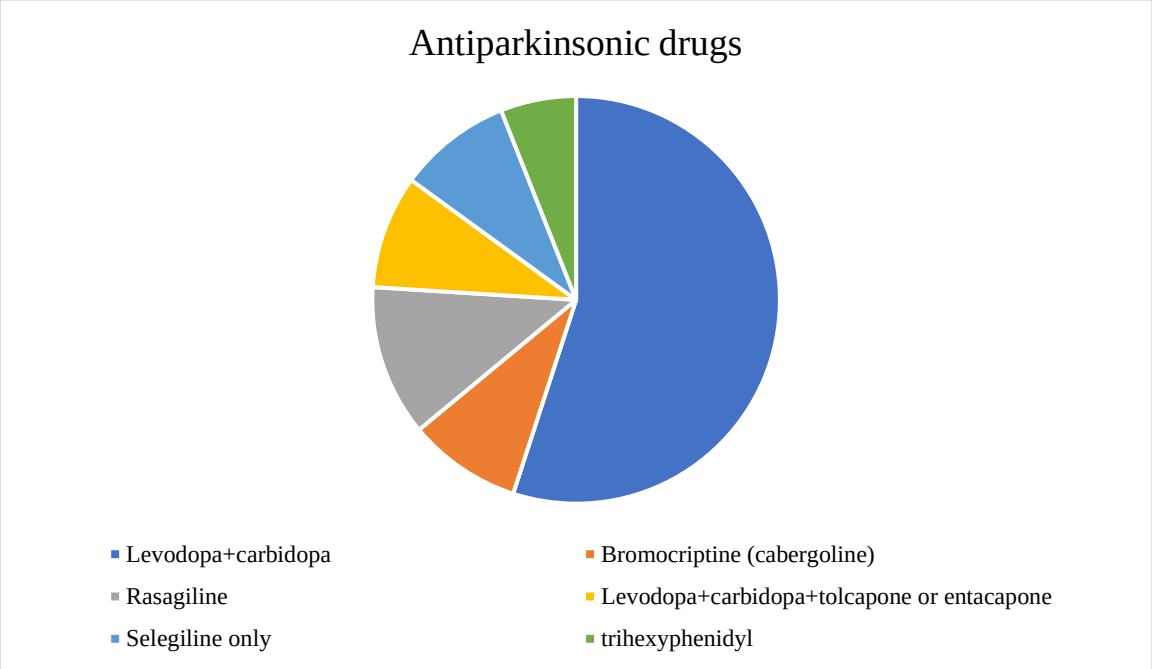

Fig. 3.6 Antiparkinsonic drugs

To monitor the effectiveness of treatment, it is necessary to find out which symptoms are improving, which we asked in the next part of the questionnaire. Tremor decreased first in 48% of respondents, muscle rigidity decreased in 24%, slowness of movement in 12%, coordination disorders in 10% and emotional disorders in 6% (Fig. 3.7). Thus, the most effective treatment was in relation to tremor, which is associated with the depletion of the stock of dopamine in dopaminergic structures and their recovery under the influence of treatment, especially containing levodopa (a structural precursor of dopamine itself).

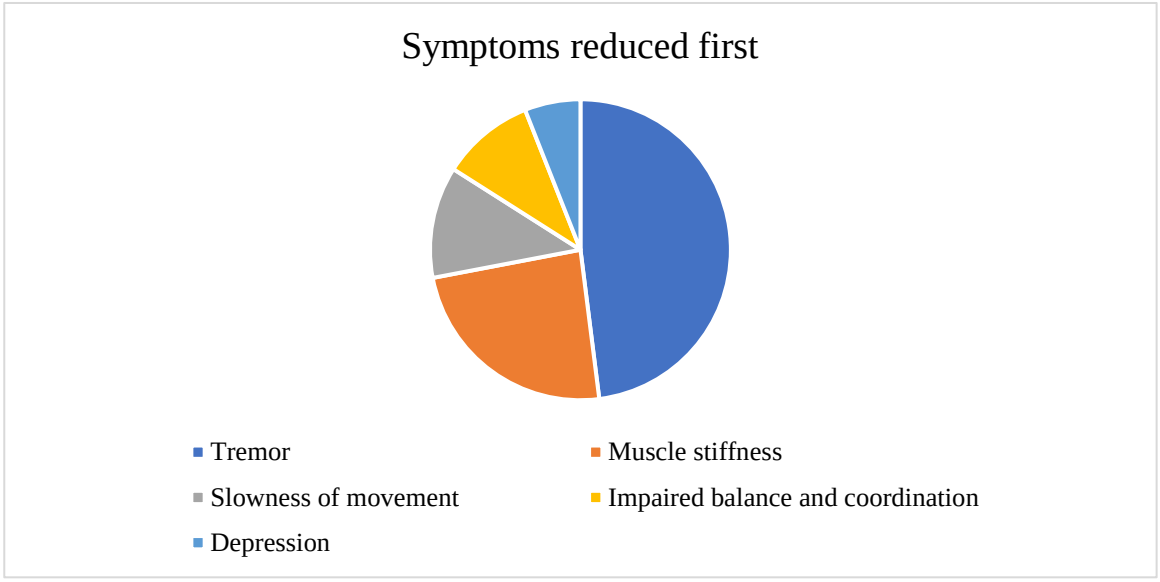

Fig. 3.7 Symptoms reduced first.

As you know, PD is an incurable disease that will accompany the patient all his life and for which there is no “magic pill”. Accordingly, antiparkinsonian drugs must also be taken for life and they may not be equally effective in different patients due to the individual characteristics of the organism and the course of the disease itself. On the other hand, over time, the effectiveness of drugs may decrease (especially true for levodopa monotherapy). All this leads to a change in drug therapy, according to the literature, in two-thirds of patients. In our study, we found that 66% percent of patients had already changed drug treatment for PD, and in 34% of them, the drugs they were taking were the first selected therapy for PD (Fig. 3.8.).

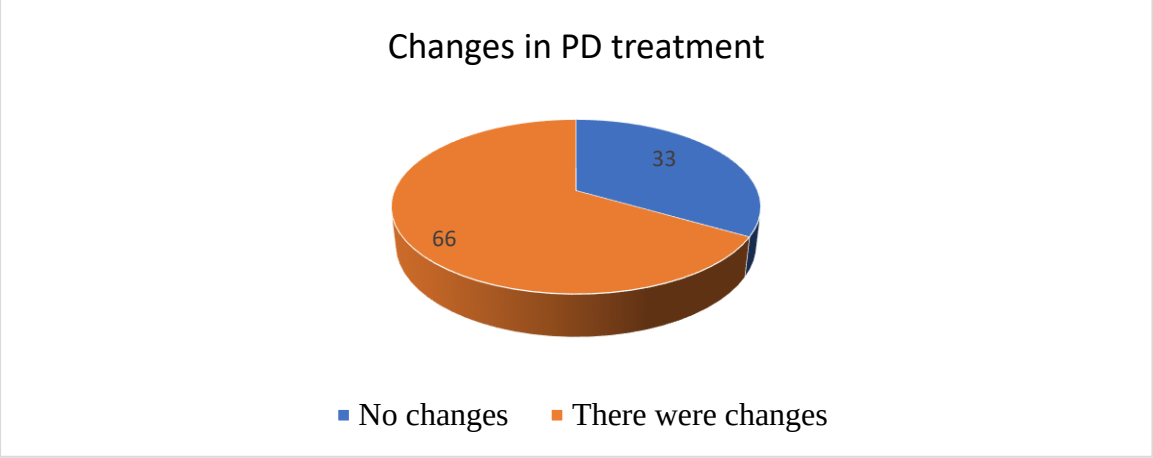

Fig 3.8 History of the PD treatment

After studying the history of medications taken, we saw that 2/3 of the patients started treatment with levodopa monotherapy, 10% selegiline, safanimide and trihexyphenidil, and 1 patient (3%) - rasagiline, but due to various circumstances, these drugs were replaced by those what patients are currently taking (Fig. 3.9).

