Effect of intramuscular depot betamethasone injection in patients with fibromyalgia and elevated C-reactive protein levels

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ABSTRACT

Fibromyalgia is characterized by diffuse musculoskeletal pain and fatigue. There are limited data about systemic steroid treatment of patients with fibromyalgia in the English literature. Patients with fibromyalgia with ongoing diffuse musculoskeletal pain despite standard treatment, extreme fatigue and elevated C-reactive protein (CRP) levels without evidence of synovitis, or other source of inflammation, were asked to participate in our study. After consent, demographic, clinical and laboratory parameters in addition to body mass index were documented. These patients were interviewed and asked to answer the Revised Fibromyalgia Impact Questionnaire (FIQR) just prior, 1 and 4 weeks following 14 mg depot betamethasone intramuscular injection. Twenty-three patients were recruited and 21 completed the study. 19 patients were women with mean age of 42±10.12 and CRP level of 14.1±3.96 mg%, and all had negative rheumatoid factor and antinuclear antibodies. All patients had significant improvement in all of the FIQR parameters, at 1 and 4 weeks, except memory, anxiety and balance. It can be concluded that systemic intramuscular depot betamethasone injection seems to have a favorable effect in patients with fibromyalgia with elevated CRP levels for at least 4 weeks.

INTRODUCTION

Fibromyalgia is a type of chronic pain syndrome.[1] It is characterized by diffuse musculoskeletal pain and fatigue.[2] Other common symptoms and signs include peripheral numbness, tenderness to touch, memory and mood problems and sleep disturbances.[3] The prevalence of fibromyalgia is about 3%–5% on average in the general population, mostly women with a female:male ratio of ~4:1.[4] The pathogenesis of this syndrome is not fully understood. Central localization of the pain is the leading theory, where the presumption is that pain perception at the brain level is exaggerated.[5] Classically, patients with fibromyalgia have negative or normal serological markers.[6] Fibromyalgia is considered in the differential diagnosis of symmetrical musculoskeletal pain and could be misdiagnosed in favor of rheumatoid arthritis (RA) or ankylosing spondylitis (AS), especially among patients with elevated inflammatory measures or patients with positive rheumatoid factor.[7 8]

Fibromyalgia is treated mainly symptomatically with different modalities, mainly medications including tricyclics, benzodiazepines, simple analgesic, duloxetine, pregabalin, non-steroidal anti-inflammatory drugs (NSAIDs), mild opiates, strong opiates, selective serotonin reuptake inhibitors (SSRIs), and/or medical cannabis.[9] Many of the patients are also treated with local injection of corticosteroids mainly at epicondyle areas, at rotator cuff areas or great trochanteric area, where pain and tenderness at these areas could be part of this syndrome. Some patients with fibromyalgia report pain relief following systemic treatment of corticosteroids, when seronegative arthritis was suspected initially, and ruled out later (personal experience).

There are nearly no data in the literature about systemic corticosteroid treatment in fibromyalgia.

In this prospective study, we wanted to evaluate a single intramuscular injection of depot betamethasone (betamethasone dipropionate+betamethasone sodium phosphate) (Diprospan) on patients with fibromyalgia with unexplained elevated inflammatory measures.

MATERIALS AND METHODS

Patients with the diagnosis of fibromyalgia according to the American College of Rheumatology criteria,[10] who were followed at the outpatient rheumatology clinics and failed at least simple analgesic, tricyclic antidepressants (if not contraindicated), simple opiates and pregabalin/duloxetine, with unexplained elevated C-reactive protein (CRP) levels higher than twice the maximal upper limits (measured at least twice over 3 months), were asked to participate in our study. These patients were offered a single intramuscular injection of combined 10 mg betamethasone dipropionate+4 mg betamethasone sodium phosphate (2 mL Diprospan). The potential adverse effects of the injection, including transient elevated blood glucose and blood pressure levels, transient increase in weight and appetite and sleep disturbances, were explained to all the patients. After signing a consent form, and

