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Covid-19 and Parkinson's disease: Nursing care, vaccination and impact on advanced therapies

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Abstract

The Coronavirus Disease 2019 (Covid-19) pandemic has created many challenges for the Parkinson's Disease (PD) care service delivery, which has been established over the past decades. The need for rapid adjustments to the new conditions has highlighted

the role of technology, which can act as an enabler both in patient-facing aspects of care, such as clinical consultations, as well as in professional development and training. The Parkinson's Disease Nurse Specialists (PNSs) play a vital role in the effective management of people with PD (PwP). Maintaining optimum functionality and availability of device aided therapies is essential in order to ensure patients' quality of life. PwP are particularly recommended to use vaccination as a basic protection from the virus. The long-term consequences of this pandemic on PwP are highly uncertain, and education, support and reassurance of patients and their families may help ease their burden.



1. Introduction

Over the past 2 years the pandemic caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has spread globally, profoundly affecting morbidity and mortality of the general population (Abate, Checkol, & Mantefardo, 2021; Piroth et al., 2021). People with Parkinson's Disease (PwP, PD) are often older and have comorbidities, which might increase the risk for severe or critical Coronavirus Disease 2019 (Covid-19) (Casella, Rajnik, Aleem, Dulebohn, & Di Napoli, 2021). This might be particularly true for those with advanced PD, as they usually experience a heterogeneous set of motor and non-motor symptoms and follow complicated therapeutic regimens.

Optimal care of PwP should involve a multidisciplinary team (MDT), with PD Nurse Specialists (PNSs) being key members. During the pandemic, PNSs have worked hard in order to assist PwP in self-isolation consequences and symptom management, reducing the risk of both hospital admission and extended hospital stays (Simpson & Doyle, 2020). The role of a PNS is particularly prominent in the care of advanced PwP, who are suitable for device-aided therapies. Moreover, the International Parkinson and Movement Disorder Society (MDS) has recommended in favor of the Covid-19 vaccinations, recognizing their paramount role in the protection of PwP, physicians and associated healthcare providers in this critical situation of the global pandemic (Bloem et al., 2021).



2. The role of the Parkinson's disease nurse specialist

Within the United Kingdom (UK) the first PNS came into post in 1989, following recommendations from a commissioned research project, investigating ways to provide up-to-date care and support to PwP (MacMahon, 1999). The PNS role has been developed with the aim of

improving PD prognosis, through better education and support, and reducing the impact of PD on patients, but also their families and caregivers. A task force for the PD Society has suggested that each individual with PD will be assigned a healthcare professional, holding a leading role in coordinating the patients' care and treatment changes in collaboration with a multi-disciplinary team (Brown et al., 2020). Today, the PNS role is still recognized as pivotal (Cook, McNamee, McFetridge, & Deeny, 2007) with around 450 PNSs working in primary, secondary, and tertiary care settings in the UK.

The PNS provides assistance with ongoing management and follow-up by providing medication review, clinical leadership, help with post-diagnostic counseling, guidance to other services, education about PD, support, and advice for PwP, their caregivers and other involving staff (Axelrod et al., 2010). Many PNSs run their own clinics, organize PD helplines, make home visits, refer to other experts and co-ordinate care packages according to patients' needs. PNSs are often the first point of contact for PwP, ensuring fast access to specialist care, whilst relieving some of the pressure from neurologists/ geriatricians with a special interest in PD, who are in short supply (Axelrod et al., 2010). The National Institute for Health and Care Excellence (NICE) guidance (Rogers, Davies, Pink, & Cooper, 2017) recommends that PwP should have regular access to:

- Clinical monitoring and medication adjustment.
- A continuing point of contact for support, including home visits when appropriate.
- Reliable sources of information about clinical and social matters of concern to PwP, their family members and their caregivers (as appropriate).

Within the UK, these recommendations are often achieved due to the services provided by the PNSs, who constitute, thus, vital team members of the PD specialist service.

2.1 Covid-19 and the impact on people with Parkinson's

In April 2020, the UK Department of Health and Social Care (DHSC) announced that all people should "Stay at home, protect the National Health Service (NHS), save lives." Further recommendations were given to people aged over 70, or those with an underlying health condition, to stay at home at all times and not to leave, even to buy food, collect medicine or exercise. Within the UK this advice lasted for months, and people have experienced a number of "lock downs" as the situation changed with

the appearance of different variants of SARS-CoV-2. Particular guidance has been given to people at high risk of developing severe complications from Covid-19, who were described as “clinically extremely vulnerable.” These individuals were contacted via the NHS and provided with extra support to ensure they were able to remain at home. PwP have been classified as “moderately vulnerable,” which means they were only recommended to leave their home in order to buy food or medicine, or to exercise once daily.

