A Randomized Controlled Trial of Acupuncture Added to Escitalopram Treatment for Fibromyalgia and Related Conditions

Fibromiyalji ve İlişkili Olduğu Semptomlar Üzerine Essitalopram Tedavisine Eklenen Akupunktur Tedavisinin Etkinliği

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ABSTRACT

Objective: The aim of this study was to investigate whether addition of acupuncture to escilatopram was a reasonable method in treating fibromyalgia and related conditions when compared to escitalopram only.

Methods: In this single blinded trial, female patients diagnosed with fibromyalgia according to ACR criteria were randomized into two groups. 1-) To the first group, together with Escitalopram 10 mg/daily, silver needles placed in fibromyalgia acupuncture sites once a week for 16 weeks (n=42). 2-) To the second group, Escitalopram was used only at a dose of 10 mg/daily for 16 weeks (n=41). For assessing the study parameters, pain was assessed by VAS-visual analog scale, depression and anxiety by Beck depression and anxiety scales, sleep disorders by Pittsburgh sleep quality index, fatigue by fatigue severity scale (FSS), duration of morning stiffness (minutes) and count of tender points. A blinded assessor to the group randomization evaluated all study parameter scales before, just after and 1 month after the study.

Results: In both groups, statistically significant decrease in pain was seen ($p<0.05$). Also, improvement in depression, anxiety, fatigue severity, sleep quality, stiffness and decrease in the count of tender points were statistically significant in both groups ($p<0.05$). No statistically significant differences were assessed in all study parameters in comparison of the groups ($p>0.05$), except much more decreased tender point count ($p<0.05$) in the acupuncture+escitalopram group.

Conclusion: Addition of acupuncture to escitalopram in fibromyalgia is generated no significant difference in fibromyalgia related symptoms except much more decreased tender point count *(J PMR Sci 2010;13:93-8)*

Keywords: Fibromyalgia, acupuncture, escitalopram, rehabilitation

ÖZET

Amaç: Bu çalışmanın amacı, essitaloprama eklenen akupunktur tedavisinin, fibromiyalji ve ilişkili olduğu durumların tedavisinde makul bir tedavi metodu olup olmadığını, yalnızca essitalopram ile karşılaştırarak değerlendirmek idi.

Yöntemler: Bu tek kör çalışmada, ACR tanı kriterlerine göre Fibromiyalji tanısı alan kadın hastalar 2 gruba randomize olarak ayrıldılar. 1-) Birinci gruba, Esssitalopram 10 mg/gün ile birlikte, fibromyalji akupunktur noktalarına gümüş iğneler, haftada 1 kez, 16 hafta süre ile yerleştirildi (n=42). 2-) İkinci gruba yalnızca essitalopram 10 mg/gün dozda, 16 hafta kullanıldı (n=41). Çalışma parametrelerini değerlendirmek için, ağrı VAS ile, depresyon ve anksiyete, Beck depresyon ve anksiyete ölçeği ile, uyku bozuklukları Pittsburgh uyku kalitesi indexi ile, yorgunluk yorgunluk

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şiddeti skalası (FSS) ile, sabah tutukluğu süresi, ve hassas nokta sayısı değerlendirildi. Tüm çalışma parametrelerini çalışma grup randomizasyonuna kör bir araştırmacı çalışma öncesi, çalışmadan hemen sonra ve çalışma bittikten 1 ay sonra değerlendirdi.

Bulgular: Her iki grupta, ağrıda istatistiksel olarak anlamlı derecede azalma görüldü (p<0,05). Ayrıca her iki grupta depresyon, anksiyete, yorgunluk şiddeti, uyku kalitesi ve tutuklukta gelişme ve hassas nokta sayısında azalma, istatistiksel olarak anlamlı idi (p<0,05). Gruplar karşılaştırıldığında, akupunktur+essitalopram grubunda, hassas nokta sayısında daha fazla azalma dışında tüm çalışma parametrelerinde istatistiksel olarak anlamlı bir fark tespit edilmedi.