Table 1 Demographics and laboratory parameters of the patients at baseline

Parameter	Result (% of all the patients)
Female:male	19:2
Age (y)*	42±10.2, 29–60
Duration of symptoms (y)*	4.5±3.4, 0.5–12
Duration of disease (y)*	1.8±2, 0–7
History of treatment	
Simple analgesics	100%
Duloxetine	43%
Pregabalin	78%
Mild narcotics	100%
Strong narcotics	12%
CRP (normal values 0–5 mg%)*	14.1±3.96
Body mass index*	32.8±4.9, 27–42

*Mean±mean, range.
CRP, C-reactive protein; y, years.

just prior to the intramuscular injection, 1 and 4 weeks later, these patients were asked to answer the Revised Fibromyalgia Impact Questionnaire (FIQR). One month following the injection, CRP levels were repeated in all the patients.

Exclusion criteria included patients with diabetes and uncontrolled hypertension, patients on anticoagulants, patients under steroids or who received steroids during the previous 3 months, patients with positive serology of either antinuclear antibodies, rheumatoid factor or antineutrophil cytoplasmic antibodies (ANCA), patients with evidence of infection anywhere (skin, urine, dental, respiratory, or other), patients with history of fever during the previous 3 months or patients with evidence of synovitis clinically or with evidence of erosions or symmetrical joint space narrowing on X-rays of the hands.

All patients had X-rays of the hands, and of the lower back and sacroiliac joints; patients with suspected sacroiliitis were also evaluated for this by MRI of the sacroiliac joints and HLA-B27 tests. The current weight and height of the patients were also documented.

RESULTS

Twenty-three patients were recruited and 21 completed the study. One patient could not be located for the repeated FIQR and the repeated test and another patient started new NSAID treatment 1 week following the depot betamethasone injection.

Table 1 summarizes the demographic and clinical parameters of the patients.

Table 2 summarizes the different parameters of the FIQR at baseline, 1 and 4 weeks later. Nearly all FIQR parameters were significantly better off following intramuscular Diprospan injection. All X-rays of the hand were negative for findings suggestive for inflammation, including erosions or symmetrical narrowing of joints, and 6 patients had negative MRI for sacroiliitis and 9 patients had negative HLA-B27. No patients had positive MRI study or positive HLA-B27.

DISCUSSION

The most important finding in our study was that most parameters of the FIQR showed a significant improvement, 1 and 4 weeks following intramuscular injection of depot betamethasone. Yet, there was no significant change in CRP level among these patients. Unfortunately, due to ethics committee restriction, a sex and age-matched control group with normal CRP levels was not possible in our study in order to control for the CRP, and see if the improvement was related to CRP level or not.

Steroids are known to have antifatigue and antistiffness effects[11] where all patients had improvement in energy and stiffness. Although steroid could cause disturbed sleep and mood, the improvement in our patients could be the result of improvement in pain, stiffness and energy attributed to steroids.

Some parameters did not show a significant change such as memory and balance.

Systemic steroids are known to be very potent in reducing inflammatory pain. However its role in non-inflammatory pain is limited as in degenerative or neuropathic pain. On the other hand, local systemic injection could be helpful in non-inflammatory pain. Enthesopathy is a typical feature in fibromyalgia,[12] and regardless of the cause, patients with enthesopathy could favorably respond to local steroid injection, mainly at the great trochanteric area and at the epicondyle area.[13]

Hidden musculoskeletal inflammation manifested also by elevated CRP levels cannot be ruled out in some of our patients.[14] Yet, CRP levels did not change significantly among our patients, alluding to the possibility that the elevated CRP levels were not related to causes responding to systemic steroids.