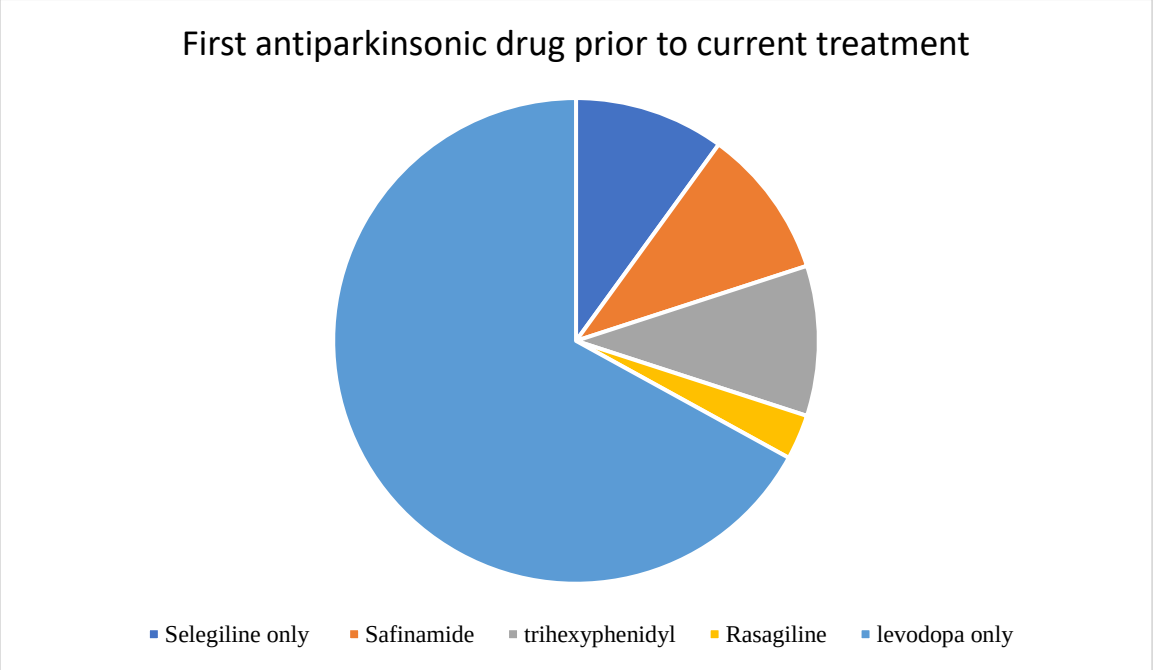

Fig. 3.9 First antiparkinsonic drug prior to current treatment/

Considering the prevalence of PD in the older age group, we can safely assume that these patients may have comorbid conditions. In the course of our study, it turned out that all patients had certain comorbidities. So, angina pectoris - in 66%, diabetes - in 51%, atherosclerosis - 91%, CKD - 12%, CHF - 45%, arterial hypertension - 75% (Fig. 3.10), that is, atherosclerosis was the most common comorbid pathology, in second place - arterial hypertension, on the third - angina pectoris. Half of the respondents were also diagnosed with diabetes.

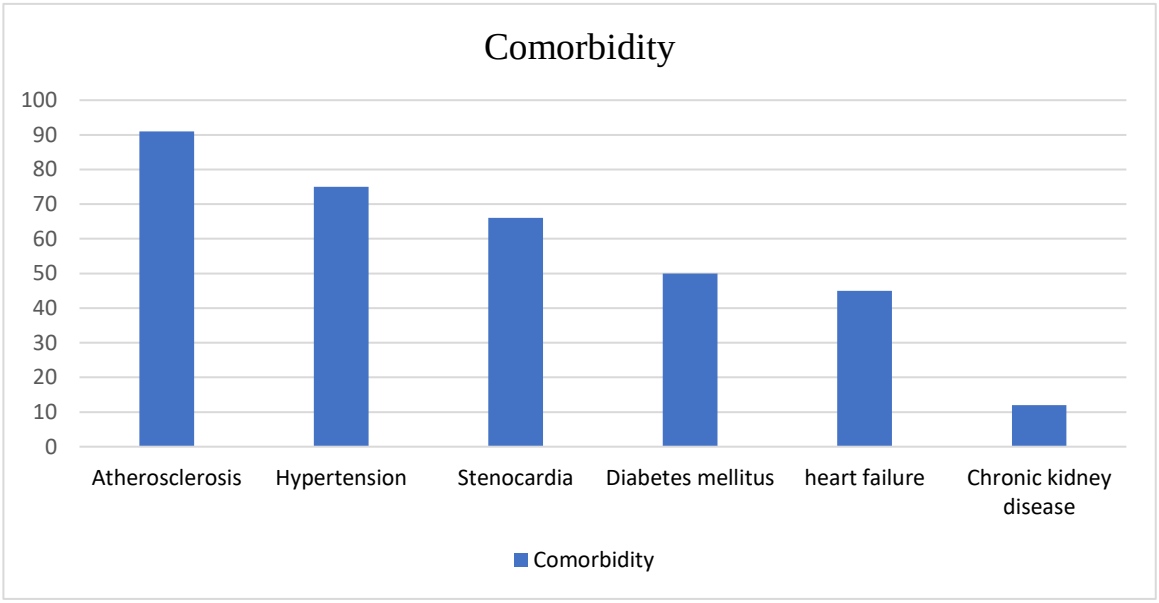

Fig 3.10 Comorbidity of the PD patients.

Considering that all patients had comorbid conditions that could be affected by the antiparkinsonian drugs taken by the patient, it was necessary to find out if the patients were aware of the presence of side effects when taking drugs? We found that 3 patients (10%) did not know about the presence of PU in drugs, in principle, despite their middle age and the presence of a certain history of taking drugs not only from PD.

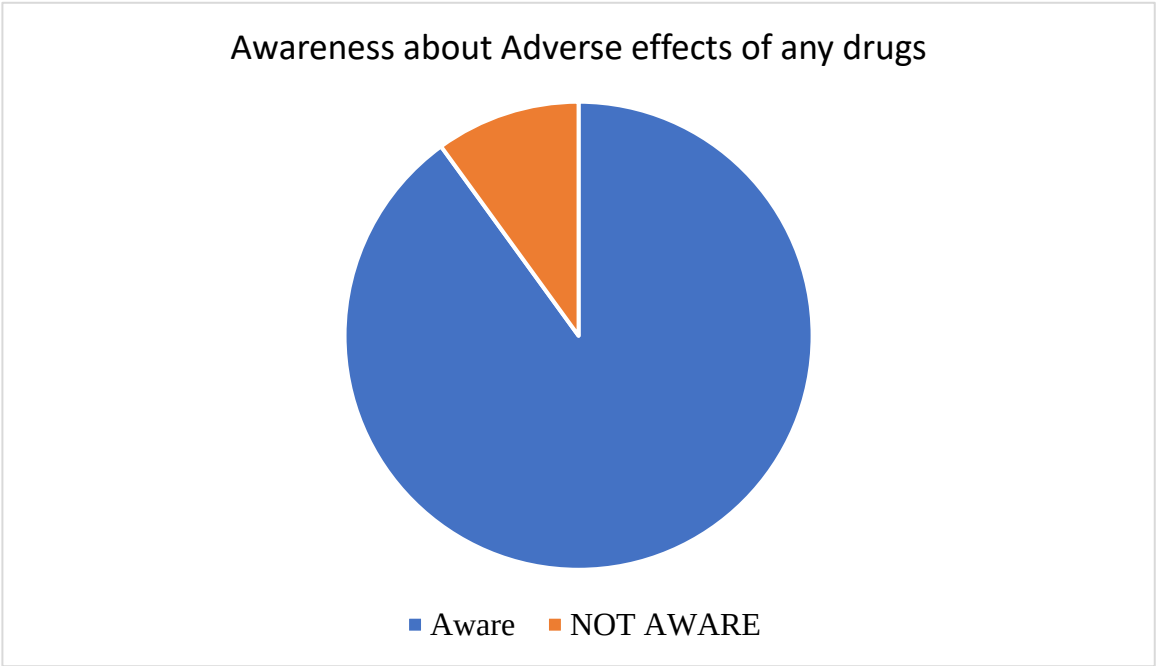

Fig. 3.11 Awareness about adverse effects of any drugs

Throughout their lives, neither doctors nor pharmacists, unfortunately, informed these patients about the presence of side effects in drugs. The

patients themselves did not read the instructions for the drugs, trusting doctors and pharmacists. The remaining 90% of patients knew about the presence of side effects when taking any drugs, which is fully explained by their age and life history and illness (Fig. 3.11).

