Rehabilitation after COVID-19: A review of recent experience

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Abstract
Corona Virus Disease 2019 that emerged at the end of 2019 has affected millions of people worldwide. In severe cases, impairment of the respiratory system requires admission of patients to intensive care unit and mechanical ventilation that may induce long-term complications and sequelae. Post-disease effects can persist also in mild cases. Recently reported experiences indicate that appropriate rehabilitation should be administered when possible and safe to improve the outcome of the treatment and to accelerate recovery of the patients. The measures taken can address nutrition, airway, posture, clearance technique, oxygen supplementation, breathing exercises, stretching, manual therapy, physical activity and social support. In this paper we review some of the recent evidences showing beneficial effect of rehabilitation on COVID-19 and post-COVID-19 patients. Keywords: COVID-19; respiratory rehabilitation; post-COVID-19 rehabilitation; intensive care unit rehabilitation, breathing technique

Rehabilitacija po COVID-19: Pregled nedavnih izkušenj

Povzetek
Koronavirusna bolezen 2019, ki se je pojavila konec leta 2019, je prizadela milijone ljudi po vsem svetu. V hujših primerih okvara dihal zahteva sprejem bolnika na oddelek za intenzivno nego in mehansko predihavanje, kar lahko povzroči dolgotrajne zaplete in posledice. Učinki bolezni so lahko dolgotrani tudi po polezni z blažjim potekom. Pred kratkim opisane izkušnje kažejo na koristnost ustrezne rehabilitacije, kadar je to mogoče in varno, z namenom, da se izboljša izid zdravljenja in pospeši okrevanje bolnikov. Ukrepi se lahko nanašajo na prehrano, prehodnost dihalnih poti, držo telesa, tehniko čiščenja dihalnih poti, dodajanje kisika, dihalne vaje, raztezanje, manualno terapijo, telesno aktivnost in socialno podporo. V tem prispevku predstavljamo pregled nekaterih nedavnih izkušenj, ki kažejo na ugoden učinek rehabilitacije na bolnike s COVID-19 in na tiste, ki okrevajo po bolezni. Ključne besede: COVID-19; dihalna rehabilitacija; rehabilitacija po COVID-19; rehabilitacija po zdravljenju na enoti za intenzivno nego; tehnika dihanja

1. INTRODUCTION

A number of severe respiratory infection cases caused by a newly identified β-coronavirus emerged in Wuhan, China in 2019. At the end of January 2020, an outbreak was declared by World health Organization (WHO) to be a public health emergency of international concern (WHO, 2020). The disease was named "COrona VIrus Disease 2019" (COVID-19) while Coronavirus Study Group of the International Committee named the new coronavirus as "Severe Acute Respiratory Syndrome Corona Virus 2" (SARS-CoV-2) (Kralj-Iglič et al., 2020). The suggested mechanism of the interaction of virus with the human was found through a particular protein (SARS-CoV-2 S-protein) which binds to the human ACE2 receptor. This receptor is expressed in several organs (e.g. lung, heart, kidney and intestine) (Hoffmann et al., 2020). The first cells that are exposed to the virus were identified to be alveolar epithelial cells and non-keratinizing squamous epithelium in the nasal and oral mucosa (Kralj-Iglič et al., 2020). However, the reported symptoms include many organs within respiratory system, cardiovascular system, brain, kidneys, gastrointestinal system and reproductive system (Gu et al., 2005, Kralj-Iglič et al., 2020). It was suggested that the virus SARSCoV-2 may enter the central nervous system through a synapse-connected route and cause severe neurological and mental dysfunction (Li et al., 2020, Pincherle et al., 2020). Mechanisms such as hypoxemia, glucose dysregulation, and sedation during the treatment also contribute to development of these effects (Pincherle st al., 2020). No effective medicine has yet been launched to treat the disease while different protocols are being used as supporting care.

