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THE ROLE OF DIETARY TRYPTOPHAN INTAKE IN FIBROMYALGIA SYNDROME

Dr. Hakan GENÇ*, Dr. Meryem SARAÇOĞLU*, Dr. Burcu DUYUR*, Dr. H. Rana ERDEM*

ABSTRACT

Fibromyalgia Syndrome (FS) is a common disease characterized by diffuse, widespread pain and multiple tender points. Syndrome was subclassified as primary fibromyalgia (PFS) and secondary fibromyalgia (SFS). The aim of this study was to evaluate the role of dietary tryptophan in FS. Twenty female patients with PFS, 20 with SFS and 20 female controls, matched by age and body mass index, participated in this study. Dietary tryptophan intakes of the FS and control subjects were assessed with "total nutrition score" (TNS) prepared for this study. Average daily consumption of tryptophan (ADCT) values were also calculated based on this scoring system. A significant difference was observed between TNS and ADCT values of FS patients and control subjects. TNS and ADCTs were significantly lower in both PFS and SFS groups. As a result, tryptophan rich diet can be recommended to these patients as a part of treatment regimen.

Key words: *Fibromyalgia, diet, tryptophan*

ÖZET

Fibromiyalji sendromu (FS) diffüz, yaygın ağrı ve çok sayıda hassas noktalarla karakterize, sık gözlenen bir hastalıktır. Sendrom primer FS ve sekonder FS olarak alt gruplara ayrılmaktadır. Bu çalışmanın amacı diyet triptofan içeriğinin FS'daki rolünü araştırmaktır. Yaşları ve beden kitle indeksleri açısından eşleştirilmiş 20 primer, 20 sekonder kadın FS hastası ve 20 kadın kontrol birey çalışmaya alınmıştır. Fibromiyaljik hastalar ve kontrol bireylerinin diyetlerinin triptofan içerikleri, bu çalışma için hazırlanmış olan "total beslenme skoru" (TBS) ile değerlendirilmiştir. Ortalama günlük triptofan alımları (OGTA) yine bu skorlama sistemi baz alınarak hesaplanmıştır. FS hastası ve kontrol bireyleri arasında TBS ve OGTA açısından anlamlı farklılık gözlenmiştir. TBS ve OGTA primer ve sekonder FS hastalarında kontrol bireylerine oranla belirgin olarak düşük bulunmuştur. Sonuç olarak FS hastalarına, tedavi rejiminin bir parçası olarak triptofandan zengin diyet önerilmesinin yararlı olacağı belirlenmiştir.

Anahtar kelimeler: *Fibromiyalji, triptofan, diyet*

INTRODUCTION

Fibromyalgia Syndrome (FS) is a common disease characterised by widespread musculosceletal pain and tenderness on palpation of spesific tendinomusculoskeletal sites, called "tender points". FS was subclassified as primary fibromyalgia (PFS) and secondary fibromyalgia (SFS). Patient with primary fibromyalgia have diffuse, widespread pain and multiple tender points in the absence of underlying, causative, or significant concomitant condition. In the presence of these conditions it is classified as secondary fibromyalgia. Studies have shown that the clinical characteristics of FS in these patients are not significantly different from those of primary fibromyalgia (1,2).

The most common characteristics of the syndrome are nonrestorative sleep, tensiontype headache, subjective soft tissue swelling, morning stiffness and paresthesias. In addition anxiety, dep-

* Ministry of Health, Ankara Education and Research Hospital 2nd Department of Physical Medicine and Rehabilitation, Ankara-TURKEY

ression, dysmenorrhea, irritable bowel syndrome, Sicca syndrome, Raynaud's phenomenon and woman urethral syndrome may be seen in fibromyalgia. Chronic fatique syndrome, restless legs syndrome, hypermobility, nocturnal myoclonus, psychogenic pain are conditions similar or related to fibromyalgia (1,3).