Staying home and isolating from others has led in dramatic changes in daily routine and lifestyle for everyone. Activities previously taken for granted, such as going shopping, attending social gatherings, collecting medications, providing childcare or attending a day center, had to stop, imposing drastic changes in people’s daily schedule. Flexible adaptations to new circumstances have been acknowledged as cognitive operations, which depend on normal dopaminergic functioning (Helmich & Bloem, 2020). An insightful paper by Helmich and Bloem (2020), based on a large body of literature, discusses how PwP experience cognitive and motor inflexibility, as a result of nigrostriatal dopamine depletion, which forms the pathophysiological substrate of PD (Helmich, Aarts, de Lange, Bloem, & Toni, 2009). Douma and de Kloet (2020) have also hypothesized that dopamine-dependent adaptation is a prerequisite for successful coping, which, when deficient, might lead to a sense of loss of control and increased psychological stress (Douma & de Kloet, 2020).

Up to now, numerous papers have been published, citing the indirect impact of Covid-19 on individuals, including stress, self-isolation, depression, and anxiety, along with the consequences of prolonged immobility due to the lockdown (Helmich & Bloem, 2020; Prasad et al., 2020). Helmich and Bloem (2020), have also identified that these increased levels of stress during the Covid-19 pandemic may have both short- and long-term negative sequelae for PwP. Indeed, high levels of psychological stress have been associated with temporary aggravation of a number of motor PD symptoms, such as tremor, freezing of gait, or dyskinesias (Macht et al., 2007; Prasad et al., 2020; Zach, Dirkx, Pasman, Bloem, & Helmich, 2017), along with a reduced efficacy of dopaminergic medication (Zach et al., 2017).

2.2 Covid-19 and the impact on Parkinson’s disease services

Due to increasing numbers of Covid-19 patients being admitted in hospitals, the pressure on healthcare professionals has been enhanced, with many

specialist nurses, including PNSs, being redeployed to different clinical areas in order to support the front line staff. As a result, many PwP have been left without their vital link to specialist knowledge, information, and support for prolonged periods of time. Regular PNSs reviews had to be canceled, helplines were closed and PwP lost their prior access to specialist service. These changes have likely contributed to the high levels of stress and anxiety already experienced by PwP.

The few PNSs, who were left to manage the specialist services, had to rapidly re-design and adjust to the new circumstances. National guidance for healthcare professionals was to avoid all face-to-face contact, unless there was a clear urgent need not to do so. This meant that many Outpatient Clinics, including Movement Disorders Outpatient Clinics, were canceled and the ability to provide standard PD care was severely compromised by the strain on healthcare systems brought about by this pandemic (Papa et al., 2020). For those services who were able to continue to assess or review PwP face-to-face, restrictions were often applied, including less new or regular patients assessed per clinic in order to allow for social distancing regulations and to ensure appropriate room cleaning between appointments.

Many PD Specialist services were only able to use telehealth and telephone-based services to continue to monitor and support PwP. Many PNSs were no longer able to conduct home visits or review those living in sheltered accommodation, residential or nursing care facilities. Many PNSs developed protocols for telephone consultations to ensure that a safe practice was followed and vital symptoms were not missed. Once PNSs were able to review patients, particularly those with complex needs or those approaching end of life, within their own home or in a community setting, appropriate personal protective equipment (PPE) guidelines were devised and followed. During this time, the use of wearable technologies was further encouraged and will be discussed later in this chapter.

Like in other specialties, further pressure has been imposed on PD specialist services, as some PNSs might be required to “self-isolate” due to their medical history or have to look after children or dependents during lockdown periods (Nune, Iyengar, Ahmed, & Sapkota, 2020). Under these circumstances, many PNSs have opted to work from home, trying to ensure continuity of care for PwP. Overall, redeployment of staff and self-isolation regulations have greatly reduced the availability of PNSs during the pandemic.

2.3 The role of the PNS in supporting people with Parkinson's disease during the pandemic

Since the onset of the pandemic, misinformation, conflicting advice, and rapidly changing instructions have contributed to increased stress and anxiety (Geldsetzer, 2020; Loomba, de Figueiredo, Piatek, de Graaf, & Larson, 2021). Misinformation has also led individuals across the globe to question the safety, effectiveness, and importance of the Covid-19 vaccine (de Figueiredo, Simas, Karafillakis, Paterson, & Larson, 2020). The PD Society of the UK (Parkinson's UK), a research and support charity within the UK, has worked closely with PNSs and other healthcare specialists to provide information, support and guidance to PwP, their families and friends. A regular roundup of news, containing the latest information and advice on what PwP need to know, as they continue to live with Covid-19, has also been published online. Furthermore, due to potential changes in people's access to PD specialist services, it was fully appreciated that contacting healthcare professionals may be different or difficult during the Covid-19 crisis. A number of resources, including information sheets, forums, videos and blogs, and webinars, have been developed, such as:

