SM Journal of Neurology and Neuroscience ISSN: 2573-6728

Research Article

Pragmatic clinical comparison of two modes of treatment in patients with ME/CFS or Post-Covid syndrome

COMHAIRE Frank[1]*, DESLYPERE Jean-Paul[1], and PEN Jan[2]

[1]Consulting specialist of internal medicine, endocrinology and metabolic diseases, Fertility-Belgium clinic. Weststraat 16, 9880 Aalter, Belgium

[2]Specialist internal medicine and ultrasonography. Chronisense, Senses praktijkhuis, Hofstraat 14; 2400 Lier; Belgium

Abstract

Background: Systemic and neurological signs and symptoms of patients suffering from Myalgic Encephalomyelitis/Chronic Fatigue syndrome (ME/CFS) or from the post-COVID syndrome (also called long-COVID) are remarkable similar, with the exclusion of impaired cardio-respiratory function related to the past viral infection. Pathogenic mechanisms common to these diseases include persistent immune and inflammatory processes inducing dysfunction of cellular/mitochondrial energy production and glucose metabolism.

Materials and methods: In the present real-life systematic registration we have compared the effectiveness of two therapeutic approaches that aim at improving general well-being, fatigue in particular. Oral therapy using a specific nutraceutical complemented with sodium-dichloroacetate and Meldonium (referred to as "oral therapy") was given to 84 consecutive patients, and compared to intravenous infusion therapy using high dose magnesium together with multivitamins and essential amino acid ("infusion therapy") given to 21 patients. After one month of treatment the effect of treatment on fatigue was measured using the Fatigue Severity Score (FSS).

Results: In a preliminary analysis both treatment approaches showed similar effectiveness with two thirds of patients reporting a variable degree of improvement, and no difference of effectiveness between ME/CFS cases and the post-Covid patients.

Conclusion: Two thirds of patients suffering from ME/CFS or from the post-COVID syndrome experienced a variable degree of reduction of fatigue thanks to treatment with a specific food supplement (QALY®) and the metabolism stimulating substances Meldonium® and sodium-dichloroacetate, or with intravenous infusions containing vitamins, minerals and selected amino acids. These preliminary finding must be interpreted with caution, and controlled trials including a larger number of patients and longer follow-up are mandatory.

Keywords: Post-COVID syndrome, long-COVID, nutraceutical, chronic fatigue syndrome, myalgic encephalomyelitis, infusion therapy.

Introduction

In both ME/CFS [1] and post-COVID patients [2-8], neurological sequelae are common. NeuroSpect imaging of the brain [9] typically shows decreased accumulation of Technetium-labelled perfusion tracer in the prefrontal region, the hypothalamus and the brain stem, corresponding with inadequate cellular metabolism and blood supply. This is associated with cognitive impairment [10] causing difficulties to concentrate and to memorise, so-called brain fog, headache, and sleep disturbance, as well as deregulation of autonomous nervous system with tachycardia, orthostatic hypotension and intestinal symptoms. The neurological manifestations suggest lowered glycolysis, decreased pyruvate transportation into the mitochondria, and inhibition of pyruvate dehydrogenase activity in brain neurons [11]. Similar metabolic alterations occur in muscles cells causing physical fatigue and exhaustion, slow post-exercise recuperation, and pain related to – among other things – oxidative overload and accumulation of lactic acid, as observed in fibromyalgia patients [12].

It is hypothesized that some of these alterations can be corrected by the delivery of specific vitamins, mineral salts, essential amino- and fatty acids [13], as well as plant extracts with antioxidant, anti-inflammatory and adaptogen potential. In addition, glucose metabolism can be optimized by the administration of sodium- dichloroacetate (DCA lab, Vilnius, Lithuania)[14], that increases pyruvate dehydrogenase activity by inhibiting dehydrogenase kinase, and of Meldonium (Mildronate®, Grindesk, Latvia), that stimulates the transfer of pyruvate from the cell cytoplasm into the mitochondria.

