Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Clinical Neuroscience 90 (2021) 132–134

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Short communication

Evolution of our understanding of MS-COVID-19 interactions and concerns for vaccination

Sanjiti Podury [a], Erum Khan [b], Medha Tandon [c], Shruti Jaiswal [e], Shitiz Sriwastava [d,e,*]

[a] Army College of Medical Sciences, India
[b] B.J. Medical College and Civil Hospital, Ahmedabad, India
[c] University of Pittsburgh Medical Center, Pittsburgh, PA, United States
[d] Department of Neurology, Rockefeller Neuroscience Institute, West Virginia University, Morgantown, WV, United States
[e] West Virginia Clinical and Translational Science Institute, West Virginia University, Morgantown, WV, United States

ARTICLE INFO

Article history:
Received 12 February 2021
Accepted 23 May 2021

Keywords:
COVID-19
Multiple Sclerosis
COVID-19 vaccine
Disease modifying therapies

ABSTRACT

As the news of approval of COVID-19 vaccination emerge, neurologists across the globe ponder upon whether to use immunotherapies in patients with Multiple Sclerosis (MS). This paper highlights the mechanism of various disease modifying therapies (DMTs) as well as the recently approved Pfizer and Moderna vaccines for COVID-19 as well as guidelines as introduced by National Multiple Sclerosis Society. As their mechanisms counteract each other at the molecular level, we believe further evidence and data might lay the foundation to formulate much needed recommendations for the usage of these medications while vaccinating MS patients on DMTs.

1. Introduction

WHO has thus far recorded 134 million confirmed cases and 2.9 million deaths due to SARS CoV-2 across the globe owing to the COVID-19 infection. A total of 547 million vaccine doses have been administered so far [1].

As our knowledge about the virus continues to grow, we observe that a major part of mortality is caused not directly by the virus, but by the response of a rather robust immune system working to fight against it [2]. This had once raised serious concerns about the cohort of patients surviving diseases requiring a modulation in the immune system, like patients of Multiple Sclerosis undergoing treatment with Disease Modifying Therapy (DMT) [3].

Vaccination and primary preventive measures will have an important role in controlling the pandemic. Patients of MS may have a higher susceptibility to COVID-19 infection due to treatment with immunosuppressive drugs. A variation also exists in the susceptibility of COVID infection in subset of MS patients based on demographics and co-morbidities [4,5].

Literature by Louapre et al. showed higher risk of severe COVID infection in patients of MS aged more than 45 years, higher expanded disability severity scale score (EDSS), male gender and co morbidities like diabetes, obesity, hypertension, heart, lung diseases and pregnancy [6]. However, there have been concerns about vaccinating patients with multiple sclerosis such as the risk of precipitating MS relapse, dangers of vaccinating immunosuppressed patients and the development of antibodies in patients on DMT therapy post vaccination. There are no studies/ trials on the efficacy of COVID-19 vaccine on MS patients currently on DMTs. In our short review we address these issues and discuss the current guidelines for vaccination of MS patients while on therapy.

2. Method

2.1. Study design

We conducted a thorough literature review in January 2021 using the terms "SARS-CoV-2 and Vaccine guidelines for MS", "SARS-CoV-2 and National MS guidelines". We reviewed all published literature on COVID-19 vaccination in Multiple Sclerosis. We searched databases including PubMed, Google Scholar and

Abbreviations: COVID-19, Coronavirus Disease 2019; n-CoV2, Novel Coronavirus 2; MS, Multiple Sclerosis; DMTs, Disease Modifying Therapies; COViMS, Coronavirus and MS Reporting Database; ARDS, Acute Respiratory Distress Syndrome; EDSS, Expanded Disability Status Scale; RCTs, Randomized Controlled Trials; WHO, World Health Organization; INF, Interferon; S1P, Sphingosine-1-Phosphate; mRNA, Messenger RNA.

* Corresponding author at: Department of Neurology, Rockefeller Neuroscience Institute, West Virginia University, United States.
E-mail address: shitiz.sriwastava@hsc.wvu.edu (S. Sriwastava).

https://doi.org/10.1016/j.jocn.2021.05.063
0967-5868/

Scopus from December, 01, 2020 to March 30, 2021. Two reviewers independently performed the literature search. So far, the following guidelines has been introduced by National Multiple Sclerosis society: 1) COVID-19 Vaccine Guidance for People Living with MS, 2) Timing MS Medications with COVID-19 mRNA Vaccine.