One of the most important pathophysiologic theories of FS is combination of central and peripheral mechanisms based on "central neurohormonal dysfunction". Decreased serotonin level which may be triggered by nonspesific stress from trauma, viral infection or mental stress is thought to be a causative factor (3).

The aim of this study was to evaluate the role of dietary tryptophan which is a precursor of serotonin in FS. We also assessed the most common characteristics of FS in our patients.

MATERIALS AND METHODS

Twenty female patients with PFS, 20 with SFS (due to type2 diabetes mellitus (DM)) and 20 woman controls, matched by age and body mass index (BMI), participated in the study. All patients fulfilled the classification criteria for fibromyalgia proposed by American College of Rheumatology (ACR) (4). First, demographic features of the patients were noted and clinical characteristics of FS such as nonrestorative sleep, tensiontype headache, morning stiffness, subjective soft tissue swelling and paresthesias were asked. Then all patients underwent detailed locomotor and systemic examination.

Tender point (TP) and control point (CP) examinations were performed with Fischer's tissue compliancemeter which may be used as a pressure pain algometer (5-7). Eighteen TP and 4 CP (mid forearm and thumbnail on the left and right sides of the body) (8) were evaluated respectively. Compliancemeter was applied to these spesific points and the amount of pressure causing pain (pain pressure treshold PPT) were recorded as kg/cm^2 . Points that were painful with less than 4 kg/cm2 pressure were accepted as tender points. Severity of fibromyalgia was assessed with total myalgic score (TMS) and control point score (CPS). The sum of the PPTs of 22 points (18TP and 4CP) were calculated as TMS (kg/cm^2) and the sum of the PPTs of the control points were recorded as CPS (kg/cm^2) (6,7).

We used "total nutrition score (TNS)", prepared for this study, for the assessment of dietary tryptophan intakes of the FS and control subjects. Tryptophan rich food intake (animal proteins; meat, egg, offal, milk, cheese, vegetable proteins; dry beans, chickpeas, lentils, oily seeds; sesamme, black cumin, sunflower seed, pumpkin seed, almond, walnut, peanut, flour; bread and chocolate) (9) was scored 0 to 4 according to consumption frequency of each food (0: none or rare, 1: once a mounth, 2: once a week, 3: more than once a week, 4: everyday; at least for one meal). The sum of the scores were calculated as TNS. Average daily consumption of tryptophan values (ADCT) of FS patients and control subjects also calculated according to consumption frequency and amount of each food based on this scoring system. The amount of tryptophan which was taken with food for 30 days was calculated and divided to 30. Final value was recorded as ADCT (g/day).

SPSS 10.0 for windows was used for statistical analysis. Chisquare and oneway ANOVA tests were selected for analysis and posthoc analysis were performed with Bonferroni test. P values less than 0.05 were accepted as significant.

RESULTS

The mean age of the 20 females with PFS was 51.25 ± 8.82 years (between 34-70), 20 females with SFS was 55.65 ± 11.06 years (between 36-78) and 20 female control was 51.40 ± 7.68 years (between 40-65). Demographic features of fibromyalgia and control groups and mean disease durations are given in Table 1. There was no statistically significant difference between the 3 groups with respect to mean age, height, weight, body mass index and duration of the disease ($p>0.05$). The mean DM duration was 9.8 ± 5.27

years and mean fasting blood glucose level was 193.5 ± 63.42 mg/dL in SFS group.

Patients with PFS were not different than SFS group in any of clinical parameters ($p>0.05$).

Nonrestorative sleep, subjective joint swelling, morning stiffness and paresthesias were found more in PFS and SFS groups than controls ($p<0.001$).

Number of tender points was found higher ($p<0.001$, $p<0.01$) and total myalgic score and control point scores were lower ($p<0.001$) in PFS and SFS groups than in control subjects (Table 2).

