

CASE REPORT

POST-COVID SYMPTOMS AND WHOLE-BODY CRYOTHERAPY: A CASE REPORT

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CASE REPORT

On 23 April 2021, a 75-year-old man, was admitted to the Covid Hospital “Sacco”, Milan, Italy, with bilateral interstitial pneumonia and acute respiratory failure secondary to SARS-CoV-2 infection. In the following days, due to worsening respiratory exchange, he was transferred to the intensive care unit (ICU) and treated with invasive mechanical ventilation. The patient underwent 6-h ventilation cycles with continuous positive airway pressure (CPAP) in the prone position every 6 h for 2 weeks. While in the ICU, a few episodes of paroxysmal atrial fibrillation occurred, which were treated with pharmacological and electric cardioversions. From 15 May, the patient ceased curarization and started weaning from mechanical ventilation. Two days later, he underwent percutaneous tracheostomy with a cuffed cannula 8. From 2 June, the patient started cycles of spontaneous breathing with heated and humidified air/oxygen mixture delivered at high volumes (40 l/min), which led to improved fraction of inspired oxygen (FiO₂) and neurological-cognitive status. Targeted antibiotic therapy and single-donor apheresis platelet concentrates transfusions were delivered following episodes of melaena in duodenal angiodysplasia. On 16 June, the patient was transferred to the Pneumology Unit of the same hospital and the tracheostomy tube was removed on 6 July. Neurophysiological investigations revealed moderate sensory-motor distal axonal neuropathy in the upper and lower limbs, with multineuropathic distribution. On 26 July, a nasal-pharyngeal swab was negative for SARS-CoV-2 (Covid-19). The next day he was transferred to our Rehabilitation Unit at the Istituto Auxologico Italiano in Piancavallo, Italy. On admission, the patient was bed-ridden and extremely deconditioned. His body weight was 61.8 kg (pre-hospitalization weight 75 kg). He presented with hypokinetic syndrome, parox-

ysmal atrial fibrillation, post-critical illness low T3 syndrome, arterial hypertension, and prostatic hypertrophy. Moderate malnutrition, according to the GLIM criteria (1), and probable sarcopaenia, as assessed by handgrip strength (16 kg), were present. The aetiological criteria of malnutrition was supported only by the presence of duodenal condition, since inflammation level due to the C-reactive protein (CRP)/albumin ratio (0.09) was in the normal range. Functional independence Measure (FIM) score was 73/126. Subjectively, the patient reported early fatigue and dyspnoea after minimal effort, and deflected mood. Biomarkers were in suboptimal range: for inflammation, ferritin 920 µg/l, transferrin 144 mg/dl, erythrocyte sedimentation rate 34 mm/h, C-reactive protein 0.3 mg/dL; for liver dysfunction, aspartate aminotransferase (AST) 167 U/l, alanine aminotransferase (ALT) 204 U/l, gamma glutamyltransferase (GGT) 387 U/l; for nutritional status, albumin 3.4 g/dl, vitamin D 35.8 ug/l and for metabolic status, total cholesterol 126 mg/dl, cholesterol HDL 29 mg/dl, glycated haemoglobin 31 mmol/mol. Colour Doppler echocardiogram (GE Medical Systems ge medical, Italy; Vivid 7 dimension) revealed normal values and absence of arrhythmias. Therefore, anti-arrhythmic and anti-coagulation therapy was ceased, maintaining only bisoprolol 1.25 mg to avoid bradycardia due to aortic valve insufficiency and adding ramipril 2.5 mg to control arterial hypertension.

Keywords: whole-body cryotherapy; post-Covid; SARS-CoV-2; rehabilitation; malnutrition.

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Rehabilitation programme

Nutritional intervention. Total energy intake was calculated at 30 kcal/die day/kg, and protein intake was calculated as in the range 1–1.3 g/die day/kg body weight. As recommended by ESPEN Guidelines (2), the patient received oral supplementation with multivitamins, essential amino acids 5 g (1,200 mg L-leucine, 650 mg L-lysine, 625 mg L-isoleucine, 625 mg L-valine, 350 mg L-threonine, 150 mg L-cystine, 150 mg L-histidine, 100 mg L-phenylalanine, 50 mg L-methionine, 30 mg L-tyrosine, 20 mg L-tryptophan), minerals and probiotics. A 1,700 kcal diet with a composition of 84 g protein (1.36 g/kg weight) 52 g lipids (0.84g/kg) and 219 g (3.5g/kg) carbohydrates was started.

