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Management of Parkinson's Disease: Challenges and Solutions

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Abstract

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. It is a progressive and disabling disease with significant impact on quality of life. Since it has no cure, available treatment is targeted to improve the symptoms due to a lack of dopamine in the central nervous system.

In this chapter, we summarized the currently available therapeutic strategies to manage the early and advanced stages of the disease.

As the disease progresses, treatment becomes more complex and it is necessary to have simple and objective tools to detect fluctuations in the motor status of patients and closely monitor their response to treatment.

Here, current difficulties and barriers to Parkinson's disease management are described. In addition, the role of new technologies is introduced as potential supporting tools to provide a more holistic approach to the treatment of the disease. For all these reasons, the need of having multidisciplinary teams accessible to the patients is also discussed.

In summary, Parkinson's disease is a complex and multisystem disorder that requires a multidisciplinary and holistic approach compressing all the aspects of the disease to improve the quality of life of the patients. New technologies are a growing field that could provide a potential solution to the current unmet of this disabling disease by real-time remote monitoring.

1.1 Introduction

Parkinson's disease (PD) is the second most frequent neurodegenerative disorder, with approximately 6.1 million people who live with PD in 2016 worldwide [1]. For several reasons that are not yet fully understood, the prevalence and incidence are expected to increase in the next years. According to the World Health Organization, globally, disability and death due to PD are increasing faster than for any other neurological disorder [2].

There is currently no cure for PD, but there are treatments available to relieve the symptoms and maintain an individual's quality of life (QoL) at least for the first years.

The PD impact on the QoL is due to an enormous number of motor and non-motor symptoms: bradykinesia, rigidity, tremor, postural instability, reduced gait speed, freezing of gait (FoG), sleep disturbances, depression, psychosis, autonomic and gastrointestinal dysfunction as well as dementia. The majority of patients will develop an increasing number of more complex symptoms over time.

The treatment in the early stages of the disease, focused on the use of levodopa, is very effective. Nevertheless, different problems related to the treatment or disease progression may start to appear depending on the advance of the disease. Thus, it might be the case of motor complications (MCs): **motor fluctuations** such as the **wearing-off** phenomenon (temporary loss of dopaminergic effect), involuntary movements known as **dyskinesia**, fluctuations between the ON stage (when a correct control of the symptoms is achieved) and the OFF stage (when motor symptoms reappear), abnormal cramps and postures of the extremities and trunk known as **dystonia**, and a variety of complex fluctuations in other motor and nonmotor functions, the nonmotor complications (NMCs). In these cases, the precise adjustment of the therapy is crucial to avoid decreasing the QoL of the patient. The motor symptoms are especially responsible for falls and gait impairments and negatively impact on QoL by reducing the ability to perform many activities of daily living. They are the major causes of institutionalization and by the way, losing independence. Daily tasks at home (self-care, food preparation, climbing stairs...) become difficult, as do many activities outside the home such as shopping, visiting friends/family, leisure activities, among others.

The management of this disease must be multidimensional. Unfortunately, there is often no integration between data at different levels of the health system: primary health physicians, occupational therapists, and social workers. Information about the general condition of the patient is also usually lacking.

PD treatment is actually symptomatic, based on dopaminergic replacement therapy, and aims to alleviate the symptoms associated with the disease, through the precise adjustment of medication. The most widely used drug, levodopa, is effective usually across the lifespan. However, the onset of MCs, as is ON-OFF fluctuations and dyskinesias, a few years after starting treatment, detracts from its value. Symptomatic management of these complications is difficult and often needs to be optimized because the improvement obtained after this adjustment is not usually stable for a long time.

As the disease progresses, treatment is primarily addressed to reduce the time spent in the OFF state, while avoiding the appearance of MCs and NMS, such as hallucinations or impulse control disorder. Reducing OFF periods is therefore one of the main parameters used to evaluate the effectiveness of therapeutic interventions, both in medical practice and in clinical trials. Gathering accurate information about the patient's condition throughout the day is essential to determine the optimal treatment plan. In clinical practice, the only method available is based on diaries filled in by patients and their caregivers about the ON – OFF periods and dyskinesias. However, this method has certain limitations that make unreliable medium-and long-term monitoring: motor difficulties and cognitive failures that hinder regular compliance and subjective evaluation. In addition to the huge time-consuming it represents for the patient as well as the clinician, to explain how the diary should be filled out. Moreover, is one of the main reasons for screening failures in clinical trials for fluctuating PD patients. Therefore, more objective solutions that can improve disease monitoring and management are of great interest and occupy an important part of current research.

