CASE REPORT

High-dose thiamine improves the symptoms of fibromyalgia

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SUMMARY

Living with fibromyalgia means living with chronic pain, fatigue, sleep disorders and other associated key symptoms. To date, pharmacotherapy generally produces modest benefits. Some observations indicate that the large majority of symptoms of fibromyalgia could be the clinical manifestation of a mild thiamine deficiency due to a dysfunction of the active transport of thiamine from the blood to the mitochondria or to enzymatic abnormalities. Between June and July 2011, we recruited three female patients affected by fibromyalgia. We proceeded with the study of the patients' history, a physical examination, an evaluation of chronic widespread pain using the Visual Numeric Scale and an evaluation of the fatigue using the Fatigue Severity Scale were also performed. The levels of thiamine and thiamine pyrophosphate in the blood were determined. After the therapy with high doses of thiamine, in the patients, there was an appreciable improvement of the symptoms.

BACKGROUND

Fibromyalgia (FM) is a chronic disorder characterised by chronic widespread pain (CWP) that may occur in multiple location and multiple extremities (usually upper and lower/right and left side of the body), spine/axial skeleton, head and/or thoraco-abdominopelvic regions. FM is a clinical diagnosis based on its signs and symptoms. The symptoms used to identify FM are CWP, fatigue and sleep disorders. Other associated symptoms include tenderness, stiffness, depression, anxiety, irritability, trouble concentrating, forgetfulness and disorganised thinking.[1] Recent research suggests that the CWP is neurogenic in origin.[1 2] Neuroimaging studies have shown that FM is associated with aberrant processing of painful stimuli in the central nervous system.[3 4] Some authors suggested a role for mitochondrial dysfunction and oxidative stress in the symptoms associated with FM.[5] Pharmacotherapy generally produces modest benefits on symptoms.[1]

We observed in June 2010 that the fatigue and the related disorders in patients with ulcerative colitis improved after a therapy with high doses of thiamine.[6] We formulated an hypothesis: chronic fatigue that accompanies inflammatory and autoimmune diseases could be the clinical manifestation of a mild thiamine deficiency probably due to a dysfunction of the intracellular transport or due to enzymatic abnormalities, and responds favourably to high doses of thiamine.[6] In fact, fatigue and related disorders seemed to have many similarities with the manifestations of a mild thiamine deficiency.[7] From that moment, we systematically searched for and treated with high doses of thiamine chronic fatigue, when present, in any type of disease. Consequently, we started treating the fatigue component of FM. We, therefore, tested this therapy on three patients reported on this study. As we approached this experimental non-controlled treatment of fatigue in FM, we monitored the most important symptom of FM, including CWP as well.

While researching in literature, we encountered a study from Monroe[8] that stated 'A number of similarities exist between Fibromyalgia and thiamine deficiency. They include irritability, frequent headaches, unusual fatigue, muscle tenderness, upon pressure palpitation, muscular weakness, irritable bowel syndrome and sleep disturbance. Studies published in *JACN* have demonstrated abnormalities of thiamine metabolism in FM'.

In the same work, Monroe[8] suggests also to study together alcohol consumption and thiamine status in patients diagnosed with FM.

Monroe's previously mentioned article was also reviewed and commented by Dr Eisinger (1998), who excluded that vitamin B_1 abnormalities, demonstrated in FM, were due to nutritional deficiencies, but proposed a theory for which these may be related to structural enzymatic abnormalities.[9]

CASE PRESENTATION

Three patients affected exclusively by FM were selected. They had a definite diagnosis performed according to the current criteria used for this disease (American College of Rheumatology, 1990). The patients throughout the years were seen by at least five different rheumatologists each, and all of them confirmed the diagnosis. The patients performed the biochemical and haematological investigations suggested for this pathology. Laboratory testing includes the measurement of erythrocyte sedimentation rate, C reactive protein levels, a complete blood cell count, a comprehensive metabolic panel and a thyroid function test. The values of all the aforementioned exams have always been normal. Moreover, the patients had done several immunological exams (ie, rheumatoid factor, antinuclear antibodies, etc) which always resulted normal. They were tested for the levels of vitamin B_{12}, vitamin D, ferritin, iron-binding capacity and percentage of saturation; all were within normal values as well. The patients were not tested for the Lyme disease. This was because our colleague rheumatologists considered the presence of this disease as very remote (15 cases over the past 10 years in

the region where our patients live). Moreover, the patients did not report to the rheumatologists any travel to endemic zones for tickborne diseases.