Unexplained elevated inflammatory markers could be seen even in normal persons without a clear explanation, especially among obese and diabetics.[15 16] Our study did not include patients with diabetes, and clearly most of our participants were obese. On the other hand, secondary fibromyalgia could develop among patients with inflammatory diseases such as RA and AS.[7 8] There was no evidence for either of RA or AS in our patients.

In conclusion, we think that systemic steroids could be a therapeutic option among patients with fibromyalgia. It needs to be seen if all patients with fibromyalgia, regardless of CRP levels, have the same favorable effect. We think that systemic steroids should not be the first line of treatment, but definitely it could be seriously considered from time to time (not on a continuous basis) in patients who are non-diabetic and non-obese with severe fibromyalgia, who have extreme fatigue and pain.

Contributors GH: conception of the study, design and planning of the study, acquisition of results, interpretation of results, drafting of the work and final approval of the version to be published. GH participated in writing of the final report and is accountable for all aspects of the work. ND: design and planning, acquisition of results, analysis of results, drafting of the work and final approval of the version to be published.

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Competing interests None declared.

Patient consent for publication Obtained.

Table 2 Performance of FIQR parameters at baseline, 1 and 4 wk following the Diprospan injection

Parameter	Result at baseline	1 wk following intramuscular injection	P value*	4 wk following intramuscular injection	P value*
Level of pain	9.45±0.82	6.55±3.11	0.012	7.64±1.29	0.007
Level of energy	8.55±1.57	6±3.35	0.017	7.18±1.94	0.016
Level of stiffness	7.91±3.33	5.36±4.37	0.027	5.91±3.33	0.017
Quality of sleep	7.64±1.63	6.18±2.93	0.027	6.73±2.61	0.104
Level of depression	8±1.18	5.64±3.2	0.011	7±1.55	0.026
Level of memory problems	6.45±1.97	6.45±2.77	0.102	6.27±1.95	0.314
Level of anxiety	8.1±1.38	6.18±3.28	0.058	7±2.65	0.136
Level of tenderness to touch	8.36±1.57	6.1±3.53	0.027	7.1±2.26	0.023
Level of balance problems	6.82±2.86	6.0±2.72	0.105	5.91±2.66	0.126
Level of sensitivity to loud noises, bright lights, odors and cold	8.36±1.96	6.45±3.5	0.026	7.45±2.85	0.04
Fibromyalgia prevented me fron accomplishing goals for the week	9.0±1.55	6.45±3.11	0.005	7.55±1.92	0.008
I was completely overwhelmed by my fibromyalgia symptoms	8.91±1.45	6.27±3.23	0.003	7.45±1.69	0.002
Go shopping for groceries	7.45±1.81	5.64±3.17	0.089	6±1.95	0.028
Sit in a chair for 45 minutes	8.15±2.9	4.85±4	0.007	5.1±3.6	0.005
Change bed sheets	7±2.55	3.92±3.33	0.018	4.62±3.48	0.034
Climb one flight of stairs	7.62±1.89	4.92±3.04	0.021	5.54±3.13	0.048
Lift and carry a bag full of groceries	8.1±2.22	5.23±3.49	0.007	5.46±3.33	0.007
Vacuum, scrup, or sweep floors	8.38±1.26	5.38±3.8	0.012	5.92±3.3	0.01
Prepare a homemade meal	7.15±2.12	4.92±3.17	0.021	5.46±2.96	0.041
Walk continuously for 20 minutes	8.46±2.1	5.77±3.77	0.007	6.31±3.22	0.01
Brush or comb your hair	7.69±2.1	5.38±3.28	0.005	5.1±3.12	0.005
CRP level	14.1±3.96			11.8±4.1	0.063

*Compared with baseline values.
CRP, C-reactive protein; FIQR, Revised Fibromyalgia Impact Questionnaire.

Ethics approval This study involves human participants and was approved by the Ethics Committee of Nazareth Hospital, Israel (IRB 36-21-EMMS). Participants gave informed consent to participate in the study before taking part.

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