Several motor and nonmotor symptoms could appear at disease onset and over time, PD might be considered a multisystemic disease instead a pure motor disease. Thus, another important aspect of the symptomatic treatment of PD is the Multidisciplinary treatment (MDT) approach. The multiple impairments occurring in Parkinson's disease have diverse functional and psychosocial consequences. While the primary treatment is pharmacological, many symptoms do not respond well to medication, such as **ON-period freezing of gait (FoG), postural instability, speech, and swallowing difficulties**. Indeed, later-stage disease may be dominated by such symptoms. In addition, there is growing evidence for the efficacy of rehabilitation therapies and exercise for specific symptoms, through the involvement of the multidisciplinary team. There is also emerging evidence for physiotherapy with external cueing for improving gait and balance; cognitive movement strategies; and strength and balance exercises. Intensive speech therapy has been shown to improve the loudness and intelligibility of speech in Parkinson's disease.

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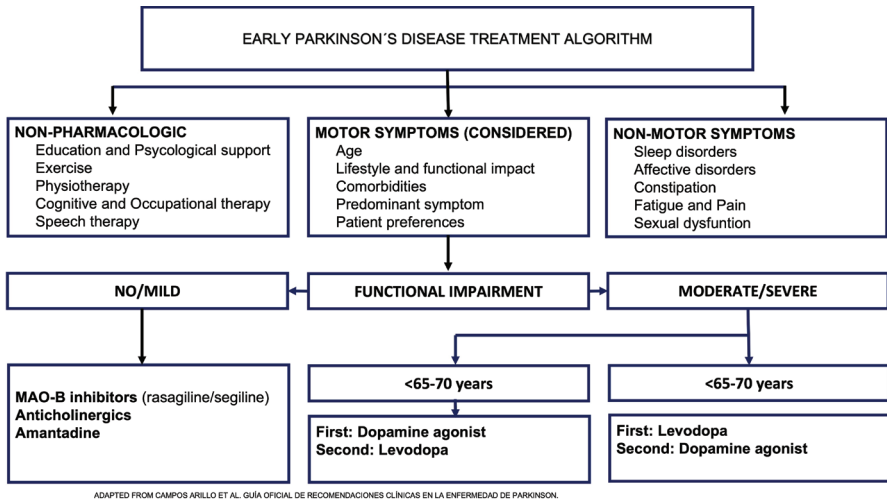


Figure 1.1 Treatment algorithm in early Parkinson's disease patients [4].

Unfortunately, the MDT is only applied in a few numbers of PD patients for economical and logistic reasons.

In the study of Winter et al. [3], a baseline and 3-, 6-, and 12-month assessments were performed on 145 Parkinson's patients. The average annual cost was calculated at 20,095 € per patient. The direct costs involved an expenditure of 13,185 € on medication, 3,526 € on hospital care, and 3,789 € on residences. The indirect costs accounted for 34.5% of the total costs (6,937 €). The costs of home care for the family accounted for 20% of direct costs. Factors associated with a higher total cost were fluctuations, dyskinesias, and younger age.

1.2 Strategies to Manage Parkinson's Disease at Different Stages

The diagnosis of PD is sometimes difficult. At the onset, the patient could show nonspecific signs, such as pain or mental depression or a slight tremor in one limb. During the first year, once the possible diagnosis is confirmed, several symptomatic treatments could be initiated depending on many factors: age, disability, and type of job, as it is summarized in Figure 1.1 [4]. Most PD patients respond very well to treatment with levodopa and dopaminergic agonists during the first years (between 3 and 7 years). This is the reason why it is called "*honeymoon period*."

