

Research Article

Boosting Health Recovery by Food Supplements: The Case of ME/CFS *versus* Post-Covid-19 Syndrome

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Abstract

Background and objectives: Other than the direct impact of cardiopulmonary sequelae, COVID-19 disease may cause persistent signs and symptoms describes as post-COVID syndrome or long COVID. The clinical presentation and neuroimaging aspects of patients suffering from this condition are remarkably similar to those seen in patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Inflammation, immune disorder and oxidative damage have been documented to cause metabolic deregulation with decreased glycolysis and impaired mitochondrial function.

Purpose of the study: It is suggested that these alterations may be improved by the oral administration of a nutraceutical, Meldonium and sodium dichloroacetate (group designated as “oral treatment”; n=79) or intermittent intravenous infusions of magnesium sulphate together with multivitamins and essential amino acids (group designated as “infusion treatment”, n=18).

Materials and methods: 97 patients suffering from ME/CFS (n=79) or post-COVID syndrome (n=9) were included in a pragmatic prospective open-label trial using either oral or infusion therapy for 1 month, and the effect of treatment was assessed by the Fatigue Severity Scale (FSS).

Results: Upon interim analysis of 97 cases of ME/CFS and/or Post-COVID-19 syndrome therapeutic approach by either the oral or the infusion therapy was found to result in a reduction of the Fatigue Severity Scale (FSS) in two thirds of patients. The quotient of FSS after treatment divided by the FSS before treatment decreased by an average for all 97 cases by 14% within one month, with no difference between oral and infusion therapy (P=0.70), nor between the ME/CFS patient (mean quotient: 0.85, SD: 0.16) and the post-COVID cases (quotient: 0.87, SD: 0.16). Among the successful cases the FSS decreased by an average of 31%.

Conclusion: Preliminary results of the oral and the infusion therapy suggest a similar beneficial effect on fatigue in a substantial proportion of patients suffering from ME/CFS or Post-COVID syndrome. The result should be confirmed in a controlled trial, while the long-term efficacy is presently being investigated in a larger group of patients.

Keywords: ME/CFS; Post-COVID 19; Long-COVID; Nutraceutical; Infusion therapy; Chronic fatigue syndrome; Sodium dichloroacetate; Myalgic encephalomyelitis

Introduction

The majority of medical interventions and health incidents induce important deregulation of the homeostatic equilibrium involving the hormonal, immunological and neurovegetative systems. This occurs after tissue damage due to surgery or traumatism, or caused by infection, as well as during radio-, chemo- or immunotherapy, but may also result from treatment with certain allopathic medications.

Physical and mental recovery after such interventions may be slow and protracted because of persistent oxidative and metabolic damage, as well as stress-related neuro-endocrine imbalance.

In the present paper we suggest that the use of natural substances, such as minerals, vitamins, essential amino acids and plant extracts

combined into certain nutraceuticals [1], together with substances enhancing glucose metabolism, or intravenous infusions containing a high dose of magnesium salt together with multivitamins, may help to boost physical and mental recovery and accelerate the return to healthy body balance. This may be relevant for the post-COVID syndrome [2,3], which shares many characteristics of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) [4].

Materials and Methods

Literature search was performed using digital platforms with specific attention to peer-reviewed publications of clinical trials. Special attention was devoted to the comparison between signs and symptoms of the “post COVID syndrome” also called “long COVID” [5] and ME/CFS. The possible application has been assessed of lessons learned from treating the latter for the benefit of patients suffering from the former [6].

The potential benefit was compared of the nutraceutical food supplement QALY[®] (Jona Pharma, Elversele, Belgium) with that of intermittent intravenous infusion therapy. All cases of ME/CFS were diagnosed by reference centers of Belgian University hospitals using relevant criteria. In addition, the effect of adding sodium dichloroacetate (DCA lab, Vilnius, Lithuania) and of Meldonium (Mildronate[®], Grindeks, Latvia), which facilitate glucose metabolism, have been studied in a prospective open-label pragmatic trial of ME/CFS cases and patients with post-COVID syndrome. Before initiation

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and after one month of treatment patient completed the Fatigue Severity Scale (FSS) [7].

