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Rehabilitation challenges in COVID-19 induced acute polyradiculoneuropathies

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Abstract

Introduction. SARS-COV 2 infection causes damage of the peripheral nervous system: loss of smell loss of taste and demyelination or axonal injury in the spinal roots and motor and sensory nerves with acute polyradiculoneuritis. As many people are affected by COVID-19, the number of patients with secondary peripheral nervous system damage is increasing. **Material and method.** There are a significant number of Guillain Barre syndrome (GBS) cases reported in COVID-19 positive patients, leading to the recognition of GBS as one of the peripheral nervous system complications of SARS-COV 2 infection. We are trying to summarise the particularities of specific rehabilitation in post-COVID patients. **Results and discussions.** The rehabilitation of a COVID patients has particularities, first – because of infectious risk carried by the patient during the procedures, second by the patient's pulmonary and physical impairments induced by the Coronavirus. **Conclusions.** There is scarce evidence for rehabilitation interventions, and many recommendations are based on methods developed in other viral infections or chronic pulmonary and neurologic conditions. There is a urgent need for studies regarding the efficacy of interventions in COVID rehabilitation, as the number of patients is constantly increasing.

Keywords: *therapeutic plasma exchange, plasmapheresis, neuroimmune disorders,rehabilitation,*

Introduction

The most common clinical presentation in COVID patients is with respiratory symptoms, but neurological impairments are increasingly reported. Neurological manifestations have been described in a significant number of COVID patients, involving both central nervous system (CNS) and peripheral nervous system (PNS), and ranging from mild to severe symptoms (1). General neurologic symptoms as headache and dizziness were also reported (2).

Neurological symptoms associated with SARS-COV 2 infection have been described with different incidence by many studies. Mao L. identified neurological manifestations only in 36,4% of patients, with dizziness, headache and alterations in smell and taste been described as most common (3). Another study reported that up to 73% of hospitalized COVID patients have neurological manifestations (4).

Peripheral nervous system involvement in COVID-19

Peripheral nervous system involvement in COVID-19 includes olfactory dysfunction (anosmia/hyposmia), gustatory dysfunction (ageusia), Guillain-Barré syndrome and variants (Miller Fisher syndrome), cranial nerves polyneuritis, facial palsies, and critical illness polyneuropathy (4). Incidence of PNS symptoms ranges between 8,9% and 13% in two observational studies (5, 6). Anosmia/hyposmia and gustatory dysfunction were the most common, and are encountered in variable incidences, ranging from 48 to 98% for olfactory dysfunction and to 71 to 88% for ageusia (7,8, 9, 10). Acute neuropathies are considered to be associated with SARS-COV 2 infection if their onset is within 6 weeks after the confirmation of COVID infection, when no other commonly associated causes were detected (1).

The pathogenetic mechanisms of PNS damage are variable. Hyposmia and dysgeusia are most probably caused by direct viral damage of olfactory and gustatory

receptor cells, which express angiotensin-converting enzyme 2 (ACE-2) receptors (11). Another postulated mechanism for dysgeusia is the direct damage of the chorda tympani nerve, a sensory branch of facial nerve (CN VII) responsible for taste, during the nasopharyngeal and middle ear colonization by SARS-COV 2 (12). PNS complications of COVID-19 are the consequence of the neurotrophic properties of the virus, and of the immune-mediated injuries of cranial nerves and spinal roots (6 ,11). Also, critical illness-associated peripheral nerves damage contributes in the severe and critical cases to the PNS injury by specific mechanisms, such as the systemic inflammatory response syndrome (SIRS), cytokine release and microcirculatory damage (2). Moreover, PNS complications were more frequent and severe in COVID patients requiring intensive-care treatment (6).

Acute polyradiculoneuropathies in COVID patients.

Acute polyradiculoneuritis (PRN) or Guillain Barre syndrome (GBS) is a severe dysimmune disease, which requires early diagnosis and intensive management. Many reports of GBS associated with COVID-19 have been published, and GBS is emerging as an important associated disease in COVID patients, representing 7-8% of reported neurological manifestations (4). The overlap between respiratory dysfunction caused by neurologic impairment of respiratory muscles and respiratory failure induced by SARS-COV 2 makes the diagnosis of GBS critically important (13). The incidence of GBS in northern Italy showed an 2,6 fold increase during the COVID-19 pandemic peak, supporting the role of SARS-COV 2 in inducing acute polyradiculoneuritis (14). Another study conducted in the UK showed that the incidence of GBS cases remained unchanged during the pandemic year (15).

