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Original Article

Gender Differences in Chronic Fatigue Syndrome☆

Mònica Faro,[a,*] Naia Sàez-Francás,[b] Jesús Castro-Marrero,[b] Luisa Aliste,[b] Tomás Fernández de Sevilla,[b] José Alegre[b]

[a] EAP CAP Terrassa Nord, Consorci Sanitari de Terrassa, Barcelona, Spain
[b] Unidad de Fatiga Crónica, Servicio de Medicina Interna, Hospital Universitario Vall d'Hebron, Barcelona, Spain

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ABSTRACT

Background and objectives: Chronic fatigue syndrome (CFS) is a chronic condition that predominantly affects women. To date, there are few epidemiologic studies on CFS in men. The objective of the study was to assess whether there are gender-related differences in CFS, and to define a clinical phenotype in men.
Patients and methods: A prospective, cross-sectional cohort study was conducted including CFS patients at the time of diagnosis. Sociodemographic data, clinical variables, comorbid phenomena, fatigue, pain, anxiety/depression, and health quality of life, were assessed in the CFS population. A comparative study was also conducted between genders.
Results: The study included 1309 CFS patients, of which 119 (9.1%) were men. The mean age and symptoms onset were lower in men than women. The subjects included 30% single men *vs* 15% single women, and 32% of men had specialist work *vs* 20% of women. The most common triggering factor was an infection. Widespread pain, muscle spasms, dizziness, sexual dysfunction, Raynaud's phenomenon, morning stiffness, migratory arthralgias, drug and metals allergy, and facial edema were less frequent in men. Fibromyalgia was present in 29% of men *vs* 58% in women. The scores on physical function, physical role, and overall physical health of the SF-36 were higher in men. The sensory and affective dimensions of pain were lower in men.
Conclusions: The clinical phenotype of the men with CFS was young, single, skilled worker, and infection as the main triggering agent. Men had less pain and less muscle and immune symptoms, fewer comorbid phenomena, and a better quality of life.

Diferencias de género en pacientes con síndrome de fatiga crónica

Palabras clave:
Síndrome de fatiga crónica
Fibromialgia
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RESUMEN

Antecedentes y objetivo: El síndrome de fatiga crónica (SFC) es una entidad que afecta predominantemente a las mujeres, con escasos estudios epidemiológicos en los hombres. El objetivo fue evaluar si existen diferencias de género en el SFC y definir el perfil clínico en el hombre.
Pacientes y método: Estudio de cohorte transversal prospectivo de inclusión de pacientes con SFC en el momento del diagnóstico. Se evaluaron datos sociodemográficos, clínicos, fenómenos comórbidos y evaluación de la fatiga, dolor, ansiedad/depresión y calidad de vida a través de cuestionarios. Se realizó un estudio comparativo de las variables entre género.
Resultados: Se estudió a un total de 1.309 pacientes con SFC, de los cuales 119 (9,1%) fueron hombres. La edad media y de inicio de los síntomas de los hombres fueron menores que en las mujeres. El 30% eran hombres solteros, *vs* el 15% de mujeres, y el 32% tenían un trabajo especializado *vs* el 20% en mujeres. El desencadenante más frecuente fue el infeccioso. El dolor generalizado, las contracturas musculares, los mareos, la disfunción sexual, el fenómeno de Raynaud, la rigidez matutina, las artralgias migratorias, las alergias a fármacos y metales, así como el edema facial, fueron menos frecuentes en los hombres. Se presentó fibromialgia en 29% de los hombres *vs* 58% de las mujeres. Los fenómenos comórbidos fueron

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* Corresponding author.
E-mail address: 34174mfc@comb.cat (M. Faro).

menos frecuentes en los hombres. Las puntuaciones en la función física, el rol físico y la salud física global del SF-36 fueron más altas en los hombres. Las dimensiones sensorial y afectiva del dolor fueron inferiores en los hombres.

Conclusiones: El perfil clínico del hombre fue el de un paciente más joven, soltero, con trabajo especializado y con un desencadenante infeccioso. Los hombres presentaron menor dolor, menor sintomatología muscular e inmune, menor número de fenómenos comórbidos y mejor calidad de vida.