For safe and effective treatment, all participants must be aware of the typical and common side effects associated with the drugs used. Physicians and pharmacists are naturally aware of this information and can recognize side effects when referred to. However, the patient spends most of his life apart from doctors and pharmacists, so it is very important for the patient to know about these side effects so that he can seek help from a pharmacist or doctor as soon as possible. In our study, we found that only half of the patients know the typical side effects of antiparkinsonian drugs, the other half do not (Fig. 3.12).

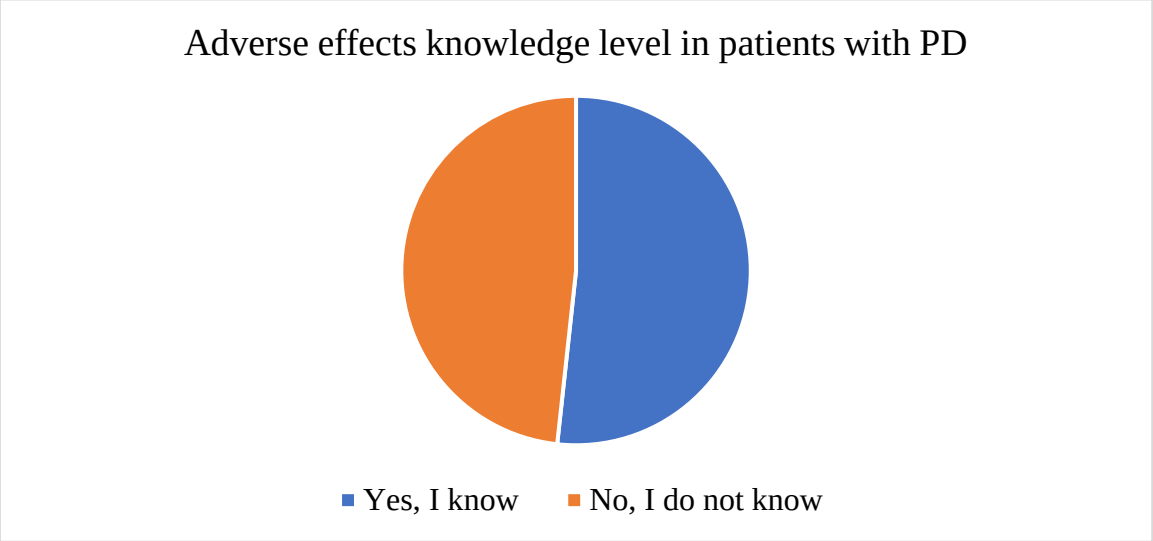

Fig. 3.13 Adverse effects knowledge level in patients with PD

Knowledge of the typical side effects of drugs should be used to identify these same side effects during treatment by the patients themselves. When asked if you had side effects of anti-pacrinsonian drugs, 1/3 of the respondents answered yes, they did - these patients recognized, but they also did not seek help from a doctor or pharmacist. Side effects are mostly on their own or with the help of a doctor or pharmacist, more

1/3 answered no, which may be a sign of insufficient awareness and attention to their condition. But the most interesting answer was in the third 1/3, who answered I don't know, which means that they had some new phenomena while taking the drugs, but neither they nor their relatives could regard these phenomena as side effects, but they also did not turn to doctors and pharmacists for help (Fig. 3.14).

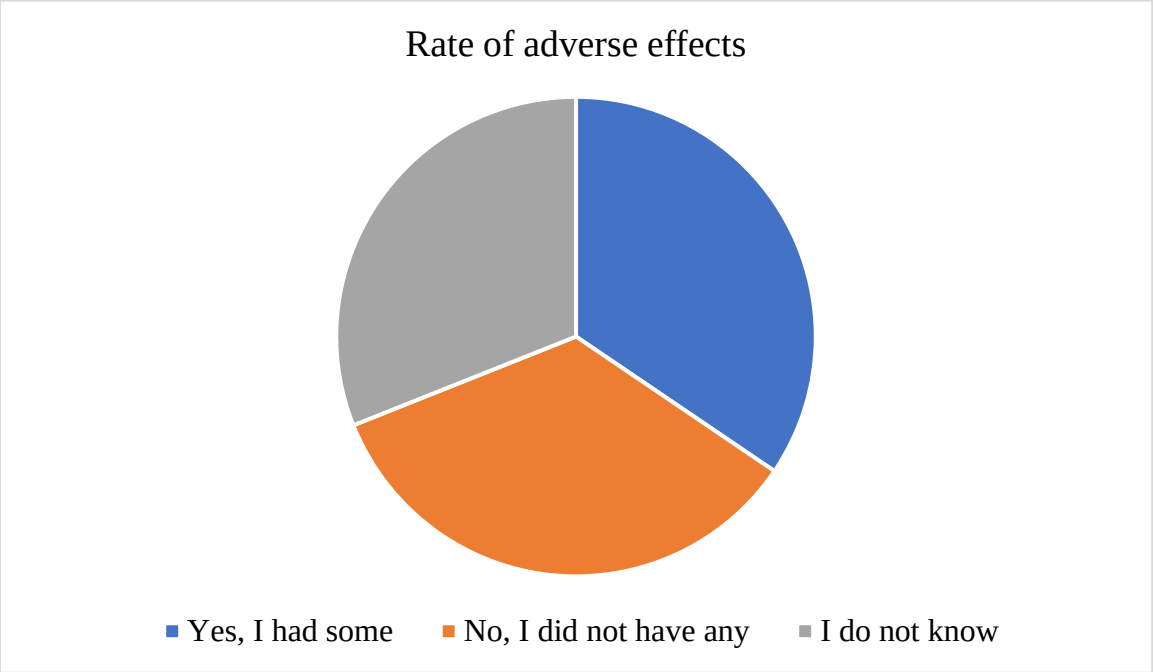

Fig. 3.14 Rate of adverse effects

However, after answering the next question, we realized that among those who answered I don't know and among those who answered that there were no side effects, there were still patients with side effects. We made this conclusion based on the fact that in all questionnaires certain side effects characteristic of antiparkinsonian drugs were noted. Such as visual disturbances (33%), muscle twitching (27%), disorientation/confusion (12%), nausea/vomiting (9%), diarrhea (6%), one patient had brief hallucinations (3%), convulsions (3%), diarrhea (6%), sweating (9%), increased blood pressure (12%), presyncope (3%), drowsiness (6%), uncontrolled facial expressions (12%), insomnia (9%)

and three people (10%) even noted worsening of the tremor (Fig. 3.15). Many patients experienced several side effects at the same time.