Particularly devastating manifestation of the disease is interstitial pneumonia. In severe cases patients are bed-ridden in the intensive care unit for longer periods. If mechanical ventilation is introduced, injury due to supportive ventilation and/or due to patient-ventilator asynchrony may occur (Tobe and Saito, 2020). Patients have to learn how to inhale and exhale to achieve sufficient oxygenation and carbon dioxide exhalation (Tobe and Saito, 2020). Also, patients often remain in a prone position for hours consequently developing post-intensive care unit dysphagia, neuropathy, myopathy, muscle weakness, reduced joint mobility, pain in the neck and shoulders, impaired balance and gait which decreases quality of life (Simpson and Robinson, 2020, Demeco et al., 2020). Furthermore, as COVID-19 is highly infectious, patients are isolated to prevent spreading the disease. This makes them feeling lonely and isolated (Demeco et al., 2020).

Patients that survive the disease, especially those that have been admitted to the intensive care unit may develop long-term complications and sequelae, such as pulmonary fibrosis, persistent dyspnoea, impaired pulmonary function, decreased functional and exercise capacity, as well as neurological and cognitive impairments (Sebio-Garcia, 2020). After the acute phase, pulmonary scarring/fibrosis with dyspnoea may reside for months. Patients who are recovering from the infection show fatigue and difficulty in movement, disorientation as well as cognitive and emotional imbalances due to the loss of the senses of taste and smell. Patients get tired even just going to the bathroom or taking a shower (Hermann et al., 2020).

The consequences of prolonged time spent in bed indicate application of rehabilitation

Physiotherapists specialized in this type of rehabilitation collaborate with medical staff in order to better manage the ventilation of patients, whether mechanical, non-invasive, with the support of oxygen therapy, etc. In order to provide optimal treatment during and post-COVID-19, several procedures have been suggested. The ultimate goal of these treatments, all combined together, is to improve respiratory functions, reduce mucus and chronic inflammation in the airways, ameliorate chest wall kinematics, and increase not only physical health but also mental wellbeing. The effectiveness of respiratory rehabilitation on different outcomes such as exercise capacity, muscle function, dyspnea and symptom control, is quite robust, so it is currently recommended in the management of different chronic respiratory conditions (Hermann et al., 2020). In this work we have reviewed some of the yet experienced rehabilitation measures in COVID-19. We have searched the literature in Web of Science and chose 20 papers reporting different protocols, case reports and research experiences yet yielded in different medical centres.

2. METHODS

Suggested measures

As regards rehabilitation in the acute phase, Chinese Association of Rehabilitation Medicine has indicated that early respiratory rehabilitation is not recommended because it may lead to rapid desaturation (Demeco et al., 2020). The risk/benefit ratio should be evaluated on a single-case basis in patients with bronchiectasis or with evident bronchial encumbrance using tools at a safe distance from the patient, which can be maintained (Pincherle et al., 2020). To minimize spreading the disease to staff, if possible, rehabilitation should be made by using telemedicine which was proved to have essentially the same outcome as person-to person interaction (Wang et al., 2020).

However, when possible and safe, respiratory rehabilitation should be implemented. In general, rehabilitation may include nutrition, airway, posture, clearance technique, oxygen supplementation, breathing exercises, stretching, manual therapy, and physical activity (Wang et al., 2020). Respiratory rehabilitation interventions were suggested to be personalized, particularly for patients with comorbidities, advanced age, obesity, multiple diseases, and complications of single or multiple organs (Demeco et al., 2020).

