FATIGUE AND ITS COORELATION WITH RHEUMATOID ARTHRITIS DISEASE ACTIVITY

A THESIS
Submitted For Partial Fulfillment of the Master Degree in Internal Medicine

BY

Maher Gaber Hafez EL-Yamani
MB.BCh, Faculty of medicine - AL-Azhar University

Under Supervision Of

Prof. Dr. Abd El-Azeim Mohammad EL-Hefny
Professor of Internal Medicine, Rheumatology and Immunology
Faculty of Medicine – Ain Shams University

Prof. Dr. Samah Abd-AL Rahman EL-Bakry
Asst. Professor of Internal Medicine, Rheumatology and Immunology
Faculty of Medicine – Ain Shams University

Prof. Dr. Sohair Helmy EL-Ghonemy
Asst. Professor of Psychiatry, Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University

٢٠١٢

الأجهاد وعلاقته بنشاط مرض الروماتويد المفصلي

رسالة
توطئة للحصول على درجة الماجستير
فى أمراض الباطنة

مقدمة من
الطبيب / ماهر جابر حافظ اليمني
بكالريوس الطب والجراحة – جامعة الأزهر

تحت إشراف
الأستاذ الدكتور / عبد العظيم محمد الحفني
أستاذ الأمراض الباطنية والروماتيزمية والمناعة
كلية الطب – جامعة عين شمس

الأستاذة الدكتورة / سماح عبد الرحمن البكرى
أستاذ مساعد الأمراض الباطنية والروماتيزمية والمناعة
كلية الطب – جامعة عين شمس

الأستاذة الدكتورة /سهير حلمي الغنيمي
أستاذ مساعد الأمراض النفسية
كلية الطب – جامعة عين شمس

كلية الطب
جامعة عين شمس
٢٠١٢

بسم الله الرحمن الرحيم

ACKNOWLEDGEMENT

In the name of Allah, the Most Gracious and the Most Merciful

Alhamdulillah, all praises to Allah for the strengths and His blessing in completing this thesis.

Special appreciation goes to my supervisor, ***Prof. Dr. Abd El-Azeim Mohammad AL-Hefny****, for his supervision and constant support. His invaluable help of constructive comments and suggestions throughout the experiment and thesis works have contributed to the success of this work.*

I am also deeply indebted to ***Prof. Dr. Samah Abd-AL Rahman EL-Bakry*** *for her great support throughout the whole work.*

I would like to express my appreciation to ***Prof. Dr. Sohair Helmy AL-Ghonemy*** *for the tremendous effort she has done in meticulous of revision of this work.*

Last but not least, my deepest gratitude goes to my parents and also to my wife for their endless love, prayers and encouragement.

Maher EL-Yamani

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects individuals in the prime of life and follows a slowly progressive destructive course. The most visible target of the inflammatory process is the synovial membrane; joint pain and swelling, and eventually irreversible damage to cartilage, tendons, and bones dominate the clinical presentation. Disease-related pathological processes are not limited to synoviocytes, tissue-infiltrating immune cells, and other cell constituents of the arthritic joint, but involve the global immune system ***(Singh et al., ٢٠١٢).***

Treatment of RA aims at inducing remission as soon as possible to prevent fatigue, structural damage and disability. This suggests that with the current early and intensive treatment strategy in RA, maintaining the ability to work will become increasingly feasible ***(Kimel et al., ٢٠٠٨).***

Fatigue has been defined in the parenting research literature as extreme tiredness or exhaustion that is not relieved by rest ***(Rychnovsky, ٢٠٠٤).***

It is a frequent and debilitating problem for patients with RA. The prevalence rate of fatigue in patients with RA is quite high, ranging from ٤٢٪ up to ٨٠٪ (due to differences in measurement) ***(Repping-Wuts et al., ٢٠٠٩)***.

In ٢٠٠٦ international consensus agreed that fatigue should be measured in all future studies of RA using a scale validated in RA ***(Kirwan et al., ٢٠٠٧).***

Four scales had some evidence of validation in RA: (١) Multidimensional Assessment of Fatigue (MAF), (٢) Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), (٣) Profile of Mood States (POMS) and (٤) Short Form-٣٦ Vitality scale (SF٣٦). MAF is RA specific ***(Nicklin et al., ٢٠٠٨).***

Turan et al., ٢٠١٠ reported that Fatigue as a major symptom in RA patients, needs to be measured properly with respect to its intensity by appropriate measures, such as MAF. The MAF provides more insight into specific dimensions of fatigue.

Patients with longstanding RA were less likely to improve fatigue and employability after effective treatment than those with early disease. Probably this is due to the fact that structural damage and comorbidity are more important in affecting work disability in late disease, whereas the effect of disease activity on work disability is reversible in early disease ***(Kimel et al., ٢٠٠٨).***

Aim of the Work

The aim of this study is to evaluate the prevalence and severity of fatigue in RA patients and to assess its correlation with disease activity.

Fatigue

Fatigue is defined as “an overwhelming sustained sense of exhaustion and decreased capacity for physical and mental work”. It is described as multidimensional symptom consisting of psychological, physical, cognitive, social and behavioral aspects ***(Repping-Wuts et al., ٢٠٠٩)***.

Epidemiology

Prevalence estimates of fatigue can be influenced by several factors, including varying methods used to classify fatigue, arbitrary cutpoints for scales, shifts over time in diagnostic conventions, population characteristics (inclusion of special populations), and external events ***(White, ٢٠٠٧)***.

Mahfouz et al., ٢٠٠١ estimated fatigue to be the most frequent symptom in Egyptian patients presenting with somatoform disorders.

In a study conducted by ***Okasha*** ٢٠٠٠, fatigue represented ٩٠٪ of the somatic symptoms in a sample of Egyptian patients, depressive disorders represented ٣٢٪ of the inpatient group and ٢٥٪ of the outpatient group. Egyptian patients mask their effect with multiple somatic symptoms, which occupy the foreground, and the affective component of their illness recedes to the background. This may be because of the greater social acceptance of physical complaints than of psychological complaints, which are either not taken seriously or are believed to be cured by rest or extra praying.

In the United Arab of Emirates fatigue prevalence was (males ٣٤,٠٪, females ٣٨. ٢٪) of general particular attenders and depression was strongly associated with fatigue in females only (its prevalence in females was ٤٥,٨٪) ***(McIlvenny et al., ٢٠٠٠)***.

A cross-sectional survey of united states (US) workers found that the two week period prevalence of fatigue to be ٣٨ percent, with an estimated annual cost to employers exceeding $١٣٦ billion in lost productive work time ***(Ricci et al., ٢٠٠٧).***

The prevalence rate of fatigue in Netherlands was up to ٣٦,٤٪ in the general population associated with unhealthy lifestyles or coping mechanisms ***(Van't Leven et al., ٢٠٠٩).***

The Office of Population Censuses and Surveys (the Office for National Statistics) conducted a large community survey in United Kingdom (UK) , in which ٢٧٪ of respondents (a third of women and a fifth of men) reported significant fatigue in the week before the interview ***(Meltzer et al., ١٩٩٥).***

Classifications of fatigue

Fatigue can be classified into categories based on origin, attribution, and duration of symptoms. The origin of fatigue may be central (brain-derived) or peripheral (usually a neuromuscular origin). It may be attributed to physical illness; psychological (e.g., Psychiatric disorder), social (e.g., Family problems), and physiological factors (e.g., Old age); or occupational illness (e.g., Workplace stress). The duration of symptoms may refer to recent fatigue (symptoms lasting <١ month), prolonged fatigue (symptoms lasting >١ month), and chronic fatigue (symptoms lasting >٦ months) ***(Prins et al., ٢٠٠٦).***

Both types of fatigue (***peripheral and central***) can potentially occur in individuals at rest and during vigorous exercise. With individuals in a rested state or performing low-intensity daily activities, ***peripheral fatigue*** is less likely to occur because fuel is readily available and acidosis within the muscle is low ***(Davis et al., ٢٠٠٠).***

Peripheral fatigue results from neuromuscular dysfunction outside the central nervous system (CNS) and relates to impaired neurotransmission in peripheral nerves and/or defects in muscular contraction, due to energy depletion, inflammation, joint abnormalities or muscle wasting ***(Jong et al., ٢٠١٠).***

Central fatigue is characterized by difficulty in initiating and sustaining mental and physical tasks in the absence of motor or physical impairment ***(Friedman et al., ٢٠٠٧).*** It results from alterations or abnormalities in neurotransmitter pathways within CNS ***(Jong et al., ٢٠١٠).***

Fatigue may be classified also as physiologic, acute, or chronic. (a) ***Physiologic 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 with rest. (b) ***Acute fatigue*** is caused by an underlying medical condition. It generally lasts less than six months. (c) ***Chronic fatigue*** lasts longer than six months and is not relieved with rest ***(Brown and Schutte, ٢٠٠٦).***

Etiology

Fatigue, as a symptom, does not occur in isolation. It is important that research measures multiple symptoms simultaneously, in an attempt to define and correlate the constellation of symptoms that may occur with fatigue or may be cofactors in the etiology of fatigue ***(Rieger, ٢٠٠١)***.

I. Rheumatological disorders

Half of SLE patients report fatigue as their most disabling symptom. Psychosocial variables seem to be strongly related to fatigue in these patients ***(Omdal et al., ٢٠٠٣)***.

In the majority of cases the cause of fatigue in SLE is not known. However, it is likely to result from a number of contributing factors, such as disease activity, mood disorder, poor sleep patterns and low levels of aerobic fitness ***(Tench et al., ٢٠٠٠)***.

Fatigue is a common symptom in RA, and interviews

with RA patients have highlighted its importance ***(Ahlmen, ٢٠٠٥)***.

II. Psychiatric disorders

There is a strong association of unexplained chronic fatigue with general psychiatric disorders, mainly depression ***(Wessely et al., ١٩٩٦)***. In an attempt to clarify this association, ***Skapinakis et al*** ٢٠٠٣ examined psychosocial variables and unexplained chronic fatigue through a community survey in UK. A greater prevalence of chronic fatigue syndrome (CFS) in subjects with psychiatric morbidity was found.

III. Neurological disorders

About ٤٠٪ of patients with Parkinson disease report fatigue among their main symptoms, and it still remains even after adjusting for the presence of depression and dementia ***(Beiske and Svensson, ٢٠١٠)***.

Two-thirds of patients reported fatigue after stroke and ٤٠٪ considered fatigue one of the worst sequelae, lasting for some patients for ≥٣ years. A pilot study suggests that fatigue correlates with the location of brain lesions, with a higher frequency in brainstem lesions ***(Staub and Bogousslavsky, ٢٠٠١)***.

Fatigue is also regarded as a common and often debilitating feature of multiple sclerosis, lateral amyotrophic sclerosis, myasthenia gravis, dystonias, and myopathies (***Krupp and Pollina, ١٩٩٦)***.

IV. Hematologic disorders

Fatigue is a cardinal symptom of anemia regardless of cause. Women without anemia but with a ferritin level <٥٠ nanograms/mL report a reduction of fatigue when given iron supplements ***(Verdon et al., ٢٠٠٣)***.

V. Cardiovascular disease

The cardinal symptoms limiting exercise in patients with heart failure are fatigue and/or dyspnea. Fatigue has