Chronic fatigue syndrome: diagnosis and treatment

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Keywords: symptoms, women,chronic fatigue, illnesses, diagnosis

Abstract

Chronic fatigue syndrome (CFS) refers to marked and prolonged fatigue, for which no indentifiable cause can be found. Despite the presence of extensive symptoms, diagnosis is made when there is profound fatigue, lasting for a duration of six months, or longer. CFS is frequently seen in association with psychiatric illnesses,such as depression and anxiety, but has not been shown to be casually related to any particular psychiatric disease.

Ⓟ Peer reviewed. (Submitted: 2011-08-11. Accepted: 2011-11-04.)© Medpharm
S Afr Fam Pract 2013;55(1):53-55

Introduction

The cause of chronic fatigue syndrome (CFS) remains unknown. Throughout the world, a number of research teams have investigated possible links to a number of infections, including Epstein Barr virus, enteroviruses and poliomyelitis; as well as fungal agents, and, in particular, *Candida albicans*).[1,2] Despite extensive studies, the evidence that CFS is caused by any particular infective agent is equivocal. Nor has it been shown that physical, or mental disease or illness, causes chronic fatigue syndrome. This syndrome occurs more commonly in women, with peak incidence in those in the third and fourth decades of their lives. Despite media references to the condition being more common in middle-income groups, evaluation of the social status of those diagnosed indicates that CFS occurs with equal frequency in all social classes. In general, no forms of treatment are shown to alter the condition's course. The definition of fatigue, accepted by most research groups, is fatigue of new onset, lasting more than six months, with a 50% reduction in activity.

Symptoms

CFS symptoms are muscle weakness and pain, low-grade fever, sore throat, painful lymph nodes in the neck and armpits, exacerbation of fatigue after moderate or strenuous exercise for periods of 24 hours or more, transient pains in a number of joints, and various disturbances of neuropsychological function, including confusion, irritability, poor concentration, and visual changes.[3]

One-fifth of family medicine patients present with fatigue, and one-third of adolescents report having fatigue at least four days per week.[4] Men and women differ in the way they describe fatigue. Men typically say they feel tired, whereas women say they feel depressed, or anxious.[5,6]

Sleepiness is the impairment of the normal arousal mechanism, and is characterised by a tendency to fall asleep. People who are sleepy are temporarily aroused by activity, whereas fatigue is intensified by activity, at least in the short term.[7] Patients with sleepiness feel better after a nap, but patients with fatigue report a lack of energy, mental exhaustion, poor muscle endurance, delayed recovery after physical exertion, and no restorative sleep.

Fatigue may be classified as secondary, physiological, or chronic. Secondary fatigue is caused by an underlying medical condition, and may last one month or longer, but it generally lasts less then six months. Physiological fatigue is an imbalance in the routines of exercise, sleep, diet, or other activity that is not caused by an underlying medical condition, and is relieved by rest. Chronic fatigue lasts longer than six months, and is not relieved by rest.[8]

Epidemiology

The mean age of onset in most series is reported as being 35 years. The majority of cases are said to occur between the ages of 18-60 years. Most studies report a predominance among females, although the ratios vary widely. Seventy-three per cent of patients shown to have CFS were female.[9] The popular perception in the media is that the condition is more prevalent in the middle- and upper-social classes. This is not substantiated by objective analysis. There is a wide variation in the incidence of the disease, with near universal acceptance that the prevalence of the condition is probably higher than reported. This is particularly so for epidemiological studies conducted using the original CDC

criteria, which include the inclusion of suspected cases with psychiatric disease, and also for disease control. Chronic fatigue occurs in all age groups, including children. Women, minorities, and people with lower educational and occupational statuses, have a higher prevalence of chronic fatigue.

On average, in his or her practice, a typical family physician sees two patients who have had fatigue for six months or longer, for which no explanation can be determined.[10] Only two per cent of patients who are chronically fatigued report complete long-term resolution of their symptoms, but 64% show limited improvement. Patients whose symptoms worsen for longer than 24 hours after physical exertion have a poor prognosis.[11,12]

The Centers for Disease Control provides the following diagnostic criteria for CFS:[13]

It is clinically evaluated, unexplained, persistent, or relapsing fatigue, that is:

- Of new or definite onset;
- Not a result of ongoing exertion;
- Not alleviated by rest;
- Results in a substantial reduction in previous levels of occupational, social, or personal activity.