In total, the patients performed 18 radiological exams (in various body parts) with normal results. The patients, at the moment of the first examination during this study, were not under any medical treatment since in the past they did not benefit from any form of therapy.

However, before the therapy with high doses of thiamine, the patients were treated with the following drugs:

Patient 1: Pregabalin, duloxetine, indomethacin.

Patient 2: Amitriptyline, indomethacin

Patient 3: Duloxetine, indomethacin, hydroxychloroquine sulfate.

These drugs were not taken during the therapy with thiamine.

After formal consensus, we proceeded with

1. A history and an objective examination of each patient
2. Evaluation of the fatigue using the Fatigue Severity Scale (FSS)
3. Evaluation of CWP using the Visual Numeric Scale (VNS)
4. Tender points (Tp) evaluation
5. Blood dosage of thiamine and thiamine pyrophosphate (TPP)
6. Immediate therapy with high doses of thiamine orally
7. Twenty days after the beginning of the therapy, points 1, 2, 3, 4, 5 were repeated.

The scores of FSS were considered as follows:

9 points: no fatigue

Up to 36 points: medium-low fatigue

From 36 to 63 points: severe fatigue

The scores of the VNS were considered as follows:

0 points: no pain

10 point: maximum pain

Patients' status before of the therapy (see table 1)

Patient 1: Female, 58 years old, weight 59 kg. From 1998, the patient began to have widespread pain accompanied by severe fatigue, depression, anxiety, irritability, sleep disorders, trouble concentrating, dry skin, general sickness, continuous headache, intolerance to low temperatures and, more recently, episodes of tachycardia and extrasystolia. Tp number: 14.

Patient 2: Female, 37 years old, weight 74 kg. From 1999, the patient has had widespread pain and all the symptoms described for patient 1, with the only exception being that of cardiac symptoms. Tp number:16.

Patient 3: Female, 60 years old, weight 65 kg. From 2006, the patient began to have widespread pain, fatigue, depression, anxiety, sleep disorders. Trouble concentrating. Tp number: 14.

Since the beginning of this study, the patients have been contacted every 3 days because, normally, the therapeutic dose shows its efficiency only after 48 h. We contacted the patients every 3 days during the first 20 days of the therapy; consequently, we contacted them every 3 months until today. Owing to the limited number of patients for this case study, we were unable to provide a control group (placebo). The lack of a placebo group makes the results preliminary and more difficult to interpret.[10] The improvements have been consistent since the beginning of the therapy to date. The lowest dose that we used is 600 mg/day (patient 1), and then a dose of 300 mg was increased every 3 days depending on the weight and the results obtained. Patient numbers 2 and 3 never reported any improvement until the dose was increased up to 1500 mg/day, orally. An abrupt improvement instead occurred at doses of 1800 mg/day.

OUTCOME AND FOLLOW-UP

The oral therapy with 600–1800 mg/day of thiamine led to an appreciable attenuation of CWP, fatigue and all other symptoms in all patients within a few days. Tp numbers in all patients remained the same; however, for the patients, these were appreciably less painful.

Patients' status after the therapy (see table 1).

Patient 1: FSS decrease: 71.3%; VNS decrease: 80%

Patient 2: FSS decrease: 37.0%; VNS decrease: 50%

Patient 3: FSS decrease: 60.7%; VNS decrease: 60%

Fianlly, the interviews after 20 days of therapy showed an appreciable reduction of all the other symptoms. All patients are currently continuing the same therapy. A recent check-up of the patients did not show any decrease in the efficacy of the therapy.