A significant difference was observed between total nutrition scores (TNS) and average daily consumption of tryptophan (ADCT) values of FS patients and control subjects. TNS was found to be significantly lower in PFS and SFS groups ($p<0.05$, $p<0.01$ respectively) than control group. ADCT was found to be significantly lower in PFS and SFS groups too ($p<0.05$, $p<0.01$ respectively). Mean TNS and ADTC values and statistical analysis are shown in Table 3.

DISCUSSION

Pathophysiologic theories of FS can be divided into the three groups based on the following proposed mechanisms. (1) Primarily central: This theory based on comorbidity of fibromyalgia with major depression, migraine, irritable bowel syndrome, chronic fatique syndrome, panic disorders and the alpha electroencephalographic sleep anomaly. (2) Combination of central and peripheral mechanisms based on "central neurohormonal dysfunction". Decreased serotonin level which may be triggered by nonspesific stress from trauma, viral infection or mental stress is one of the possible mechanisms. (3) Primarily peripheral: This theory focused on localised ischemia due to disturbed microcirculation that causes muscle pain. To explain widespread pain at rest, characteristic of FS, this theory invokes disturbed pain modulation in the central nervous system (CNS) (3).

One of the ACR criterion for the diagnosis of FS is the existence of "sensitive points". While former data indicated pain only in these described points, recent studies have shown an increase in the sensitivity throughout the body (10). Moreover, it is stated in the recent studies that a central hyperexcitability exists in FS patients and as a consequance of this, the afferent input originated from periphery is amplified and continued by the central nervous system (11-13).

Tryptophan, which is an amino acid and a precursor of serotonin, not only inhibits the descending pain pathways, but also is an important neurotransmitter in stage 4 sleep. Decrease in restorative nonREM sleep, occurence of somatic complaints, depression and an increase in the perceived pain ensues as a consequence of its decrease in the brain. Decreased serotonin level is one of the most studied mechanisms in the etiopathogenesis of fibromyalgia (13,14). 5 Hydroxy-L-tryptophan is used per oral in the treatment of patients with fibromyalgia and is reported to have success (15).

A number of studies have reported the effects of diet on the symptoms of rheumatic disease, but almost all have dealt with rheumatoid arthritis, so very little information on fibromyalgia is available (16,17). Kaartinen et al.(17), assessed the effect of uncooked vegan diet on symptoms in 18 FS patients. They concluded that vegan diet had beneficial effects on fibromyalgia symptoms. Vitamin B6 plays a role in the synthesis of serotonin from tryptophan. Tryptophan metabolism was altered, with urinary excretions of xanthurenic acid after tryptophan loading. Pyridoxine repletion corrected all of the abnormalities noted. Vitamin B6 in natural foods was as available as crystalline pyridoxine (18). Futher studies were necessary about this issue. Markus et al. also showed the effects of whey protein on plasma tryptophan levels. They reported that whey protein rich in ?lactalbumin increased the ratio of plasma tryptophan to the sum of other large neut-

Table 1. Demographic features of FS and control groups and mean disease durations

	Age (year)	Height (m)	Weight (kg)	BMI (kg/m²)	Duration of FS(year)
PFS	51.25±8.82	1.60±0.06	72.05±10.71	28.09±4.97	4.00±2.73
SFS (Type-2 DM)	55.65±11.06	1.56±0.07	73.55±10.87	30.12±4.43	4.45±2.37
Control	51.40±7.68	1.58±0.05	75.50±10.69	30.00±4.39	
p	>0.05	>0.05	>0.05	>0.05	>0.05

FS: Fibromyalgia, PFS: Primary Fibromyalgia, SFS: Secondary Fibromyalgia, DM: Diabetes Mellitus, BMI: Body Mass Index

Table 2. Clinical features of primary, secondary FS and control groups.

