The need for Rapid Vaccination Coverage against COVID in People with Neuromuscular Diseases

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Abstract:

Infections may affect the therapeutic course of neuromuscular disorders, both in immunocompetent individuals and in those with reduced immunocompetence due to immunomodulating/ /immunosuppressive therapies. Infections can also cause NMDs as well. In patients with diminished immunocompetence, there is a risk for decreased effectiveness of immunizations. Countries across Europe have started considering vaccination roll-out plans in recent months, which are widely seen as a means of addressing high mortality rates and extensive lockdowns over the course of 2020. Vaccines are not compulsory in most European countries, and so the population's ability to be vaccinated against COVID-19 must be high in order to meet the high targets of obtaining herd immunity from the virus. This article examines emerging vaccination rollout co-

ordination methods in many European countries: the Switzerland, Sweden, Germany, France and UK. It centered on the need for rapid vaccination in patients with NMD and the protection and effectiveness of immunization in NMD patients, with a focus on COVID-19 vaccination.

Introduction

More than 13 million COVID-19 cases have now occurred across the UK and the EU/EEA, resulting in over 320,000 deaths. Several politicians including World Health Organization Director-General have aligned COVID-19 vaccinations with a 'light at the end of the tunnel' in order to resolve COVID-19 infection rates and eliminate potential lockdowns (1). For this to be done, a high consumption of any safe and effective vaccine is required. Many concerns about the treatment of people with neuromuscular conditions have arisen from the coronavirus disease pandemic-2019. For the most recent two COVID-19 vaccines (PfizerBioNTech and Moderna) and more in the pipeline were granted emergency use clearance by the U.S Food and Drug Administration (2). The development of NMDs varies based on the underlying etiology and pathophysiology and can be determined by concomitant diseases and infections. The risk of aspiration is due to: dysphagia; impaired ability to take a deep breath; impaired cough reflex; and poor airway clearance of secretions with resulting atelectasis and pneumonia; respiratory or bulbar muscle weakness (3). In some of these conditions, the use of immunosuppressive and immunomodulating agents which can increase susceptibility to infections and at the same time reduce the humoral response to immunizations, is of special concern.

Immunization against a disease can be given by natural infection or vaccines against a certain agent or agents. The aim of vaccination is to create an immune response against a particular antigen and to shield vulnerable populations from communicable diseases. This can be achieved by adding a living manipulated agent ('live vaccine'; e.g. yellow fever vaccine), suspending killed animals (e.g. pertussis vaccine), antigen expressed in a heterologous organism (e.g. hepatitis B vaccine), or inactivated toxin (e.g. tetanus) (4). In this Practice Subject we use the terms immunization and vaccination interchangeably to refer to immunity gained in relation to vaccines.

Infections and Underlying NMDS

In terms of symptom severity and patient experience, the wide spectrum of neuromuscular disorders differ but typically include the peripheral nervous system resulting in gradual muscle weakness involving both skeletal muscles and internal organ muscles. The hallmarks of neuromuscular disorders, including: ALS; muscular dystrophies; SMA; along with certain myopathies; and mitochondrial diseases, among others; are mobility difficulties as well as cardiac, respiratory and intestinal complications. Our elderly patients and those with cardiorespiratory issues are at extremely high risk and the highest priority should be given. A multisystem influence of their disorders is faced by most people dealing with neuromuscular diseases. If they develop, these illnesses can weaken the pulmonary muscles and diaphragm raising the risk of significant pulmonary infection. There are also underlying coronary disorders of many neuromuscular patients. Research is gradually finding that, during the duration of their disease, these patients are at high risk of acute heart injury. For their future COVID-related effects; these variables do not bode well. To prevent muscle weakness, people with neuromuscular conditions are also administered corticosteroids. The CDC has reported that because of the resulting weakening of the immune system, people who take corticosteroids "may be at increased risk." Immunosuppressive therapy is needed for individuals with certain neuromuscular disorders such as myasthenia gravis and Lambert-Eaton myasthenia syndrome leaving them more prone to extreme COVID-19.