Sonuç: Fibromiyaljide, essitaloprama eklenen akupunktur tedavisi, hassas nokta sayısında daha fazla azalma dışında, fibromiyalji ile ilişkili diğer semptomlarda istatistiksel olarak anlamlı bir fark oluşturmamaktadır. *(FTR Bil Der 2010;13:93-8)*

Anahtar kelimeler: Fibromyalji, akupunktur, essitalopram, rehabilitasyon

Introduction

Fibromyalgia (FM) is a non-arthritic rheumatic disease of which etiology is indefinite and is characterized with widespread chronic pain, sensitivity on specific anatomic points (tender points), stiffness, sleep disorders, fatigue and frequently with psychological distress (1,2).

Acupuncture is a well-known and effective treatment method for pain; but studies on its effect on FM is a few (3). Non-steroid anti-inflammatory drugs have minor effects on FM and has never been the primary or unique choice (4,5). Central nervous system drugs may have decrease pain, fatigue and sleep disorders of seen in FM. For this purpose amitriptyline, cyclobenzaprine and selective serotonin reuptake inhibitors (SSRI) have been successfully used in the treatment of FM(5,6). Serotonin and somatostanine analogs are being used in the treatment of FM. This experience illustrates the value of serotonin receptor type 2 (5HT2) inhibition with atypical neuroleptics, of neural cation channel and glutamate inhibition with anticonvulsants, and the potential usefulness of antidepressants after establishing 5HT2 control to enhance downward inhibitory tracts (7).

Escitalopram is the therapeutically active S-enantiomer of RS-citalopram, a commonly prescribed selective serotonin reuptake inhibitor (SSRI) as an antidepressant. We seek an answer to the question if acupuncture addition to escitalopram has a role on FM treatment, taking into consideration that it has therapeutic effect by a 16-session implementation for 16 weeks.

The purpose of this study was to compare the effects of escitalopram only and addition of acupuncture to escitalopram in the treatment of FM.

Patients and Methods

Eighty-nine female patients who admitted to Physical Medicine and Rehabilitation, and Rheumatology departments with widespread aches, diagnosed with FM based on 1990 American Collage of Rheumatology fibromyalgia diagnostic criteria (2). Female patients have been randomly divided into two groups without taking into consideration of age. Hemogram, biochemistry, erytrocyte sedimentation rate, anti-streptolysin O antibody, C-reactive protein, rheumatoid factor , antinuclear antibody titers, brucella antibody, vitamin B12, hepatitis markers, thyroid function tests (FT3, FT4, TSH) and parathyroid hormone levels were studied just before starting treatment process. Those patients in whom of the above-mentioned laboratory evaluation was found abnormal, were excluded from the study. Patients were informed about the study and received a written consent. 6 patients (four in the first group, two in the second group) excluded the study because lack of contact. A total of 83 female patients completed the trial.

Measurement parameters and tests used in this study: 10 cm. Visual Analogue Scale(VAS) for pain severity measurement, duration of morning stiffness (minutes), fatigue measurement (fatigue severity scale), the number of tender points, Pittsburgh sleep quality index for sleep disorder, Beck depression inventory for depression measurement, Beck anxiety scale for anxiety measurement (8,9,10).

Abnormal systemic clinical findings such as headache, paresthesia, dysmenorrhea, Raynaud's syndrome, irritable bowel syndrome, and irritable urethral syndrome of FM had been inquired in all patients.

A total treatment of 16 acupuncture sessions (once a week) added to Escitalopram (10 mg/daily), was implied to the first group. Sharply ended handle silver needles with 80 mm long, 0.63 mm diameter were used during the acupuncture session. In each session, at least 6, mostly 12 points were needled regarding the symptoms and pain patterns of the patients. Du 14 have been surely needled in each session and besides, at least two or three of UB 41, UB 42, UB 43, UB 44, UB 45, UB 46 points have been symmetrically needled. Some extra-meridian points, identified by palpation and named as Ah-shi points in Chinese literature, have also been needled. Hand manipulation of needles nearly 30 seconds and sessions was carried on for 20 minute.

In the second group the patients was treated by only Escitalopram (10 mg/daily) for 16 weeks. Both groups were evaluated by a blinded assessor before, at the end and one month after the end of the treatment. Patients didn't used any other drugs during their treatment process.

Statistical analysis was performed using SPSS version 11.0 package for Windows. After performing descriptive statistics of variables at baseline, the Kolmogorov-Smirnof test was applied to evaluate the normal distribution of variables. Continuous data were expressed as means+SD. A paired t-test was used to examine changes in scores between baseline and follow-up examinations. Inter- group differences in variables were analyzed by using repeated measures analysis of variance. Alpha criterion for significance was set at $p<0.05$ in all tests.