DISCUSSION

Overall, we had a favourable response to thiamine administration. The presence of symptoms of a mild thiamine deficiency in patients with normal concentration of thiamine and TPP in the blood may be explained if referred to a form of thiamine deficiency due to a dysfunction of the vitamin B_1 active transport mechanism from the blood to the mitochondria or, perhaps, due to a structural enzymatic abnormalities. The administration of large quantities of thiamine orally increases the concentration in the blood to levels at which the passive transport restores the normal glucose metabolism. According to different authors, the dysfunction of the active transport could

Table 1 Patient's characteristics

Laboratory examinations, FSS, VNS	Patient 1	Patient 2	Patient 3
Thiamine before therapy (nv 2.1–4.3 µg/l)	10.2 µg/l	6.4 µg/l	9.6 µg/l
Thiamine after therapy	435.5 µg/l	107.0 µg/l	44.0 µg/l
TPP before therapy (nv >49 µg/l)	96.6 µg/l	106.1 µg/l	96.2 µg/l
TPP after therapy	184.3 µg/l	164.5 µg/l	126.5 µg/l
FSS before therapy	49	46	61
FSS after therapy	14	29	24
VNS before therapy	10	6	5
VNS after therapy	2	3	2

FSS, Fatigue Severity Scale; nv, normal value; TPP, thiamine pyrophosphate; VNS, Visual Numeric Scale.

be overcome by diffusion mediated at supranormal thiamine concentrations.[11]

The glucose metabolism of all organs goes back to normal values and all symptoms are reduced. We deem it necessary to prescribe a lifelong use of high doses of thiamine in the affected subjects.

Patient numbers 2 and 3 never reported any improvement of neither fatigue nor CWP until the dose was increased to1500 mg/day. Instead, an abrupt improvement instead occurred at doses of 1800 mg/day.

The therapy seems to be characterised by an 'all or nothing' effect. In other words, below a given daily minimum dose, there was no improvement observed. Empirically, we learned that once an appreciable improvement of the fatigue and related symptoms is achieved, a further increase in thiamine doses has led in few cases to mild tachycardia (90–100 bpm) and difficulties in falling asleep.

A dysfunction of intracellular thiamine transport was described for genetic diseases characterised by mutations in thiamine-transporter genes.[11–13]

A number of inborn errors of metabolism have been described in which the clinical improvements can be documented following the administration of pharmacological doses of thiamine.

Fatigue in Spinocerebellar ataxia type 2 and in inflammatory bowel diseases can be treated with large doses of thiamine.[6 14]

It is our opinion that fatigue, sleep disorders, depression, anxiety and cardiac troubles are the expressions of a classic mild thiamine deficiency. CWP pain in a patient with FM is not a symptom of a classic thiamine deficiency; rather, it may because, within spinal and upper-spinal circuits that control sensory inputs, a more severe focal dysfunction of the transport-metabolism of the thiamine exists that produces this irritative symptom.

No side effects owing to the dose of thiamine administered to the patients were observed during this study. In literature, there is no study that has observed side effects linked to the daily use of high doses of thiamine.[15] The patients under treatment for FM did not show any collateral effect. However, side effects such as tachycardia and insomnia were observed in some of our patients treated with this regimen for other conditions.[6]

Metabolic studies were not performed on patients affected by fibromyalgia, and the mechanism of action of thiamine remains speculative for this disease.

Further studies are necessary to confirm our observations. We strongly believe that our observations represent an important contribution to the relief of many patients.

Learning points

- The treatment described in this paper is immediately available for the care of fibromyalgia.
- In the literature, there is no study that has observed side effects linked to daily use of high-dose thiamine.
- We believe that this report opens a ray of hope for the therapy of fibromyalgia.

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