The onset of GBS symptoms was variable: in the first days after viral detection, concurrent with COVID-19 symptoms (so called ‘’para-infectious’’ pattern), but also after the acute phase of viral infection (‘’the post-infectious’’ pattern – described in acute polyradiculoneuritis not associated with SARS-COV 2) (2). Other studies reported longer interval since viral detection and neurologic symptoms, ranging from 2 to 24 ±11 days, both para- and post-infectious GBS being reported (14, 16). The occurrence of concurrent neurologic symptoms in the acute phase of SARS-COV 2 infection is the consequence of an acute dysimmune attack against PNS during the ‘’cytokine storm’’ (11). For the ‘’post-infectious’’ pattern of SARS-COV 2 triggered GBS, a molecular mimicry mechanism between the viral protein–associated gangliosides and peripheral nerve gangliosides have been described (13).

The clinical presentation of PRN in COVID 19 patient is heterogenous; the typically ascending motor and sensory deficits with loss of deep tendon reflexes is the most common (more than 75% of patients had an ascending course); facial weakness and respiratory failure were also described (14, 16, 17). In an observational study of adult COVID-19 patients, the most common neurological symptom was motor weakness (in 34,4% of patients), with higher incidence (51%) in Intensive Care Unit (ICU) patients; tetraparesis was noted only in 15% of patients (6). In a systematic review, most common features of COVID-associated GBS were sensory symptoms in 72% of patients, para- or tetra-paresis in 65%, cranial nerves involvement in 16%, areflexia in 10% and gait ataxia in 37,5%. Only 16,7% of patients developed autonomic symptoms . Mean age of the patients was 55 years, with male predominance (17). Compared to COVID negative GBS patients, COVID – positive GBS patients had a more severe motor deficit, a more frequent involvement of all four limbs, and they were more predisposed to be admitted in the ICU (14).

Among the 3 main subtypes identified based on electrophysiological features, the acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most frequent, affecting 66 to 77% of patients, the axonal variants (acute motor axonal neuropathy - AMAN, acute motor sensory axonal neuropathy - AMSAN and Miller-Fisher syndrome - MFS) accounting for the rest (between 6,7 to 34%) (13, 14, 17). The cerebrospinal fluid (CSF) studies showed typical albumino-cytological dissociation in 71% of patients (17). Despite elevated protein levels, most studies reported negative PCR test for SARS-COV 2 in the CSF, supporting the immune-mediated pathogenetic mechanisms (16).

An UK study showed that the neurological recovery prognosis in COVID-associated GBS is similar to non-COVID GBS (15). In COVID positive patients, favourable prognosis occurred in 72% of patients with GBS, 10 % had no clinical improvement, 11,8% required ICU admission and 5,8% died (17). One fifth of patients required mechanical ventilation. It has been hypothesized that ventilatory support in COVID-related GBS was also required due to viral-induced pulmonary damage, not only to neuromuscular weakness (15, 18). Patients with poor outcome were older and had a severe form of COVID-19 (17). The modified Erasmus GBS Outcome Score (mEGOS) is an useful tool designed to assess GBS prognosis, predicting long term outcome pf patients based on their clinical presentation at day 7 after admission (19). The mEGOS scores did not show any statistically significant difference between COVID-induced and ‘’classical’’ GBS (13). Also, mortality was 11% in GBS related to SARS-COV 2 infection, identical to classical GBS.

Rehabilitation interventions in acute polyneuropathies

Regardless of the cause, GBS is an important cause of long-term disability, requiring a wide range of rehabilitation interventions (20). After the acute phase, it was reported that approximately 40% of patients require intensive inpatient rehabilitation, and in the chronic phase 16% of patients are still reporting limitations in work and social activities (20). At 6 months after GBS onset, 20% of patients required help or assistive devices for waking. The most frequent deficits in acute PRN survivors are motor and sensory deficits, fatigue and pain (21).

Rehabilitation methods proposed for GBS patients before COVID pandemic include multidisciplinary rehabilitation and specific interventions. Multidisciplinary rehabilitation delivered patient-centred, functional-oriented and coordinated interventions by two or more disciplines: physiotherapy, occupational therapy, nursing, psychological counselling or social support, provided in inpatient settings, or ambulatory (20). Physiotherapy techniques are addressed especially to mobility impairments: maintenance of postures, joint range of motion exercises, endurance training, muscular strengthening and reinforcement, cycling, progressive ambulation programs. Also, physiotherapy programs should be non-fatiguing, and should avoid muscle groups overworking (20). The use of assistive devices, orthoses and ambulatory aids should optimise the gait and the motor function. Occupational therapy focuses on reacquisition of skills required for patient autonomy, use of adaptative equipment or environment changes.

