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Physiological parameters as a tool in the diagnosis of fibromyalgia syndrome in females: A preliminary study

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ABSTRACT

Aims: Although fibromyalgia (FM) syndrome is associated with many symptoms, there is as yet no specific finding or laboratory test diagnostic of this syndrome. The physical examination and laboratory tests may be helpful in figuring out this syndrome.
Materials and methods: The heart rate, respiration rate, body temperature (TEMP), height, body weight, hemoglobin level, erythrocyte sedimentation rate, white blood cell count, platelet count (PLT), rheumatoid factor and C-reactive protein levels and electrocardiograms (ECG) of FM patients were compared with those of control individuals. In addition, the predictive value of these tests was evaluated via receiver operating characteristic (ROC) analysis.
Key findings: The results showed that the TEMP and the PLT were higher in the FM group compared with the control group. Also, ST heights in ECGs which corresponds to a period of ventricle systolic depolarization, showed evidence of a difference between the FM and the control groups. There was no difference observed in terms of the other parameters. According to the ROC analysis, PLT, TEMP and ST height have predictive capacities in FM.
Significance: Changes in hormonal factors, peripheral blood circulation, autonomous system activity disorders, inflammatory incidents, etc., may explain the increased TEMP in the FM patients. The high PLT level may signify a thromboproliferation or a possible compensation caused by a PLT functional disorder. ST depression in FM patients may interrelate with coronary pathology. Elucidating the pathophysiology underlying the increases in TEMP and PLT and the decreases in ST height may help to explain the etiology of FM.

1. Introduction

Fibromyalgia (FM), which is a chronic pain syndrome, is a disease defined by widespread musculoskeletal pain accompanied by fatigue, sleep disturbance, memory and mood disorders. A subjective feeling of swelling, paresthesia, cognitive disorders, dizziness and weakness are also frequent symptoms of the disease. The etiology of FM remains uncertain.

Though it has many various symptoms, as yet, there is no specific physical examination finding or laboratory test to diagnose a patient with FM syndrome [1]. Because there is no specific test for the diagnosis of FM syndrome, specialists apply subjective tests. The most commonly used diagnostic tests are the 1990 American College of Rheumatology (ACR) Fibromyalgia Diagnostic Criteria and the 2010 ACR criteria, which represent a revised version of the criteria established in 1990 [2,3]. In these tests, patients are assessed for the criteria, and FM is diagnosed according to a certain score. In the 1990 ACR FM criteria, specialists need to explore tender points to find scores. The aim of the 2010 ACR FM criteria was to simplify FM diagnosis, such that a tender point examination would not be required. Another objective of the 2010 ACR criteria was to identify the significance of perceived cognitive impairment, fatigue, and sleep disturbance, or other non-pain symptoms of the disease, when it comes to making a diagnosis. However, up to 25% of patients diagnosed FM syndrome satisfy neither the 1990 or 2010 ACR classification criteria. Because inflammatory and other non-somatoform disorders with pain have been excluded, the 2010 ACR classification criteria cannot be applied to patients with systemic

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lupus erythematosus, rheumatoid arthritis, or other conditions [4]. Scientists are still working toward providing much more sensitive FM tests than the 2010 ACR criteria [5]. If specific parameters for FM syndrome can be found, they may replace subjective tests; more specific and sensitive new diagnostic criteria could be created using such parameters.

Identifying possible differences in FM may also be helpful in understanding the etiology of the disease. We hypothesized that the physical examination and laboratory tests that can be easily applied in clinics may be different for FM patients compared to control subjects. In the present study, we aimed to compare parameters with a control set of FM patients. Frequently observed characteristic properties in FM syndrome can be a good starting point in searching for parameters specific to FM.

Autonomous neural system disorders have frequently been observed in FM, such as sympathetic hyperactivity, para-sympathetic hypoactivity and a decline in the sympathetic response to different stimulants [1]. Distorted autonomous system activity might affect the operation of the cardiovascular and pulmonary system, thereby changing the heart rate (HR) and the respiration rate (RR). Similarly, it might alter the microcirculatory circulation of the autonomous neural system and sweating functions, thereby also changing the body temperature (TEMP). Some studies have reported an increase in the HR of FM patients [6,7]. Moreover, one study mentioned a decrease in TEMP on FM patients' tender points [8]. However, there is no consensus in the literature on the results of other studies conducted on such parameters [9–13].

Distorted autonomous system activity might also affect electrocardiogram (ECG) results. ECG changes in patients with FM syndrome have not been demonstrated extensively in the past. Recent studies show us that FM syndrome can be associated with heart trouble [14,15]. However, in these studies, detailed ECG analysis was not performed, and probable ECG changes were not shown. If there is any heart trouble in FM syndrome patients, that can be seen by analyzing ECGs.