Physiotherapy and physical activity. On 27 July, the patient started physiotherapy in bed, consisting of progressive postural trunk control, passive/assisted exercises and muscle strengthening. The rehabilitation programme included 2 h/day, divided into 2 sessions, monitored with subjective perception of fatigue (Borg's CR10 scale) and oxygen saturation (SpO₂). Exercises were stopped when a score of 5 on the Borg scale was reached. After 1 week, the patient succeeded in reaching the standing position and maintaining this position supported, for 15 s. The intensity of strengthening exercises for the trunk and lower/upper limbs was increased progressively. Three weeks after admission to our unit, the patient was able to stand unsupported for 2 min and walk a few steps with a walker. On that day, he underwent a first 1-min familiarization session of whole-body cryotherapy (WBC). From the following day, he underwent a daily morning WBC session in a Cryochamber (CryoScience, Giovanni Antonelli, Roma) at a temperature of -110°C for 2 min, before starting physiotherapy (**Fig. 1**). A week later, the patient also began moderate aerobic

training with a cycloergometer at an intensity of 3.5 metabolic equivalents (METs) and for a duration of 5–10 min at a moderate subjective perception of fatigue. SpO₂ value, while exercising moderately was 89% and 92% at rest. A few days later, the patient was able to walk with one cane for 20 m, and balance training was started. At the end of week 5 of rehabilitation, he was able to walk without support for more than 100 m, aerobic training volume was increased (intensity 4.5 METs, duration 20–25 min), SpO₂ during exercise was 97%. At the end of week 6, the patient walked outdoors for approximately 400 m. The total duration of his rehabilitation stay was nearly 7 weeks.

Whole-body cryotherapy. WBC exposes patients to extremely cold dry air in an environmentally controlled cabin for 2 min. Such stimulus induces vasoconstriction (3), stimulation of dermal thermoreceptors, slower nerve conduction (3). WBC is currently mostly used to relieve inflammatory symptoms in rheumatoid arthritis (4), fibromyalgia (5) or ankylosing spondylitis (6). A few studies have shown improvements in depression and anxiety syndromes (7), in functional status and fatigue in patients with multiple sclerosis (8), and in quality of sleep (9). WBC is widely used as a recovery technique after physical exercise in elite athletes (10) and positive effects of 10 serial WBC sessions have been registered one month after discontinued treatment (11). To the best of our knowledge, no studies have so far investigated the effects of WBC on post-Covid symptoms. Given the absence of medical contraindications, WBC was proposed to the patient and informed consent was provided. The WBC protocol included 15 sessions of cryotherapy. Before and after each session, the patient's superficial temperature was recorded at the level of the popliteal fossa, thigh, and neck.



Fig 1. Parts A: Example of the cryostimulation session. Parts B: Cryochamber (CryoScience, Roma, Italy).

RESULTS

After the first 2-min session of WBC, 3 weeks after admission to rehabilitation, the patient reported an immediate subjective improvement in breathing. The mean reduction in skin temperature recorded was -16.75°C , with a maximum delta value of -19.9°C between pre- and post-session temperature. The minimum temperature recorded at the level of the popliteal fossa was 14.2°C . During the following hours, he also reported reduced weakness and improved quality of sleep at night. From then on, improvements in subjective fatigue, joint mobility, muscle strength, as well as SpO_2 values during exercise and inflammatory, metabolic and nutritional markers continued until discharge nearly 7 weeks after admission (**Table I**). The reported patient's satisfaction, tolerance and compliance specifically related to WBC treatment were all excellent. No adverse events related to WBC were recorded.