- How to get the support you need from healthcare professionals, including who to contact and how the communication with a healthcare professional might be modified due to the use of telephone or video consultations.
- Information on anti-parkinsonian medication, including guidance on how review appointments may change and what to do if an individual is unable to obtain their usual anti-PD medication.
- Advice on what to do if an individual is experiencing new or worsening PD symptom.
- Information and advice for PwP or their caregivers, related to working, furlough and redundancy due to Covid-19.
- Benefits to support those who may have found that their financial situation changed due to Covid-19.
- Information on the Covid-19 vaccine in order to answer any queries or concerns PwP might have.

Support, information, and advice have also been provided via social media sites and on-line support groups, as a way for people to stay in touch, reduce isolation and engage with others.

During the Covid-19 pandemic, many PwP have seen their health deteriorate and have experienced an aggravation of their parkinsonian symptoms, including tremor, stiffness, anxiety, hallucinations and others (Simpson & Doyle, 2020). Family members and friends of PwP have also taken on more caring responsibilities, such as assistance with personal care and mobility, with reported impacts on their own physical and mental health (Simpson & Doyle, 2020). Access of PwP to a multi-disciplinary team is essential to improve self-management, limit deterioration of any symptoms and lower the risk of exposure to Covid-19. Those PNSs who were able to continue in their usual clinical role, have assisted individuals with self-isolation and have provided symptoms management, reducing both the risk of hospital admission and extended hospital stays. More specifically, PNSs may:

- support PwP in overall clinical management of their condition and guidance, including provision of therapy, via remote consultation. Potential misunderstandings or delays in the doses or regimen of anti-parkinsonian drugs and other medication commonly used in PD, such as anti-depressants or anti-psychotics, can lead to adverse incidents and life-threatening situations.
- refer PwP to other medical care and social services, when needed, and facilitate their navigation across multiple referral pathways.
- recognize and advise on PD symptoms that could mimic Covid-19 manifestations, such as loss of smell, nausea, or hallucinations (Andrews, Cai, Rudd, & Sanger, 2021; Parra et al., 2020).
- provide advice and proper guidance to PwP and their caregivers in case of medical emergencies (e.g., who to contact, how to proceed).
- support other healthcare professionals, such as General Practitioners (GPs) and non-specialist secondary care teams, by providing expert consultation when needed.
- assist PwP in registering to and familiarizing with Parkinson's UK and other support organizations.

For all the above reasons, Parkinson's UK has called for PD specialist services to be retained as a matter of priority. Parkinson's UK, with support from the leaders of the Parkinson's Nurse Associations across the UK, has produced a national statement urging managers and commissioners that the role of the PNS is crucial during this time and that PNSs should not be redeployed, but maintain their original role during the pandemic.



3. Covid-19 vaccinations

3.1 General information on the available Covid-19 vaccines

As the prevalence of Covid-19 continues to surge globally, constituting a major global public health threat, and with limited therapeutic interventions available up to now, the development of Covid-19 vaccines has brought hope to humanity, especially in low- and middle-income countries (Choi, 2021), as an effective mean to prevent severe disease and control the pandemic. As of January 2022, at least nine Covid-19 vaccines have obtained Emergency Use Listing (EUL) by the World Health Organization (WHO), based on their safety and efficacy characteristics (World Health Organization: Coronavirus disease (COVID-19): Vaccines, 2022), while more than 15 vaccines are currently investigated or await approval (Phanhdone et al., 2021). Nevertheless, authorizing the use of specific Covid-19 vaccines on a local basis remains at the discretion of each country and complies to national regulations.

Currently, there are few main types of Covid-19 vaccines available globally, including mRNA-1273 (Moderna INC., USA), BNT162b2 mRNA (Pfizer, New York, USA), AZD1222 (Oxford/ AstraZeneca, UK), Janssen Ad26.CoV2.S (Johnson & Johnson, New Jersey, USA), and others (World Health Organization: Coronavirus disease (COVID-19): Vaccines, 2022). Both Pfizer and Moderna vaccines are mRNA-based vaccines and are estimated to have an efficacy rate of more than 94% (Hippisley-Cox et al., 2021). As of March 14, 2022, 4.46 billion people worldwide have completed the whole course of vaccination, with 65.1% of the global population having received at least one vaccine dose (Coronavirus (COVID-19) Vaccinations, 2022; Holder, 2022). Six types of Covid-19 vaccines, including BBIBP-CorV (Sinopharm, Shanghai, China), WIBP-CorV (Sinopharm, Shanghai, China), Ad5-nCoV (CanSinoBIO, Tianjin, China), CoronaVac (Sinovac Biotech, Beijing, China), have been approved in China (6 Vaccines Approved for Use in China, 2022).