Table 1.1 Modified Hoehn and Yahr scale.

Stage	Modified Hoehn and Yahr scale
1	Unilateral involvement only
1.5	Unilateral and axial involvement
2	Bilateral involvement without impairment of balance
2.5	Mild bilateral disease with recovery on pull test
3	Mild to moderate bilateral disease; some postural instability; physically independent
4	Severe disability; still able to walk or stand unassisted
5	Wheelchair-bound or bedridden unless aided

During the years 2–4, there is relative normality, and the medication is generally effective. As the disease progresses, the patient encounters a limitation of the effect of medical treatment due to the appearance of motor and non-motor complications: wearing off and dyskinesias. These entail a progressive difficulty in carrying out activities of daily living and leading an independent life. Between the years 5 through 9, the effectiveness of medication usually decreases, and treatment may need to be modified. Problems with driving, finances, and work may appear at this time. During years 10–13, there is an increasing disability: 60%–75% of patients present with some cognitive deficit, worsening immobility, incontinence, and increased risk of falls.

We can distinguish five evolutionary stages of the disease, such as the Hoehn & Yahr stages (HY) (Table 1.1). Patients do not necessarily have to go through all of them. The main problems presented by patients in the different evolutionary phases and the strategies currently recommended are considered in the following points.

1.2.1 Patients at early stages

In stage I of PD, facial expression and posture are generally normal. A tremor of a limb is the most common initial manifestation. It is often quite annoying, and it is the symptom that draws the attention of both the doctor and the patient. Typical Parkinsonian tremor appears at rest and rarely interferes with the activities of daily living (ADL), although it disturbs and distresses the patient and caregiver. Patients sometimes report difficulties in performing activities that require motor skills such as buttoning, typing, or cutting food. In the careful exploration of these patients, other Parkinsonian signs in a limb, such as bradykinesia or slow movement, and stiffness, which contribute to these fine motor difficulties, are detected in addition to tremors. Decreased arm swing or dragging of a leg when walking can also be observed. These symptoms, often present for several years, are better tolerated than tremors.

In stage II of PD, there is bilateral involvement. There may be a loss of facial expression with decreased blinking. Slight flexion of the body may be present and, in general, arm swing when walking is diminished, without altering balance. Patients slow down when performing ADLs, and they require more time to dress, clean themselves up, get up from a chair, or tie their shoes on their own.

Depressive symptoms are also frequent, and these are detected in between 30% and 50% of the cases. Medical treatment will be administered according to the severity of the symptoms. Sometimes they can produce side effects.

In these initial stages, patients are advised to learn about the disease, learn to speak naturally about their problems, learn to share difficulties and go to the doctor accompanied by someone. Standardized psychoeducational programs, such as the “EduPark” program [5] are a great help at this stage of the disease. From the diagnosis, it is recommended to initiate MDT, which includes physical exercise, and cognitive stimulation. It is better for patients to continue doing things by themselves, even if it is done slowly, without rushing, and with enough time. It is advisable to adapt the setting in which patients must perform their ADLs and to be physically and mentally as active as possible. Family members should also be informed and should know how to convey their support. It is recommended to see a doctor if depressive symptoms or side effects occur with medications.

1.2.2 Moderately affected patients

People at III-IV Hoehn and Yahr stages have already a degree of moderate-severe disability, as they experience gait and balance difficulties. They explain that their gait is shortened and that sometimes they have difficulties making turns while they walk, in the corners of the rooms, or while crossing the doors. Balance problems can cause falls. Sometimes while walking, they present FoG, or difficulty to stand, either forward (propulsion), or backward (retropulsion). The feeling of fatigue is a very frequent symptom. They have the feeling of needing a lot more effort to perform certain tasks and often notice pains in the cervical, lumbar, or shoulder region. Symptoms of autonomic dysfunction may also be present in the form of orthostatic hypotension, extreme sensations of heat or cold, sweating not related to physical activity, sometimes in the form of crisis, and urinary, gastrointestinal, or sexual dysfunction.

