

EVALUATION OF HEADACHE TREATMENT IN PATIENTS WITH FIBROMYALGIA

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Abstract. *Fibromyalgia (FM) is characterized by chronic widespread pain lasting for a minimum of three months and pain at mechanical pressure in at least 11 of the 18 tender points. Four treatment groups with FM patients and a healthy control group were followed within 3 months in the Clinic of Rheumatology, Sofia. The accompanying clinical symptoms were evaluated by a 5-point grading system. These results are useful for the everyday clinical practice and treatment of fibromyalgia.*

Key words: *fibromyalgia, headache, clinical manifestations*

INTRODUCTION

Hippocrates described diffuse musculoskeletal pain. Since the mid-20th century, scientists have been looking for a connection between diffuse muscle pain, headache, fatigue, unrefreshing sleep, and mental stress [7]. In 1990, the American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia (FM) were introduced. FM is characterized by generalized pain persisting for more than 3 months, which is spontaneous, diffuse, prolonged, and unexplained; pain with mechanical pressure in 11 of 18 points. The pain threshold at these points should be less than 4 kg/cm² pressure [9]. The clinical picture of FM is very diverse – headache, which may be tension-type or true migraine (40% of cases), changes in circulation (Raynaud's syndrome), vascular play, dermatographism, palpitations accompanied by anxiety up to cardiac neurosis, skin rashes, decreased ability to concentrate, decreased vision and hearing, dizziness and nausea, profuse sweating, myalgias, arthralgias with a feeling of swelling of the fingers, myoclonic tremor of the limbs [4]. To this day, measuring the chronic pain threshold with a dolorimeter in combination with assessing the accompanying symptoms of fibromyalgia remains an objective method for diagnosing this disease.

CLINICAL CONTINGENT AND METHODS

The present study is prospective and was performed at the Rheumatology Clinic of the University Hospital "Sv. Ivan Rilski" and the Medical Center "Focus 5", Sofia. The studied patients were divided into 4 therapeutic groups, treated with different medications – trazodone, pregabalin, mydocalm and tizanidine for 3 months, 1 group of untreated patients, and 1 control group of healthy individuals [1]. Table

1 presents the demographic characteristics of the treated patients, and Table 2 presents the demographic characteristics of the healthy subjects. The patients did not differ from the healthy subjects in terms of demographic characteristics.

Table 1. Demographic characteristics of patients with FM

Demographic characteristics	Values
Number of patients	97
Number (% women)	86 (88,5%)
Female:male ratio	8:1
Age (years), mean±SD (standard deviation) rank	20-71; 46.5±11.4
Duration of FM (years)	1-44; 6.1±8.68
Mean age at onset of complaints (years) ± SD (standard deviation) rank	19-63; 40.5±11.3

Table 2. Demographic characteristics of healthy individuals

Demographic characteristics	Age
Number of healthy	39
Number (% women)	38 (97.44%)
Age (years), mean ± SD (standard deviation) rank	21-70; 45.8±13.73

METHODS

1. Anamnesis and examination of the patients. In the anamnesis of the patient, special attention was paid to the duration of FM, the etiological factors for the occurrence of FM, the social employment and education of the patient, the presence of fatigue, tension-type headache, sleep disorders and autonomic disorders.

2. Measurement of pain threshold at 18 points for the diagnosis of FM.

The change in pain threshold at all painful points was precisely monitored with dolorimetry, measured in kg/cm² with a Fisher dolorimeter.

3. Assessment of the accompanying clinical complaints of the patients – sleep disorders, headaches, autonomic disorders, and presence of diffuse pain. The assessment is carried out by an independent answering of questions about all accompanying symptoms, which are assessed on a 5-point scale.

4. Paraclinical methods – exclude active inflammatory and systemic disease by examining laboratory parameters

5. Statistical methods – ANOVA, factor analysis, correlation analysis, Paired Samples Test. Statistical processing of the data was performed using the statistical software program SPSS-13.0 [1].

