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Mini Review

The Lesson Learned from Covid-19 and Patients with Neuromuscular Disorders

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Abstract

After 3 years of the Covid-19 pandemic, it is possible to explain what impacted mostly neuromuscular patients and treating physicians. There were many challenging items, such as determining if patients with neuromuscular disease (NMD) present a higher risk for Covid-19 and determining the consequences of the risk of Covid-19 infection for treatments used in patients with NMD, it was important to find out if cases with NMD that developed after Covid-19 infection or pre-existing conditions were exacerbated. Positive effects were observations regarding vaccines for Covid-19, that did not harm neuromuscular disease, finally, teleconsultations were the most frequent types of telemedicine used during the COVID-19 in different European countries to face worsening of NMD, therapy or physical therapy advice, diagnosis, and general follow-up.

Keywords: *Neuromuscular Diseases; Covid-19; Pandemic; Risk Factors; Telemedicine*

Introduction

The Covid-19 pandemic has hit in the last 3 years the neuromuscular patient community, there have been reports in several countries i.e. Italy, France, and Taiwan of its impact on these kinds of patients. The following are conclusions that apply to both acquired and genetic numerous neuromuscular disorders. These are designed mainly for patients, specialists, and non-specialist medical providers. They might inform neuromuscular specialists, regarding frequently asked questions and future requirements. Neuromuscular diseases include different entities with different etiology and progression.

Considerations

Did patients with neuromuscular disease (NMD) present a higher risk for Covid-19?

National neurological associations and neuromuscular networks have produced papers [1,2] on the impact of Covid-19 on these patients.

Clinical features conferring a high or very high risk of severe disease included: muscular weakness, respiratory forced vital capacity less than 60% predicted, especially in patients with kyphoscoliosis, patients with weak cough, oropharyngeal weakness or presence of tracheostomy, neuromuscular patients with cardiac involvement or on medication for heart involvement, neuromuscular cases suddenly deteriorating for fasting, or infection, or at risk of rhabdomyolysis, patients with obesity or diabetes and, patients on steroids and undergoing immunosuppressants.

In a large study [1] collecting cases of COVID-19 in patients with NMDs, cases were collected across a region. They have identified factors associated with higher odds of more severe COVID-19 outcomes, including older age, gender, and severe course.

Within the different NMDs, Guillain Barrè syndrome (GBS) was associated with higher odds of worse COVID-19 severity, compared to mitochondrial disease, further obesity, hypertension, diabetes, gender, immunosuppressive drugs/corticosteroids, which could be additional risk factors playing an important role.

Patients with pre-existing chronic inflammatory demyelinating polyneuropathy, in association with SARS-CoV-2 infection, were found at high risk as a consequence of cytokine hyperactivation triggered by the virus. In parallel, a higher risk of mortality was found in myasthenic patients.

It was found that the risk factors for the general population such as obesity, hypertension, diabetes, gender, immunosuppressive drugs/corticosteroids, and age could be similar risk factors playing an important role in the impact or degree of severity of COVID-19 in NMD patients.

What did patients with NMD do to avoid infection?

COVID-19 accumulates in the particular patient group with ventilatory support.

Patients with motor neuron disease and dystrophinopathies might present ventilatory muscle weakness or cardiomyopathy. Thus, the COVID-19 pandemic did severely affect such NMD patients.

There was an impulse to properly modify the respiratory care methodology for NMD patients, especially during the COVID-19 spread, in fact managing COVID-19 was a rapidly evolving field, and patients with NMD and at high risk of a severe course of Covid-19 infection underwent the following precautions: A social distancing of at least 2 meters, while for high-risk patients, self-isolation was advised.

While visiting physiotherapy was discontinued, physiotherapists provided advice by telemedicine to try to maintain physical activity remotely.

The person responsible for organizing the home tried to face the situation, making plans to best meet the needs of the patient, and avoiding hospitalization.

Consequences of the risk of Covid-19 infection for treatments used in patients with NMD

Patients and carers tried to make use of online and telephone-based pharmacy and equipment ordering and delivery services, however, they were not fully comfortable with emergency procedures, and delivery services for their condition.

DMD patients on various steroid regimens did continue their regimen, since it is advised that steroids must not be stopped suddenly, and eventually increased the steroid dose when worsening.

Similarly in cases of polymyositis, myasthenia gravis, and CIDP immunosuppression was not discontinued, except in consultation with the neuromuscular physician.

Isolation requirements impacted treatment regimens requiring hospital procedures (i.e. spinraza, Myozyme, IVIg, and rituximab infusions or treatments related to clinical trials) and in a few cases, home services were tried, and when possible moved to a non-hospital setting using home-visiting or outreach nurses, i.e. IVIg was changed to subcutaneous immunoglobulin.

What happened when isolating in real life?

Backup and advice guidelines were offered by the patients' neuromuscular physicians.

Few patients had an alert card/medical bracelet providing their neuromuscular contact.

Neuromuscular specialists tried actively to contact patients on ventilatory support, to give advice.

During the whole three years of the Covid-19 pandemic, many of these practical recommendations have been lost, there was a sense of isolation and most neuromuscular cases were left to themselves for their management.