It is now acknowledged that SARS-CoV-2 is constantly evolving and mutating, producing multiple novel variants with varying characteristics. Most of these mutations are expected to have an unremarkable clinical effect, however, a minority of them is anticipated to significantly differentiate from the original pattern of the virus interaction with the immune system of human hosts (Harvey et al., 2021). Recently, the newly recognized

Delta and Omicron variants have attracted considerable attention due to reported alterations in transmissibility, the duration of incubation period, along with the potential for severe clinical manifestations (Bai, Gu, Liu, & Zhou, 2021). Moreover, one of the biggest concerns of the scientific community lays on whether the emergence of these new variants might lower the Covid-19 vaccine efficiency, leading to insufficient immunization cover around the world (Karim & Karim, 2021).

According to a recent, large study analyzing surveillance data collected from the Center for Disease Control and Prevention (CDC) from 13 United States of America (US) jurisdictions, the rate of deaths among unvaccinated citizens was found to be about 11 times higher compared to those fully vaccinated since the Delta variant became the dominant strain in the affected population (Scobie, Johnson, & Suthar, 2021). Although results from various studies have suggested a constant vaccine effectiveness against severe Covid-19 from the Delta variant, a relative decline in vaccine efficacy was found compared to previous variants (Bruxvoort et al., 2021; Lopez Bernal et al., 2021). Another US study, analyzing data from 32,867 adults derived from nine states during the summer months of 2021, when the Delta variant was predominant in the country, revealed that vaccinated people were significantly less likely to be hospitalized due to Covid-19 or contract SARS-CoV-2 than those unvaccinated (Grannis et al., 2021). Interestingly, vaccines were 89% (85% to 92%) effective in preventing hospital admissions due to Covid-19 among adults aged under 75, but 76% (64% to 84%) effective in those older than 75. According to the researchers, these tendencies might reflect a declining immunity in people who were vaccinated early, as older vaccine recipients were, indeed, given priority in the vaccination campaigns around the world. Following rapid distribution and administration of the mRNA Covid-19 vaccines (Pfizer-BioNTech and Moderna) under an Emergency Use Authorization by the Food and Drug Administration (FDA), early observational studies among nursing home residents have demonstrated a vaccine effectiveness ranging from 53% to 92% against SARS-CoV-2 infection, a percentage which dropped significantly to 53.1% after the predominance of the Delta variant (Nanduri, Pilishvili, & Derado, 2021). The UK Health Security Agency revealed early estimates indicating that the Omicron variant has significantly reduced the effectiveness of vaccines against symptomatic infection, when compared with the previously dominant Delta infection; however, a booster dose was expected to lead to a moderate to high vaccine effectiveness ranging from 70% to 75% (UK Health Security

Agency: COVID-19 variants identified in the UK, 2022). A large study, using data from more than 1.1 million people aged over 60 (30 July to 31 August 2021), reported that a third dose of the Pfizer vaccine was found to substantially reduce rates of infection and of severe illness in this population, when compared to those who only had two doses (Mahase, 2021).

3.2 Covid-19 vaccines and people with Parkinson's disease

Increasing evidence suggests that PwP are particularly vulnerable to the sequelae of SARS-CoV-2 infection due to intrinsic features of PD, including, but not limited to, rigidity of respiratory muscles, abnormal posture and impaired cough reflex (Lau, Lau, & Ibrahim, 2021; van Wamelen et al., 2020), while they are likely to experience an aggravation of their motor and non-motor symptoms, especially in cases of advanced PD (Merello, Bhatia, & Obeso, 2021). Restrictions of mobility, often accompanying PD, limited access to healthcare resources, and reduced social interactions due to the imposed lockdown regulations might further deteriorate patients' health and quality of life.

Among PwP, pneumonia has been reported as the most common cause of death and inpatient admissions (Okunoye, Kojima, Marston, Walters, & Schrag, 2020), while PwP are considered at increased risk of vaccine-preventable infections of the respiratory system, including influenza and pneumococcal pneumonia (Leibson et al., 2006; Pilishvili & Bennett, 2015). Nevertheless, in a recent study of 143 homebound and ambulatory PwP, almost 10% of individuals reported having missed all influenza vaccinations within the last 5 years and almost one out of three had never been vaccinated against pneumococcus (Phanhdone et al., 2021). More specifically, approximately 35% and 19% of the participants reported hesitation or refusal, respectively to be vaccinated, while, surprisingly, 13% thought vaccination is contraindicated in PD. The study has also highlighted that a significant percentage of household members of PwP would opt out from getting vaccinated as well, thus, posing a threat to more vulnerable individuals (Nordström, Ballin, & Nordström, 2021).