Rehabilitation interventions in COVID patients with PNS impairments

Patients with severe COVID infection usually recover with sequelae in multiple systems: respiratory, cognitive or neurological, associated with deconditioning; all dysfunctions should be addressed by specific interventions (22). In patients recovering after COVID-19, rehabilitation of neurologic sequelae is not possible without concomitant rehabilitation of respiratory function and of deconditioning. Another important challenge is that COVID patients recovering from severe forms could be potentially unstable and had a low exercise tolerance. For that reason, monitoring of heart rate (HR), respiratory rate (RR) and oxygen saturation (SaO2) is mandatory during physical therapy. Patients which had moderate forms of SARS-COV 2 infection frequently showed fatigue and exercise intolerance, with decrease in oxygen saturation. Post-COVID sequelae should be considered in all patients, it was predicted that approximatively half of discharged patients will need further rehabilitation support or social care (23).

There is a conflicting evidence regarding early rehabilitation for severe forms of SARS-COV2 infections. There are recommendations for starting early progressive rehabilitation programmes, within the first 30 days after diagnosis, for a maximal impact on recovery (23). Moreover, an international task force in the field of pulmonary rehabilitation recommended initiation of inpatient rehabilitation during the acute COVID infection, addressing immobility, muscle weakness or neurological impairment (24). In contrast, there are recommendations against early rehabilitation in severe COVID patients, because of the associated risk of rapid desaturation during exercises (25). The timing of respiratory rehabilitation should be individualized, depending on patient's status and comorbidities (26).

Before discharge, it is recommended to assess patient's oxygen needs during rest and during exercise. Also, patient's ability to perform physical exercises and his functional capacity should be assessed by simple tests, such as 6-minute walk test and 1 minute sit-to-stand test (27). After discharge, there is a strong recommendation for performing regular daily activities and for continuing low or moderate-intensity physical exercise during the first 6 to 8 weeks. After this interval, patient's limitations, needs and dysfunctions should be reassessed, and new rehabilitation goals should be established. Pulmonary sequelae were found at 6-8 weeks after discharge (mild to moderate restrictive dysfunction), but also after 1 year follow up (23). If persistent lung function impairment is identified, the patient will continue the comprehensive pulmonary rehabilitation programme, which includes exercise training, (respiratory muscle training, coughing exercises, diaphragmatic training, stretching exercises), patient education, psychosocial support, and behavioural modification strategies (23). If lower limb weakness of mobility problems are diagnosed, a muscle strengthening programme is recommended (24).

Rehabilitation of patients with COVID and associated GBS with pulmonary dysfunction is challenging. Usually, one third of GBS patients had respiratory dysfunction, caused by respiratory muscles weakness with incomplete recovery. Even before COVID pandemic, post-GBS respiratory dysfunction required specific interventions, such as breathing exercises, chest percussion or resistive respiratory training (20). In COVID-19 survivors, respiratory problems secondary to lung fibrosis are difficult to manage, requiring long rehabilitative interventions with specifical physical therapy methods, such as endurance training or strengthening exercises (22, 28). For endurance training, the patient could use ground walking or an ergometric bicycle, with continuous HR, blood pressure (BP) and SaO2 monitoring, until 60% of maximal HR or 80% of gait speed are attended after 6 minutes walking (28). Also, upper and lower limb exercises are recommended, depending of individual effort tolerance.

Breathing training exercises are, and many techniques were proposed: pursed-lip breathing, diaphragmatic control techniques, thoracic expansion techniques, training of thoracic respiratory muscles. The results obtained after respiratory rehabilitation should be monitored with specific scales: St-George Respiratory Questionnaire (29) and the 6 minutes walking test (30).

Rehabilitation of post-COVID deconditioning is mandatory, and it will also improve respiratory functions, as well as GBS-induced muscles weakness. Interventions should include aerobic training, breathlessness management, energy conservation, with or without oxygen supplementation (31). Also, in chronic phase, stable patients with pulmonary dysfunction and neurologic impairments could benefit of specific balnear methods of rehabilitation and relaxation (32).

In the pandemic context, virtual (remote) rehabilitation of COVID outpatients have been proposed. Tele-rehabilitation with a physiotherapist following the patient performing recommended exercises during a session, could be considered an useful tool in patient care, which maintain the connection between the patient and the medical team (33).

Conclusion

As SARS-COV 2 continues to spread, more patients with associated neurologic symptoms, including acute PRN, will be diagnosed. Clinicians should be aware of the possibility of COVID-associated neurologic manifestations, detailed clinical and paraclincal investigations should be performed, and appropriate treatment and rehabilitation interventions should be recommended, concomitantly with specific COVID treatment. Recognition of these different entities is important for improving care for COVID patients

Rehabilitation is an essential tool in the management of complex, multisystem post-COVID dysfunctions. Until today, there are no researches relevant to rehabilitation in post-COVID patients. There is scarce evidence for rehabilitation interventions, and many recommendations are based on methods developed in other viral infections or chronic pulmonary and neurologic conditions. There is a urgent need for studies regarding the efficacy of interventions in COVID rehabilitation, as the number of patients is constantly increasing.

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