Results

83 patients completed the study. 6 patients were dropped out of the treatment because of contact lacking. Demographical data of the patients who completed the trial is presented in the (Table 1). There was no statistically significant difference ($p>0.05$) in comparison of baseline characteristics of the study parameters between groups (Table 2).

The analysis of results showed that there were statistically significant differences ($p<0.01$) on depression, anxiety, duration of morning stiffness, fatigue severity, the number of tender points, VAS and Pittsburgh sleep quality index parameters between the pre-treatment and after treatment values and pre-treatment and one month after treatment values in acupuncture+escitalopram group (Table 3).

In escitalopram group, we also found statistically significant differences ($p<0.01$) on anxiety, morning stiffness, fatigue severity, the number of tender points, VAS parameters, Pittsburgh sleep quality index, and significant differences on depression by means of pre-treatment and after-treatment and one month post treatment period (Table 3).

When efficiency of the both treatment methods was compared, no statistically significant difference ($p>0.05$) in all study parameters was seen except much more decreased tender point count ($p<0.05$) in the acupuncture+escitalopram group (Table 4).

Escitalopram and acupuncture have generally been well tolerated. The most observed Escitalopram depended side effects were nausea, diarrhea. Four patients (two in the first group, two in the second group) have informed nausea, two diarrhea (two in the second group). Those side effects were mild and did not necessitate drug interruption. No patient have lived a fainting or pain shock during the acupuncture application.

When the results of acupuncture+escitalopram group were compared to escitalopram group. It was seen that there were no significant differences in all study parameters in comparison of the groups ($p>0.05$), except much more decreased tender point count ($p<0.05$) in the acupuncture+escitalopram group (Table 4).

Discussion

Fibromyalgia-related pain is treated with analgesics, antidepressants, physical exercise, relaxation techniques, and educational programs, but there is no unanimous protocol for treating the condition. While antidepressants have shown themselves to be effective in the treatment of symptoms (5), the best recommendations available are based on the opinions of committees of experts. One of the alternative treatments used to ameliorate the symptoms is acupuncture, though the various studies which have addressed acupuncture and fibromyalgia to date, have failed to furnish solid evidence of its efficacy (3).

For the fact that the etiology of FM is indefinite, treatment selection is difficult and symptomatic. There is no reliable measurement method for fibromyalgia patient follow-up and

Table 1: Demografhic analysis of the patients who completed the study

	Acupuncture+Escitalopram group(n=42)	Escitalopram group(n=41)	p value
Female / Male	42/0	41/ 0	p>0.05
Mean age (year) (mean+SD)	33.63±7.06	34.20±8.86	p>0.05
Disease duration (year) (mean+SD)	3.89±3.39	3.71±4.42	p>0.05

Table 2: Baseline characteristics of the study parameters

Study Parameters	Acupuncture+Escitalopram group(n=42) (mean±SD)	Escitalopram group(n=41) (mean±SD)	P value
Beck depression inventory score	23.17±11.62	23.47±11.39	p>0.05
Beck anxiety scale score	30.23±13.40	29.90±12.97	p>0.05
Pittsburgh sleep quality index score	9.93±4.18	10.30±5.11	p>0.05
Morning stiffness duration (minutes)	1.46±0.72	1.57±0.63	p>0.05
Fatigue severity scale	5.73±1.15	5.77±1.23	p>0.05
Tender points count	16.87±1.48	16.57±1.63	p>0.05
VAS (Visual Analog Scale) (10 cm)	7.80±1.24	7.97±1.07	p>0.05

treatment (11,12,13,14). Researchers pointed out that citalopram had significant effect on pain and well being (15), whereas acupuncture had been effective on pain and other clinical symptoms in fibromiyalgia (3,14).

Some researchers claimed that FM is a clinical reflection of depression and is seen in 22-68% of patients (16,17). However the relation between FM and major depression has not been proved (18). In our study the majority of patients had minor depression (scale marks between 14 and 24 was accepted as minor, marks over 25 was accepted as major depression). Both of the treatment methods were effective ($p<0.05$) for the depression in FM but not superior to each other in this current study ($p>0.05$).