Four, or more, of the following symptoms that persist, or recur, during six, or more, consecutive months of illness, and that do not predate the fatigue:

- Self-reported impairment of short-term memory or concentration;
- Sore throat;
- Tender lymph nodes;
- Muscle pain;
- Multi-joint pain, without swelling or redness;
- Headaches of a new type, pattern, or severity;
- Interrupted sleep;
- Post-exertion malaise (a feeling of general discomfort or uneasiness) lasting more than 24 hours.

Exclusion criteria for CFS are:

- Active, unresolved, or suspected, disease, that is likely to cause fatigue;
- Psychotic, melancholic, or bipolar depression (but not uncomplicated major depression);
- Psychotic disorders;
- Dementia;
- Anorexia, or bulimia nervosa;
- Alcohol, or other substance misuse;
- Severe obesity (body mass index equal to, or greater than, 45).

The University of Oxford's diagnostic criteria are the following:[14]

Severe, disabling fatigue of at least six months' duration that:

- Affects both physical and mental functioning;
- Is present for more than 50% of the time.

Other symptoms, particularly myalgia, and sleep and mood disturbance, may be present.

According to the University of Oxford criteria, the exclusion criteria are:

- Active, unresolved, or suspected disease, likely to cause fatigue;
- Psychotic, melancholic, or bipolar depression (but not uncomplicated major depression);
- Psychotic disorders;
- Dementia;
- Anorexia, or bulimia nervosa.

Misdiagnosis

Whichever definition is being used to define CFS, it should be clearly referenced and substantiated.

Pathogenesis physiology

The mechanisms and pathogenesis of chronic fatigue syndrome are unknown.[15] Research studies have examined, and hypothesised about, the possible biomedical and epidemiological characteristics of the disease, including oxidative stress, genetic predisposition, infection by viruses and pathogenic bacteria, hypothalamic-pituitary-adrenal axis abnormalities, immune dysfunction, as well as psychological and psychosocial factors.[16]

Treatment

Cognitive behavioural therapy (CBT), a form of psychological therapy often used to treat chronically ill patients, is a moderately effective treatment of CFS, that "can be useful in treating some CFS patients".[17-20] Since the cause or causes of CFS are unknown, CBT tries to help patients understand their individual symptoms and beliefs, and develop strategies to improve day-to-day functioning.[21]

Graded exercise therapy

Graded exercise therapy (GET) is a form of physical therapy. A meta-analysis of five randomised trials, published in 2004, found that patients who received exercise therapy were less fatigued after 12 weeks than the control participants, and the authors cautiously concluded that GET shows promise as a treatment.[22] Meta-analyses confirm the effectiveness of regular structured exercise. Four weeks of aerobic, strength, or flexibility training, is associated with improved energy and decreased fatigue.[23] Moderate aerobic exercise, e.g. a daily 30-minute walk, has a more consistently positive impact on fatigue than any other intervention studied.[24] With the exception of patients with depression, pharmacological

therapy (including stimulants) only has a short-term impact.[25,26]

Pacing

Pacing is an energy management strategy that encourages behavioural change, while acknowledging patient fluctuations in symptom severity, and delayed exercise recovery. Patients are advised to set manageable daily activity and exercise goals, and to balance activity and rest to avoid overexertion, which may worsen symptoms.

Many patients perceive that physicians and their staff are more responsive to them when they describe physical symptoms.[27] Fatigue, even when linked with a disease process, is associated with an imbalance of sleep, stress, or psychological coping skills. Balancing these factors reduces reliance on, and is more effective than, medication.[28] Regular visits, i.e. every two weeks to two months, allow physicians to focus on fatigue as a central problem, and circumvent the tendency for these patients to present at urgent care appointments.[29]

Medication

Medications thought to have the potential to alleviate symptoms include antidepressant and immunomodulatory agents.[30] Many CFS patients are sensitive to medications, particularly sedatives, and some patients report chemical and food sensitivities.[31] CFS patients have a low placebo response, especially to psychological-psychiatric interventions, perhaps due to patient expectations.[32]

Conclusion

The major criterion for chronic fatigue syndrome is fatigue lasting for more than six months, in the absence of any other medical, or psychiatric cause thereof. There is no evidence that heredity, genetic, or developmental factors, play a part in the onset of CFS. Nor is there any consistent evidence that the condition is associated with particular types of occupation, lifestyle, mental, or physical stress, or pre-existing psychiatric illness. Treatment of the condition aims to ensure an adequate degree of rest, in conjunction with a supervised course of gentle graded exercises, throughout the course of the illness. Treatment of specific symptoms, such as muscle pains and depression, is recommended as being appropriate, but in the most cases, the use of narcotic and other addictive forms of medication would appear to be inappropriate. A range of other therapies have been tried at various times, but none have shown any particular benefit yet.

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