	Primary FS (n:20) (%)	Secondary FS (n:20) (%)	P	Primary FS (n:20) (%)	Control (n:20) (%)	P	Secondary FS (n:20) (%)	Control (n:20) (%)	P
NRS	16 (80)	18 (90)	>0.05	16 (80)	6 (30)	<0.001	18 (90)	6 (30)	<0.001
SJS	19 (95)	15 (75)	>0.05	19 (95)	9 (45)	<0.001	15 (75)	9 (45)	<0.05
MS	18 (90)	18 (90)	>0.05	18 (90)	7 (35)	<0.001	18 (90)	7 (35)	<0.001
Paresthesia	15 (75)	16 (80)	>0.05	15 (75)	5 (25)	<0.001	16 (80)	5 (25)	<0.001
Headache	18 (80)	18 (90)	>0.05	18 (80)	17 (85)	>0.05	18 (90)	17 (85)	>0.05
NTP	14.70±2.27	14.65±1.87	>0.05	14.70±2.27	4.75±2.79	<0.001	14.65±1.87	4.75±2.79	<0.01
TMS (kg/cm²)	71.50±4.53	70.15±4.75	>0.05	71.50±4.53	102.30±4.34	<0.001	70.15±4.75	102.30±4.34	<0.001
CPS (kg/cm²)	14.78±2.60	14.93±2.14	>0.05	14.78±2.60	23.77±3.26	<0.001	14.93±2.14	23.77±3.26	<0.05

FS: Fibromyalgia, NRS: Non-Restorative Sleep, SJS: Subjective Joint Swelling, MS: Morning Stiffness, NTP: Number of Tender Points, TMS: Total Myalgic Score, CPS: Control Point Score,

Table 3. Total nutrition scores (TNS) and average daily consumption of tryptophan (ADCT) values of primary fibromyalgia (PFS), secondary fibromyalgia (SFS) patients and control group.

	Primary FS (n:20)	Secondary FS (n:20)	P	Primary FS (n:20)	Control (n:20)	P	Secondary FS (n:20)	Control (n:20)	P
TNS	15.40±2.95	14.15±3.46	>0.05	15.40±2.95	17.60±3.35	<0.05	14.15±3.46	17.60±3.35	<0.01
ADTC (g/day)	1.06±0.39	0.98±0.58	>0.05	1.06±0.39	1.25±0.96	<0.05	0.98±0.58	1.25±0.96	<0.01

mance in stressvulnerable subjects (19).

This is the first study to investigating the role of dietary tryptophan intake in FS using TNS which is prepared for this study. TNS is a simple and useful scoring system under limited laboratory conditions. We found using this scoring system that our patients with PFS and SFS had lower dietary tryptophan intake as compared to the control group. We also found that our patients with PFS and SFS had lower average daily consumption of tryptophan values (1.06±0.39 g/day and 0.98±0.58 g/day respectively) as compared to control subjects. These values also lower than the average daily consumption of tryptophan in USA (1.2 g/day)(20).

Multiple theories about the pathogenesis of this disease dictates various therapy regimens. As the difficult, current therapeutical approaches seem to be inadequate. Ledingham et al. (21) were received seventytwo patients with PFS in their study and they reported a poor prognosis characterised by a high degree of functional impairment and persistence of symptoms.

In conclusion, considering the central hyperexcitability exists in FS patients, tryptophan may play an important role in fibromyalgia as a causative factor and also plays a role in persistence of fibromyalgia symptoms. Thus tryptophan rich diet (for example including whey proteins, milk, meat, vegetable proteins, chocolate etc.) can be recommended to these patients. The amount and frequency of dietary triptophan intake and also the effect of tryptophan on symptoms in FS patients should be confirmed with further studies.