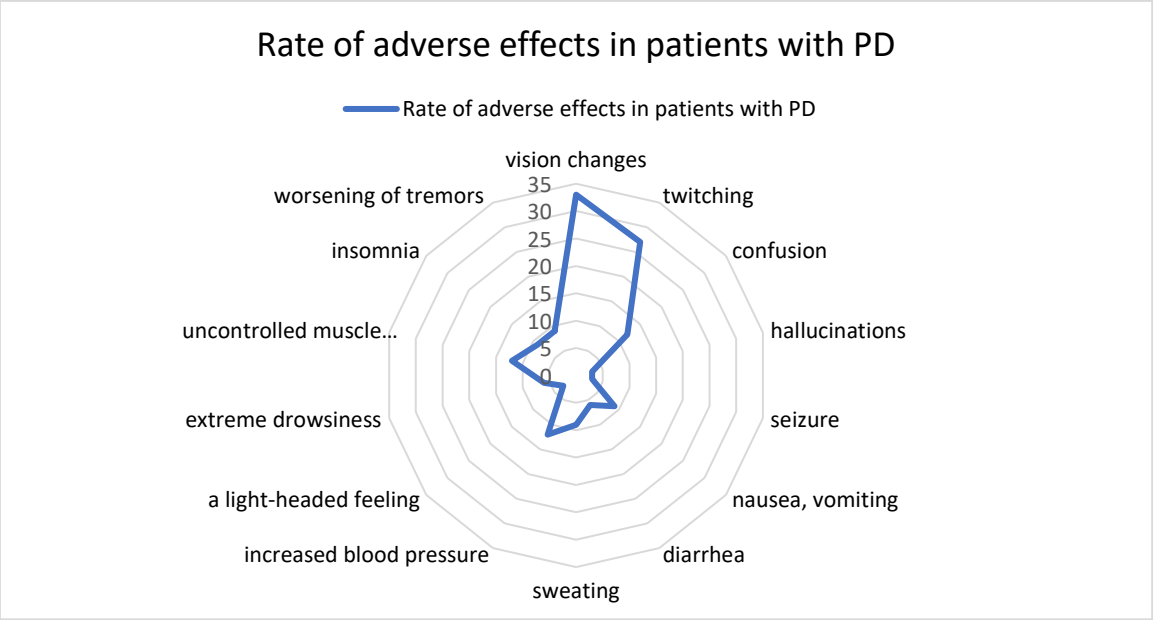

Fig. 3.15 Rate of adverse effects in patients with PD

We found in our study that only 60% of all cases of side effects were recognized by medical or pharmaceutical professionals (physicians 27%, pharmacist 33%), the remaining 40% were identified by the patients themselves and their families and friends.

Thus, it can be concluded that the widespread prevalence of PD and the peculiarities of the course of this pathology in the older age group require special attention to these patients from both doctors and pharmacists. The selection of safe and effective therapy is a serious medical and social task. Both the patients themselves and their environment should be involved in solving this problem. At the same time, it is necessary to increase the awareness of patients about the drugs they take, including by doctors and pharmacists.

PRACTICAL RECOMMENDATIONS

Community pharmacists are highly visible, easily accessible health care providers who are valued by patients for their knowledge about medications. Pharmacists are well trained to address medication-related concerns and are the ideal health professionals to assess and refer patients requesting assistance with determining the treatment for symptoms indicative of PD. Additionally, pharmacists have long-standing established relationships with their patients and comprehensive appreciation of their patients' drug therapy, whether prescribed by the patient's family physicians or specialists or obtained by the patient for self-care. Pharmacists can therefore support both patients and physicians in the choice, adjustment and monitoring of ongoing pharmacotherapy for safety, effectiveness, drug interactions, affordability and adherence.

Communication

Good communication is the key to assisting patients, whether it is answering queries about the disease process, medications used to treat it, or helping patients navigate the health care system. Communication should be designed to meet the needs of the patient with PD.

Recommendations

Pharmacists should do the following:

Empower people with PD to participate in the judgment and choices about their own care.

Tailor information to the needs of the individual.

Provide both verbal and written material.

Frequently reinforce information, especially with those people with PD who are cognitively impaired and/or are depressed.

Inform family and caregivers about the condition, entitlement to care assessments and support services available.

II. Diagnosis

As outlined earlier, the clinical presentation of PD is characterized by tremors, rigidity, bradykinesia and postural instability. Patient complaints or visual

observation of any of these symptoms should result in advising patients to seek an assessment and diagnosis from a family physician or specialist immediately (see Figure 1 for summary of identification, diagnosis and prognosis in PD).

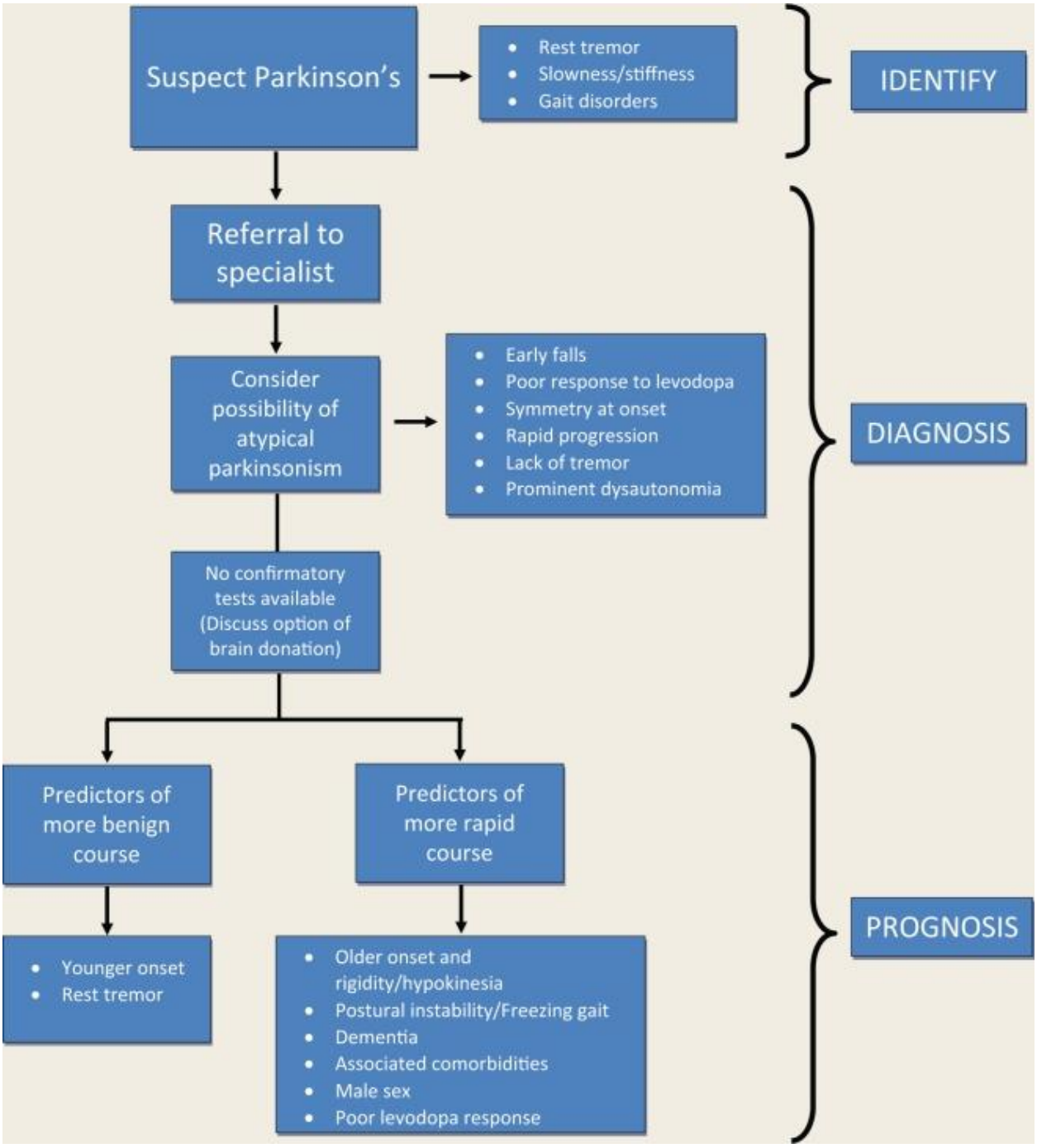

Figure 1

Summary of the identification, diagnosis and prognosis in Parkinson's disease

Recommendations

Pharmacists should do the following:

Suspect PD in people presenting with or complaining about tremors, stiffness, slowness, balance problems and/or gait disorders.

Refer such patients to their family physician immediately for an assessment, diagnosis and further referral to a specialist.

III. Prognosis, neuroprotection, and treatment

Prognosis

The rate of progression of PD is dependent on a number of factors such as age, presence of comorbidities and primary symptom of presentation.

