Editorial

Chronic fatigue syndrome: an overview

Síndrome da fadiga crônica: uma visão geral

Medically unexplained symptoms (MUS) – those lacking identifiable underlying physical disease – are common in all levels of the health care system, and can be associated with severe disability and distress to patients and high cost to health services. Common MUS include pain (including back, chest, abdominal pain, and headache), fatigue, dizziness and ENT (Ear, Nose and Throat) symptoms. Similarly, functional somatic syndromes refer to groups of symptoms lacking disease-specific, demonstrable abnormalities of structure, and are usually defined by specialty or organ system.[1] They include irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, multiple chemical sensitivity, chronic pelvic pain, temporomandibular joint dysfunction and more recently Gulf War syndrome. These conditions overlap in their symptoms, aetiology and treatment; prompting some to point out that the similarities outweigh differences between them and that there is utility in considering them collectively rather than separately.[2]

Chronic fatigue syndrome (CFS) is an exemplar of a medically unexplained syndrome. It is characterised by severe physical and mental fatigue and fatigability, associated with impairment in function, and which cannot be explained by any other medical condition. It also must have persisted for a minimum of 6 months. The core symptomatology is usually accompanied by other symptoms such as muscle pain (which is usually post-exertional and often delayed in onset), joint pain, sleep disturbance, impaired memory, mood disturbance and headache.

The aetiology of CFS is elusive and this uncertainty has fuelled many debates and much controversy surrounding this illness, polarising physical and psychological perspectives. To avoid the often acrimonious nature of such debates, a multifactorial approach has been proposed to explain the pathogenesis of CFS, integrating psychological, social and physical factors into a coherent model. According to this model, aetiology can best be divided into predisposing, precipitating, and perpetuating factors. Hence a person might be pre-disposed to develop CFS by genetic and lifestyle factors. The illness is then triggered by a viral infection such as glandular fever and finally there is a lack of the usual recovery because of the development of certain perpetuating factors.

Perpetuating factors have particular importance in understanding CFS for two reasons. Firstly, many consider that amplification and maintenance of acute or subacute somatic symptoms that happen in our daily lives is a core factor underpinning the perpetuation of many unexplained medical syndromes.[1] We know that acute or subacute fatigue is very common in both the community and those who use health services. The real issue is less why fatigue develops in the first place, but why it persists and causes disability in a lesser number. Secondly, modification of these factors is the main focus of what are the currently most successful treatments for CFS, i.e., cognitive-behavioural therapy and graded exercise therapy.[3]

Several factors have been reported to be associated with the perpetuation of CFS.[4] These include a fixed somatic attribution for the cause of fatigue, which may in turn be associated with fear and avoidance behaviour related to exercise or activity (as noted in chronic pain). The belief that exercise may cause

damage or permanent harm is linked to poor response to treatment. Physical deconditioning as a consequence of reduced activity may in turn contribute towards greater experience of symptoms.

Numerous interventions have been used for the treatment of CFS, often based on very different models of illness and disability. For example, several immunological and virological agents have been used on the basis of a possible immunological or virological explanation for symptoms. Pharmacological agents have also been used, which may be linked to psychiatric (antidepressants) or neuroendocrinological (corticosteroids) models of illness. Behavioural therapies have been employed focusing on the cognitive-behavioural aspects of CFS. Empirically, dietary supplements and alternative medicine have also been tried for the treatment of CFS. However, recent systematic reviews have concluded that at present the only interventions with some reasonable evidence of effectiveness are the cognitive-behavioural therapy and graded exercise therapy.[3] For the others, there is inconclusive or insufficient evidence about the effectiveness. Meanwhile, one strategy that is adopted by some sufferers to reduce symptoms in the short term – namely prolonged rest – seems to be ineffective in the longer term and may even perpetuate or worsen fatigue.

One novel area of research on CFS, which has not received much attention so far, is the placebo response. There are numerous articles that claim that CFS is associated with a high placebo response, with figures ranging from 30% to 50%. This is because CFS is associated in the minds of many with the features that are thought to maximise the placebo effect: highly subjective symptoms lacking identifiable physiologic correlates and a fluctuating nature often influenced by patients' selective attention. Nevertheless, our systematic review with meta-analysis revealed a pooled placebo response of 19.6% in the clinical trials of CFS.[5] This suggests that anecdotal experiences have tended to overestimate the placebo effect in CFS. Researchers have suggested that the response rate in the placebo arm of a clinical trial may not include only the pure placebo effect but also the other components such as spontaneous improvement, regression to the mean, measurement bias and unidentified parallel interventions. A controversial meta-analysis of the trials comparing placebo with no treatment – an attempt to distinguish the pure placebo effect from the other components – has found little evidence that placebos had powerful clinical effects.[6] In other words, the low placebo response in CFS could relate to its natural history. By definition it is a chronic condition with duration of at least six months. Many of the CFS sufferers recruited to the clinical trials have illnesses which have lasted many years and the disorder has a poor prognosis. Given this context, the finding of our meta-analysis may be partly explained by the low rate of spontaneous remission in CFS.

Brazilian data on CFS is scarce, but a preliminary analysis of the epidemiological study we carried out in primary care centres across Sao Paulo revealed an approximate prevalence of 1.5% according to the CDC-1994 (Centers for Disease Control and Prevention) criteria, slightly lower than the prevalence reported by several British primary care studies. We are currently exploring whether the profile of risk factors for CFS in Brazil is similar to that reported in the UK and USA.

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