The Italian societies of respiratory healthcare professionals, AIPO (Associazione Italiana Pneumologi Ospedalieri), ARIR (Associazione Riabilitatori dell'Insufficienza Respiratoria), SIP (Societŕ Italiana di Pneumologia) AIFI (Associazione Italiana Fisioterapisti) and SIFIR (Societŕ Italiana di Fisioterapia e Riabilitazione) promoted a multidisciplinary international consensus on physiotheraphy (Vitacca et al., 2020). The experts considered relevant questions regarding personal protection needs, phenotypes of patients, importance of frailty measurements, timing of respiratory rehabilitation start, assessment of the patient, the choice of imaging to individualize the program, the time and method to assess gas exchanges, the choice of lung function tests, the choice of exercise capacity and muscle status tests, the methods on respiratory muscle assessment, the secretion encumberance, the nutritional status, the quality of life assessment, the identification of emotional aspects regarding rehabilitation, types of intervention, re-assessment possibilities and risks and benefits of exercise training in patients with cardiovascular complications (Vitacca et al., 2020). They supported the idea of personalized rehabilitation programs; airway clearance techniques were recommended to be continued only for hyper-secretive patients. Oxygen, at rest and during efforts, aerosol-therapy and drug-inhalers must be delivered with caution and adaptation to avoid droplet dispersion. As the effects of muscle activity in viral infections is not known, the professionals suggested aerobic low load exercise based on subjective symptoms with low intensity, together with daily patient counselling and education.

3. RESULTS

Patients with severe COVID-19

In patients in the intensive care unit breathing exercises and bed mobility may be the initial intervention given. Bed mobility exercises include ankle pumps, sliding legs into flexion/extension, over-head arm stretches, sit-to-stand at bedside (Wang et al., 2020).

Early mobilization, can be initiated during the mechanical ventilation to counteract intensive care unit-acquired weakness. Mobilization of the patients can be achieved by using an automatic system for leg movement in a supine position that induces movements similar to riding a bicycle. This equipment allows for passive, active or assisted mobilization or a tilting table with an integrated leg movement system to attain vertical position of the patient, adjustable to the patient's needs, and possibilities. Mobilization can be applied as soon as cardiovascular stability of the patient is attained. Frequent changes of posture, passive mobilization, and/or neuromuscular electrical stimulation should be planned especially in the unconscious patient. In addition, evaluation of peripheral muscle strength trends should be recorded as soon as practicable (Pincherle et al., 2020).

Respiratory muscle weakness from diaphragm proteolysis may be suspected in those patients with prolonged mechanical ventilation (Wang et al., 2020). Inspiratory and expiratory muscle training can be

implemented in these patients starting with incentive spirometry and progressing to inspiratory muscle training devices if available (Wang et al., 2020).
Early (defined as during and immediately after discharge from intensive care unit) rehabilitative interventions are fundamental for reducing the neurological burden of a disease. In addition, ameliorating neuromuscular weakness with early rehabilitation could improve the efficiency of respiratory function (Pincherle et al., 2020). Effective auditory stimulation can be achieved by providing information about a time and place. Patient's favourite music or the voice of a loved one could be played, the patient should be told about happy daily events in his/her family, pleasant memories and enjoyable experiences. Tactile and proprioceptive stimulation can be provided by massaging the patient's hands and legs and performing passive range of motion activities several times. Patient should be provided by picture of a family member or encouraging motif. An olfactory stimulation can be applied by using the patient's favourite aroma scents, gustatory stimulation can be achieved by flavours using a cotton bud. Rehabilitation can be key element of the patient-centred care where rehabilitation professionals have a critical role. It was suggested that rehabilitation by a multidisciplinary team should start as early as possible by means of an individualized treatment plan (Pincherle et al., 2020).