Recommendations

Pharmacists should expect a more rapid rate of motor progression in newly diagnosed PD if, at onset, the person is/does the following:

Is male or older.

Presents with rigidity/hypokinesia as an initial symptom. Such persons may also develop cognitive decline and dementia earlier.

Presents with associated comorbidities such as stroke, auditory deficits, visual impairments and/or postural instability/gait difficulty.

Pharmacists can expect a slower rate of progression in newly diagnosed PD in persons

who present with tremors as the primary symptom. Such persons may also experience benefit from levodopa for a longer period of time.

Neuroprotection

Neuroprotection in PD has been defined as an intervention with the potential to slow, stop or reverse the progression of PD.[8] Although none of the medications used in the treatment of PD has been conclusively shown to have this effect, clinical trials with other agents are ongoing.

Recommendations

Pharmacists should do the following:

Not recommend vitamin E, coenzyme Q10, dopamine agonists or monoamine oxidase inhibitors for neuroprotection in PD, except in the context of clinical trials.

Understand that there is no long-term evidence to recommend levodopa for neuroprotection.

Treatment

The treatment for PD is primarily pharmacological, although an increasing number of nonpharmacological treatments are gaining favour. Surgical treatment for PD is presently limited to patients who have advanced disease and in whom pharmacological treatment is failing to manage motor symptoms. Only a few highly specialized centres offer these treatment options, thereby limiting access.

With the progression of PD, a patient's medication may need to be finely adjusted, as it often becomes difficult to balance side effects with the therapeutic effects of the medication (see Table 2 for side effects of medications used in the treatment of PD). Patients will develop motor complications such as "wearing off" (where the duration of the beneficial effect of levodopa becomes progressively shorter), "on/off" (where beneficial effects of the treatment are unpredictable), "freezing" (where there is no beneficial effect of levodopa for periods of time), and dyskinesias (involuntary movements). During this time, pharmacists can serve as invaluable partners in the care of people with PD by assisting with complex medication schedules, addressing side effects, assisting with different formulations of medications, obtaining approval for medications on emergency release, ensuring appropriate intake to maximize the absorption of medications and guiding the choice of medication based on patient preference, other concurrent medications and medical conditions, and affordability.

Table 2

Medications for PD[9]

Drug (trade name)	Dosage	Adverse effects	Comments
Anticholinergic drugs: block cholinergic activity in the brain.			
Benztropine (Cogentin)	Initial: 0.5 mg daily	Anhidrosis, nausea/vomiting,	May help with

Drug (trade name)	Dosage	Adverse effects	Comments
	Usual: 1-2 mg/d Maximum: 6 mg/d administered 1-4 times daily Titration: adjust dose in 0.5-mg increments every 5-6 days	constipation, confusion, memory impairment, depression, hallucinations, weakness, tachycardia, blurred vision	drooling; use caution in the elderly as they can cause confusion and cognitive impairment
Trihexyphenidyl (Artane)	Initial: 1 mg daily Usual: 6-10 mg/d administered 3-4 times daily Maximum: 6-10 mg/d Titration: increase 2 mg every 3-5 days		
COMT inhibitors: reversibly and selectively inhibit COMT.			
Entacapone (Comtan)	Initial: 200 mg with each dose of	Nausea, dyskinesias, orthostatic	Adjunctive treatment with

Drug (trade name)	Dosage	Adverse effects	Comments
	levodopa/carbidopa Maximum: 8 times daily (1600 mg/d)	hypotension, syncope, dizziness, fatigue, hallucinations, somnolence, diarrhea, constipation, vomiting, brown-orange urine discoloration	levodopa; liver function test every 6 months

Dopamine agonists (nonergot derived): dopamine agonist binding to the D_2 subfamily of dopamine receptors; also shown to bind to D_3 and D_4 receptors and believed to stimulate dopamine activity in the striatum and substantia nigra.

Pramipexole (Mirapex)	Immediate release: Initial: 0.125 mg 1-3 times daily Usual: 0.5-1.5 mg 3 times daily Maximum: 4.5 mg/d Extended release: Initial: 0.375 mg daily	Symptomatic hypotension, somnolence, dyskinesias, weakness, nausea/vomiting, constipation, hallucinations, impulse control, rhabdomyolysis, pleural/retroperitoneal fibrosis	Dosing adjustment needed in renal impairment

Drug (trade name)	Dosage	Adverse effects	Comments
	Maximum: 4.5 mg/d Titration: gradually increase every 5-7 days		
Ropinirole (Requip)	Immediate release: Initial: 0.25 mg 3 times daily Usual: 1-8 mg 3 times daily Maximum: 24 mg/d Extended release: Initial: 2 mg daily for 1-2 weeks Maximum: 24 mg/d Titration: gradually increase every 5-7 days		
Dopamine agonists (ergot derived)			

Drug (trade name)	Dosage	Adverse effects	Comments
Bromocriptine (Parlodel)	Initial: 1.25 mg 3 times daily Usual: 10-30 mg/d Maximum: 100 mg/d Titration: gradually increase by 2.5 mg/d every 1-2 weeks	Impulse control disorders, sedation, pleural/retroperitoneal fibrosis, dizziness, fatigue, headache, constipation, nausea, weakness, rhinitis, hypotension, Raynaud's phenomenon, hypoglycemia, increased risk of infection	Monitor for cardiac valvular fibrosis
Cabergoline (Dostinex)	Initial: 0.25 mg daily Maximum: 2-6 mg/d Titration: increase 0.5-1 mg every 1-2 weeks		
Dopamine precursors: Levodopa: dopamine precursor; crosses the blood-brain barrier and is converted to dopamine. Benserazide and carbidopa: inhibit the peripheral plasma breakdown of levodopa.			
Levodopa/benserazide (Prolopa)	Initial: 100/25 mg 1-3	Nausea/vomiting,	Long-term

Drug (trade name)	Dosage	Adverse effects	Comments
Carbidopa/levodopa (Sinemet)	times daily Usual and maximum dose: patient dependent Titration: increase by 100/25 mg every 3-4 days	confusion, orthostatic hypotension, hallucinations, hypersexuality, somnolence, gambling behaviour, melanoma	treatment associated with motor fluctuations and dyskinesias
Carbidopa/levodopa (Duodopa intestinal gel)	Initial: 1:1 ratio to/from oral tablet formulations Morning bolus dose: usually 100-200 mg levodopa (5-10 mL) Maximum: 300 mg levodopa (15 mL) Continuous maintenance dose: usually 40-120 mg levodopa per		For intestinal gel therapy, any condition that prevents the placement of a percutaneous endoscopic gastrostomy tube

Drug (trade name)	Dosage	Adverse effects	Comments
	hour (2-6 mL/h) for up to 16 hours; adjust in increments of 2 mg/h (0.1 mL/h); range: 20-200 mg levodopa per hour (1-10 mL/h)		
Carbidopa/levodopa controlled release (Sinemet CR)	Initial: 50 mg carbidopa/200 mg levodopa daily Titration: may adjust dosage every 3 days		Useful at dopamine ≥300 mg/d; slower absorption than immediate release; can improve motor fluctuations in people with later PD
Carbidopa/levodopa/entacapone (Stalevo)	Initial: 1 tablet daily	Refer to sections on dopamine	Use after individual

Drug (trade name)	Dosage	Adverse effects	Comments
	Maximum: 8 tablets	precursors and COMT inhibitors	dosages have been established; transfer to a combined product once the dose is stabilized; fractionated doses are not recommended

MAO-B inhibitors: irreversibly and selectively inhibit brain MAO-B, reducing the breakdown of dopamine.