Vaccination against SARS-CoV-2 should be a priority in the management of PwP during the pandemic (Lau et al., 2021). The MDS has released a Covid-19 vaccine statement to address aspects of Covid-19 vaccination among PwP (Bloem et al., 2021). More specifically, PwP are strongly encouraged to receive Covid-19 vaccination, unless there is a specific contraindication. The MDS highlights that the benefits and risks of PwP being

vaccinated against Covid-19 are similar to those reported in the general, age-matched population, while the administration of Covid-19 vaccination is not expected to interfere with regular anti-parkinsonian medications and is not known to interact with any subjacent neurodegenerative processes observed in PD (Bloem et al., 2021). Of notice, it has been reported that even though vaccines seem safe for older adults, it is important to remain cautious when administering the vaccine to very frail and terminally ill elderly patients, as a small number of deaths has been reported shortly after vaccination (within 6 days) in markedly frail patients over 75 years old (Torjesen, 2021). Cosentino and colleagues have reported two cases of patients with a PD diagnosis, who developed some degree of temporary aggravation of their motor symptoms soon after the first dose of the Pfizer/bioNTech vaccine with symptoms subsiding spontaneously without any interventions or changes in the patients' regular regimen (Cosentino et al., 2022). More specifically, the first patient manifested a 2-day increase in rigidity and gait impairment, while the second patient exhibited an increased resting tremor, lasting approximately two weeks. Erro and colleagues had earlier reported two cases of PwP, who presented with severe dyskinesia after receiving the BNT162b2 mRNA vaccine (Erro, Buonomo, Barone, & Pellicchia, 2021). In both cases, dyskinesias were managed by reducing the total levodopa dose received by the patients, with the first patient exhibiting a good response to this modification. Considering the second patient, dyskinesias were also accompanied by fever, confusion, delusions and increased levels of D-dimers. Although severe symptoms did abate after 2 weeks, mild confusion and worse than baseline dyskinesias persisted. The reasons underlying these phenomena remain unclear, however, it has been postulated that a subjacent systemic inflammatory response, triggered by excessive anxiety or due to an interaction with regular anti-dopaminergic medication, might have contributed. These cases represent a very low incidence of adverse events following vaccination in PwP and, therefore, PwP should not be discouraged from receiving Covid-19 vaccines. Booster doses should also be offered to PwP according to international guidelines in order to strengthen their immunity against SARS-CoV-2.

Many countries have rolled out vaccination programs, as well as booster doses for their citizens, with a clear priority given to the elderly, especially those with reported comorbidities, including PD. Vaccinated PwP are still expected to strictly comply to the national health guidelines to reduce exposure to and transmission of SARS-CoV-2 (Beauchamp, Finkelstein, Bush, Evans, & Barnham, 2020).

Effective communication strategies between the treating neurologist, PwP, and their household members may limit misinformation and vaccine hesitancy in the community, encourage people to get vaccinated, increase immunization cover against SARS-CoV-2 and, thus, strengthen public health, by reducing rates of Covid-19 morbidity and mortality (Harrison & Wu, 2020). Importantly, the role of nursing care is integral to the success of the Covid-19 vaccines, as it significantly contributes to patients' and caregivers' education or the promotion of outreach programs with regards to vaccination, as well as identifying any barriers to PwP receiving vaccination. For instance, nursing home and long-term care facility residents live in congregate settings and are often elderly and frail, thus, at increased risk of Covid-19 (Nanduri et al., 2021). Nursing home residents remain vulnerable despite vaccination, and, hence, Covid-19 prevention strategies, including infection control, frequent testing, and vaccination of nursing home staff members, residents, and visitors are critical. These interventions could be delivered by dedicated nurses through organizing focused campaigns, providing relevant reading or audio-visual material with regards to Covid-19 and PD, and advocating vaccination.

Difficulty traveling to specialized clinical settings (Outpatients Clinics, vaccination centers) has been identified as an obstacle to administering Covid-19 vaccinations to homebound PwP (Harrison & Wu, 2020). Furthermore, homebound women with advanced PD were more often found to live alone and encounter considerable difficulties in accessing healthcare facilities (Nwabuobi et al., 2019). In one recent meta-analysis, living alone was strongly associated with lower vaccine uptake (van der Heide, Meinders, Bloem, & Helmich, 2020). PwP, particularly those with advanced disease and/ or homebound have been reported to be at an increased risk of complications from Covid-19 (Brown et al., 2020; Del Prete et al., 2021; van der Heide et al., 2020). Trained nurses could overcome such difficulties by providing vaccination through home visits to this group of patients (Harrison & Wu, 2020).