REFERENCES

1. Yunus MB, Masi AT. Fibromyalgia, Restless Legs Syndrome, Periodic Limb Movement Disorder and Psychogenic Pain. In: Mc Carthy DJ, Koopman WJ eds. Arthritis and Allied Conditions. 12th Ed. Lea and Febiger, Philadelphia, 1993. p.1383-1406.
2. Clauw DJ. Musculoskeletal Pain and Dysfunction. Fibromyalgia. In: Ruddy S, Harris ED, Sledge CB eds. Kelley's Textbook of Rheumatology. 6th ed. WB Saunders Company, Philadelphia, 2001 . p.417-428.
3. Jeffrey M, Thompson MD. The Diagnosis and Treatment of Muscle Pain Syndromes. In: Braddom RL ed. Physical Medicine and Rehabilitation.. 2nd Ed. WB Saunders Company, Philadelphia, 2000. p.934-956.
4. Wolfe F, Smythe HA, Yunus MB, Bennet RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria commitee. Arthiritis Rheum 1990; 33:160-172.
5. Fischer AA. Clinical use of tissue compliancemeter for documentation of soft tissue pathology. Clin J Pain 1987;3:23-30.
6. Fischer AA. Tissue compliance recording method for objective documentation of soft tissue pathology. Arch Phys Med Rehabil 1981; 62:542-545.
7. Ineel NA, Erdem HR, Açıkgöz G, Özgöçmen S, Yorgancıoğlu ZR. Analysis of painpressure threshold values in healthy subjects with repeated manual and algometric measures. Magyar Rheumatologia 1990; 40:139-142.
8. Malyak M. Fibromyalgia. In:West SG ed. Rheumatology Secrets.. Hanley and Belfus Inc., Philadelphia, 1997. p.354-362.
9. Williams SR. Aminoacid contents of foods. In: Nutrition and Diet Therapy. 6th ed. Times Mirror / Mosby College Publishing. St Louis, 1989.
10. Granges G, Littlejohn G. Pressure pain threshold in painfree subjects, in patient with chronic regional pain syndromes, and in patients with fibromyalgia syndrome. Arthritis Rheum 1993; 36:642-644
11. Johnson BW. Pain Mechanisms: Anatomy, Physiology, and Neurochemistry. In: Raj PP ed. Practical Management of Pain.3rd. ed. Mosby Inc., St Louis,2000.p.117-144.
12. Sörensen J, GravenNielsen T, Henriksson KG, Bengtsson M, Arendt Nielsen L. Hyperexcitability in fibromyalgia. J Rheumatol 1998;25: 152-155.
13. Bennett RM. Fibromyalgia and the disability dilemma. A new era in understanding a complex, multidimensional pain syndrome. Arthritis Rheum 1996;39: 1627-1634.
14. KrsnichShriwise S. Fibromyalgia syndrome: an overview. Phys Ther 1997;77:68-75.
15. Puttini PS, Caruso I. Primary fibromyalgia syndrome and 5hydroxyLtryptophan: a 90day open study. J Int Med Res 1992;20:182-189.
16. Nenonen MT, Helve TA, Rauma AL, Hänninen OO. Uncooked, lactobacillirich, vegan food and rheumatoid arthritis. Br J Rheumatol 1998;37:274-281.
17. Kaartinen K, Lammi K, Hypen M, Nenonen M, Hänninen O, Rauma A.L. Vegan diet alleviates fibromyalgia symptoms. Scand J Rheumatol 2000;29:308-313.
18. Sauberlich HE, Canham JE. Vitamin B6. In: Goodhart RS, Shils ME Eds. Modern Nutrition in Health and Disease. Philadelphia: Lea&Febiger;1980:216-229.
19. Markus CR, Olivier B, de Haan EHF. Whey protein rich in ?lactalbumin increases the ratio of plasma tryptophan to the sum of other large neutral amino acids and improves cognitive performance in stressvulnerable subjects. Am J Clin Nutr 2002;75:105-116.
20. Munro NH, Crim MC. The proteins and amino acids. In: Goodhart RS, Shils ME Eds. Modern Nutrition in Health and Disease. Philadelphia: Lea&Febiger;1980:5198.
21. Ledingham J, Doherty S, Doherty M. Primary fibromyalgia syndrome an outcome study. Br J Rheumatol 1993;32:139-142.