CONCLUSION

Pain, fatigue and inflammatory symptom alleviation after WBC appear to be related to reduced nerve conduction and acetylcholine formation and lower levels of oxidative stress and inflammation (12). A surprising number of extra-pulmonary manifestations of severe acute respiratory SARS-CoV-2 infection have been described with review of imaging (13), shedding some light on a range of musculoskeletal, nerve, joint and bone involvement and leading to the manifestation of prolonged symptoms. Although no specific literature is currently available, the rationale for prescribing WBC sessions for post-Covid symptoms appears to be in line with the existing evidence for clinical and functional benefits following WBC documented in other musculoskeletal, neurological and psychiatric conditions. Since we delivered a range of interventions, we cannot establish to what extent WBC per se may have accounted for the clinical and functional improvements

Table I. Admission and discharge parameters of body composition, physical performance, muscle strength, joint mobility and biological markers

Values		Admission	Discharge		
Body composition	Weight, kg	61.800	63.200		
	BMI, kg/m^2	21.63	22.13		
Physical performance	FIM	73/126	124/126		
	Hand grip, kg	16.6	17.5		
	Timed Up & Go Test, s	NS	11"31		
	VAS	Pain/100	20/100		
	Disability/100	90/100	10/100		
Upper and lower limbs mobility and strength	Left shoulder	Active mobility	Flexion, $^{\circ}$	80	110
			Abduction, $^{\circ}$	70	100
			Rotation int./est, $^{\circ}$	60/40	85/60
		Manual Muscle Strength Test	Flexion, $^{\circ}$	2+	4
			Abduction, $^{\circ}$	2+	4
			Rotation int./ext., $^{\circ}$	3/2	4/4
	Right shoulder	Active mobility	Flexion, $^{\circ}$	50	100
			Abduction, $^{\circ}$	40	90
			Rotation int./ext., $^{\circ}$	30/10	60/50
		Manual Muscle Strength Test	Flexion, $^{\circ}$	2	4
			Abduction, $^{\circ}$	2	4
			Rotation int./ext., $^{\circ}$	2/2	4/4
	Left hip	Active mobility	Flexion, $^{\circ}$	45	100
			Abduction, $^{\circ}$	20	35
			Rotation int./est, $^{\circ}$	10/10	30/30
		Manual Muscle Strength Test	Flexion, $^{\circ}$	2	4
			Abduction, $^{\circ}$	2	4
			Rotation int./ext., $^{\circ}$	2/2	4/4
	Right hip	Active mobility	Flexion, $^{\circ}$	45	100
			Abduction, $^{\circ}$	20	35
			Rotation int./ext., $^{\circ}$	10/10	30/30
		Manual Muscle Strength Test	Flexion, $^{\circ}$	2	4
			Abduction, $^{\circ}$	2	4
			Rotation int./ext., $^{\circ}$	2/2	4/4
Biomarkers	Inflammatory	ESR mm/h	34	18	
	C-reactive protein mg/dl	0.3	0.1		
	CRP/albumin ratio	0.09	0.03		
	Liver dysfunction	AST U/L	167	14	
		ALT U/l	204	14	
	GGT U/l	387	28		
	Nutritional	Albumin g/dl	3.4	3.5	
		vitamin D ug/l	35.8	Not rescreened	

BMI: body mass index; FIM: Functional independence Measure; TUG: Timed Up & Go; VAS: visual analogue scale of pain (0: no pain, 100: max pain) and disability (0: no functional difficulty; 100: maximal functional difficulty); SPO2: blood oxygen level; ESR: erythrocyte sedimentation rate; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma glutamyltransferase.

observed. However, it was observed from the very first session, 3 weeks after admission, that the introduction of WBC sessions represented a turning point in the patient's subjective and objective improvements, which continued noticeably until discharge, nearly 7 weeks after admission. This case report, written according to the CARE checklist (available from <https://smj.org.sa/sites/default/files/PDF/CAREchecklist-English-2013.pdf>), provides some novel suggestions that WBC, in addition to a multidisciplinary rehabilitation programme, may represent an effective adjuvant in recovery from post-Covid symptoms. However, larger studies are needed. Given the severity and prevalence of post-Covid symptoms in the general population, optimizing rehabilitation programmes is of paramount importance.

The authors have no conflict of interest to declare.

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