4. Impact on advanced therapies

4.1 Management of advanced therapies in times of Covid-19

Device-aided therapies constitute effective therapeutic options for patients with advanced PD, whose symptoms are so severe that are no longer

sufficiently controlled with optimum medical therapy. These treatments, including continuous subcutaneous apomorphine infusion (CSAI), levodopa/ carbidopa intestinal gel (LCIG) infusion, and deep brain stimulation (DBS), have been found to decrease the intensity and frequency of motor fluctuations, improve non-motor aspects of PD and ameliorate the patients' and their caregivers' quality of life (Dafsari et al., 2019; Santos-García, Añón, Fuster-Sanjurjo, & de la Fuente-Fernández, 2012), while some benefits are maintained in the long-term (Antonini et al., 2021; Limousin & Foltynie, 2019). Although device-aided therapies, especially DBS, appear to be cost-effective in the long-term (Smilowska et al., 2021), regular follow-up visits are still required, while the role of nursing care in the management of these patients, including home-visits, is essential (Antonini, Mirò, Castiglioni, & Pezzoli, 2008; De Rosa, Tessitore, Bilo, Peluso, & De Michele, 2016).

As mentioned above, the pandemic of Covid-19 has taken a toll on PwP using advanced therapies, not only because of the direct effects of the virus on these vulnerable patients (worse Covid-19 outcome due to older age, comorbidities and inherent characteristics of PD, including the fact that advanced stage PwP might be frail, bedridden, incontinent or cognitively impaired), but also due to limitations considering their access to healthcare services and specialized personnel (Fasano et al., 2020).

In order to overcome the Covid-19-related reductions in scheduled visits, many changes have been implemented considering care and management of PwP on device-aided therapies, with healthcare professionals having to re-design services and update medical procedures according to individual situations, while struggling to minimize the risk for infections. Keeping as a priority to provide high quality of care with a concurrent feeling of safety, along with psychological comfort, are of the utmost importance, especially nowadays. Depending on the type of advanced therapy, the product manufacturers have implemented novel possibilities for phone communication, personal assistance and device replacement, when needed. Consequently, and similarly to measures applied in periods predisposing to flu, especially during autumn and winter, direct contacts, not only in consultation rooms, but also with homebound patients and those in nursing homes, had to be reduced. Movement disorders specialists and PNSs have begun to take advantage of modern telemedicine applications to support the needs of PwP on advanced therapies, while carefully picking those specific cases who might need face-to-face assessments at patients' homes with respect to safety rules.

To ensure and maintain constant care of PwP on advanced therapies, it has been recommended to use video or telephone consultations, strengthen the caregiver's role and authorize patients to use electronic prescriptions with simultaneous home delivering of medication via the caregiver or courier. In situations requiring a home visit and a direct contact with the patient, special caution measures have been recommended:

1. A more detailed history, along with a distant assessment of the patient's physical and neurological condition can take place via phone, before the actual face-to-face visit. The collected information and given instructions might suffice for the patient's management at the moment or lead the healthcare professional to schedule a traditional visit.
2. Informing patient and their caregiver about the possibility of providing services through tele- or video-consultation, plus suggesting possible methods of conducting it, such as video-calls using available and patient-friendly platforms.
3. Setting up convenient times and settings (especially for patients and caregivers) to conduct the tele- or video-consultation.
4. Informing patients and their caregivers about:
 - a. the need to report any symptoms of health deterioration by phone.
 - b. refrain from visiting the Emergency Department and/ or Outpatient Clinics when not necessary.

4.2 Initiating device-aided therapies during the Covid-19 pandemic

The Covid-19 pandemic had a major impact both on the potential of introducing new patients to advanced therapies, as well as on ensuring continuation of treatment in patients who are already enrolled. More specifically, the pandemic has significantly reduced the number of new patients included in device-aided practices, mainly due to the widespread limitations on scheduled hospitalizations, which in most countries are necessary for the qualification and initiation of DBS, LCIG infusion or CSAI. The hospitalization period is expected to last an average of 4–6 days for LCIG infusion (including the naso-jejunal test phase, the percutaneous endoscopic gastrostomy (PEG) with jejunal extension tube (J-tube; PEG-J) insertion procedure, and the titration phase), 3–4 days for the CSAI (preparation for initiation, starting infusion, and titration phase), 1 day after the implementation (neurosurgery ward) and 2–3 days for the DBS stimulation setting (Mikos et al., 2010), although timelines might differ among various clinical settings.