Risk of Infections in Individuals with NMDS

In the treatment of autoimmune neuromuscular conditions, Immunosuppressive /Immunomodulatory agents are commonly used and vaccines play a significant role in minimizing the morbidity associated with vaccine-preventable infections in this population (5). There is a general belief that both typical and atypical Immunosuppressive

agents increase the risk of infections. A systematic study of 631 patients who were on Immunosuppressive/immunomodulatory agents with *myasthenia gravis*, chronic inflammatory demyelinating polyneuropathy, and dermatomyositis showed a 19% infection rate in all three diseases, with the most common being pneumonia. In multivariate studies, there has been an important independent correlation between infections and the use of plasmapheresis, mycophenolate mofetil, and corticosteroids. In retrospective analysis, line infections due to plasmapheresis were not analyzed separately (6). An elevated risk of illnesses, including the reactivation of latent tuberculosis, is associated with corticosteroids (7). HBV infections can be reactivated by B-cell depleting therapies, such as rituximab. For rituximab or high-dose corticosteroid treatment, the chance of reactivation is estimated at over 10% (8). It is calculated that the chance of HBV reactivation with azathioprine, methotrexate, or low-dose corticosteroids is less than 1% (8). Through the use of rituximab, reactivation of varicella zoster virus infections has also been reported (9). The most serious infectious complication of immunosuppressive therapy, for which no appropriate vaccination or cure is presently available, is progressive multifocal leukoencephalopathy due to reactivation of infection with the John Cunningham virus (10). The risk of Pneumocystis jirovecii pneumonia is increased by immunosuppressive agents. In patients taking corticosteroids in conjunction with other immunosuppressive agents, the risk of Pneumocystis jirovecii pneumonia is higher (11). A chance of severe meningococcal infections is linked with eculizumab. It binds to the protein C5 complement to inhibit the cleavage of C5a and C5b, thus preventing the combination of C5b with the C6 to C9 complement proteins that form the membrane attack complex. Due to the absence of sufficient serum bactericidal action and compromised opsonization with decreased phagocytic degradation of the encapsulated organism, the lack of membrane attack complex prevents the capacity of the immune system to respond effectively to acquire Neisseria infections (12).

Effectiveness of Vaccinations in NMDS Patients

The benefits of vaccines can be diminished by altered immunocompetence. There is insufficient evidence, however, on the efficacy of vaccines in people that are on IS/IM agents (13). Methotrexate reduces the humoral response to pneumococcal vaccine (14). CD19+ B cells, preplasma cell bursts, and interferon-γ-secreting T cells are depleted by rituximab. After rituximab, antibody responses may be compromised for at least 6 months (15). It appears that this medication has the most significant effect on the immune response to vaccinations, including vaccines against influenza and pneumococcal vaccines. It is also expected to affect the effectiveness of other vaccines (14). High-dose immunosuppression is more likely than low-dose immunosuppression (prednisone >20 mg/day for >14 straight days, azathioprine >3 mg/kg/day, methotrexate >0.4 mg/kg/week) to influence vaccine reaction (16).

Vaccination and Infection Prophylaxis in Individuals with NMDS

NMDs, which influence all age ranges, are complex. Two fairly distinct classes of NMDs arise from the viewpoint of diseases and immunizations: 1) those that are allergic and often treated with IS/IM agents, and 2) those that are inherited/degenerative and treated mostly with supportive management. It is likely that the risk of infection in people with NMD undergoing long-term IS/IM treatments could be higher than in people with NMD who do not undergo these treatments, but there is no evidence to support this. Furthermore, in these two classes, separate concerns about immunization emerge. Underlying heart and respiratory failure puts people with NMD at greater risk of severe complications and increased mortality, independent of treatment with IS/IM agents, from infections such as influenza. Vaccine-related deterioration of the underlying condition, activation of new autoimmune NMDs, and suboptimal vaccine effectiveness provide additional concerns in patients infected with NMD on IS/IM agents.

Conclusion

People with neuromuscular conditions, health care professionals and patients and employees at long-term care facilities should be among the first to receive COVID-19 vaccines. Finally, a single neuromuscular disorder is found to be rare (fewer than 100,000 cases in the US and Germany). There is little or no study on the im-

pact of COVID-19 on these patients due to this "rare" status. This suggests that we might be unaware of additional risk factors that improve vulnerability to serious COVID-19 infection.