Many patients, at stage III or IV, experience side effects of chronic dopaminergic medication. The most annoying side effect for patients is the

ON-OFF phenomenon that can manifest with MCs or with NMCs. This phenomenon is often disabling and causes fear and insecurity. During the ON phase, patients can enjoy good mobility and carry out activities outside the home, such as shopping or social activities. However, during the OFF phase, the patient may be completely disabled, with difficulties in walking, thinking and speaking, getting up from a chair, or manipulating objects with hands among others. The appearance of OFF phases limits the social activities of the patient, often preventing them from going out with consequent worsening in terms of QoL. In this state, patients may find themselves in really dangerous situations, such as if this phenomenon occurs when crossing a street.

Dyskinesias, or abnormal involuntary movements, are another important and disabling problem that many patients present with during stages III and IV. In general, they have a choreiform nature: creeping and twisting movements of the extremities, or masticatory movements of the lower jaw, protrusion of the tongue, oscillations as they walk, and reciprocating movements with head and neck. Dyskinesias are a long-term side effect of dopaminergic medication, which usually occurs during the levodopa plasmatic peak dose. If they are mild, the family is more aware of these movements than the patients themselves, who usually associate it with the free time of Parkinsonian symptoms. When they are severe, they can become disabling as much as the symptoms themselves.

NMS may appear in form of sleep disorder, vivid dreams, and nocturnal vocalizations. Night-time vocalizations, reported by the bed partner, consist of loud cries during sleep often accompanied by the agitation of arms and legs (acting out). It is called "*REM behavior disorder*." These events can disrupt sleep. Other frequent behavioral disorders in these stages are visual hallucinations, delusional ideation, and confusing states of the paranoid type. Visual hallucinations in general are not very threatening in PD. They often describe the vision of family members, animals, or shadows that become animated objects.

The strategies recommended in these phases are aimed at understanding the MCs and NMCs and knowing how to monitor them. This will allow the patient to adjust the activities in each period. If MCs or behavioral changes appear, the neurologist can be informed to assess the possibility of adjusting the drug. It is, therefore, important to learn to do the patient's diary. This information will be crucial to optimize pharmacological treatment.

Patients at these stages should continue to maintain an active life and perform MDT, such as physical exercise, occupational therapy, speech therapy, and cognitive stimulation, according to individual needs. It is also

recommended that patients continue doing things by themselves, for as long as possible.

1.2.3 Severely affected patients

Patients with PD, stage V, are severely affected. They are usually confined to a wheelchair or bedridden and require great assistance to make transfers. They are totally dependent to carry out ADLs and have a great limitation on a personal level.

Difficulties in speech and voice are often accentuated: these patients are often difficult to understand due to their low volume and poor articulation of words. They may eventually develop contractures and present decubitus ulcers or recurrent urinary tract infections.

Since the emergence of effective therapies for the treatment of this disease, not all patients reach a state of total dependence. However, they are experiencing a progressive reduction in time spent in ON and an increase in dependency time. In the lasted stages of this disease, the presence of progressive dysphagia can cause recurrent aspiration pneumonia, which is a possible cause of death. Other conditions that may contribute to this outcome are infections of pressure ulcers or urinary tract.

Since a causal treatment of the disease is still not possible, the objective for an optimal treatment will be to obtain for the patient a good QoL and the maximum independence possible. In the advanced stages, it is recommended to follow extreme hygiene, take care of mobilization, adapt the feeding, and above all take care of communication. The Lee Silverman Voice Treatment (LSVT) method has demonstrated efficacy in the treatment of speech and speech disorders. However, in very severe situations, it is advisable to maintain communication, even if external technical support is necessary.

Possible behavioral disorders should be addressed, while enhancing the hobbies and pleasures that can still take place, such as listening to music, reading, or watching movies. Caregivers should make them feel their support, while they should seek a replacement that allows them to have their own space and thus avoid the burden of care and better adaptation when the patient passes away.

1.3 Impact on the Quality of Life

PD is one of the chronic degenerative disorders with the most impact on patients' lifestyles. Most patients survive many years after the first symptoms. The mean survival rate of patients with this disease (when diagnosed

after age 50) is 26 years, not very different from the nonaffected population of PD.