For infusion therapies, many difficulties have arisen in patients' and caregivers' face-to-face education considering the pump, as the pandemic restrictions have limited the opportunities for family and caregivers to participate in the initial education and training needed for the self-management and self-care support of patients. In the pre-pandemic era, such processes would normally take place during the patient's hospitalization. These processes constitute key elements, affecting infusion therapies long-lasting success, as they allow caregivers to expand their skills in real life conditions in order to cope with the needs of home care. Routine care would, thus, be much faster and better results would be produced with the reinforcement of caregivers' self-esteem and self-management abilities at home. Both infusion therapies require training in pump operation, skin care routine and many other important, practical issues. During the Covid-19 pandemic, the educational training is carried out mainly at the end of hospitalization, when the patient is about to be discharged.

4.3 Supporting patients and caregivers during Covid-19

4.3.1 Initiation phase for advanced therapies

Placement of device-aided therapies and dose titration in infusion therapies traditionally take place in a hospital. However, there are examples of countries where significant parts of the initiation phase, including medication titration, might take place at patients' homes using telemedicine services or during home visits by healthcare professionals (Willows et al., 2017). Such initiatives might be more comfortable for the patient and are expected to reduce any infection risks in the Covid-19 era. Nevertheless, implementing such measures on a worldwide basis might not be easy or even possible in many countries due to regulatory issues or shortage in personnel.

Movement disorder centers were forced to work out their own possible individual solutions for continuing enrollments and after-care management. While PwP are hospitalized in a ward for the device implementation, it is challenging to secure them from infections during the Covid-19 pandemic. Despite any precautionary measures taken by the hospital authorities and healthcare professionals, the infection risk remains high. The majority of adverse events occurring during the first few post-procedural weeks after implementing LCIG infusion can be, in most cases, easily managed by movement disorders specialists or PNSs by phone (Fasano et al., 2020; Wirdefeldt, Odin, & Nyholm, 2016).

4.3.2 Educational phase for advanced therapies

A possible way to cope with the difficulties encountered by patients and caregivers during the educational and preparation process of device-aided therapies might be a simulation—focused medical training, which would offer useful opportunities to improve learners' competence and confidence, maintaining patient safety. Specially prepared educational material (e.g., an abdomen phantom, dummy infusion pumps and PEG-J tubes), may successfully substitute for patients' and/or caregivers' training, as it is necessary for them to practice skin care routine, drug connection and flushing, possible ways of puncturing the abdomen skin and pump management. Patients could also be equipped with a list of recommendations for possible troublesome issues (concerning the pump, skin care hygiene, high pressure alarm). Finally, patients and their caregivers should be aware of any alarming or dysregulation symptoms and should be properly informed about the advised procedures that need to be followed in case of an emergency (e.g., contact details of treating physician or nurse).

4.3.3 Continuation phase

All device-aided therapies are recommended to be continued in the event of contracting a SARS-CoV-2 infection, as undisturbed continuation of treatment is expected to keep the patients' motor and non-motor PD symptoms under control and reduce OFF periods and fluctuations. Moreover, a non-oral administration of dopaminergic treatment might be more desirable and adequate for patients suffering from conditions impeding oral medication, like dysphagia.

4.4 LCIG infusion therapy

Using tele- or video-consultation might be very convenient for LCIG infusion patients, as photos or video visualization of the pump, PEG and abdomen are not difficult to access. Changing pump settings can be done on an unlocked pump by the caregiver with proper guidance by phone, although this must be based on good cooperation with a caregiver or a patient without a subjacent dysregulation syndrome. Patients should be aware of the need to keep at home a stock of oral medications (with individual administration instructions) in case of pump or system failure. LCIG infusion treatment may need PEG-J tubes exchange due to tube blockage, loops or any other adverse event which may occur any time. If continuing the therapy through the stomach tube is possible, this might allow the patient some time to book

an appointment in order to have the complication properly addressed. Sometimes, though, an acute situation may require immediate intervention.

It is also of notice that during the pandemic hospitals have extra obligatory safety procedures; typically patients and their accompanying caregivers need to be fully vaccinated and/ or a negative PCR or antigen test must be demonstrated on entrance. These extra procedures are time-consuming and might feel uncomfortable for the patients.

