

Commentary

COVID-19 Vaccination for Persons with Parkinson's Disease: Light at the End of the Tunnel?

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Abstract. Several COVID-19 vaccines have recently been approved for emergency use according to governmental immunization programs. The arrival of these vaccines has created hope for people with Parkinson's disease (PD), as this can help to mitigate their risk of becoming infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which can lead to serious, life-threatening disease, at least among those with more advanced PD. However, both persons with PD and physicians looking after these individuals have expressed concerns about the vaccine's efficacy and safety in the specific context of PD and its symptomatic treatment. Here, we discuss our perspective on these concerns, based on our interpretation of the literature plus the unfolding experience with widespread vaccination in the population at large. Because the benefits and risks of COVID-19 vaccines do not appear to be different than in the general population, we recommend COVID-19 vaccination with approved vaccines to persons with PD, unless there is a specific contraindication. Some caution seems warranted in very frail and terminally ill elderly persons with PD living in long-term care facilities.

Keywords: Parkinson's disease, movement disorders, COVID-19, SARS-CoV-2, pandemic, vaccination, vaccine, efficacy, safety, adverse effects

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INTRODUCTION

The risk of becoming infected with the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which leads to the coronavirus disease 2019 (COVID-19), is a serious concern for persons with Parkinson's disease (PD) worldwide. Reports indicate that the likelihood of becoming infected is not higher for those living with PD, but the risk of experiencing the serious respiratory disease and sequelae of COVID-19 does appear to be elevated, at least in later stages of PD [1]. Furthermore, both motor and non-motor symptoms of PD can worsen considerably as a result of COVID-19 [2]. Finally, the risk of dying in conjunction with SARS-CoV-2 infection also appears to be higher for persons with PD compared to the general population [3, 4]. Until recently, physical distancing, face masks and eye protection were the only strategies to prevent person-to-person transmission of SARS-CoV-2 [5]. Thus, recommendations from public health agencies have been to stay at home and limit direct contact with others to mitigate the risk of becoming infected. This social isolation and the justifiable fears of infection can be associated with stress, anxiety and depression [6, 7]. The risk for mental health challenges seems extra high for people living with PD who are particularly vulnerable to the deleterious effects of stress and the inability to exercise adequately [8, 9].

Fortunately, there may now be light at the end of the tunnel, thanks to several COVID-19 vaccines that have been approved in multiple countries for emergency use according to governmental immunization programs. In many countries, these programs start with the inoculation of high-risk people—health care providers, seniors, and people with co-morbidities, so the initial vaccination wave will likely also include people with PD. The rapid development and approval of COVID-19 vaccines have created some concerns in the scientific and medical communities, as well as among the general public, in regard to the benefits and risks of these new vaccines. Many physicians have already received phone calls from worried persons with PD or their families, asking about the safety of COVID-19 vaccination in the specific context of PD and the dopaminergic medications. We are in a unique situation where concerted global efforts are being made to rapidly combat a catastrophic pandemic, at an unprecedented pace. We fully understand that this speed of development may give rise to concerns about the vaccine's efficacy and safety, both among per-

sons with PD and among physicians looking after these individuals. To address critical questions about these vaccines, some of them based on new technologies (e.g., mRNA-based and viral vector vaccines), it is important to first discuss the path leading to vaccine approval for emergency or limited-term use by the regulatory agencies. We will then discuss the present perspectives of the International Parkinson and Movement Disorder Society, who has asked its Scientific Issues Committee (IPMDS-SIC) to provide information regarding the COVID-19 vaccinations, which are paramount to the protection of our community of patients, physicians and associated health providers in the current critical situation of the global pandemic.