Quality of life (QoL) means well-being or satisfaction with aspects of life that are important to the person according to social standards and personal judgments. Because of this latter characteristic, each person understands the QoL in different ways and, therefore, it is difficult to define. The World Health Organization (1995) defines it as: “*an individual perception of the position in a person’s life, in the context of the culture and value system in which he lives, in relation to his goals, expectations, standards, and concerns.*”

When it is not possible to cure, maintaining the quality of life of the patient is a priority of medical care. Quality of Life, as related to Health (QoLRH), is the self-perception and assessment of the impact that the disease has on a patient’s life and what its consequences are [6]. This assessment is extremely important and includes physical aspects related to the ability to perform activities, mental aspects related to mood and cognition, social aspects, and economic aspects. Several studies have been done to assess QoLRH in PD [7]. The three most important factors determining QoLRH in PD were depression, the stage of the disease, and the time that has elapsed since the onset of the disease.

In another study [8] performed with 100 patients, the most important predictor for poor QoL was depression, followed by motor complications. Motor complications, especially nocturnal akinesia, and dyskinesias, significantly decrease the QoL of Parkinson’s patients [9–11]. Dyskinesias can also increase health costs in patients with PD. This should be considered when planning treatment [12].

Despite the high impact of motor symptoms in PD, nonmotor symptoms seem to influence patients’ QoL even more. Nonmotor symptoms tend to accumulate. The average was 10 symptoms per patient in the populations studied and symptoms tend to intensify over time. Depression, anxiety, fatigue, sleep disorders, pain, orthostatic hypotension, and profuse sweating are some of those that have shown an individual relationship with loss of quality of life. In fact, any symptom that, due to its intensity, is installed as a central problem in the life of the patient has a direct and important impact on his/her quality of life. For example difficulty swallowing, persistent constipation, urinary urgency, night-time urination, delusions and hallucinations, memory problems, or a sense of choking when breathing. At the global level, the main factors influencing the poor QoL of those affected by PD are (in order):

1. Depression
2. Overall disease intensity (stage)

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3. Dyskinesia
4. On-off fluctuations
5. Age
6. Insomnia
7. The tremor
8. Cognitive dysfunction

To assess, in a more global fashion, the impact of motor and nonmotor symptoms in terms of QoL a new staging of the disease has been proposed. The combination of HY and Nonmotor symptoms score could reflect the severity of the disease more accurately [13].

Another element that must be considered is the QoL in caregivers. Forty percent of them indicate that their health suffers due to the care. Nearly half have increased depression, and two-thirds report that their social life has suffered. The caregiver becomes burned out more (*burden of care*) if the patient has more disability, affective problems, mental confusion, or falls. There is a correlation between those caregivers that are most affected and the degree of a patient's depression and one of the main determinants of QoL in caregivers is mood changes, especially depression [14].

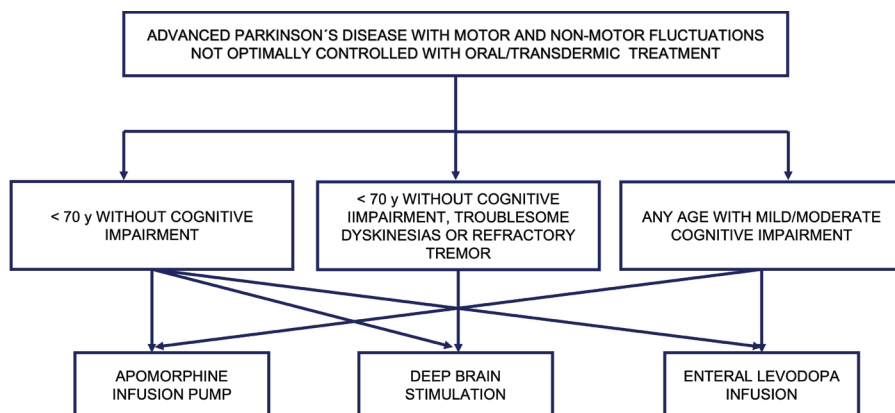
The conclusion is that more attention should be given to caregivers' care, particularly in advanced stages and/or with psychiatric and fall complications. These findings demonstrate that the quality of life of both the patient and the caregiver depends, to a great extent, on the inclusion of the burden of care as one of the problems associated with PD [15].