All data were collected and analysed by appropriate methods using the MedCalc programme for medical statistics [8].

Results

Similarity between “long COVID” and ME/CFS

The most common symptoms of the post-COVID syndrome reported in Wuhan, China, are fatigue, sleep disturbance, anxiety and depression [9]. Persistent fatigue was found to be common following SARS-Cov-2 infection, independently from the severity of initial infection [10,11]. In addition, post-exertional malaise and cognitive dysfunction were experienced by many patients [12]. The “fiches SFCRL”, as well as the Belgian “home publications” and the NICE-guideline, report respiratory symptoms and dyspnoea, which may be typical cardiopulmonary sequelae related to the viral pneumonia or its treatment [13], and headache to complete the syndrome [14]. Neurological manifestations among hospitalized COVID-19 patients are associated with higher in-hospital mortality [15], whereas brain imaging revealed post infectious loss of grey matter and impaired blood supply in certain brain regions [16], similar to those seen in ME patients [17]. The mechanisms causing these signs and symptoms [18] are suspected to be comparable to those alleged to be involved with the pathogenesis of ME/CFS [19,20].

Hypothetic pathophysiology

In 2018 the first author has emitted a hypothesis concerning the pathogenesis of ME/CFS and suggested a possible treatment [21]. Hereby the interplay of external factors, including infection, affecting persons with particular genetic predisposition and/or personality characteristics, trigger a disordered immunological [22,23] and inflammatory reaction. This then induces a multitude of deregulations of vital systems, including vascular, neuro-endocrine and metabolic mechanisms. Among the latter disturbed energy production and affected glucose metabolism within the cellular cytoplasm and mitochondria is considered of pivotal importance. So far, it seems that this sequence of events also does occur in the post-COVID syndrome [24,25], with complementary signs and symptoms related to the primary cardiopulmonary, neurological and additional localization of the infection [26].

Treatment options

Therapy targeting bronchopulmonary recovery as well as cardiovascular support is necessary. Also Graded Exercise Therapy (GET) and muscular revalidation should be applied whenever possible and indicated [27]. However, general complaints of exhaustion and fatigue, as well as cognitive and emotional impairment require complementary treatment. In patients suffering from ME/CFS treatment by Cognitive Behaviour Therapy (CBT) does not bring any measurable benefit, nor does it in post-COVID cases [28]. Among available options, hormonal substitution should be considered whenever neuro-endocrine dysfunction results in thyroid, adrenal, or gonadal failure.

Supplementation with vitamins, minerals and essential amino acids probably has a favourable benefit/risk ratio. These may be provided through an oral nutraceutical, or by means of repeated intravenous infusions. Plant extracts with anti-inflammatory and adaptogenic potential may equally be helpful.

Impairment of cellular glycolysis and mitochondrial pyruvate

metabolism can be corrected by sodium dichloroacetate and by Meldonium, which were proven efficacious in patients with ME/CFS, particularly when complemented with antioxidants [29]. The effect of treatment with the oral nutraceutical plus sodium dichloroacetate and Meldonium (referred to as “oral treatment”) was compared with that using repeated intermittent intravenous infusions of high-dose magnesium sulphate combined with multivitamins and essential amino acids (referred to as “infusion treatment”).

Preliminary clinical findings and treatment outcome

A total of 97 patients have been included in the ongoing open-label trial, of which 79 in the group treated with the oral treatment, and 18 have received infusion therapy. The mean age of ME/CFS patients (n=88) was 43.2 yrs (SD: 11.04 yrs), and that of the post-COVID cases (n=9) was 44.9 yrs (SD: 12.4 yrs). Eighty two percent (82%) of patients were female. The average duration of disease of the ME/CFS patients was 9.5 yrs (SD: 5.5 yrs), that of the post-COVID cases was 7 mths (SD: 3.1 mths).

In 66.7% of cases the fatigue severity scale decreased indicating significant improvement of their health situation (P=0.0001) (Figure 1). The average decrease of the fatigue severity scale among the successful cases was 31%, and the average FSS scale in the total population decreased by 14%.

There was no significant difference (P=0.70) between the two treatment approaches regarding the change of FSS, nor between the outcome in patients with ME/CFS (quotient FSS after treatment/FSS before treatment: mean=0.87; SD: 0.16) as compared to the post-COVID cases (quotient FSS after treatment/FSS before treatment: mean=0.85; SD: 0.16).

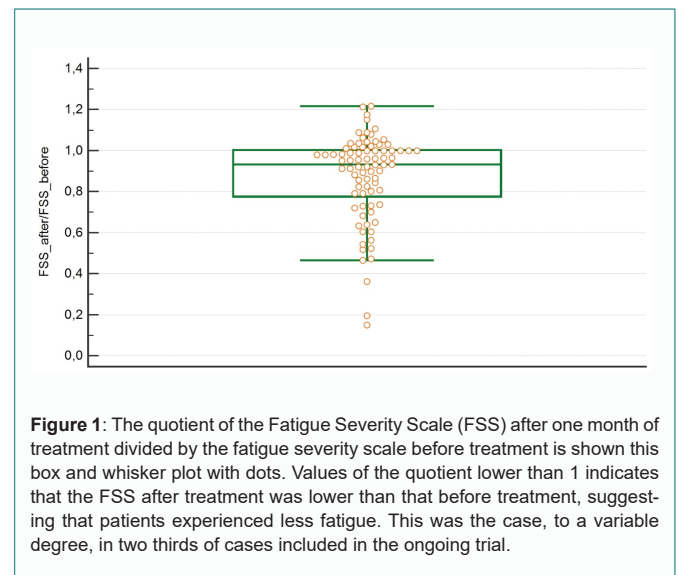


Figure 1: The quotient of the Fatigue Severity Scale (FSS) after one month of treatment divided by the fatigue severity scale before treatment is shown this box and whisker plot with dots. Values of the quotient lower than 1 indicates that the FSS after treatment was lower than that before treatment, suggesting that patients experienced less fatigue. This was the case, to a variable degree, in two thirds of cases included in the ongoing trial.

Discussion

Post-COVID syndrome affects approximately one out of every seven patients after COVID-19 disease, independently of the severity of the initial disease. The syndrome has a strong impact on the quality of life of patients during several months, and some signs and symptoms may persist as long-term sequelae. These include fatigue, post exercise exhaustion, cognitive and emotional disorders, and are comparable to the clinical presentation of ME/CFS.

Though the exact mechanisms of the both diseases remain largely

unknown, it is hypothesized that chronic inflammation, associated with neuro-endocrine and metabolic deregulations are common to both the post-COVID syndrome and ME/CFS. Therefore, treatments used in the latter may be beneficial for the recovery of the former. Preliminary results of an ongoing pragmatic trial, using either the oral or the intravenous approach, tend to sustain this hypothesis. As many as two thirds of patients seem to experience a variable degree of benefit from a short course of treatment.

Conclusion

Aside from sequelae typically related to COVID-19-associated cardiopulmonary inflammation, the general complaints of the post-COVID syndrome are remarkably comparable to those of patients with ME/CFS. We have studied the possible beneficial effects of treatments used for the latter in post-COVID cases. Overall treatment using oral agents or intravenous infusions resulted in similar results in patients suffering from either disease. In fact, approximately two out of every three patients experienced improvement of fatigue within one month of treatment.

Given the small number of cases included and the open-label design, these conclusions should be interpreted with caution, and controlled studies are needed. Also, the potential benefit of protracted treatment should be studied.

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