In clinical inquiries of FM patients, sleep disorders can bee seen as high rates as 60-90% (19,20,21,22). In our work, sleep disorder's rate was also high. It was detected that a significant improvement on sleep quality was provided by use of Amitriptyline (13) and moclobemide (21). In a controlled study with electro-acupuncture; there had been an improvement in sleep quality (14). In our study it was seen that Pittsburgh

Table 3: Comparison of study parameters results for acupuncture+escilatopram and escitalopram groups after the treatment and one month after treatment.

Study Parameters	Treatment group	Pre-treatment (PT) Values (mean±SD)	Just after end of the treatment (AT) values (mean±SD)	PT-AT comparison	One month after end of the treatment (C) values (mean±SD)	PT-C comparison
Beck depression inventory score	Ac+Es	23.17±11.62	14.29±9.70	p<0.01	14.39±9.07	p<0.01
	Es	23.47±11.39	14.38±9.20	p<0.01	14.47±8.24	p<0.01
Beck anxiety scale score	Ac+Es	30.23±13.40	17.50±11.22	p<0.01	17.21±12.37	p<0.01
	Es	29.90±12.97	17.77±10.27	p<0.01	16.97±10.19	p<0.01
Pittsburgh sleep quality index score	Ac+Es	9.93±4.18	6.90±3.79	p<0.01	6.87±3.63	p<0.01
	Es	10.30±5.11	6.97±4.38	p<0.01	6.93±4.73	p<0.01
Morning stiffness duration	Ac+Es	1.46±0.72	0.50±0.57	p<0.01	0.54±0.56	p<0.01
	Es	1.57±0.63	0.53±0.65	p<0.01	0.56±0.65	p<0.01
Fatigue severity scale	Ac+Es	5.73±1.15	4.33±1.56	p<0.01	4.37±1.63	p<0.01
	Es	5.77±1.23	4.35±1.69	p<0.01	4.43±1.59	p<0.01
Tender points count	Ac+Es	16.87±1.48	6.47±3.18	p<0.01	6.93±3.54	p<0.01
	Es	16.57±1.63	9.97±3.75	p<0.01	9.93±3.71	p<0.01
VAS (10 cm)	Ac+Es	7.80±1.24	4.43±1.89	p<0.01	4.90±1.84	p<0.01
	Es	7.97±1.07	4.67±1.97	p<0.01	4.73±2.00	p<0.01

Ac+Es: Acupuncture+ Escitalopram Es : Escitalopram PT: Pre-treatment AT: Just after end of the treatment C: One month after end of the treatment

Table 4: Study parameters comparison of the groups at the end of the study and one month after end of the study

Study parameters	Evaluation Time	Acupuncture+Escitalopram Group values (mean±SD)	Escitalopram Group values (mean±SD)	Comparison of the groups p value
Beck depression inventory	AT	14.29±9.70	14.38±9.20	p>0.05
	C	14.39±9.07	14.47±8.24	p>0.05
Morning stiffness duration (minutes)	AT	0.50±0.57	0.53±0.65	p>0.05
	C	0.54±0.56	0.56±0.65	p>0.05
Fatigue severity scale	AT	4.33±1.56	4.35±1.69	p>0.05
	C	4.37±1.63	4.43±1.59	p>0.05
VAS (10 cm)	AT	4.43±1.89	4.67±1.97	p>0.05
	C	4.90±1.84	4.73±2.00	p>0.05
Beck anxiety scale	AT	17.50±11.22	17.77±10.27	p>0.05
	C	17.21±12.37	16.97±10.19	p>0.05
Pittsburgh sleep quality index	AT	6.90±3.79	6.97±4.38	p>0.05
	C	6.87±3.63	6.93±4.73	p>0.05
Tender points count	AT	6.47±3.18	9.97±3.75	p<0.05
	C	6.93±3.54	9.93±3.71	p<0.05

AT: Just after end of the treatment C: One month after end of the treatment

sleep quality index values were recovered by both methods and efficiency was continued after treatment.

Morning stiffness was detected in FM patients about 75-78 % (16,19) and fatigue rate was declared 86% (23). In our trial, fatigue severity was as well high and stiffness rate in pre treatment period was detected in the majority of the patients. It is known that lack of serotonin can cause pain on FM and therefore antidepressants are used in the treatment (24,25). In two studies were informed that venlafaxine and escitalopram made significant decrease on VAS scores and on morning stiffness in Fibromyalgia patients (24,25).