1.4 State of the Art of the Current Trends in Illness Management

As has been previously mentioned the current treatment of PD is symptomatic and is applied through pharmacological and/or surgical treatment, associated with MDT.

The pharmacological treatment of PD is focused on balancing the lack of dopamine and other neurotransmitters, and aims to alleviate the symptoms associated with the disease, by precise drug optimization. During the first years of treatment, dopaminergic drugs (levodopa and dopaminergic agonists) are usually very effective. At 2 years of levodopa treatment, 38% of patients had ON-OFF fluctuations [16].

When the ON-OFF phenomena are already present, the objective of the treatment will be essentially concentrated on reducing the time that the



ADAPTED FROM VALLEDEOROLA SERRA ET AL. GUÍA OFICIAL DE RECOMENDACIONES CLÍNICAS EN LA ENFERMEDAD DE PARKINSON.

Figure 1.2 Decision tree algorithm to manage advanced Parkinson's disease.

patient spent in the OFF state. To determine the optimal and personalized treatment plan, gathering accurate information about a patient's condition throughout the day is essential. In clinical practice, the method currently available is based on clinical recall or diaries filled in by patients and their caregivers, recording hours of ON-OFF and the presence of dyskinesia. However, this method has limitations that make it unreliable in conditions of the real clinical setting, such as motor difficulties, failures in memory and in compliance, and subjective evaluation. It is necessary to know precisely and objectively the effect of drugs on the OFF stage reducing hours and increasing the ON hours in PD patients. **Reliable and easy-to-use tools are therefore needed for detecting and monitoring the motor condition of the patients.**

When both, motor and nonmotor symptoms, are not adequately controlled with oral or transdermal treatment, patients may benefit from second-line or device-aided therapies (DAT). These therapies include continuous infusions of apomorphine, enteral levodopa, and deep brain stimulation. Subcutaneous formulations of levodopa are likely to be available in the future. The main objective of these strategies is to provide continuous dopaminergic stimulation (CDS) by different mechanisms to manage and control both motor and nonmotor fluctuations. All of these therapies have shown significant efficacy in terms of increasing the quality of ON time (without troublesome dyskinesias), decreasing OFF time, and reducing the burden of nonmotor symptoms [17]. Figure 1.2 summarizes a decision tree considering the second-line therapy options [4].

However, these techniques are expensive and often difficult to manage the patient. Well-designed clinical studies on these DATs provided evidence for the efficacy of DBS and CDS in advanced PD and currently, we have new perspectives for their use also in earlier disease stages.

On the other hand, there is growing scientific evidence of the benefit of the application of MDT, such as physiotherapy, speech therapy (e.g., LSVT), occupational therapy, cognitive stimulation, and psychoeducation in the treatment of PD. Intensive and multidisciplinary rehabilitation slows the progression of motor decay and slows the need to increase treatment with levodopa, which is postulated to have a neuroprotective effect [18]. Therefore, the application of MDT from the moment of diagnosis seems of great interest. There are several studies of multidisciplinary care in Parkinson's disease comparing outcomes before and after the intervention. Outpatient multidisciplinary care programs have reported short-term improvements in motor skills, gait speed and stride length, speech, depression, and health-related quality of life. Long-term improvements in motor function have also been reported, and the authors comment that a close collaboration among members of the multidisciplinary team was essential to obtain the best results.

For the implementation of an effective multidisciplinary approach, there may be limitations, such as living far away, insufficient experience among health professionals, poor interdisciplinary collaboration, poor communication, and lack of financial support for a multidisciplinary team approach.

Regular face-to-face team meetings are important for the effective functioning of the team. These meetings allow sharing of accurate information and ensure the team is working toward shared goals for any given patient. The meetings can be a forum and stimulus for staff education, driving up the quality of care. This type of coordinated multidisciplinary approach is sometimes referred to as interdisciplinary.