Rasagiline (Azilect)	Monotherapy: 1 mg daily With levodopa: Initial: 0.5 mg daily May need to reduce levodopa dosage	Orthostatic hypotension, dyskinesias, falls, headache, nausea, angina, chest pain, syncope, depression, hallucinations, constipation, arthralgia, flu syndrome, dyspepsia	Use caution with the concomitant use of cyclobenzaprine, dextromethorphan, methadone, propoxyphene, St. John’s wort or tramadol

Drug (trade name)	Dosage	Adverse effects	Comments
Selegiline	Initial: 5 mg daily Dose early in the day For patients receiving levodopa/carbidopa, may start with 2.5 mg daily and then increase gradually to 5 mg twice daily Maximum: 10 mg/d	Headache, dizziness, nausea, hallucinations, confusion, vivid dreams, dyskinesias, dry mouth	Use caution with the concomitant use of cyclobenzaprine, dextromethorphan, methadone, propoxyphene, St. John's wort or tramadol; metabolized to amphetamine derivatives; contraindicated with meperidine
Miscellaneous			
Amantadine	Initial: 100 mg twice daily or 100 mg daily if receiving other	Nausea, dizziness, insomnia, confusion, hallucinations,	Do not discontinue abruptly; dosing adjustment

Drug (trade name)	Dosage	Adverse effects	Comments
	PD drugs Adjustment: after 1 week on 100 mg daily, can be increased to 100 mg twice daily if necessary Maximum: 400 mg/d	depression, livedo reticularis, orthostatic hypotension	needed in renal impairment

COMT, catechol-O-methyl transferase; MAO-B, monoamine oxidase B; PD, Parkinson's disease.

Recommendations

Prior to commencing initial drug treatment for early PD, pharmacists should do the following:

Ensure that the drug choice is based on the clinical and lifestyle characteristics of the patient and patient preference.

Ensure that the patient is aware of the short- and long-term benefits and drawbacks of the drug classes.

Be aware that levodopa, dopamine agonists and monoamine oxidase inhibitors may be used to initiate symptomatic treatment.

Be aware that amantadine may be used as a treatment in early PD but is not a drug of first choice.

Be aware that anticholinergics may be used as a treatment in young patients with early PD and severe tremors but are not drugs of first choice, given the limited efficacy and propensity to cause neuropsychiatric side effects.

Be aware the β-adrenergic agonists may be used to treat postural tremors in selected people with PD but are not drugs of choice.

Be aware that nonergot dopamine agonists are preferred over ergot-derived dopamine agonists for the treatment of PD.

Ensure that the baseline erythrocyte sedimentation rate, renal function result, and chest radiograph finding have been obtained for those patients prescribed an ergot-derived dopamine agonist.

During pharmacotherapy for PD, pharmacists should do the following:

Assist with the clinical monitoring of safety and effectiveness.

Assist with medication adjustment.

Ensure that antiparkinsonian medications are administered at appropriate times.

Ensure that antiparkinsonian medications are adjusted after a discussion with a specialist.

Ensure that antiparkinsonian medications are not withdrawn abruptly or allowed to fail suddenly due to poor absorption (e.g., gastroenteritis, abdominal surgery) to avoid the potential risk for akinesia or neuroleptic malignant syndrome.

Ensure that patients are not withdrawn from their antiparkinsonian drugs (so-called drug holidays) because of the risk of neuroleptic malignant syndrome.

Assist patients with keeping the dose of levodopa as low as possible to maintain good function in order to reduce the development of motor complications.

Not recommend modified-release levodopa preparations to delay the onset of motor complications in people with early PD.

Titrate dopamine agonists to clinically effective doses. If side effects prevent this, recommend replacing this drug with another dopamine agonist or a drug from another class.

Be aware of dopamine dysregulation syndrome (impulse control disorders), an uncommon disorder in which dopaminergic medication misuse is associated with abnormal behaviours, including hypersexuality, pathological gambling, and stereotypical motor acts.

In patients who present with motor fluctuations, pharmacists should do the following:

Recommend entacapone and/or rasagiline to reduce off time.

Recommend pramipexole or ropinirole to reduce off time.

Recommend modified-release levodopa preparations to reduce motor fluctuations but not as drugs of first choice.

Recommend amantadine to reduce dyskinesias.

IV. Nonmotor features of PD

Nonmotor features of PD have been recognized as occurring in persons with PD, worsening disability and significantly impacting quality of life. The frequently occurring nonmotor features of PD are highlighted in this section, followed by recommendations for the treatment of these conditions.

Depression

Recommendations

In the management of patients with PD and depression, pharmacists should do the following:

Personalize the approach to management, taking into consideration patients' coexisting therapy.

Recommend amitriptyline as an option for drug therapy.

(C60, C61).

Psychosis

Recommendations

In the management of patients with PD and psychosis, pharmacists should do the following:

Refer patients for medical evaluation and treatment for precipitating conditions.

Reduce polypharmacy, reduce or stop anticholinergic antidepressants, and reduce or stop anxiolytics and/or sedatives.

Recommend gradually withdrawing any antiparkinsonian medications that might have triggered psychosis: anticholinergics, amantadine, dopamine agonists,

monoamine oxidase B and catechol-O-methyl transferase inhibitors, and levodopa. Note: Stopping antiparkinsonian drugs can worsen motor symptoms.

Recommend no treatment for mild psychotic symptoms if they are well tolerated by the patient and caregiver.

Recommend against the use of typical antipsychotic drugs (such as phenothiazines and butyrophenones) due to the risk of exacerbating motor symptoms.

Be aware that olanzapine should not be routinely considered, quetiapine may be considered, and clozapine may be considered, but registration with a mandatory monitoring scheme is required. Note: Few specialists caring for people with PD have experience with clozapine.

(C62-C70).

Dementia

Recommendations

In the management of patients with PD and dementia, pharmacists should do the following:

Recommend the discontinuation of potential aggravators such as anticholinergics, amantadine, tricyclic antidepressants, benzodiazepines, tolterodine and oxybutynin.

Recommend donepezil for the treatment of dementia in PD.

Recommend rivastigmine for the treatment of dementia in PD or dementia with Lewy bodies.

Sleep disorders

Recommendations

In the management of patients with PD and sleep disorders, pharmacists should do the following:

Take a full sleep history from patients who report sleep disturbance.

Educate patients on good sleep hygiene including

the avoidance of stimulants (e.g., coffee, tea, caffeine) in the evening;

the establishment of a regular pattern of sleep;

comfortable bedding and temperature;

the provision of assistive devices, such as a bed lever or rails to aid with moving and turning, allowing the person to get more comfortable; and

the restriction of daytime naps.

Recommend regular and appropriate exercise to induce better sleep.

Review all medications and recommend the discontinuation of any drugs that may affect sleep or alertness or may interact with other medications (e.g., selegiline, antihistamines, H2 antagonists, antipsychotics, and sedatives).

Advise against driving or other potential occupational hazards in patients who have a sudden onset of sleep. Adjust medications to reduce this occurrence.

Autonomic dysfunction

Recommendations

In the management of patients with PD and autonomic dysfunction, pharmacists should do the following:

Refer and assist in the appropriate treatment for the following autonomic disturbances:

urinary dysfunction,

weight loss,

dysphagia,

constipation,

erectile dysfunction,

orthostatic hypotension,

excessive sweating, and

sialorrhea (hypersalivation).

For urinary dysfunction, pharmacists should do the following:

Recommend general measures for treating urinary urgency and incontinence including avoiding coffee before bedtime and limiting water ingestion before bedtime, among others.

Recommend peripherally acting anticholinergic drugs as options for drug therapy.

For constipation, pharmacists should do the following:

Recommend general measures for treating gastrointestinal motility problems in PD. These can include dietary modifications and the use of laxatives, among others.

Recommend reducing or discontinuing drugs with anticholinergic activity.

Recommend domperidone for drug therapy.

For orthostatic hypotension, pharmacists should do the following:

Recommend general measures including

avoiding aggravating factors such as large meals, alcohol, exposure to a warm environment, and drugs known to cause orthostatic hypotension, such as diuretics or antihypertensive drugs. Levodopa and dopamine agonists may also induce orthostatic hypotension.

increasing salt intake in symptomatic orthostatic hypotension.

head-up tilt of the bed at night.

wearing elastic stockings.

highlighting postprandial effects. In some patients, only postprandial hypotension occurs. Educate patients about this effect, and recommend frequent small meals.

Recommend midodrine and fludrocortisone as options for drug therapy.