The MDA is urging the CDC and state and local governments to assign high priority to vaccinating persons with neuromuscular diseases against COVID-19 for all of these reasons.

References

1. WARREN GW, LOFSTEDT R. (2021) *COVID-19 vaccine rollout risk communication strategies in Europe: a rapid response*. Journal of Risk Research. 2021:1-11.
2. ZIVKOVIC SA, GRUENER G, NARAYANASWAMI P, QUALITY A, COMMITTEE PS, NARAYANASWAMI P, et al. *Doctor–Should I get the COVID–19 vaccine? Infection and Immunization in Individuals with Neuromuscular Disorders*. Muscle & nerve.
3. PANITCH HB (2017) *Respiratory implications of pediatric neuromuscular disease*. *Respiratory care*. 2017;62(6):826-48.
4. KIMBRELL DA, BEUTLER B (2001) T*he evolution and genetics of innate immunity*. *Nature*. Reviews Genetics. 2001;2(4):256-67.
5. CARTWRIGHT SL, CARTWRIGHT MS (2019) *Health maintenance for adults with neuromuscular diseases on immunosuppression*. Muscle & nerve. 2019;59(4): 397-403.
6. PRIOR DE, NURRE E, ROLLER SL, KLINE D, PANARA R, STINO AM, et al. (2018) *Infections and the relationship to treatment in neuromuscular autoimmunity*. *Muscle & nerve*. 2018;57(6):927-31.
7. MALPICA L, MOLL S (2020) *Practical approach to monitoring and prevention of infectious complications associated with systemic corticosteroids, antimetabolites, cyclosporine, and cyclophosphamide in nonmalignant hematologic diseases*. Hematology 2014, the American Society of Hematology Education Program Book. 2020;2020(1):319-27.
8. SMALLS DJ, KIGER RE, NORRIS LB, BENNETT CL, LOVE BL (2019) H*epatitis B virus reactivation: \ risk factors and current management strategies*. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2019; 39(12): 1190-203.
9. AKSOY S, HARPUTLUOGLU H, KILICKAP S, DEDE DS, DIZDAR O, ALTUNDAG K, et al. (2007) *Rituximab-related viral infections in lymphoma patients*. Leukemia & lymphoma. 2007;48(7):1307-12.
10. CORTESE I, REICH DS, NATH A (2020) *Progressive multifocal leukoencephalopathy and the spectrum of JC virus-related disease*. Nature Reviews Neurology. 2020: 1-15.
11. AVINO LJ, NAYLOR SM, ROECKER AM (2016) *Pneumocystis jirovecii pneumonia in the non–HIV-infected population*. Annals of Pharmacotherapy. 2016; 50(8): 673-9.
12. KONAR M, GRANOFF DM (2017) *Eculizumab treatment and impaired opsonophagocytic killing of meningococci by whole blood from immunized adults*. Blood, The Journal of the American Society of Hematology. 2017;130(7):891-9.
13. RUBIN LG, LEVIN MJ, LJUNGMAN P, DAVIES EG, AVERY R, TOMBLYN M, et al. (2013) IDSA clinical practice guideline for vaccination of the immunocompromised host. Clinical infectious diseases. 2014;58(3):e44-e100.
14. HUA C, BARNETCHE T, COMBE B, MOREL J (2014) E*ffect of Methotrexate, Anti–Tumor Necrosis Factor α, and Rituximab on the Immune Response to Influenza and Pneumococcal Vaccines in Patients With Rheumatoid Arthritis: A Systematic Review and Meta–Analysis*. Arthritis care & research. 2014;66(7):1016-26.
15. NAZI I, KELTON JG, LARCHE M, SNIDER DP, HEDDLE NM, CROWTHER MA, et al. (2013) *The effect of rituximab on vaccine responses in patients with immune thrombocytopenia*. *Blood*. 2013;122(11):1946-53.
16. ESPOSITO S, BRUNO C, BERARDINELLI A, FILOSTO M, MONGINI T, MORANDI L, et al. (2014) *Vaccination recommendations for patients with neuromuscular disease*. *Vaccine*. 2014; 32(45): 5893-900.