Most hospitals in Europe do not have a multidisciplinary service for the care of people with PD. These types of therapies are expensive and in addition, their application requires patients to frequently go from one place to another. This entails a number of limitations, both economic and logistical, for those affected with PD before having access to these therapies.

1.5 Challenges for the Best PD Management

Current management of advanced PD is complicated and problems arising from poor quality of life affect many patients. In 2001, *the Committee on Quality of Health Care in America Institute of Medicine* provided an objective analysis of healthcare. The report listed 6 aims, proposing that health

care should be: safe, effective, patient-centered, timely, efficient, and equitable. However, current care for PD in the United States, Europe, and likely the majority of the world, frequently does not meet these six aims [19]. PD care is often not safe. Individuals with PD who are hospitalized are often subjected to delayed treatment, contraindicated medications, prolonged immobility, lengthy stays, and high mortality [20, 21]. There are some comprehensive and distributed PD care models that are quite effective, but only a few patients receive such care. Many PD-related hospitalizations are likely preventable. The patient-centered care that is timely has been rarely studied. Despite the limited evidence, focus groups and surveys suggest that individuals with PD want more personalized information from multiple disciplines that are delivered remotely in a timely manner [22]. PD care is very inefficient. Patients and their caregivers spend hours traveling and waiting in the clinic for routine follow-up appointments or for the application of complementary therapies. A recent technical publication from WHO underlines the importance of multidisciplinary teams in the holistic approach to the disease and lists a series of key actions to be implemented by health systems [2].

Finally, probably what may be most concerning, is that there exists inequity in current PD care. **A primary determinant of the care that will be received is where you live.** In the United States, 42% of individuals with PD older than 65 and up to 100% of individuals in some rural areas do not see a neurologist soon after diagnosis [23]. In Europe, the first right expressed in the European Parkinson's Disease Association Charter is care from a physician with a special interest in PD. However, 44% of Europeans do not see a PD specialist in the first 2 years after diagnosis. Beyond neurological care, access to specialist nurses, occupational therapists, and counselors is often more limited [24]. In less wealthy countries, the situation is even worse. China only has approximately 50 movement disorder specialists to care for more than 2 million individuals with PD. Bolivia only has 15 professionals. A door-to-door epidemiology study found that none of the individuals identified with PD had ever seen a physician, much less received treatment.

It is possible to make the treatment safer, effective, patient-centered, efficient, and equitable only if the following two conditions apply [25]:

- The treatment is applied, mostly, at the patient's home.
- Tools, based on new technologies, are used (sensors, communication platforms, and smartphones).

These conditions will overcome economic barriers and physical distance. However, the **potential digital gap** and the **population's access to such**

technological resources should be considered when developing health program policies.

The simple fact of detecting accurately and reliably the clinical condition of the patient can mean a 360°-change in the QoL of the patient, as this will affect a much more accurate adjustment of medication. In addition, with the help of adequate platforms, many more patients, as well as their caregivers, will receive more specialized medical care, complementary therapies, and psychoeducation as often as necessary, regardless of where they live.

In addition, **reliable detection of the motor status of PD patients throughout the day can drastically change the value of drug clinical trials**. Finally, the careful selection of patients amenable to semi-invasive therapy options becomes more and more important and should be timely. An interdisciplinary setting is required to account for optimal patient information and awareness, selection of best individual treatment modality, training of relatives and caregivers, management of complications, and follow-up care.

From a clinical point of view, the development of new technologies in the management of Parkinson's disease must be validated so that the improvement of the QoL related to health is the main objective. Symptoms' monitoring tools should be based on the following premises [26]:

- They provide a valid and accurate parameter of a clinically relevant characteristic of the disease.
- The evidence that the parameter has an ecologically relevant effect on the specific clinical application is found.
- A target interval can be defined in which the parameter reflects the appropriate treatment response.
- The implementation is simple to allow repetitive use.

Remote monitoring from devices, such as wearable sensors, smartphones, platforms, disease management applications, smart beds, wall-mounted cameras, smart glasses, etc., can monitor a patient's symptoms and function objectively in their environment, facilitating the delivery of highly personalized care.