RESULTS

1. Results of headache dynamics.

Graph 1 presents the results of headache dynamics (tension type) – reduction in its intensity after a 3-month treatment period in 4 therapeutic groups, compared with a group of healthy individuals.

The best success was achieved with tizanidine – the reduction in headache intensity was 1.01, 36%, $p>0.05$ (before treatment – arithmetic mean $\pm$ standard deviation 2.81 ± 1.69 , min. 0, max. 5, after treatment 1.8 ± 1.64 , min. 0, max. 4); pregabalin – 0.8, 29.7%, $p>0.05$ (before treatment 2.69 ± 1.67 , min. 0, max. 5, after treatment 1.89 ± 1.53 , min. 0, max. 4); trazodone – 0.8, 21.9%, $p>0.05$ (before treatment 3.64 ± 1.09 , min. 0, max. 5, after treatment 2.96 ± 0.93 , min. 0, max. 4); mydocalm – 0.44; 21.5%, $p>0.05$ (before treatment 2.04 ± 1.65 , min. 0, max. 4, after treatment 1.6 ± 1.43 , min. 0, max. 3). The arithmetic mean value of the headache intensity score in the control group was 0.897, and in the groups

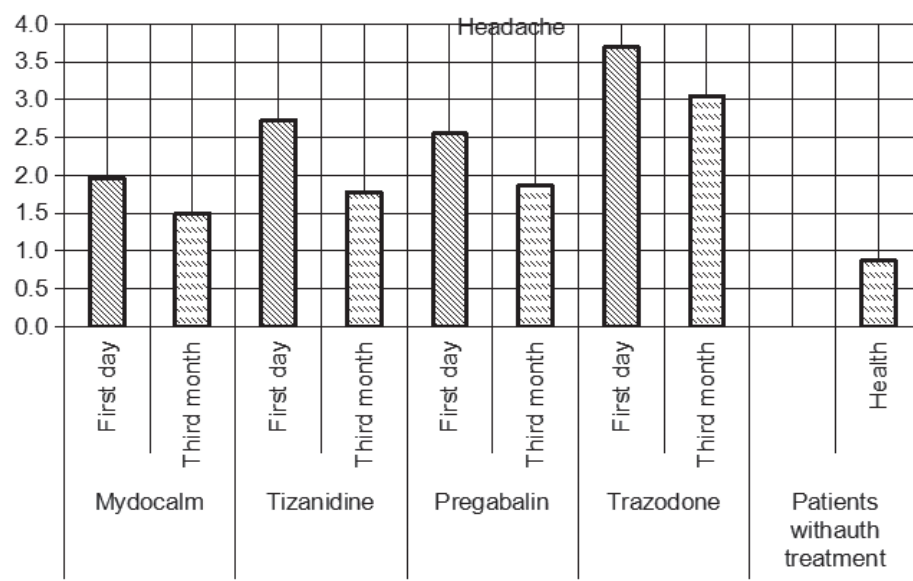
with patients it reached 3.636. A statistically significant difference in symptoms was observed between healthy individuals and all patients before treatment, and in the mydocalm group after treatment. Therefore, after treatment, the patients approached the healthy group. Practical results of the treatment of headaches in FM show the highest effectiveness of tizanidine, followed by pregabalin, trazodone and mydocalm. The qualities of tizanidine as a muscle relaxant with a primary central effect influence spasticity of the muscles of the head and neck, which is one of the causes of tension-type headaches. In the practice of treating tension-type headache in FM, medications can be selected in the following order.

2. Percentage distribution of patients with tension-type headache.

Before treatment, 80.4% of patients (treated and untreated) had headaches (tension-type). In the control group, healthy participants (no fibromyalgia) without headaches were 68% of the participants. Before starting mydocalm, 62% of the patients reported having tension-type headaches. It disappeared in some patients, and at the end of treatment, 46% reported having headaches.

In the tizanidine group, the percentage of patients reporting tension-type headache at baseline and at the end of treatment was 77% and 59%, respectively, compared with 76% and 69% in the pregabalin group. Tension-type headache was reported in 91% of the untreated patients.