Patients with mild COVID-19
According to their protocol, Wang et al (2020) (Wang et al., 2020) suggest following activities in patients with mild COVID-19: Patient education on the disease, encouragement to lifestyle improvement (adequate sleep, hydration and nutrition), physical activities (exercise intensity appropriate for Borg dyspnoea score smaller than 3, 1-2 times per day, 3-4 times per week; the exercises should be 10-15 minutes in the beginning but can incrementally increase to 45 minutes per session to target Borg score 4-6), psychological support consisting of social support and professional help, educational support (cleaning of airways by using a proper technique to avoid entrance of sputum in aerosol and Huff cough), and breathing exercises (diaphragmatic breathing pursued lip breathing, active abdominal contraction, Yoga, Pranayama, Tai Chi and singing, 2-3 times per day, daily, 10-15 minutes initially with incremental increase towards 30-60 minutes sessions). The activities suggested for moderate and severe disease include also bed mobility, sit to stand, ambulation and breathing rehabilitation exercises. Stretching including neck, upper chest, pectoralis major, lateral chest and flexion and extension to mobilize the facet joints is encouraged three times per day.
Initial intensity of exercise should be graded and approached with caution and monitoring. Exclusion criteria include the following: body temperature greater than 38 degrees, time from diagnosis or symptom onset smaller than 3 days, onset of dyspnoea smaller than 3 days; progression of disease assessed from chest image in 24 - 48 hours larger than 50%, oxygenation below 90%, blood pressure lower than 90/60 mmHg or higher than 180/90 mmHg, respiratory rate larger than 40 times per minute, heartbeat rate smaller than 40 beats per minute or greater than 120 beats per minute, new onset of arrhythmia and myocardial ischemia and altered level of consciousness (Wang et al., 2020). It was suggested that respiratory rehabilitation or breathing exercises should be stopped if oxygenation does not reach the required level, if the patient is unable to maintain Borg scale dyspnoea score smaller than 4 with rest and oxygen supplementation and if the patient is feeling chest pain, palpitations and dizziness (Wang et al., 2020).
Zha et al (2020) have suggested that rehabilitation exercises for patients recovering from mild COVID-19 should take into account specific pathological alterations in COVID-19 patients. In these exercises, special attention was payed to achieve smoot respiration and easy expectoration. The suggested exercises was designed to reduce total airway resistance, smoothen inflow of fresh air and improve gas exchange efficiency were divided into four sets: Overhead chest and shoulder stretch with holding breath at each inspiration; Standing heel raises and upper body acupressure by patting the Yunmen acu-point located in the infra-clavicular fossa (according to traditional Chinese medicine this point is associated with lungs) to free the mucus for the epithelial lining of the respiratory tract; Upper body rotation while patting the lateral side of thorax to enable mucus clearance; and Massage of three lung-associated acupressure points (Shaoshang, Yuji and Lieque) on each hand to support respiratory

function and decrease fatigue (Zha et al., 2020). The exercises should be practiced at least twice per day (Zha et al., 2020).

Post-COVID-19 patients

The intensive care unit-acquired weakness affects both peripheral and respiratory skeletal muscles of critical patients and represents one of the most serious consequences of prolonged immobilization. It was previously observed within a 5 years follow up study including initially 109 relatively young patients who survived acute respiratory distress syndrome in Toronto, Canada (median age at 5 years post – disease 44 years) that exercise limitations and a reduced physical quality of life were still present 5 years after their critical illness (Herridge et al., 2011). It was suggested that this was a consequence of the weakness and physical and neuropsychological impairments caused by the disease (Herridge et al., 2011). The decrements in the 6-minute walk distance and the physical evaluation 5 years after the disease suggested that previously functional and relatively young patients may undergo an irreversible decrease in function after critical illness; the decrease being even greater in older patients with more coexisting comorbidities (Herridge et al., 2011). Similar effects could be expected also in COVID-19 patients. Indeed, post-disease effects of COVID-19 were observed by Halpin et al. (2020) (Halpin et al., 2020) who found that more than half of patients that were hospitalized for COVID-19 were still experiencing fatigue, breathlessness, and decreased health-related quality of life 48 days after discharge (Halpin et al., 2020).

Antonelli and Donelli (2020) have suggested that in order to outline a standard/baseline model of care, already existing rehabilitative plans with a long-standing tradition should be applied, such as those ones prescribed for work-related respiratory diseases in which long-term outcomes share some clinical characteristics with post-infective lung fibrosis. Furthermore, health spa centres should be engaged to offer the post-COVID-19 patients the appropriate rehabilitation programs including physiological and psychological support, provided that they are no longer contagious. The rehabilitation programs for work-related respiratory diseases consist of respiratory physio-kinesiotherapy and postural drainage for lungs, mechanical pulmonary ventilation for rehabilitative purposes, inhalation therapies with mineral waters, physical activity and psychological support. Patient specific program can include also water kinesitherapy, belneotherapy, dietary advice and relaxation under the guidance of physiotherapists and physicians.