Neuromuscular disorders that developed after Covid-19 infection or pre-existing conditions that were exacerbated

Regarding immunosuppressive therapies, the need for therapy dosage reduction vs. discontinuation in NMD patients is uncertain. There was no significant increased mortality or risk for a severe disease course in immunosuppressed NMD patients with COVID-19. A limited number of polymyositis patients have been followed and it is possible to conclude a modest impact of immunosuppression in infected NMD patients.

The isolation measures probably affected the QoL of patients in different regions worldwide, particularly those with chronic debilitating neuromuscular diseases. It remains unanswered how the underlying NMDs precautions and immunosuppression affected the COVID-19 disease course.

Several neuromuscular conditions, including Guillain-Barré syndrome, rhabdomyolysis, and myositis, have been reported in patients infected with COVID-19, but even with a temporal association, a causal relationship remains unproven. The virus could have a direct invasion of neurons or myocytes or cause immune-mediated damage. In addition, the factors causing a significant reduction in diaphragm muscle contractility as represented by the post-COVID-19 conditions need accurate detection, since treatment and rehabilitation should not be delayed, if necessary. Patients with NMD became aware of the limitation of emergency services at disposition and this impacted the potential for intensive care admission for patients with NMD. Unfortunately, the words "incurable" and "untreatable" were confused by physicians. However, even if several neuromuscular diseases might still be incurable, they are not untreatable, and this implies different treatment decisions.

Did treatments or vaccines for Covid-19 harm neuromuscular disease?

The Covid-19 vaccines focusing on the spike glycoprotein had a major impact in diminishing the spread of Covid-19, but their efficacy was possibly attenuated by locally circulating variants. The frontrunner Covid-19 vaccines had good neutralizing activity against the Alpha variant, less impact on Gamma and Delta variants, and a reduced efficacy on the Beta variant, long-term evaluation of neutralizing activity is needed to evaluate the persistence of protective antibodies against novel variants.

Rare adverse events have also been reported following Covid-19 immunization such as anaphylaxis, myocarditis, and Guillain-Barrè syndrome.

Some drugs used during Covid-19 infection can affect neuromuscular function significantly: for example, chloroquine and azithromycin are unsafe in myasthenic patients.

Other treatments had adverse effects on metabolic, mitochondrial, myotonic, and neuromuscular junction disorders and anatomical peculiarities are important for treatment (e.g. prolonged prone position).

One should avoid new treatments for Covid-19 on an experimental basis, offered "compassionately", i.e. outside trial conditions. They should only be looked at with great caution, and consultation with the patient's neuromuscular specialist is advisable.

Neuromuscular specialists' collaboration in intensive care decisions, admissions, escalation of treatment, and care of NMD

Unfortunately during the Covid-19 pandemic often decisions on patient admission to Intensive Care were limited by existing capacity problems, but in this, there was a close collaboration between neuromuscular and pneumology specialists.

The neuromuscular physician was available to play a role in ensuring fair access to intensive care for NMD patients and was involved in decision-making and providing documentation.

Neuromuscular specialists developed guidelines suggesting a policy that ensures patients should remain at home, if possible.

Support of neuromuscular centers and critical requirements, a lesson to be learned

It was inevitable that the Covid-19 pandemic delayed the regular course of clinical trials. Further control visits and exams were performed without major problems only in a few centers.

A series of services such as home care nursing and psychological support were markedly affected worldwide and substituted with new modalities.

To avoid the risk of infection from the patient to the therapist, most rehabilitation services were suspended. Remote physiotherapy was rarely provided, because of the difficulties experienced by neuromuscular-specific patients and their caregivers in conducting such treatment. Home nursing care was provided in a fair number of cases, compared to physical therapy, despite their risks. Psychological support for patients and caregivers was generally available since it could be provided through remote contact [3-7].

Conclusion

Neuromuscular specialists should aim in the future to provide the following services:

- Outreach ventilatory support strategies should be provided,
- Ensure specific treatment access for a series of neuromuscular diseases, in particular, ERT. In metabolic cases, drugs for mitochondrial diseases, myotonic, and neuromuscular junction disorders.

El Hassar data [8] show that teleconsultations and phone consultations were the most frequent types of telemedicine used during the COVID-19 in different European countries and contests such as worsening of NMD, therapy or physical therapy advice, diagnosis, and general follow-up.

The worsening of NMD symptoms was reported in NMD patients with pre-existing respiratory impairment, and/or suffering from swallowing difficulty, and/or on long-term immunosuppressive therapy, who were classified "at high risk" for developing severe forms of COVID-19.

Patients with motoneuron diseases (including spinal muscular atrophy), with associated ventilatory muscle deficit, were particularly susceptible to the infection by SARS-CoV-2.

In addition, some other types of NMD patients were found at increased risk of developing a severe form of COVID-19; for example patients with muscular dystrophies, including myotonic dystrophies, or metabolic myopathies (e.g. Pompe disease), with ventilatory muscle weakness and/or associated cardiomyopathy.

Because of this experience, telemedicine will likely be more often used in the future as previously reported. Clinical trials will be resumed with better outcome measures, that will fit the available time of neuromuscular specialists.

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