Fibromyalgia: its prevalence in haemodialysis patients and its relationships with clinical and laboratory parameters

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Abstract
Objective. Our aim was to determine the prevalence of fibromyalgia syndrome (FS) in chronic haemodialysis (HD) patients and to identify possible links between FS and various clinical and laboratory parameters.

Methods. We studied 122 chronic HD patients and 89 healthy age- and sex-matched controls, classified according to the American College of Rheumatology (ACR) classification criteria for FS. Age, sex, causes of renal failure, length of time on dialysis and marital status were recorded, and questions were asked about symptoms related to FS. All subjects completed the Fibromyalgia Impact Questionnaire (FIQ). Laboratory data obtained in the preceding 6 months were re-evaluated.

Results. Nine (7.4%) of the 122 HD patients and four of the 89 control subjects (4.5%) fulfilled the ACR criteria for definite FS ($P = 0.56$). The mean ages of the subjects who had definite FS and those who did not were similar. Most of the subjects diagnosed with definite FS were female (11 out of 13). The HD patients had higher FIQ scores than the controls, regardless of FS diagnosis. Among the HD patients, those with definite FS had a significantly higher mean FIQ score than all the other HD patients combined. In the all HD patients group, fatigue, irritable bowel syndrome and personal histories of depression were correlated with FS, whereas duration of HD, aetiology of renal failure, laboratory parameters and hepatitis B or C virus infection were not.

Conclusion. The prevalence of FS appeared to be similar in chronic HD patients and the general population; also, FS-related symptoms appear to be similar in HD patients and the general population who have FS. No laboratory parameter was correlated with frequency of FS.

Keywords: fibromyalgia; haemodialysis

Introduction

Fibromyalgia syndrome (FS) is characterized by widespread chronic pain in the musculoskeletal system, and also includes non-musculoskeletal clinical features, such as fatigue, anxiety, sleep disturbance, headache and irritable bowel syndrome [1,2]. In 1990, the American College of Rheumatology (ACR) announced classification criteria for the diagnosis of FS that were based on the combination of widespread chronic pain and detection of specific ‘tender points’ on palpation. These proposed criteria are chronic widespread pain of at least 3 months duration and tenderness at $\geq 11$ of 18 specific tender points. For the diagnosis of FS, widespread pain is defined as four-quadrant pain (right side, left side, and upper and lower body) and pain in the axial skeleton (neck and back).

FS is relatively frequent in the general population (prevalence between 0.5 and 6%), and affects females more often than males [3]; its prevalence is reported to increase with age [3]. The aetiology of this disease is unknown, but several aspects of its pathogenesis are being investigated, and this research is shedding light on the possible pathophysiological mechanisms underlying it [4–7].

Rheumatic disorders are major complications of renal disease, and approximately two-thirds of haemodialysis (HD) patients develop musculoskeletal problems and that incidence rises with time on dialysis [8–10]. The current literature contains no reports of FS prevalence in patients with end-stage renal disease (ESRD) on HD.

The aim of this study was to determine the frequency of FS in patients on HD, and to assess whether this syndrome is associated with any of the following variables: age, sex, various laboratory parameters, duration of HD, cause of renal disease and presence...
of hepatitis B virus (HBV) or hepatitis C virus (HCV) infection.

**Subjects and methods**

We investigated 122 patients with ESRD who had undergone 4h HD sessions with cuprophane membranes three times weekly between September 1 and December 31, 2002. A control group of 89 age- and sex-matched healthy volunteers who were relatives of the patients were also included. The study was done after being granted approval by the local ethics committee.

FS was diagnosed according to the ACR classification criteria detailed above [1]. Subjects were asked if they had experienced chronic widespread pain (see definition above) for at least 3 months. Each subject was also examined for tenderness at 18 tender points by digital palpation. One score point was assigned for each tender point noted; thus, each individual’s tender point score was between 0 and 18. Based on the findings, each individual was assigned to one of three groups: group 1 (‘definite fibromyalgia’) subjects had a combination of chronic widespread pain and tenderness at ≥11 of the 18 tender points; group 2 (‘probable fibromyalgia’) subjects had a combination of chronic widespread pain and tenderness at a minimum of six, but not more than 10, tender points [13]; and group 3 (‘normal’), which comprised the subjects who did not meet the criteria for either group 1 or group 2.

Each individual’s age, sex and marital status were recorded. Subjects were also asked about symptoms of paraesthesia, restless leg syndrome, sleep disturbance, irritable bowel syndrome (according to Roma criteria [11]), and personal and family histories of depression. For each HD patient, the aetiology of renal failure and duration of HD were noted.

Each subject also completed the Fibromyalgia Impact Questionnaire (FIQ). This self-administered questionnaire has been validated for use in people with FS [2]. It measures physical function, work status and overall well being, and also contains six separate visual analogue scales (VAS) for pain, sleep, fatigue, morning stiffness, anxiety and depression. After completion of this questionnaire, a total score, between 0 and 100, is calculated for each responder by normalizing certain items and summing all the VAS scores. The highest total score possible is 100, with a higher value indicating more severe adverse impact on quality of life. In this patient group, the FIQ has been shown to be the most accurate way to measure the effect of pain on the individual’s daily activities [12].