3. Discussion

Since the WHO first announced the COVID-19 pandemic in March 2020, potential therapeutic and vaccination options have been the most extensively reviewed and studied. Immunization will not provide complete protection and primary preventive measures to reduce person to person transmission will be the most critical tool to bring the pandemic under control. The current FDA approved vaccines are given in two doses and are mRNA vaccines that code for spike protein found on the surface of SARS-CoV-2. Both vaccines have been shown to be 95% effective in their phase II/III trials in individuals older than 16 years of age and have been reported to lower further risk of severe illness from COVID-19 by more than 90%. However, these trials excluded the immunocompromised patients such as patients with autoimmune disorders on immunosuppressants [7,8].

Regarding the concern for MS relapse post vaccination, previous studies have shown a risk of MS exacerbation after influenza immunization but there is no evidence that Hep B, tetanus, varicella and BCG increase the risk of exacerbation [9]. With respect to the risk of infection due to vaccination of patients on DMTs there is a consensus that these vaccines will do no harm even in immunosuppressed patients as they are inactivated vaccines. Live vaccination should be avoided during immunosuppressive therapy. mRNA vaccines and vector vaccines (component of vaccinating viral strain are implanted into a harmless virus, a vector) can be considered in immunosuppressed patients as there is no viral replication [4,5].

National MS society recommends vaccinating all patients with relapsing and progressive forms of MS as the risks of CoVID-19 disease outweigh any potential risks from vaccine. In addition, family members should also be vaccinated in order to reduce risk and impact of infection in MS patients. Vaccines can cause fever as a side effect, which can worsen MS symptoms temporarily, however they should subside and return to normal once the fever is gone. It is important to get the second dose despite the temporary flaring of symptoms [10].

There are concerns regarding the effectiveness of vaccination and boosters in patients with depleted immune cells and decreased ability to generate memory B cells as seen in patients of MS on DMTs. So far there have been no studies evaluating the efficacy of the vaccines while on DMTs approved for MS. Most trials included very few individuals resulting in non-uniform results [4]. The VELOCE study states that patients receiving peripheral B-cell depleting drug Ocrelizumab mounted an attenuated humoral response to the vaccine antigens [11].

So far efficacy of vaccination has been tested for S1P receptor modulators, Natalizumab and Alemtuzumab. Antibody titers should be measured to confirm adequate protection in patients on DMT therapy.

The guidelines set by the National MS society for COVID-19 vaccination in patients living with MS apply only for the people living in the United States and receiving the Pfizer and Moderna vaccines. Vaccination against COVID-19 while on DMTs is safe. Some DMTs make the vaccine less effective, but the vaccine will still provide some protection. For patients on Alemtuzumab, Ocrelizumab, Rituximab or Ofatumumab a coordination between timing of vaccine and therapy must be considered [10]. Also, there is guidelines on the timing of DMTs with vaccination (Table 1). Patients should consult their MS healthcare provider to determine the best schedule as decisions should be individualized and should consider factors like age, disease factors, risks and benefits of DMTs and risks associated with COVID-19.

Table 1
National MS society Guidelines on Timing MS Medications with COVID-19 Vaccines.

DMT	Adjustment of therapy with vaccination
Interferons	Do not delay therapy
Glatiramer acetate	No adjustment required if already on therapy
Sphingosine 1 phosphate receptor modulators (Fingolimod, Ozanimod, Siponimod)	Fully Vaccinate 2–4 weeks prior to starting medication If already on therapy continue therapy as it is and get vaccinated
Alemtuzumab (Lemtrada)	Fully Vaccinate 4 or more weeks prior to starting therapy If already taking therapy vaccinate 24 or more weeks after last dose
Cladribine	Fully Vaccinate 2–4 weeks prior to staring therapy Insufficient data on scheduling vaccination if already on therapy
Anti-CD20 infusions (Ocrelizumab and Rituximab)	Fully vaccinate 2–4 weeks or more prior to starting therapy If already on therapy consider vaccination 12 weeks or more after the last dose
Anti-CD20 infusions Ofatumumab	Fully vaccinate 2–4 weeks or. More prior to starting therapy Insufficient data on scheduling vaccination if already on therapy
High dose steroids	Start vaccination 3–5 days after the last dose steroids

MS, Multiple Sclerosis.