Introduction

Chronic fatigue syndrome (CFS) is a multisystem condition of unknown cause that affects mostly young adults, with ages ranging between 20 and 40 years; the male to female ratio is 1:4 in some series.[1,2] The prevalence is estimated to be between 0.2% and 2.6% of the general population.[3,4] Chronic fatigue syndrome should be suspected in patients with signs and symptoms of inexplicable fatigue that have persisted for at least 6 months and do not improve with rest. The fatigue should be accompanied by 4 or more of the following symptoms: impaired short-term memory and concentration, odynophagia, tender cervical or axillary lymph nodes, muscle pain, arthralgia with no signs of inflammation, headache of a new kind, with different characteristics or severity, unrefreshing sleep, and exhaustion lasting more than 24 h after exercise. All these symptoms should be indicative of a serious functional disorder, as proposed by the international diagnostic criteria established by the Centers for Disease Control (CDC) in Atlanta, Georgia, in 1994.[5] In 2003, a new case definition for CFS was proposed with the intention of excluding psychiatric cases, as was put forward in the Canadian consensus document on CFS.[6] The Canadian criteria are useful and complementary to the CDC criteria, and enable us to study the symptoms in clusters (neurological, muscle, cognitive, neurovegetative and immunological). In 2011, these criteria were updated, and postexertional exhaustion was proposed as a hallmark of the disease.[7] Chronic fatigue syndrome is associated with different comorbid phenomena (sicca syndrome, regional myofascial pain syndrome, anxiety-depressive disorders, plantar fasciitis, degenerative or mechanical disk disease, tendinopathy of the shoulder and fibromyalgia (FM),[8,9] that are more prevalent in CFS patients than in non-CFS individuals.[10] Because of the smaller number of men with CFS—in our experience, the ratio of men to women is 1:9[9]—epidemiological and clinical studies in CFS have basically been carried out in women, and there are few studies on the profile of men with CFS. The differences between men and women in terms of health are partly determined by biological differences that, in addition to reproductive functions, involve genetic, hormonal and neurometabolic factors. At the present time, the most widely accepted hypothesis for the pathogenesis of CFS characterizes it as a genetic-based process, with different triggering factors and subsequent neuroimmunological and immunoinflammatory dysfunction, which would produce the different symptoms observed in patients.[11] There are clinical phenomena in CFS that are also observed in immunoinflammatory diseases that are more prevalent in women (systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis, Sjögren's syndrome and irritable bowel syndrome),[12] with improvement in the symptoms during pregnancy and worsening during menstruation and childbirth. For all the above, it is logical to hypothesize that CFS will affect more women than men, although, at the present time, the clinical phenotype that differentiates men from women has not been defined. The objective of this study was to evaluate the clinical characteristics of men with CFS and compare them with those of women in order to determine whether there are gender differences in patients with CFS and, thus, to establish a differential clinical profile, with implications involving the prognosis and therapeutic management.

Patients and Methods

We studied 1309 patients who were diagnosed with CFS in the chronic fatigue unit of Hospital Universitario Vall d'Hebron in Barcelona, Spain, on the basis of the diagnostic criteria[5] and who, after receiving the diagnosis, agreed to be included in a database. Table 1 shows the inclusion and exclusion criteria for the study. The design was that of a prospective, cross-sectional, cohort study in which patients were enrolled at the time of diagnosis. We evaluated the influence of gender on the clinical presentation of the disease, the presence of associated comorbidities, symptom scores and questionnaires administered. The majority of the patients had been referred to the unit from the first level of care or specialized care, from all of the Spanish autonomous communities, because they showed compatible clinical signs. They were consecutively enrolled from January 2008 to May 2011. The interviews were conducted by 2 internists skilled in the diagnosis of the disease. All of the patients were requested to give their written informed consent and the study was approved by the ethics committee of the Hospital Universitario Vall d'Hebron. Sociodemographic data (age, sex, marital status, profession, employment status and level of education) were gathered for all the participants in the study, and are shown in Table 2. These patients were asked about the features of their fatigue (form and moment of onset, course and duration) and those of their pain (age at onset, length of time with continuous pain). The clinical interview was structured according to clusters of symptoms (muscle, cognitive, neurological, autonomic/neurovegetative and immunological) defined by the Canadian criteria for CFS.[7] It took into account the presence of recurrent headache and sleep disorders (unrefreshing sleep, insomnia, nightmares and poor quality of sleep) and associated comorbidities (restless leg syndrome, sleep paralysis and mild sleep apnea-hypoapnea syndrome). The patients were asked about the existence of FM, defined according to the American College of Rheumatology[13]; sicca syndrome, defined as the presence of mouth dryness plus eye dryness, and demonstrated by the Schirmer test; regional myofascial pain syndrome, defined

Table 1
Criteria for Inclusion and Exclusion of Patients With Chronic Fatigue Syndrome.

Inclusion criteria	1. Patients over 18 years of age of both sexes 2. Patients with CFS according to established diagnostic criteria[5] from the chronic fatigue unit, Hospital Universitari Vall d'Hebrón, Barcelona, Spain 3. Patients who willingly give their written informed consent to participate in the study
Exclusion criteria	1. Patients who are participating in another study of the same or a different nature, or have been within the 30 days prior to inclusion 2. Any individual who the investigator considers to be unable to follow the instructions of the study or complete the self-administered questionnaires 3. Individuals who do not give their written informed consent to participate in the study