Materials and Methods

In a prospective, open-label, two-centre real life systematic registration 105 consecutive patients diagnosed with ME/CFS or Post-COVID syndrome were requested to complete the Fatigue Severity Scale (FSS) [15] before initiation, and again after one month of treatment. During this month the first group of patients (n=84) received "*oral treatment*" with the nutraceutical QALY® (JonaPharma, Elversele, Belgium; formulation in annex) together with a capsule composed of 400 mg of sodium-dichloroacetate, Vitamin B1, and alfa lipoic acid. In addition, they had to take 500 mg of Meldonium once or twice per day. The second group (n=21) were given "*infusion treatment*" containing between 1

Submitted: 28 January, 2022 | **Accepted:** 25 February, 2022 | **Published:** 28 February, 2022

***Corresponding author(s):** COMHAIRE Frank, Consulting specialist of internal medicine, endocrinology and metabolic diseases. Fertility-Belgium clinic. Weststraat 16, 9880 Aalter, Belgium

Citation: COMHAIRE F, DESLYPERE JP, PEN J (2022) Pragmatic clinical comparison of two modes of treatment in patients with ME/CFS or Post-Covid syndrome. SM J Neurol Neurosci 8: 4.

and 3 grams of magnesium-sulphate, multivitamins, and selected essential amino acids as needed.

The results of the FSS were introduced into the spreadsheet of the MedCalc® statistical program (MedCalc ltd, Ostend, Belgium)[16] and analysed using student's t-test for paired or for independent samples as indicated. For each individual patient the quotient was calculated of the FSS after treatment divided by the FSS before treatment (FSS after/FSS before). Quotients were plotted in box and whisker graphs (Figures 1 and 2) with dots. Quotients less than 1 indicate the FSS to be lower after treatment than before, suggesting improvement of fatigue.

Results

The epidemiologic characteristics of the patients of the two groups were not statistically different, with mean age of 43.2 (SD: 12.0) yrs in the oral group and 44.5 (SD: 11.4) yrs in the infusion cases (P=0.67). Eighty two % were female. The average duration of disease was significantly longer in the ME/CFS patients (9.37 yrs; SD: 5.42) than in de the post-COVID cases (10.6 mths; SD: 4.7).

There was no significant difference in the outcome of oral as compared to infusion therapy regarding the effect of treatment on the FSS quotient (P=0.70), nor between the ME/CFS patients and the post-COVID cases.

The paired t-test for comparison of FSS before (mean: 5.97, SD: 0.74) and after treatment (mean 5.21: SD:1.30), was highly significant (p<0.0001) with overall two thirds of patients reporting a beneficial effect on fatigue, albeit in a variable degree (Figures 1 and 2). The FSS quotient of value after divided by value before treatment decreased by an average of 21% among the successful cases.

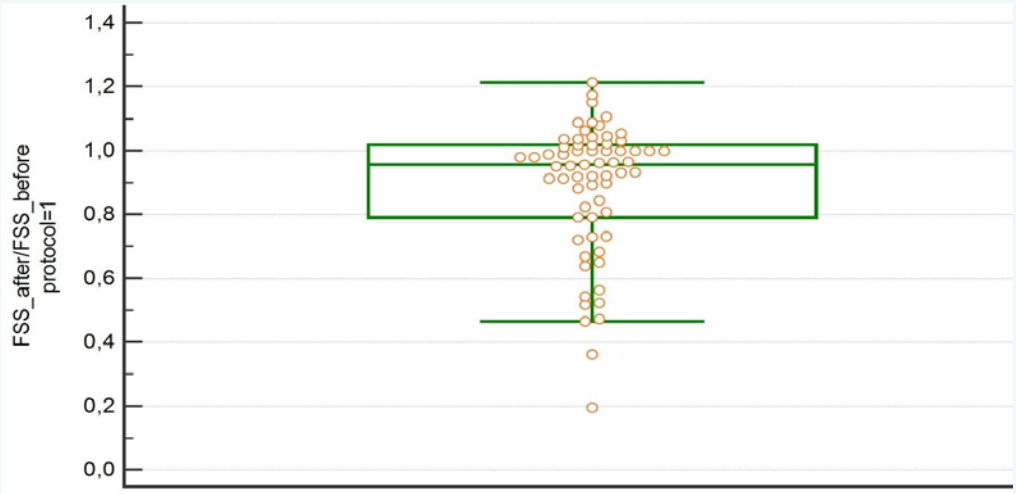

Figure 1 Box and whisker plot with dots presenting the quotient of Fatigue Severity Scale (FFS) after "oral treatment" divided by the FFS before in individual patients. Values lower than 1.0 correspond to cases reporting less fatigue after treatment.