4.5 Continuous Subcutaneous Apomorphine Infusion therapy

CSAI seems to be the easiest among the device-aided therapies to be implemented. However, it still needs careful preparation and education in order to cope with the most frequently encountered difficulties and complications. Patients and caregivers should be aware of potential skin problems, nausea, somnolence, orthostatic hypotension, neuropsychiatric issues and the rarely occurring, but severe, drug-induced hemolytic anemia or eosinophilia. Such situations require regular check-up examinations of blood results and caregiver knowledge about the symptoms of anemia. Routine laboratory tests can be postponed after confirming patients' status or can be done at patient's home. Similarly, to LCIG infusion therapy, it is advised to continue CSAI if the patient is admitted in the Intensive Care Unit (ICU). Sudden withdrawal of CSAI might be very dangerous, as patients might experience acute lethargy, malignant akinesia, and symptoms of dopaminergic agonist withdrawal syndrome (prominent psychiatric features, dysautonomia, generalized pain) (Chaudhuri et al., 2015). Under these circumstances, caregivers should be properly informed and prepared in order to proceed with substitution treatment.

4.6 Deep brain stimulation

DBS, like other device-aided therapies, constitutes an established treatment option during the pandemic. A possible limitation might be related to artifacts in conducting an electrocardiogram or electroencephalogram, but this can be solved by turning DBS off during the time of the procedure. Patients should be educated on how to use their handheld controller for DBS and be aware of the situations that it might be useful.

Another issue in DBS therapy comes with battery replacement, as delayed or postponed outpatient visits may cause an abrupt cessation of DBS function. Limited access to ambulatory consultations and to scheduled surgeries might also restrict battery exchange procedures. Postponing

follow-up visits can result in depletion of the implanted pulse generator (IPG), leading to the life-threatening situation of DBS—withdrawal syndrome, characterized by a severe akinetic state, mimicking the parkinsonism-pyrexia syndrome (Reuter et al., 2018). It is, thus, highly recommended to regularly perform tele- or video-consultations to check on the DBS status and be vigilant for any signs indicative of abnormal function.

4.7 Outlook for best care and caregiver support

Clinical experience supports the use of device-aided therapies for PwP who are severely affected by pneumonia, possibly needing ventilation, and for those in a palliative stage (Antonini, Leta, Teo, & Chaudhuri, 2020; Chaudhuri, 2020).

The Covid-19 pandemic has had a big impact on lifestyle, with many changes forced by isolation, restriction of social contacts, limitations in regular stationary exercise classes, physiotherapy, functional or rehabilitation therapy and other relevant sessions. PwP, including those using device-aided therapies, have been forced to stay at home, a situation that has brought more duties for the caregiver, burdening them even more. Consequently, caregivers might be in extra need for support and free time. For example, the time spent by the patient during the aforementioned sessions (exercise, physiotherapy etc.) could also be used by the caregiver to rest.

Telemedicine services can be of great use during the Covid-19 pandemic, supporting PwP in their routine and promoting a healthy lifestyle. Reorganization is needed, for example establishment of comprehensive rehabilitation programs suitable for tele- or video-consultations with PwP (Langer et al., 2021; Vellata et al., 2021). Especially for PwP on advanced therapies, a positive attitude and proper information technology (IT) infrastructure to conduct tele- or video-consultations is deemed necessary, although the application of these services might not always be feasible for this group of patients due to practical difficulties. In some situations, patients may not have computers, tablets, or phones, and sometimes may require assistance in using the relevant software. Families and caregivers are often able to operate the system on their own, but sometimes may need prior training in this field. Taking actions and looking for solutions is worthwhile, because studies on continuing care and therapy in a remote fashion, like PwP attending online dancing sessions, have had a beneficial effect on PwP, reducing their anxiety levels (Morris et al., 2021).

Our own experience from clinical practice indicates that during the Covid-19 pandemic, patients' needs have been focused on closer communication with assurance of maintaining an ongoing care. There was a need to educate patients for video consultations, but only minor problems have arisen during this process. Some patients might have even enjoyed video consultations and the feeling of being home, while receiving safe and professional consultation.

4.8 Conclusion

In conclusion, embracing the new norm with a practical and careful approach towards the care of PwP is of utmost importance to ensure that patients are not unnecessarily exposed to SARS-CoV-2 and that all aspects of PD management are optimized. The role of the PNS in organizing this multi-faceted task is invaluable. Given the widespread impact of the Covid-19 pandemic among PwP, it is crucial that timely vaccination must be provided to reduce morbidity and mortality, while PNSs hold an important role in thoroughly informing PwP and facilitating vaccinations. The device-aided therapies-related procedures in PD, especially when hospitalization is required, have become more complicated during the pandemic, highlighting even more the need for coordination by the PNS in order to make these processes as comfortable as possible for patients and caregivers, but also for the implicated healthcare professionals.

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