Some investigators (1,6) claimed that tender points were a measure of general disease. In another study (24), significant decrease on tender points in FM patients with venlafaxine therapy was reported. As in this current study, in some studies (3,26) noted that acupuncture significantly decreased the number of tender points.

Aside from depression and anxiety, stress was also common in patients with FM (27,28,29,30). Yunus et al detected that fibromyalgia patients had various psychological problems (28). Anxiety and mental distress were seen as rates of 50-70 %(27.28). In this current study, scores of depression and anxiety scales were highly positive in all patients before treatment.

Various investigators have pointed out the importance of serotonin and endorphins in the regulation of sleep, anxiety and pain in fibromiyalgia and other rheumatologic conditions (23,25). Levels of endorphins and serotonin in the brain may be changed by taking a number of drugs including alcohol, heroin and other opiates and centrally acting drugs (tricyclic anti depressants or selective serotonin reuptake inhibitors). Electro-acupuncture has been used to stimulate the production of endorphins (29,30,31,32).

Those clinical findings in our work showed that escitalopram, a selective serotonin reuptake inhibitor, could have positive clinical effects on sleep disorders, anxiety and depression by regulating serotonin levels in the brain, as well as addition of acupuncture to escitalopram treatment had similar effects as escitalopram only on symptoms including sleep disorders, anxiety and depression in fibromiyalgia.

In conclusion, both acupuncture+escitalopram and escitalopram only have significant recovery effect on all parameters in fibromyalgia in this study. Along side with sleep quality, anxiety and depression; morning stiffness, the count of tender points and fatique severity have been effectively treated both in acupuncture added to escilatopram group and in only escitalopram group. But when efficiency of the both treatment methods was compared, no significant difference was seen except much more decreased tender point count in the acupuncture+escitalopram group. In this currrent study we found no evidence of benefit resulting from acupuncture addition to escitalopram treatment versus escitalopram only except much more decreasing of tender point count in acupuncture group, as a treatment for fibromyalgia. These findings indicate that addition of acupuncture to escitalopram treatment in fibromyalgia treatment may be preferred only for much more decreasing of tender point count with its cost effectiveness and no major side effects.

References

1. Williams DA, Schilling S. Advances in the assessment of fibromyalgia. Rheum Dis Clin North Am 2009;35:339-57.
2. Bennett RM. Clinical manifestations and diagnosis of fibromyalgia. Rheum Dis Clin North Am 2009;35:215-32.
3. Martin DP, Sletten CD, Williams BA, Berger IH. Improvement in fibromyalgia symptoms with acupuncture. Results of a randomized controlled trial. Mayo Clin Proc 2006;81:749-57.
4. Goldenberg DL. Treatment of fibromyalgia syndrome. Rheum Dis Clin North Am 1989;15:61.
5. Russel II, Fletcher EM. Michalek JE. Treatment of primary fibrositis / fibromyalgia syndrome with ibuprofen and alprazolam, A double blind, placebo controlled study. Arthritis Rheum 1991;34:552-6.
6. Yourself P, Coffey J. For fibromyalgia, which treatments are most effective. J Fam Pract 2005;54:1094-5.
7. Smith NL. Serotonin mechanisms in pain and functional syndromes: management implications in co morbid fibromyalgia, headache, and irritable bowl syndrome - case study and discussion. J Pain Palliat Care Pharmacother 2004;18:31-45.
8. Yücel Ağargün M, Kara H, Anlar Ö. Turkish validation of the Pittsburgh Sleep Quality Index. Türk Psychiatry Dergisi 1996;7:107-15.
9. Watnick S, Wang PL, Demadura T, Ganzini L. Validation of 2-depression screening tools in dialysis patients. Am J Kidney Dis 2005;46:919-24.
10. Lambert MV, Senior C, Fewtrell WD, Phillips ML, David AS. Primary and secondary depersonalisation disorder: a psychometric study. J Affect Disord 2001;63:249-56.
11. Martin-Sanchez E, Torralba E, D´az-Dom´nguez E, Barriga A, Martin JL. Efficacy of acupuncture for the treatment of fibromyalgia: systematic review and meta-analysis of randomized trials. Open Rheumatol J 2009;16:25-9.
12. Bennett RM., Gatter PA, Campbell SM. A comparison of cyclobenzaprine and placebo in the management of fibrositis. Arthritis Rheum 1988;31:1535-42.
13. Carette S, McCain GA, Bell DA. Evaluation of amitriptyline in primary fibrositis. Arthritis Rheum 1986;29:655-9.
14. Langhorst J, Klose P, Musial F, Irnich D, Häuser W. Efficacy of acupuncture in fibromyalgia syndrome–a systematic review with a meta-analysis of controlled clinical trials. Rheumatology (Oxford). 2010;49:778-88.
15. Andrberg UM, Marteinsdottir I, von Knorring L. Citalopram in patients with fibromyalgia–a randomized, double-blind, placebo-controlled study. Eur J Pain 2000;4:27-35.
16. Epstein SA, Kay G,Clauw D, Heaton R, Klein D, Krupp L. Psychiatric disorders in patients whit fibromyalgia, A multicenter investigation. Psychosomatics 1999;40:57-63.
17. Kravitz RM, Katz R, Kot E, Helmke N. Biochemical c1ues to a fibromyalgia-depression link: Irniprarnine binding in patients with fibromyalgia or depression and in healthy controls. J Rheumatol 1992;19:1428-32.
18. Anthony KK, Schanberg L. Juvenile fibromyalgia syndrome. Curr Rheumatol Rep 2001;3:165-71.
19. Hench PK. Evaluation and differential diagnosis of fibromyalgia. Rheum Dis Clin North Am 1989;15:19-29.
20. Dwight MM, Arnold LM, O'Brien H, Metzger R, Morris-Park H, Keck PE. An open clinical trial of venlafaxine treatment of fibromyalgia. Psychosomatics 1998;39:14-7.