In FM syndrome, the hemoglobin (Hb) level, erythrocyte sedimentation rate (ESR), white blood cell count (WBC), platelet count (PLT), rheumatoid factor (RF) level and C-reactive protein (CRP) level are expected to be within the normal range of values accepted for healthy individuals [1]. FM can be confused with several other medical conditions, including infections, hormonal and inflammatory diseases in which most of these parameters are not within the normal range. If such parameters are not within the normal range of values, the patients may be deemed to have a disease other than FM. Indeed, in the literature, we have not identified any study indicating that such values are high or low in FM patients. Even if these values in FM patients were within the range of values accepted for normal individuals, there might be differences in a good comparison made between FM patients and control subjects.

2. Method

We received approval from Mugla Sitki Kocman University Scientific Research Ethics Committee for this study. Participants provided their written informed consent to participate in this study.

In our study, the following parameters that are taken into consideration during the physical examination and laboratory tests that are frequently applied in rheumatology clinics were investigated in FM patients: HR, RR, TEMP, height, body weight, Hb, ESR, WBC, PLT, RF and CRP levels and ECG. Other tests that are not frequently used and are difficult to apply have not been included in the study.

Female patients from 24 to 52 years old attending the Physical Medicine Clinic at the Faculty of Medicine, Süleyman Demirel University were chosen as subjects. Patients diagnosed with FM for the first time were selected as the FM group ($n = 30$), and an age-matched control group made up of healthy people attending the same clinic were selected as the control group ($n = 30$). 2010 ACR Fibromyalgia Diagnostic Criteria were chosen to identify patients as having a FM syndrome [3].

Control group made up of people who need to undergo a check-up, for example; driving license, health insurance, travel visa or gun license. Therefore, specialists in internal medicine, neurology, general surgery, orthopedics, psychiatry, ophthalmology and otorhinolaryngology performed examination and laboratory tests to clarify whether they have any disease. According to results of these specialist physicians and our results, if anyone pass this medical examination, we accept them healthy for our study.

Those with cardiovascular, neurological, or any other diagnosed disease, as well as those who had taken medication in the past 10 days for any reason were not included in the experiment. These individuals were excluded because the parameters that we wanted to measure can be altered by medication or disease (for example, in the case of a cold, temperature can increase; with diabetes, weight and BMI can decrease; beta-blocker medication can decrease HR). None of the subjects received any dietary restrictions.

During the study, the same devices were used for the measurement of all parameters. A Powerlab 8/30, Bridge Amp, Dual BioAmp tools and a LabChart 7 Pro software compatible piezo-electric pulse transducer, a piezo-respiratory belt transducer and a temperature probe (all from ADInstruments, Castle Hill, NSW, Australia) were used for evaluating the HR, RR and TEMP. An examination room of the hospital was allocated to perform data collection and psychological testing. The room temperature was kept between 22 and 24 °C. The piezo-electric pulse transducer was belted to the second digit of the left hand, the piezo-respiratory belt transducer was belted to the thoracic cage, and the temperature probe was belted to the inside of the right arm. To obtain DII records in the ECG, a negative electrode (−) was fixed to the subject's right arm, a positive electrode (+) was fixed to the subject's left foot, and a neutral electrode (e) was fixed to the subject's right foot. To obtain noiseless ECG recordings, filters suitable for the software were selected (the settings were Range = 500 μV; Sampling rate = 1000 Hz; Single-ended = checked; Mains Filter and 50 Hz Notch filter selected; High pass = 0.3 Hz; and Low pass = 100 Hz). Care was taken to ensure that the skin surface to which the transducers were belted was not a tender point. The subjects then rested in a reclining position for 15 min. Recordings were then taken for 5 min with the subjects' eyes closed. The recordings were analyzed with the LabChart 7 Pro software, and an average value was taken for each parameter (ECG calculations are shown in Fig. 1).

Subjects were seated on a blood sampling chair after the recording. The venous blood samples of the subjects were collected from the forearm collective venous blood vessels. For Hb, WBC and PLT measuring EDTA-containing tubes, for RF and CRP measuring clot activator with gel tubes, and for ESR measuring sodium citrate-containing tubes were used.

Hb, WBC and PLT were measured with a Mindray BC-5500 Autohematology Analyzer (Shenzhen, China) device; the RF and the CRP levels were measured with a Beckman Coulter Immage Immunochemistry System (Fullerton, California, USA) device and the ESR was measured with the Greiner Bio-One Sed Rate Screener 100 (Kremsmünster, Austria) device, with original reagents.

The height and body weight were measured with the ELW-200 (Saglam, Istanbul, Turkey) scale. The body mass index (BMI) was calculated as (body weight / height^2) $*$ 100.

Before the experiment, to avoid type I and II errors, we performed sample size calculations, using GraphPad StatMate 2.0 (Windows 8.1) software (GraphPad Software Inc., San Diego, CA, USA). In order to have minimal significant intraclass correlation coefficient (ICC) value of 0.60 (1-$\beta = 0.80$; $\alpha = 0.05$), a minimum of 27 subjects was required. An n value of 30 persons for each group was accepted as suitable. After the experiment, post hoc power analysis was performed using the same software. For the statistical analysis, the values obtained from each