The presented results show the different distribution of patients with and without tension-type headache in the therapeutic groups. The least patients without tension-type headache were allo-



Graph 1. Dynamics of headache intensity before and after treatment in 4 therapeutic groups and a control group of healthy subjects ($p>0.05$)

cated to treatment with mydocalm. The headache disappeared completely in 18% of the patients treated with tizanidine and in 16% of the patients after treatment with mydocalm. For practical work with patients with FM it is important that muscle relaxants have a good effect on the accompanying tension-type headache.

DISCUSSION

In many scientific reports, headache is a common and troublesome symptom in FM. In the study by Wolfe et al. [9] to develop the ACR 1990 diagnostic criteria, 97.6% of FM patients had chronic pain, 75.6% had sleep disturbances, 78.2% had fatigue, and 54.3% had headaches. Although surprising, the percentage of our patients with chronic pain before treatment is identical – 97.6%, 88.4% have sleep disorders, 97.5% have fatigue. A higher percentage of patients have headaches – 80.4% [9]. Various receptors in the sensory pathways – opiate receptors, α_2 -receptors, 5-hydroxytryptamine receptors, γ -aminobutyric acid receptors – are important in influencing headache. Tizanidine (an α_2 -adrenergic agonist) is used to treat various types of pain syndromes, such as headache, joint, myofascial or neuropathic pain, and back pain [3]. Tizanidine has an antinociceptive effect that is independent of the endogenous opioid system. Its effectiveness in headache has been studied in various clinical trials. At a dose of 14 mg daily, tizanidine reduces the frequency, duration, and intensity of headaches [3]. Our results on the effect of tizanidine on tension-type headache in patients with FM are similar when administered at a dose of 12 mg daily. Of all the groups of medications, tizanidine has the most pronounced effect on headache.

Krusz, J. K. summarizes the positive effect of pregabalin and gabapentin in patients with FM and headache, as well as another antiepileptic drug, topiramate [3]. According to our results, pregabalin is second among the drugs in terms of effect on headache intensity, diffuse pain, and pain threshold.

The pain in FM is considered to be neuropathic (central or “centralized” neuropathic). There are clinical trials with types of medications that affect pain at all pathophysiological levels. Antidepressants and α_2 -adrenergic agonists act on the cerebral cortex. Antiepileptics and α_2 -adrenergic agonists affect the descending modulation of the dorsal horn pathway in the spinal cord and peripheral nerves [6]. According to a retrospective study

conducted with tizanidine in 430 (7% with FM) patients over 3 years by Russel and colleagues, tizanidine improves sleep quality, chronic pain, and muscle spasms in discogenic disease, osteoarthritis by 50%; with good effects on chronic pain and sleep in FM, myofascial pain, migraine and spinal surgery [5]. According to our results, the effect of tizanidine is weaker – sleep quality improves by 16% and chronic pain is reduced by 23.4%. The difference in effect is probably due to the different pathogenesis in FM, compared to chronic pain of a mixed type – neuropathic and nociceptive. Our results from the treatment of FM with tizanidine show a 36% reduction in headache intensity. Tizanidine administration in FM has been found to affect the concentration of substance P in the cerebrospinal fluid and reduce the intensity of pain in FM [2]. The ACR 1990 criteria are embedded in the European League Against Rheumatism (EULAR) diagnostic and treatment guidelines, developed in 2008 by rheumatologists from 11 European countries [2]. They are intended to guide physicians in the proper approach to monitoring and treating patients with FM. In the presented observation, these guidelines were fully used. In most cases, EULAR indicated treatment with antidepressants and pregabalin, with a good effect on the pain syndrome. In our study, the effect of SSRI with a specific mechanism of action and pregabalin on pain and tension-type headache in patients with FM was monitored [1]. Medications affect complaints to varying degrees, with mydocalm, trazodone, and pregabalin being effective in reducing pain, muscle relaxants improving headaches and diffuse pain, and being ineffective in autonomic disorders. Therefore, an individual assessment of the leading clinical complaints of each patient is necessary, and then treatment should be applied according to the intensity of the clinical complaints [1].

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