DMTs suppress/modify the immune system of the body and some may increase the risk of developing complications of covid infection and post risk–benefit assessment, a decision to delay/stop treatment should be made.

With the realization that extreme cautiousness by imposing stringent restriction measures, though effective immediately, could never be a permanent solution, heads have turned towards vaccine development for good. Since the coronavirus has been predating on the aged and comorbid cohort, several institutions have recommended prioritizing them through vaccination strategies. However, concerns have been raised regarding the effectiveness of a vaccine in patients with depleted immune cells and decreased ability to generate memory B cells. MS patients with elderly age and receiving disease modifying therapy are at more risk of infection compared to general population.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] WHO. WHO Coronavirus Disease (COVID-19) Dashboard [Available from: https://covid19.who.int/?gclid=Cj0KCQiA6t6ABhDMARIsAONIYywpPDg3HucQtbypR3MmCf9RzstxhVodEx73VZCfpbDuLfpNoy-73caAvp_EALw_wcB.
[2] Yazdanpanah F, Hamblin MR, Rezaei N. The immune system and COVID-19: Friend or foe? Life Sci. 2020 Sep 1;256:117900. doi: 10.1016/j.lfs.2020.117900. Epub 2020 Jun 2. PMID: 32502542; PMCID: PMC7266583.
[3] Kataria S, Tandon M, Melnic V, Sriwastava S. A case series and literature review of multiple sclerosis and COVID-19: Clinical characteristics, outcomes and a brief review of immunotherapies. eNeurologicalSci. 2020 Dec;21:100287. doi: 10.1016/j.ensci.2020.100287. Epub 2020 Nov 2. PMID: 33163634; PMCID: PMC7605741.

[4] Ciotti JR, Valtcheva MV, Cross AH. Effects of MS disease-modifying therapies on responses to vaccinations: A review. Mult Scler Relat Disord. 2020 Oct;45:102439. doi: 10.1016/j.msard.2020.102439. Epub 2020 Aug 1. PMID: 32769063; PMCID: PMC7395588.
[5] Sellner J, Rommer PS. Multiple Sclerosis and SARS-CoV-2 Vaccination: Considerations for Immune-Depleting Therapies. Vaccines (Basel) 2021;9 (2):99. https://doi.org/10.3390/vaccines9020099. PMID: 33525459; PMCID: PMC7911298.
[6] Louapre C, Collongues N, Stankoff B, Giannesini C, Papeix C, Bensa C, et al. Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis. doi: 10.1001/jamaneurol.2020.2581. PMID: 32589189; PMCID: PMC7320356.
[7] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020;383 (27):2603-15. doi: 10.1056/NEJMoa2034577. Epub 2020 Dec 10. PMID: 33301246; PMCID: PMC7745181.
[8] Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021;384 (5):403-16. doi: 10.1056/NEJMoa2035389. Epub 2020 Dec 30. PMID: 33378609; PMCID: PMC7787219.
[9] Rutschmann OT, McCrory DC, Matchar DB. Immunization Panel of the Multiple Sclerosis Council for Clinical Practice Guidelines. Immunization and MS: a summary of published evidence and recommendations. Neurology 2002;59 (12):1837–43. https://doi.org/10.1212/wnl.59.12.1837. PMID: 12499473.
[10] COVID-19 Vaccine Guidance for People Living with MS. National MS Society Guidelines for COVID-19 Vaccine Guidance for People Living with MS: https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/covid-19-vaccine-.
[11] Bar-Or A, Calkwood JC, Chognot C, Evershed J, Fox EJ, Herman A, et al. Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis: The VELOCE study. Neurology. 2020 Oct 6;95(14):e1999-e2008. doi: 10.1212/WNL.0000000000010380. Epub 2020 Jul 29. PMID: 32727835; PMCID: PMC7843152