For the HD patients, the results of laboratory tests that had been done monthly in the previous 6 months were reviewed, and the mean values from these tests were used for statistical correlation analyses. Serum calcium, phosphorus and alkaline phosphatase were measured by enzymatic colorimetric testing (Stanbio Laboratory, Boerne, TX). Serum albumin and alanine aminotransferase were measured in a clinical chemical analyser (Roche Modular, Roche Diagnostics, Indianapolis, IN). Serum parathyroid hormone and thyroid-stimulating hormone were measured by microparticle enzyme immunoassay (Abbott TDX System, Abbott Laboratories, Abbott Park, IL). Serum C-reactive protein was measured nephelometrically. Serological testing for HBV surface antigen and antibodies to HCV was performed using microparticle enzyme immunoassay (Abbott-AxSYM System) and appropriate assays manufactured for the system (Abbott-AxSYM HBsAg version 2 and HCV version 3.0 assays).

**Statistical methods**

Analyses were done to identify correlations between FS and the above-mentioned laboratory and clinical parameters. The Statistical Package for the Social Sciences (SPSS, version 11.0, SSPS Inc., Chicago, IL) was used to process and statistically analyse all data. Group results are presented as the mean±SD. *P*-values <0.05 were considered statistically significant. The χ² and Kruskal–Wallis tests were used to assess for correlations between FS and measurable variables. Relationships between the presence of FS and symptoms such as joint swelling, paraesthesia, restless legs, sleep disturbance, headache, irritable bowel symptoms, and personal and family histories of depression were statistically evaluated using Fisher’s exact test.

**Results**

Table 1 shows demographic data for all 211 subjects and, for the 122 patients on chronic HD, lists the aetiologies of ESRD and the distribution of definite FS patients according to the aetiology of ESRD. Table 2 shows the prevalence of FS in the HD and control groups. Of the 122 HD patients, nine (7.4%) met the ACR criteria for FS, eight (6.6%) patients had probable FS and the remaining 105 (86%) individuals were defined as ‘normal’. The prevalence rates of FS and probable FS in the control group were 4.5% (four patients) and 3.4% (three patients), respectively.

The mean age of the 13 (total) subjects with definite FS was not significantly different from that of the remaining subjects (*P* = 0.3). There was also no statistical age difference between the HD patients with definite FS and the control subjects with definite FS (*P* = 0.35). Females predominated significantly in the subgroup with definite FS (*P* = 0.019).

The mean FIQ score in the HD group overall was significantly higher than that in the control group (*P* = 0.014). The mean FIQ score for the controls with FS was statistically similar to the mean for the HD patients with FS (*P* = 0.15). Within the HD group, the individuals with definite FS had a significantly higher mean FIQ score than the individuals who did not have definite FS (*P* < 0.01).

FS-related clinical features, such as fatigue, irritable bowel symptoms and a personal history of depression, were significantly more common in the HD patients with definite FS than in the HD patients without definite FS. Sleep disturbance, paraesthesia and restless legs were more common in the HD patients with definite FS; however, none of the differences for these parameters was statistically significant. There were no statistically significant correlations between definite FS and a family history of depression, duration of HD, aetiology of renal failure, or HBV or HCV infections. The laboratory parameters that were
Fibromyalgia in haemodialysis patients

Table 1. The demographic characteristics of the haemodialysis (HD) and control groups

<table>
<thead>
<tr>
<th></th>
<th>HD patients (n = 122)</th>
<th>Definite FS in the HD group</th>
<th>Controls (n = 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>44.5 ± 15.7</td>
<td>43.9 ± 14.5</td>
<td></td>
</tr>
<tr>
<td>Sex (female/male)</td>
<td>55/67</td>
<td>45/60</td>
<td></td>
</tr>
<tr>
<td>Cause of renal failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>41 (33.7%)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>17 (13.9%)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>11 (9%)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Vesico-ureteral reflux</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>9 (7.4%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Amyloidosis due to FMF</td>
<td></td>
<td>7 (5.7%)</td>
<td></td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>7 (5.7%)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Nephrolithiasis</td>
<td>5 (4.1%)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>14 (11.5%)</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

FMF = familial Mediterranean fever; FS = fibromyalgia syndrome.

Table 2. Prevalence of fibromyalgia syndrome in the haemodialysis and control groups

<table>
<thead>
<tr>
<th></th>
<th>HD patients (n = 122)</th>
<th>Controls (n = 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS</td>
<td>9 (7.4%)</td>
<td>4 (4.5%)</td>
</tr>
<tr>
<td>PFS</td>
<td>8 (6.6%)</td>
<td>3 (3.4%)</td>
</tr>
<tr>
<td>Normal</td>
<td>105 (86%)</td>
<td>82 (92%)</td>
</tr>
</tbody>
</table>

FS = fibromyalgia syndrome, PFS = probable fibromyalgia syndrome.

studied were also not statistically correlated with FS (Table 3).