Another aspect to improve PD care is that most of it must be done at home. Current care models frequently require caring for older people with mobility and cognition problems, with loss of the ability to drive, and needing to be transferred by overburdened caregivers, to large and complex urban medical centers.

Moving care to the patient's home would make PD care more patient-centered. Demographic factors, including aging populations, and

social factors, such as the splintering of the extended family, will increase the need for home-based care.

Technological advances, especially the ability to assess and deliver care remotely, will enable the transition of care back to the home. However, despite its promise, this next generation of home-based care will have to overcome barriers, including outdated insurance models and a technological divide. Once these barriers are addressed, home-based care will increase access to high-quality care for the growing number of individuals with PD.

Emerging care models will combine remote monitoring, self-monitoring, and multidisciplinary care to enable the provision of patient-centered care at home and decrease the need for in-clinic assessments. The demand for in-home care is likely to grow as a result of demographic, economic, social, and technological factors. Both the absolute number and proportion of older individuals with PD will increase.

A system for PD management will be necessary in the near future. It must be able to reliably assess the symptoms, facilitate patient disease management, and give them independence and the best QoL. At the same time, the tools must help the patient to stay physically and mentally active as much as possible. Finally, they must provide the neurologist with disease management tools to optimize the treatment.

Emerging available systems, like STAT-ON™, try to improve the efficacy of disease management and treatments, and detect the onset of motor complications, and monitor treatment response in the current clinical practice that presents the following major obstacles:

- **Barrier 1: Lack of accuracy and completeness when reporting about own symptoms.** Due to the cognitive impairments, distress, or evasive nature of some of the symptoms caused by PD, the patients often find difficulties or lack sufficient ability to provide reliable/consistent clinically relevant information about the symptoms they experience in order to optimize the treatment. In particular, often the patients are not aware of the onset of dyskinesia and sometimes it is even difficult for them to distinguish between ON/OFF periods. However, these are key information items for the physician to adjust the treatments.
- **Barrier 2: Missing information about the PD symptoms and signs of disease progression at the clinical level.** The currently available means to report and monitor the symptoms are modest compared to the huge challenge posed by the variety of PD symptoms and their fluctuations. The patient's visits and self-reporting may not throw reliable or complete evidence for the physician to cope with the entire picture and

overall phenomena surrounding their patients day-to-day. Most of the evidence used builds on reporting provided by the patients themselves and they often lack the ability to undertake this task.

- **Barrier 3: Compromised self-care and adherence to treatments.** Treatment regimens (medications, times, and doses) and adherence to treatment are crucial for correct PD management and for the QoL of the patients. PD patients resort to prescribed regimes, but this seemingly simple commitment may represent a nontrivial feat since patients must add on top of the overall burden the challenge of self-care, which is often difficult to achieve due to the many impairments and distresses linked to the disease. Cognitive deficits such as attention, communication, memory, and executive functions; depression and impulsive behaviors play a key role in the common lack of adherence and self-efficacy in co-management of the disease.
- **Barrier 4: Symptoms recognition in time to better administrate the medication dose.** Another related barrier is the capability of the professional to properly assess the number of OFF hours the patient has experienced to judge, based on that information, the therapeutic effect of the administered therapy since it is based on diaries or patient recall. When an infusion pump therapy is used, the practitioner has difficulties adjusting the infusion rate, and parameters of stimulation, as well as controlling the administration of extra doses.
- **Barrier 5: Usability from the patient's point of view.** Some patients with Parkinson's have OFF phases so severe that they cannot even self-administrate extra doses or medications. Patients with severe OFFs, which have no caregivers who can perform this task for them, often cannot choose the treatment with continuous infusion pumps. So, for these treatment modalities, it is important an accurate evaluation of socio-functional status and resources since support from others is often required.

1.6 Conclusion

As a concluding remark, it could be said that the current knowledge about PD is continually growing, opening the possibilities of new strategies. Many treatments are currently available, requiring a multidisciplinary approach to improve the QoL of the patients. In order to advance in a more personal and patient-centered treatment, the new technologies could help to address new

scenarios from a more global perspective, allowing closer and more objective monitoring in real time.

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