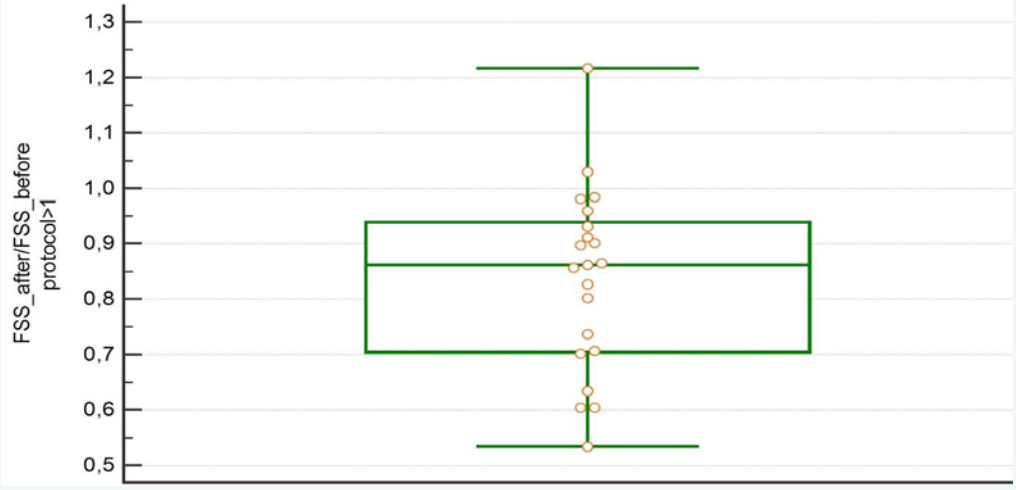

Figure 2 Box and whisker plot with dots presenting the quotient of Fatigue Severity Scale (FFS) after "infusion treatment" divided by the FFS before in individual patients. Values lower than 1.0 correspond to cases reporting less fatigue after treatment.

There was no relationship between the efficiency of treatment and the duration of disease, nor with its severity estimated from the FSS before.

Discussion

The results of the present pilot study, extending previous findings [17], should be interpreted with due caution, because of the limited number of cases, the open-label design, and the short duration of observation. Also, no data are available concerning the overall quality of life, or other disease aspects, such as brain function, metabolic associations [18] or self-management [19].

Whereas graded exercise therapy (GET)[20], cognitive training [21], and psychological support may be helpful in the rehabilitation of ME/CFS and post-COVID patients, complementary nutraceutical [13] and/or infusion treatment may be beneficial as well. The result of the present study is in agreement with that of a previous trial [14] and suggests both oral and infusion therapy to generate a variable degree of improvement of fatigue. The similarity of results among patients with either ME/CFS or post-COVID syndrome may support the concept of comparable pathogenic mechanisms being involved in both diseases [11, 22]. Since oral and infusion therapy could act in synergism at different steps of the pathogenetic process, it may be favourable to combine both approaches.

Conclusion

Preliminary findings of a real life, two-centre study using an oral nutraceutical together with metabolism stimulating substances, or intravenous infusion of vitamins, minerals and essential amino acids suggests a beneficial effect on fatigue in the majority of patients suffering from ME/CFS or the Post-COVID syndrome. This approach may be considered as an add-on in the totality of rehabilitation treatments.

Acknowledgments

The authors express their gratitude to the members of the nursing staff of the Fertility-Belgium clinic and of the Chronisense outpatient consultation facility.

Conflict of interest

The first author owns the Belgian patent of the fixed combination of 3 ingredients of QALY®. There has been no financial support for the present study.

Addendum

Formulation of QALY ® (Jona Pharma Ltd, Elversele, Belgium).

Each box contains one flask with 60 capsules QALY 1 and one flask with 60 softgels of Qaly 2. Take one of each flaks once per day, after breakfast.

QALY 1: Composition per vegetarian capsule:

Rhodiola rosea 175 mg; Haematococcus pluvialis 97,5 mg; Coenzyme Q10 25 mg; Pinus maritima 21 mg; Zinc 3 mg; Folic acid 200 mcg; Selenium 70 mcg; Vitamin B12 1,25 mcg

QALY 2: Composition per softgel

Lipid extract from Antarctic Krill (Euphausia superba) 500 mg.