Discussion

The reported prevalence rates for FS range from 0.5 to 6% [3], and females are affected more frequently than males. Work by Wolfe and co-workers [3] in a random sample of 3006 adults revealed FS prevalence rates of 3.4% in women and 0.5% in men. In the current study, the prevalence rates of this condition in the HD and control groups were statistically similar (7.4 vs 4.5%, respectively; P = 0.56). In accord with the literature, we found that FS was more frequent in females, with rates of 10.4% (11 out of 106) in women and 1.9% (two out of 105) in men.

The above-mentioned study by Wolfe and co-workers also showed that the prevalence of FS increases with age, and noted that the highest rates are seen in those between the ages of 60 and 79 years [3]. They found a 2% prevalence rate of FS in individuals aged 30–39 years, whereas the rate in the group aged 70–79 years was 7.4%. Of our 13 subjects with definite FS, seven (54%) were in the 31–50 age group, two were younger than 30 years, three were in the 51–59 age group, and only one was older than 60 years. In contrast to the literature, only one of the 37 total subjects in our study who were older than 60 years had definite FS. However, the number of subjects we studied was relatively low, so it is difficult to have a clear indication of the prevalence of FS in the different age groups. The mean age of the nine HD patients with definite FS was not significantly different from that of the four control subjects with this diagnosis (P = 0.35).

In some cases, the subject did not fulfill the ACR criteria for definite FS, but we felt the person could not be considered unaffected. Middleton and colleagues have defined cases of this type as ‘probable’ FS, and we used this term in our study [13]. However, we included the patients with ‘probable FS’ in the ‘normal’ group for statistical analysis, because most papers published on FS have not treated this group separately in the analyses.

Rheumatic disorders are frequent complications of renal disease, and most data indicate that the risk of such complications increases with time on HD. To date, no reports have published the prevalence rates of FS in HD patients. As detailed above, in our study, FS rates were similar in HD patients and control subjects. Each of our subjects completed the FIQ. The mean FIQ score in all of the HD patients was higher than the mean score in the control group overall. This is not surprising, because the questionnaire items are not specific for FS; they also reflect general health status and factors that affect daily activity. When the FIQ results for the 13 subjects with definite FS were analysed, there was no significant difference between the mean scores of the nine in the HD subgroup and the four among the controls. Within the HD group, the patients with definite FS had higher FIQ scores than those without definite FS (P < 0.01). These results indicate that FS causes additional functional disability and has distinct negative effects on general health, even within chronic disease states such as ESRD.

The many features that frequently accompany FS include fatigue, sleep disturbance, irritable bowel, paraesthesia, psychological problems, restless legs and a personal history of depression [5,14,15]. We found that the frequencies of fatigue, sleep disturbance,
paraesthesia, depression and restless legs were higher in HD patients than in control subjects, regardless of whether or not the individual was diagnosed as having FS. This is not surprising, since musculoskeletal and psychological problems are common in patients on HD, and are related to metabolic and neurological disorders [16–19]. Within the HD group, fatigue and irritable bowel symptoms were significantly more frequent in the definite FS subgroup. These results are in line with those of other studies that have compared these symptoms in FS patients in study populations without chronic systemic illness [3,14]. We also detected a correlation between a personal history of depression and the presence of FS in HD patients—this too is supported by the literature [15]. The analysis revealed no statistical link between FS and history of depression in family members. We did not use a standard scale or clinical criteria to diagnose depression; only information in medical records was used to establish this diagnosis. Most of the 13 HD patients and control subjects with definite FS had received professional help for depression and had taken medication for it.

Currently, there are no special laboratory tests to diagnose FS. We tested for correlations between FS and a range of laboratory parameters, including markers for hepatitis. Analysis of the HD patient data revealed no significant relationships between definite FS and serum levels of C-reactive protein, alanine aminotransferase, albumin or thyroid-stimulating hormone. These results show that neither chronic inflammatory state nor malnutrition are associated with FS in the HD patient group. We also detected no association between definite FS and serum levels of parathormone, alkaline phosphatase, calcium or phosphorus in the HD group. This is surprising, because most musculoskeletal problems in ESRD patients can be attributed to altered metabolism of calcium, phosphorus and parathormone.

**Conclusion**

In this study, the prevalence of definite FS in the HD group was 7.4%, which was similar to that in the healthy controls. In the HD group, definite FS was correlated with fatigue, irritable bowel symptoms and a personal history of depression, but not with the aetiology of ESRD, duration of HD or any of the laboratory parameters investigated. Our sample was relatively small; however, the results suggest that the prevalence of FS in patients on chronic HD is similar to that in the general population, and that the symptoms that accompany FS in HD patients are similar to those that affect FS patients in the general population. None of the laboratory parameters was correlated with FS, and this syndrome does not seem to be connected with chronic inflammatory illness, malnutrition or any disorders of calcium or phosphorus metabolism.

**References**


*Conflict of interest statement.* None declared.