4. DISCUSSION

Experiences with rehabilitation involving COVID-19 patients

A retrospective cohort study was performed including 28 patients undergoing cardiopulmonary rehabilitation program after hospitalization in acute care hospitals for COVID-19 in Zurich, Switzerland (Hermann et al., 2020). Program consisted of personalized aerobic exercises (supervised indoor and outdoor walking or stationary cycling), strength exercises (3x20 repetitions with the maximal tolerated load within 25-30 therapy sessions, 5-6 days per week), teaching breath control (pursed lip breathing, secretion mobilization, and diaphragmatic breathing), energy-saving techniques, and controlled coughing exercises. Patients were offered educational sessions, nutritional advice, smoking cessation program and psychosocial support. It was concluded that cardiopulmonary rehabilitation could be performed safely and with beneficial effect in COVID-19 patients; functional capacity and subjective health status improved significantly. There were no differences observed between patients that were previously on the mechanical ventilation and those in whom the mechanical ventilation was not needed.

In July, 2020, the Northern Sydney Local Health District evidenced 550 cases of COVID-19. A telehealth rehabilitation program was offered to patients recovering from the disease who experienced breathlessness, fatigue and reduced physical capacity (Wotton et al., 2020). Wotton et al. (2020) reported on first three cases who had moderate to severe COVID-19 with relatively short hospital stays and who underwent the programme. The programme consisted of pre-rehabilitation assessment, initial six weeks individualized rehabilitation programme with multidisciplinary team and post-rehabilitation assessment. Fatigue, dyspnoea, oxygenation and heartbeat frequency were measured during the

exercises. Cognitive status and anxiety/depression were assessed by questionnaires. Educational program was offered. Aerobic exercise consisted of ground-based walking (Borg score of <3) 5-10 min which extended to 30 min [18]. In case of excessive fatigue, intermittent exercise was prescribed starting with 2-minute intervals with a 1-minute rest. Strengthening exercises were also prescribed with a focus on large muscle groups (exercise examples: sit-to-stand, heel raises, lunges, bicep curls with hand weights, wall push ups, and tricep dips). The patients were all males (73 (Case 1), 59 (Case 2) and 80 (Case 3) years of age, respectively). In all three, the lungs were affected, showing in images bilateral pulmonary infiltrates and/or ground-glass opacities. Patients 1 and 3 were admitted to intensive care unit while all three have spent 9 (case 1), 12 (case 2) and 15 (case 3) days in the hospital. Patients 1 and 2 were employed and patient 3 was retired, but was a full time carer of his wife. Patient 1 was highly compliant and was able focus entirely on his rehabilitation. In contrast, patients 2 and 3 progressed more slowly and only completed one to two sessions during the first three weeks before increasing compliance to the amount prescribed. Six weeks after the initiation of the program, depression score worsened in one of the patients (patient 2) while fatigue score worsened in 2 patients (patients 2 and 3) as they felt the burden of returning to work and carer roles. 11 weeks after the onset of COVID-19 symptoms, patient 2 was reporting persistent dyspnoea connected to still persisting bilateral ground-glass opacities and a small pulmonary embolism. Feedback regarding the programme from the patient experience measure was highly positive with patients reporting that they had significantly improved their confidence in what to do during their recovery. The authors concluded that it is valuable to provide early support to people recovering from COVID-19 (Wotton et al., 2020).

A case report from Italy considered a 51-year old man, non-smoker with no comorbidities, who was admitted in the emergency department with persistent fever, cough, and dyspnoea, while the chest x-ray showed bilateral interstitial thickening and consolidation of the lung parenchyma (Pancera et al., 2020). The following day, the patient was transferred to the intensive care unit for invasive mechanical ventilation and life support due to acute hypoxemic respiratory failure. 8 days later, percutaneous tracheostomy was performed for the prolonged necessity of mechanical ventilation. 12 days after admission the patient was transferred to isolation ward set up for COVID-19 infection where 2 physiotherapists with intensive care respiratory rehabilitation experience carried out the assessment and initiated treatment (30-45 minutes, once per day). After 2 consecutive negative swabs for COVID-19 infection, the patient was moved to a COVID-free ward, where he exercised 6 days per week for 30-45 minutes twice per day. 12 days after administration of mechanical ventilation, the weaning procedure started, however, during the first attempt the patient's oxygenation fell below 90% and heart rate increased to 130 beats per minute within 30 minutes and mechanical ventilation was re-introduced. Two days later, a second attempt for the spontaneous breathing was performed using a threshold positive expiratory pressure device and supplemental oxygen. Rehabilitation progressed to maintenance of the sitting position and quadriceps strengthening with neuromuscular electrical stimulation. 16 days after the admission the patient progressed to maintain spontaneous breathing during the whole day, with supplemental oxygen via nasal cannula. Besides, the training program was integrated with sit-to-stand training and seated leg or arm cranking for 20-30 min. On day 17, the patient was successfully weaned from MV with supplemental oxygen. Walking with assistance and balance training, both limited to the patient's room, were added to the rehabilitation program and continued until the patient progressed to walk without assistance and independently carried out activities of daily living. Tracheal cannula was removed on day 23 after the admission. The rehabilitation was continued with resistance exercises using elastic bands or free weights. Despite the improvement in exercise tolerance, the patient still required supplemental oxygen via nasal cannula for another week. Patient was discharged from hospital 37 days after the admission. This case report (Pancera et al., 2020) reported the first case of beneficial effect of rehabilitation in severely ill patient that achieved complete functional recovery after COVID-19.

Yoga and respiratory rehabilitation

Increasing evidence suggests that Yoga and related meditation techniques are effective in modern clinical practice for improving respiratory function and reducing chronic pain. Moreover, some

techniques of respiratory rehabilitation have parallels in Yoga techniques. By practicing Yoga breathing technique, patients may learn how to take longer and deeper breaths, decrease the frequency of breaths, keep the airways open longer and maintain a proper upright position of the body to allow for maximum lung expansion. Patients also learn how to use the diaphragm and abdominal muscles, rather than accessory respiratory muscles, to more effectively breathe in and out and oxygen saturation, and thus ameliorate dyspnoea (Tobe and Saito, 2020). Inhalation, holding the breath and exhalation are the three basic steps of yogic breathing exercises. Normally inhalation and exhalation are done for the equal time while breath hold is for twice the duration of inspiration or expiration.

Pranayama is a typical way of breathing in Yoga. During Pranayama lungs and the rib cage (thorax) undergo horizontal expansion, vertical ascension, and circumferential expansion. This ensures expansion of both the lungs in all its lobes in the front as well as back aspect. *Ujjayi* breathing, a diaphragmatic breathing starts by filling the lower belly, rises to the lower rib cage, and finally moves into the upper chest and throat. Inhalation and exhalation are both done through the nose. The length and speed of each breath are controlled by the diaphragm. Inhalations and exhalations are equal in duration and are controlled in a manner that causes no distress to the practitioner. This helps bring air into all parts of the lungs, increases oxygenation, builds internal body heat and regulates blood pressure. *Kapalabhati* involves short and strong forceful exhalations followed by automatic inhalation. It is thought to be effective for cleaning the cranial sinuses. *Nadi Shodhana* is an alternative nostril breathing method that helps in becoming calm. Pranayama and other breathing exercises have gained more importance these days due to its definite role in improving blood oxygenation and utilization of the greater capacity of lungs, thereby helping in the prevention of many diseases. It was found that regular Yoga practice increases vital capacity, maximum voluntary ventilation, breath-hold time and maximal inspiratory and expiratory pressures (Dhaniwala et al., 2020).

5. CONCLUSIONS

COVID-19 is a disease that may require intensive and long-term rehabilitation involving a multidisciplinary team and personalized program. Existing evidences indicate that rehabilitation may be beneficial for patients. Specific protocols should be elaborated for its optimal administration. Respiratory rehabilitation program can take advantage of traditional methods which have mastered breathing techniques.

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