For erectile dysfunction, pharmacists should do the following:

Recommend sildenafil for drug therapy.

CONCLUSIONS

1. Parkinson's disease affects men twice as often as men, which coincided with our data. The main age group of patients with PD is aged 75-84 years.

2. tremor is the most common symptom of Parkinson's disease occurred in all respondents, muscle rigidity, as still very a frequent and important symptom for diagnosing PD in 97% of respondents. Also among the most frequent symptoms were: slowness of movement - 81%; impaired coordination of movements up to falls - 33%, emotional disorders and depression - 66%, difficulty in swallowing - 10%, urinary disorders and constipation - 43%, skin rash - 12%. The study found that 18% of patients were diagnosed with PD less than 3 years ago, 55% from 3 to 10 years ago, and 27% more than 10 years ago. It can be concluded that the majority of respondents suffer from PD for 3 to 10 years

3. We found out what drugs our respondents take: 55% receive a combination of levodopa and carbidopa, 12% rasagiline, 9% seligiline, bromocriptine and a combination of levodopa, carbidopa and entacapone, another 6% are treated with trihexyphenidyl. Thus, the vast majority of patients receive a combination of levodopa and carbidopa as the main drugs, which is in line with modern global trends in the treatment of PD

4. We found that 3 patients (10%) did not know about the presence of Adverse effects in drugs, in principle, despite their middle age and the presence of a certain history of taking drugs not only from PD. The remaining 90% of patients knew about the presence of side effects when taking any drugs, which is fully explained by their age and life history and illness/

5. Thus, it can be concluded that the widespread prevalence of PD and the peculiarities of the course of this pathology in the older age group require special attention to these patients from both doctors and pharmacists. The selection of safe and effective therapy is a serious medical and social task. Both the patients themselves and their environment should be involved in solving this problem. At the same time, it is necessary to increase the awareness of patients about the drugs they take, including by doctors and pharmacists.

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Appendex 1

COMMON SIDE EFFECTS AND PRECAUTIONS

Antiparkinsonian drugs	Common side effects	Precautions
1. Levodopa	• Nausea • Vomiting • Lightheadedness • Drowsiness • Involuntary movements • "On-off" effect if long-term use [sudden switch between being able to move (on) and being immobile (off)]	• Use with caution in patients with severe pulmonary or cardiovascular disease, psychiatric illness (discontinue if deteriorate and avoid if severe), endocrine disorders and in those with a history of convulsions or peptic ulcer • Use with caution in patients susceptible to angle-closure glaucoma, and in hepatic or renal impairment. • Avoid abrupt withdrawal • Patient should be alert to the possible sedative effect and should not drive or operate machinery if they feel drowsy
2. Dopamine agonists	• Nausea • Vomiting • Tiredness • Dizziness • Swelling • Compulsive behaviours such as hypersexuality, gambling and eating	• Use with caution in elderly who are more susceptible to confusion or hallucinations • Rule out cardiac valvulopathy with echocardiography before starting treatment with ergot-derivatives dopamine-receptor agonists such as bromocriptine and cabergoline

		• Patients should be warned of the risk of sudden onset of sleep. They should not drive or operate machinery if they feel drowsy • Hypotensive reactions can occur in some patients and if affected, they should not drive or operate machinery
3. MAO-B inhibitors	• Nausea • Headache • Abdominal pain • Dry mouth • Gastrointestinal disturbance	• Avoid abrupt withdrawal • Increased risk of hallucinations and muscle problems when used with levodopa • Should not be taken with certain types of antidepressant, as the drugs can interact to raise blood pressure to dangerous level
4. COMT inhibitors	• Nausea • Vomiting • Diarrhoea • Abdominal pain • Increased risk of involuntary movements	• Avoid abrupt withdrawal • Concurrent levodopa dose may need to be reduced • Should not be used in patients with phaeochromocytoma, history of neuroleptic malignant syndrome or rhabdomyolysis • Should not be used in patients with hepatic impairment
5. Antimuscarinics	• Dizziness • Nausea and vomiting • Constipation • Rapid/irregular heartbeat • Urinary urgency and retention • Blurred vision	• Use with caution in children and elderly • Use with caution in patients with cardiovascular disease, prostatic hypertrophy, hypertension,

	• Dry mouth • Rash	psychotic disorders, pyrexia, and those who are susceptible to angle-closure glaucoma • Use with caution in hepatic or renal impairment • Should not be given to patients with myasthenia gravis and gastro-intestinal obstruction
6. Amantadine	• Gastro-intestinal disturbances • Anorexia • Dry month • Palpitation • Lethargy • Dizziness • Purple mottling of the skin • Ankle swelling • Hallucination	• Avoid abrupt withdrawal Use with caution in elderly • Use with caution in patients with congestive heart disease, confused or hallucinatory states and hepatic impairment • Should not be used in women who are pregnant or breast-feeding • Patient should be alert to the possible sedative effect and should not drive or operate machinery if they feel drowsy

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department of clinical pharmacology and clinical pharmacy

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
Acting the Head of
Department of
clinical pharmacology
and clinical pharmacy

_____
_____
Tetiana SAKHAROVA
"02" of September 2022

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Jad AL KHATIB

1. Topic of qualification work: «Clinical and pharmacological aspects of the use of antiparkinsonian drugs», supervisor of qualification work: : Stanislav ZIMIN, PhD, assist.

approved by order of NUPh from "06" of February 2023 № 35

2. Deadline for submission of qualification work by the applicant for higher education: April 2023.

3. Outgoing data for qualification work: _ Parkinson disease, tremor, muscle stiffness, levodopa, carbidopa, _____

4. Contents of the settlement and explanatory note (list of questions that need to be developed): conduct a literature review on the problem of Parkinson disease, its treatment and prevention, to analyze pharmaceutical market of medicinal products for the treatment of Parkinson disease, conduct a survey of pharmacy visitors with Parkinson disease, develop practical recommendations for patients regarding non-pharmacological methods of treating Parkinson disease, develop practical recommendations for patients regarding the rationality of using antiparkinsonic drugs.

5. List of graphic material (with exact indication of the required drawings):
pictures – 16, tables – 7 _____

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
CHAPTER 1	Stanislav ZIMIN, assistant of department of clinical pharmacology and clinical pharmacy	02.09.2022	02.09.2022
CHAPTER 2	Stanislav ZIMIN, assistant of department of clinical pharmacology and clinical pharmacy	02.09.2022	02.09.2022
CHAPTER 3	Stanislav ZIMIN, assistant of department of clinical pharmacology and clinical pharmacy	02.09.2022	02.09.2022

7. Date of issue of the assignment: «___02__» ___of september____ 2022.

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Analyze the literature on rational use of beta-blockers	September-November 2022	done
2.	Developing a questionnaire on the rational use of beta-blockers	December 2022	done
3.	Conducting a survey of patients using beta-blockers	January 2022	done
4.	Statistical data processing	February 2023	done
5.	Development of practical recommendations for pharmacists	March 2023	done
6.	The final design of the thesis	April 2023	done

An applicant of higher education _____ Jad AL KHATIB

Supervisor of qualification work _____ Stanislav ZIMIN

ВИТЯГ З НАКАЗУ № 35
По Національному фармацевтичному університету
від 06 лютого 2023 року

нижченаведеним студентам 5-го курсу 2022-2023 навчального року, навчання за освітнім ступенем «магістр», галузь знань 22 охорона здоров'я, спеціальності 226 – фармація, промислова фармація, освітня програма – фармація, денна форма здобуття освіти (термін навчання 4 роки 10 місяців та 3 роки 10 місяців), які навчаються за контрактом, затвердити теми кваліфікаційних робіт:

Прізвище студента	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• **кафедри клінічної фармакології та клінічної фармації**				
Аль Хатіб Жад	Клініко-фармакологічні аспекти застосування протипаркінсонічних лікарських засобів.	Clinical and pharmacological aspects of the use of antiparkinsonian drugs	асистент Зімін С.М.	доцент Должикова О. В.