DEVELOPMENT AND APPROVAL OF COVID-19 VACCINES

Two COVID-19 vaccines—BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna)—were recently approved via emergency use authorization by several international entities (U.S. Food & Drug Administration [FDA]; and current regular but restricted authorization of the European Medicines Agency [EMA], among other agencies). This process included thorough analyses of completed Phase III data provided by vaccine developers in a transparent process with peer-reviewed publication of full data sets [10–15]. The recent FDA and EMA approval of these vaccines met the high standards required for use authorization after complete data scrutiny and validation, as required in the normal process of a vaccine approval. The process ensures that the efficacy and safety requirements have been met and people can be inoculated because the vaccine benefits outweigh its risks. Additional COVID-19 vaccines that are still in clinical development Phases II and III will eventually undergo the same scrutiny before emergency use authorization. Transparency about the development and approval process is very important. The efficacy and safety of the approved vaccines are fully disclosed in the published papers [10–15]. We should note that, in addition to the Pfizer/BioNTech and Moderna vaccines, different vaccines are currently also being used in various countries. This includes the ChAdOx1 nCoV-19 vaccine (AZD1222, Oxford-AstraZeneca), a chimpanzee adenovirus-vector vaccine, which has been approved for temporary supply in the United

Kingdom, and recently also for wider use in the European Union by the EMA, based on a Phase I/II, single-blind, randomized controlled trial [16] and a single-blind, randomised, controlled, Phase II/III trial [14]. This vaccine appears to have an acceptable safety profile, but it is uncertain how effective this vaccine is for those over 55 years of age because this age group was unrepresented in the studies. We must await publication of the Phase III trial results. Still other vaccines are being used in countries such as China and Russia, but we cannot make any statements about their efficacy or safety as we do not have access to published data.

To date, the approved COVID-19 vaccines have proven to be highly effective in preventing the severe and even the mild forms of the disease. High efficacy (>90%) has been demonstrated regardless of race, gender, age, and medical conditions. By comparison, data obtained during the 2019-20 influenza season indicate that the overall effectiveness of seasonal influenza vaccine for preventing influenza virus infection in children and adults is estimated at only 45% [17]. Similar to other vaccines, there are some side effects with the recently approved COVID-19 vaccines. For the most part, side effects have been mild (pain and irritation at the injection site, fatigue, muscle pain, headache, low fever/chills) [11, 15]. In addition, reactogenicity (allergic reaction to vaccines) was observed only occasionally, as is typically seen with other vaccines. A finding with possible importance for the elderly PD population is the notion that younger adults (18-55 years) tended to have more severe reactions than older adults (65-85 years), at least within the framework of the published clinical trials. However, a word of caution is in place here, because the experience with adverse events will grow as an increasing number of persons will

be vaccinated. To illustrate this, recent observations in Norway have revealed that following vaccination of around 42,000 persons, a total of 33 deaths have occurred that were considered possibly related to vaccination, as these persons were treated within six days prior to death [18, 19]. It is uncertain whether a truly causal relationship exists between these deaths and the preceding vaccination. It is important to note that these deaths all occurred in severely frail and elderly (over 75 years of age) persons living in long-term care facilities, and many of them had serious underlying medical conditions or terminal illnesses [19]. All symptoms and adverse events post-vaccination are being reported and data thoroughly collected to determine the actual relation to the vaccine. At this point and until details of the reported deaths are analyzed, no conclusion can be drawn about causality.

IMPLICATIONS FOR PERSONS LIVING WITH PARKINSON'S DISEASE

Vaccines with proven efficacy and what appears to be a satisfactory safety profile are now hopefully going to significantly contribute to ending the COVID-19 pandemic that has already taken many lives. The question remains as to what the impact of COVID-19 vaccination is for the worldwide population of people living with PD. In this regard, it is important to emphasize that as of today, there are currently no scientific data that have specifically looked at the efficacy and safety of COVID 19 vaccination for persons with PD. Any specific claims about the efficacy and safety for this specific population therefore have to be made cautiously, and are merely based upon extrapolating the evidence from general

Table 1
Take home messages with respect to COVID-19 vaccination for persons with Parkinson's disease