References

1. Davis HE, Assaf GS, McCorkel L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine 2021; 38:101019. Doi: 10.1016/j.eclinm/2021.101019.
2. Taquet M, Geddes JR, Husain M, et al . 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. Lancet Psychiatry 2021; 8: 416-427.
3. Fiani B, Coverrubias C, Desai A, et al. A contemporary review of neurological sequelae of COVID-19. Front Neurol 2020; 23 June. Doi: 10.3389/fneur.2020.00640.
4. Iwu CJ, Iwu CD, Wiysonge CS. The occurrence of long COVID: a rapid review. Pan Afr Med J 2021; 38: 65 Doi 10.11604/panj.2021.38.65.27366.eCollection 2021.
5. Huang C; Huang L, Wang Y et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 2021; 397: 220-232.
6. Townsend L, Dyer AH, Jones K, et al. Persistent fatigue following SARS-COV-2 infection is common and independent of severity of initial infection. PloS ONE 15(11): e0240784.
7. Chou SH-Y, Beghi E, Helbok R et al. Global incidence of neurological manifestations among patients hospitalized with COVID-19. A report for the GCS-NeuroCOVID consortium and the ENERGY consortium. JAMA Netw Open 2021; 4(5): e2112131. Dor: 10.1001/jamanetworkopen2021.12131.
8. Nauen DW, Hopper JE, Steward M et al. Assessing brain capillaries in Coronavirus disease 2019. JAMA Neurol published online February 12, 2021.doi: 10.1001/jamaneurol 2021.0225.
9. Douaud G, Lee S, Alfaro-Almagro F, et al. Brain imaging before and after COVID-19 in UK biobank. MedRxiv 2021. Doi 10.1101/2021.06.11.21258690.
10. Manca R, De Marco M, Ince PG et al. Heterogeneity in regional damage detected by neuroimaging and neuropathological studies in older adults with COVID-19: a cognitive-neuroscience systematic review to inform the long-term impact of the virus on neurocognitive trajectories. Front Aging Neurosci 2021 jun3.13646908. Doi: 10.3389/fnagi.2021-646908.eCollection2021.
11. Comhaire F. Treating patients suffering from myalgic encephalopathy/chronic fatigue syndrome (ME/CFS) with sodium dichloroacetate. An open-label, proof of principle pilot trial. Medical Hypotheses 2018; 114:45-48.
12. Aschman T, Schneider J, Greuel S, et al. Association between SARS-COV-2 infection and immune-mediated myopathy in patients who have died. JAMA Neurol 2021 june 11. Doi: 10.1001/jamaneurol.2021.2004.
13. Wang MX, Gwee SXW, Pang J.+ Micronutrients deficiency, supplementation and novel Corona infection. A systemic review and meta-analysis. Nutrients 2021; 13: pii:nu 13051589. Doi:10.3390/nu13051589.
14. Comhaire F, Deslypere JP. News and views in myalgic encephalopathy /chronic fatigue syndrome (ME/CFS): the role of co-morbidity and novel treatments. Medical hypotheses 2020; 134:109444 (pp1-5).
15. Krupp LB, LaRocca NG, Muir-Nash J, et al. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus

erythematosus. Arch Neurol 1989;46(10):1121–3. https://doi.org/10.1001/archneur.1989.00520460115022.

16. Schoonjans F, Zalata A, Depuydt CE, et al. MedCalc: a new computer program for medical statistics. Computer Methods and Programs in Biomedicine, 1995; 48: 257- 262.

17. Comhaire F, Pen J. Boosting health recovery by food supplementation: the case of ME/CFS *versus* Post-Covd-19 syndrome. J Clin Pharmacol Ther. 2021; 2: 75-77.

18. Milic J, Barbieri S, Gozzi K, et al. Metabolic associated fatty liver disease is highly prevalent in the post-acute COVID syndrome. Open forum infectious diseases (Oxford academic) 10 January 2022; Doi: 10.1093/ofid/ofac/ofac003.

19. Brown K, Yahyouche A, Haroon, S et al. Long COVID and self-management. Lancet 2022; 399: 355.

20. Barker-Davies RM, O'Sullivan O, Senaratne KPP et al. The Stanford Hall consensus statement for post-COVID-19 rehabilitation. Sports Med 2020 ; 54: 949-959. Doi: 10.1136/bjsports-2020-102596.

21. Vink M, Vink-Niese A. Could Cognitive Behavioural Therapy Be an Effective Treatment for Long COVID and Post COVID-19 Fatigue Syndrome? Lessons from the Qure Study for Q-Fever Fatigue Syndrome. Healthcare (Basel) 2020; 8:552. doi: 10.3390/healthcare8040552.

22. Maltezou HC, Pavil A, Tsakris A. Post-COVID syndrome: an insight on its pathogenesis. Vaccines 2021; 9: 497 doi:10.3390/vaccines9050497.: