



Commentary

Differential diagnosis between “chronic fatigue” and “chronic fatigue syndrome”

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Fatigue is a common complaint experienced by most of subjects during lifetime, which affects approximately 30–50% of general population as point prevalence.¹ According to the fatigue-lasting duration, it is classified as acute (<1 month), prolonged (>1 month, <6 months), and chronic fatigue (≥ 6 months), respectively. Acute fatigue is generally disappears after taking a rest or treating the causative diseases, while uncontrolled prolonged and chronic fatigue limit the physical and social activities.² Especially, medically unexplained chronic fatigue is a debilitating status, such as idiopathic chronic fatigue (ICF) and chronic fatigue syndrome (CFS).

On the other hand, to distinguish CFS from chronic fatigue or ICF is very important in clinical practice. The reason is that although patients present fatigue symptom as their main complaint in subjects suffering from chronic fatigue or CFS, CFS is considered as to being in totally different pathologic illness.³ In 2015, US Institute of Medicine (IOM) reported diagnostic criteria for CFS as follows; three mandatory symptoms, a substantial impairment in activities accompanied by fatigue persisting for more than 6 months, post-exertional malaise (PEM) and unrefreshing sleep, and one optional symptom among cognitive impairment or orthostatic intolerance.⁴ Unlike chronic fatigue, CFS has characteristics of brain and CNS symptom and is counted as a complex, multisystem neuroimmune disease. As commonly referred to myalgic encephalomyelitis (ME)/CFS together, brain inflammation is frequently implied in pathology of CFS.⁵

Above facts brought a necessity of new name which distinguishes CFS from chronic fatigue, without the word “fatigue”. IOM therefore recommended “systemic exertion intolerance

disease (SEID)” instead of CFS. The changed conception of CFS is summarized in Fig. 1. The accumulated evidences may indicate the possibility that CFS is not a part of chronic fatigue-related diseases but rather an isolated and different disease with chronic fatigue.^{6,7} The major differences may come from the pathogenesis related to neuroinflammation in brain of CFS patients.^{8,9}

Regarding therapeutics for CFS, a large-scale clinical study (called the PACE trial) results supported the cognitive behavior therapy (CBT) and graded exercise therapy (GET) as more effective therapies improving both fatigue and physical function.¹⁰ They were however abandoned or revised in both the U.S. and UK due to serious criticism by both scientists and patients. The criticisms were for the biases and limitations of their results as well as the unmatched recommendation of GET in contrary to PEM, a main feature of CFS by IOM diagnosis criteria.^{11,12} Another trial using rituximab, anti-CD20 antibody, did not show therapeutic effects, and then no curable therapy exists to date.¹³ Unlike CFS, chronic fatigue generally shows the favorable clinical course. One systemic study revealed the recovery rate of 54–94% chronic fatigue, but <10% of CFS.¹⁴ Thus it is essential and therapeutically effective to stratify chronic fatigue-related diseases, at least chronic fatigue and CFS, for clinical practitioners.^{15,16} Briefly, the differential diagnosis between chronic fatigue and CFS can be produced as show in Fig. 2. This was modified based on the diagnostic algorithm for ME/CFS suggested by IOM in 2015.¹⁷ In this differential diagnosis, the keys are the severity of impaired individual activities due to fatigue, and complaints of PEM, unrefreshing sleep, cognitive dysfunction.

ICF is another group with unexplained chronic fatigue, but does not meet the criteria for CFS. Prevalence of CFS is estimated approximately 1%, while ICF is higher by 10-fold of CFS in general population worldwide including in Korea.^{18–20} Many patients suffering from chronic fatigue traditionally have used alternative medicines including traditional herbal drugs.²¹ There is expecta-

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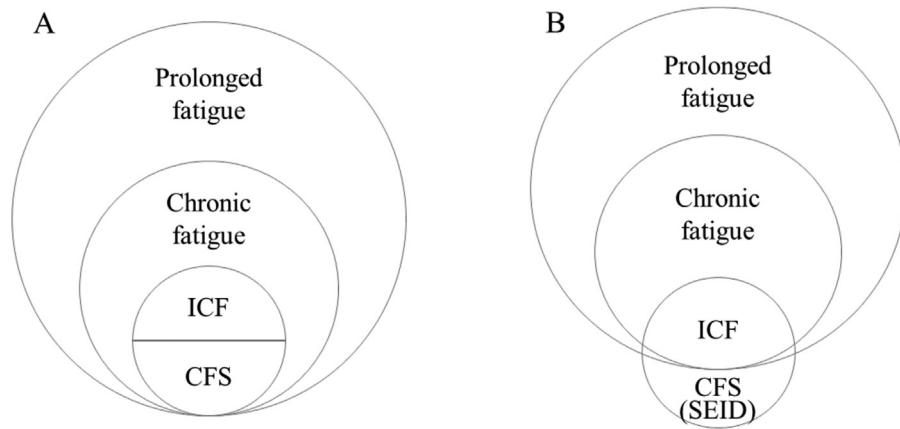


Fig. 1. Chronic fatigue and CFS. The conventional concept (A) and newly changed concept (B) are presented.

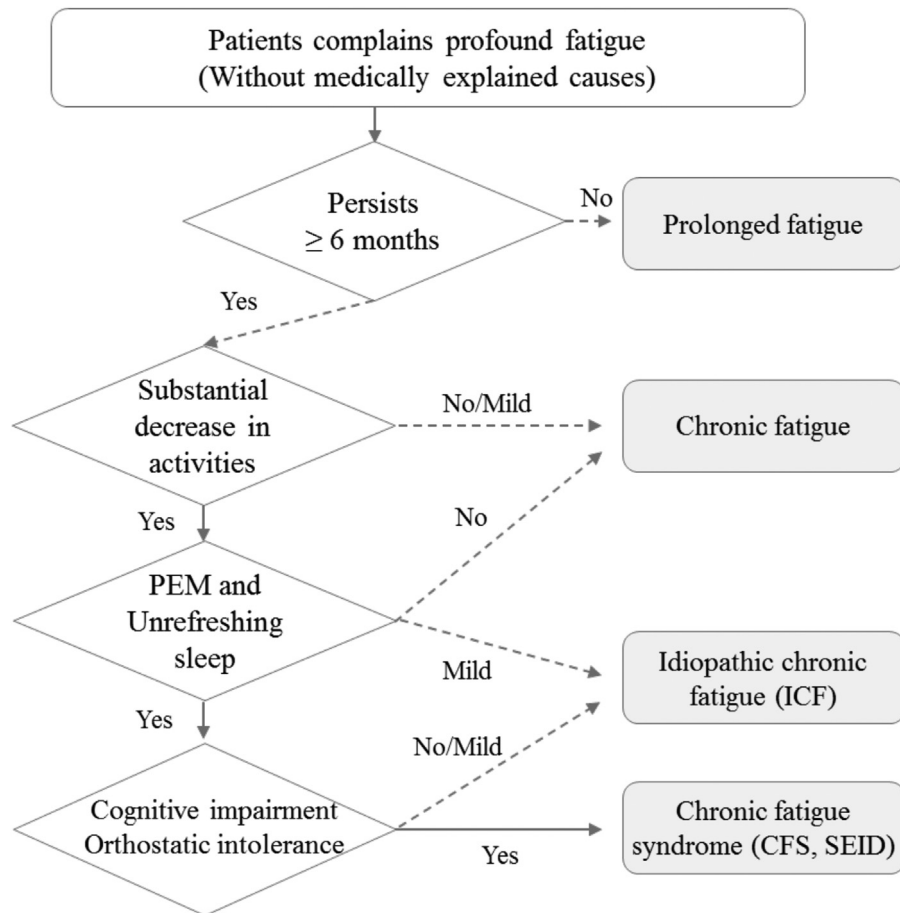


Fig. 2. Suggested algorithm for chronic fatigue, ICF and CFS.

tion that herbal remedies would be a suitable strategy for chronic fatigue-associated disorders in aspect of “multiple compounds and multiple targets” linked to especially CFS treatment. This article hopefully will provide a concise guide to manage patients with chronic fatigue-related complaints.

Conflict of interest

The author declares no conflict of interest.

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