- Compared to the general population, the risk of SARS-CoV-2 infection causing serious, life-threatening disease seems higher for people living with PD, at least among those with more advanced disease.
- The approved mRNA-based vaccines and viral vector vaccines under development are not known or expected to interact with the neurodegenerative process in PD.
- The types or incidence of side effects of these vaccines in persons with PD seem no different than in the general population.
- The vaccines also seem safe for older adults, but caution is needed for the specific subgroup of very frail and terminally ill elderly persons with PD living in long-term care facilities.
- COVID-19 vaccination is not known to interfere with the current therapies of PD.
- Taken together, we recommend COVID-19 vaccination with approved vaccines for persons with PD, unless there is a specific contraindication.
- Vaccinated persons with PD must continue to comply with the public health guidelines to reduce exposure and transmission of COVID-19.
- Insights may change, and we must consciously monitor newly emerging data from both trials and real-life vaccination programs.

elderly populations, and the experience as progressively more people with PD are being vaccinated worldwide.

Bearing these caveats in mind, and based on our interpretation of the literature plus the unfolding experience with widespread vaccination in the population at large, the IPMDS-SIC has the following considerations in relation to PD. (1) The approved mRNA-based vaccines and the viral vector vaccines under development induce immunization through mechanisms that are not known to interact with the neurodegenerative process in PD. With respect to the inflammation that is associated with the pathogenesis of PD, there is no evidence of a direct interaction with the immune response to these vaccines. (2) The reported Phase III data of the approved vaccines showed that the types or incidence of side effects in persons with PD have not been different than in the general population. The vaccines appear to be safe for older adults, with less side effects than in younger adults. The Norwegian experience with very frail elderly persons living in long-term care facilities suggests that extra caution is needed for this specific subgroup of the frail elderly with several clinically relevant comorbidities [19]. It therefore seems prudent to remain careful with administering the vaccine to very frail and terminally ill elderly persons with PD, and to openly discuss the risks with patients and families prior to vaccination, set against an already limited life expectancy. (3) Similar to reactions to other immunizations, COVID-19 vaccination is not known to interfere with the current therapies of PD. (4) As some persons with PD may be part of the first groups in the current vaccination programs because of their age, residency in long-term care facilities, or other reasons related to PD disabilities, more data will become available in the near future for further analysis of the impact of these vaccines on PD. A cautious approach remains necessary, as we have seen historical examples in our field where drugs such as tolcapone initially appeared to be safe within the setting of a clinical trial (albeit in only several hundreds of patients), but where very serious hepatotoxicity emerged in a few individuals only after more widespread introduction into daily clinical practice [20]. Studies of vaccines, including those of the COVID-19 vaccines, typically include much larger study populations (tens of thousands of participants), but this does not preclude detection of possible adverse effects after the introduction of widespread vaccination campaigns [21]. We therefore strongly encourage readers to periodically refer

to the website of the International Parkinson and Movement Disorder Society, where the recommendations will be updated in a live document, as new data are published and as we gain more experience from both further trials and real-life clinical practice (<https://www.movementdisorders.org/MDS-Files1/COVID-19vaccination01042021.pdf> for medical professionals, <https://www.movementdisorders.org/COVID-19-Pandemic-MDS/MDS-COVID-19-Vaccine-Statement-for-Patients.htm> for persons with PD).

CONCLUSION

Taken together, we encourage our community of movement disorder specialists to recommend COVID-19 vaccination with approved vaccines to their patients with PD (or their responsible caregivers), unless there is a specific contraindication. Some caution seems warranted in very frail persons with PD living in long-term care facilities. We also recommend that persons with PD come forward themselves to discuss the vaccine with their physician. This recommendation to both physicians and patients is given because the benefits and risks do not appear to be different than in the general (age-matched) population, while the risk of developing the serious, life-threatening complications of a possible SARS-CoV-2 infection does appear to be higher for persons living with PD, at least among those with more advanced disease. Finally, even after vaccination, it is important that persons with PD continue complying with the public health guidelines to reduce exposure and transmission of COVID-19 as recommended by WHO and CDC.

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CONFLICT OF INTEREST

The authors have no conflict of interest to report.

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