Підстава: подання декана, згода ректора

Ректор

Вірно. Секретар

Ф А2.8-47-110

ВИСНОВОК

Комісії з академічної доброчесності про проведену експертизу

щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

№ 114505 від « 1 » червня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Аль Хатіб Жад, 5 курсу, _____ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Клініко-фармакологічні аспекти застосування протипаркінсонічних лікарських засобів / Clinical and pharmacological aspects of the use of antiparkinsonian drugs», Комісія з академічної доброчесності дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,

професор **Інна ВЛАДИМИРОВА**

5%

30%

Ф А2.2.1-32-353

REVIEW

of scientific supervisor for the qualification work of the second (master's) level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Jad AL KHATIB

on the topic: «Clinical and pharmacological aspects of the use of antiparkinsonian drugs»

Relevance of the topic. Community pharmacists are highly visible, easily accessible health care providers who are valued by patients for their knowledge about medications. Pharmacists are well trained to address medication-related concerns and are the ideal health professionals to assess and refer patients requesting assistance with determining the treatment for symptoms indicative of PD. Additionally, pharmacists have long-standing established relationships with their patients and comprehensive appreciation of their patients' drug therapy, whether prescribed by the patient's family physicians or specialists or obtained by the patient for self-care. Pharmacists can therefore support both patients and physicians in the choice, adjustment and monitoring of ongoing pharmacotherapy for safety, effectiveness, drug interactions, affordability and adherence

Practical value of conclusions, recommendations and their validity. The practical significance of the work consists in clarifying the issue of patients' awareness of the drugs and non-drugs they use to increase the effectiveness and safety of treatment of Parkinson's disease. Practical significance follows logically and consistently from conclusions that are based on a sufficient amount of data obtained in the course of the study.

Evaluation of work. The work made a positive impression, it is a well-integrated scientific work carried out at a sufficient research level and with a high level of analysis of the obtained data. The work is presented on 72 pages of printed text, illustrated with 16 figures and 7 table, the list of used sources contains 94 names, all of them in Latin.

General conclusion and recommendations on admission to defense. The work is a completed and full-fledged scientific work, the design of which meets the

requirements for works of this level according to the "Regulations on the Procedure for the Preparation and Defense of Qualification Works at the National Pharmaceutical University POL A 2.2-25-025" and is recommended for official defense in the state examination commission

Scientific supervisor _____ Stanislav ZIMIN

«11» of April 2023

Ф А 2.2.1-32-356

REVIEW

for qualification work of the second (master's) level of higher education, specialty 226 Pharmacy, industrial pharmacy

Jad AL KHATIB

on the topic: "Clinical and pharmacological aspects of the use of antiparkinsonian drugs"

Relevance of the topic. Community pharmacists are highly visible, easily accessible health care providers who are valued by patients for their knowledge about medications. Pharmacists are well trained to address medication-related concerns and are the ideal health professionals to assess and refer patients requesting assistance with determining the treatment for symptoms indicative of PD. Additionally, pharmacists have long-standing established relationships with their patients and comprehensive appreciation of their patients' drug therapy, whether prescribed by the patient's family physicians or specialists or obtained by the patient for self-care. Pharmacists can therefore support both patients and physicians in the choice, adjustment and monitoring of ongoing pharmacotherapy for safety, effectiveness, drug interactions, affordability and adherence.

Theoretical level of research. In the theoretical part of the work, the relevance is substantiated, modern ideas about the etiology, pathogenesis, symptoms and methods of treatment of Parkinson's diseaseare presented, special attention is paid to drug treatment, lifestyle modifications. The theoretical level of work seems quite sufficient.

The author's proposals on the research topic. The author's proposals presented in this work are fully justified and logical, capable of increasing the effectiveness and safety of the therapy of Parkinson's disease.

Practical value of conclusions, recommendations and their validity. The practical value of the conclusions and practical recommendations lies in the need to work more carefully with the patient regarding his treatment, informing him about the properties of the drugs and necessarily about the presence of side effects of the

drugs, which must be recognized in a timely manner in order to take timely measures to minimize the negative consequences for the patient All conclusions and practical recommendations are based on a sufficient amount of data obtained during the study, their careful analysis and consideration.

Disadvantages of work. Among the shortcomings of the work, you can list some grammatical and stylistic errors, the questionnaire may have had to be placed in the appendices. But these shortcomings in no way reduce the scientific and practical significance of the work

General conclusion and evaluation of the work. The work generally leaves a pleasant impression, it is a finished, consistent and logically constructed scientific work. The author conducted a scientific study at a sufficient research level, made reasonable conclusions and provided important practical recommendations. The work is well illustrated, which sufficiently visualizes the data obtained during the research. Thus, the work was performed at a high scientific level and meets the requirements of the "Regulations on the procedure for preparation and defense of qualification papers at the National Pharmaceutical University POL A 2.2-25-025" and is recommended for official defense in the state examination commission.

Reviewer _____ assoc. prof. Olena DOLZHYKOVA

«15» of April 2023

МОЗ України
Національний фармацевтичний університет

ВИТЯГ З ПРОТОКОЛУ №10

Засідання кафедри клінічної фармакології та клінічної фармації

м. Харків «19» квітня 2023 р.

СЛУХАЛИ: Про представлення до захисту в Екзаменаційній комісії випускної кваліфікаційної роботи на тему: **«Клініко-фармакологічні аспекти застосування протипаркінсонічних лікарських засобів». («Clinical and pharmacological aspects of the use of antiparkinsonian drugs»)** здобувача вищої освіти 5 курсу, спеціальність – 226 Фармація, промислова фармація, освітня програма – Фармація, ступінь вищої освіти – магістр, термін навчання – 4 р. 10 міс., денна форма навчання, НФаУ 2023 року випуску

Жад Аль Хатіб

прізвище, ім'я та по батькові

Керівник: асистент кафедри клінічної фармакології та клінічної фармації, к.мед.н., Зімін С.М.

Рецензент: доцент закладу вищої освіти кафедри клінічної лабораторної діагностики, д.фарм.н., доцент Должикова О.В.

В обговоренні кваліфікаційної роботи брали участь:

В.о. зав. кафедри, професор Т.С. Сахарова; професор В.Є. Доброва; професор С.К. Шебеко; доцент О.О. Андрєєва; доцент Н.П. Безугла; доцент С.В. Місюрьова; доцент І.А. Отрішко; доцент О.О. Тарасенко; доцент К.М. Ткаченко; асистент Зімін С.М.; асистент Т.С. Жулай; асистент Н.В. Давішня; асистент Т.Ю. Колодєзна; асистент К.В. Вєтрова; асистент Ю.В. Тимченко

ПОСТАНОВИЛИ: Рекомендувати до захисту в ЕК кваліфікаційну роботу здобувача вищої освіти

Жад Аль Хатіб

прізвище, ім'я та по батькові

На тему: **«Клініко-фармакологічні аспекти застосування протипаркінсонічних лікарських засобів». («Clinical and pharmacological aspects of the use of antiparkinsonian drugs»)**

В.о. завідувачки кафедри _____ Тетяна САХАРОВА

(підпис)

Секретар _____ Катерина ТКАЧЕНКО

(підпис)

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Жад АЛЬ ХАТІБ до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: ««Клініко-фармакологічні аспекти застосування протипаркінсонічних лікарських засобів».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Жад АЛЬ ХАТІБ

виконав усі необхідні експериментальні дослідження, власне підготував огляд літератури та написав роботу за консультативної участі керівника. Студент є добре підготовленим фахівцем, готовим до самостійного виконання наукової роботи. Робота написана грамотно з дотриманням усіх необхідних вимог та може бути рекомендована до захисту в ДЕК.

Керівник кваліфікаційної роботи

_____ Станіслав ЗІМІН

«11» квітня 2023 року

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Жад АЛЬ ХАТІБ допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

В.о. завідувачки кафедри
клінічної фармакології та
клінічної фармації __

_____ Тетяна САХАРОВА

«19» квітня 2023 року

Qualification work was defended

of Examination commission on

« ___ » _____ 2023

With the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____ / Oleh SHPYCHAK /