21. Yunus MB, Masi AT, Aldag JC. A controlled study of primary fibromyalgia syndrome: features and association with other functional syndromes. J Rheumatol 1989;16:62-71.
22. Jennum P, Drewes AM, Andreasen A, Nielsen KD. Sleep and other symptoms in primary fibromyalgia and in healty controls. J Rheumatol 1998;20:1756-9.
23. Sommer C, Häuser W, Gerhold K, Joraschky P, Petzke F, Tölle T, Uçeyler N, Winkelmann A, Thieme K. Etiology and pathophysiology of fibromyalgia syndrome and chronic widespread pain. Schmerz 2008;22:267-82.
24. Sayar K, Aksu G, Ak I, Tosun M. Venlafaxine treatment of fibromyalgia. Ann Pharmacother 2003;37:1561-5.
25. Anderberg UM, Marteinsdottr I, Knorring L. Escitalopram in patients with fibromyalgia a randomized, double-blind, placebo-controlled study. Eur J Pain 2002;4:27-35.
26. Berman BM, Ezzo J, Hadhazy V, Swyers JP. Is acupuncture effective in the treatment of fibromyalgia. J Fam Pract 1999; 48:213-8.
27. Hudson JL, Pope HG. The relationship between fibromyalgia and major depressive disorder. Rheum Dis Clin North Am 1996;22:285-303.
28. Yunus BM, Ahles TA, Aldag JC, Masi AT. Relationship of clinical features with psychological status in primary fibromyalgia. Arthritis Rheum 1991;34:15-25.
29. Jang ZY, Li CD, Qiu L, Guo JH, He LN, Yue Y, Li FZ, Qin WY. [Combination of acupuncture, cupping and medicine for treatment of fibromyalgia syndrome: a multi-central randomized controlled trial]. Zhongguo Zhen Jiu. 2010 ;30:265-9.
30. Itoh K, Kitakoji H. Effects of acupuncture to treat fibromyalgia: a preliminary randomised controlled trial. Chin Med. 2010; 23;5-11.
31. Targino RA, Imamura M, Kaziyama HH, Souza LP, Hsing WT, Imamura ST. Pain treatment with acupuncture for patients with fibromyalgia. Curr Pain Headache Rep 2002;6:379-83.
32. Iguchi Y, Tokuda H, Tamura S, Kishioka S, Ozaki M, Yamamoto H. Effects of electroacupuncture on beta-endorphin contents in rats. Nippon Yakurigaku Zasshi 1985;86:105-14.