Therapeutic effect of duloxetine combined with ozone trigger point injection on fibromyalgia—A retrospective observational study

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Abstract

Importance

Fibromyalgia (FM) is a common clinical chronic disease, mainly manifested as generalized chronic muscle pain and discomfort throughout the body, often accompanied by various emotional disorders such as depression, anxiety, cognitive impairment and sleep disorder, which seriously affects the quality of life of patients. However, there has not been adequately good treatment methods in clinically, so it is urgent to seek a better treatment method. In this study, duloxetine combined with ozone pain point injection was used to treat FM patients, and the clinical efficacy of the patients was observed.

Objective

To determine whether duloxetine combined with ozone pain point injection is safe and efficacious in the treatment of Fibromyalgia.

Methods

According to the final treatment plan selection, the patients diagnosed with FM in the Pain Department of Shiyan Taihe Hospital, were selected from July 2017 to July 2020. After communication and written consent, 66 patients were injected with drugs and ozone pain point. Actually 60 cases finished the study procedure and follow-up. The age ranged from 22 to 57 years, and the course of the disease ranged from 2 to 8 years. In this study, a crossover design was adopted, and random number table method was used to enter the group. The patients were randomly divided into duloxetine group (group D), ozone injection group (group O) and duloxetine-ozone injection group (group D+O), with 20 patients in each group. Each group was given corresponding treatment. VAS, FIQ, PSQI and HAMD scales were used to evaluate and calculate the number of pain points, so as to observe and evaluate the clinical efficacy of patients.

Results

In terms of pain, there was no significant difference among the groups before treatment. After 2 weeks and 4 weeks of treatment, the VAS scores in each group were significantly lower than before intervention ($F=324.365$ $P < 0.05$). The number of pain points in each group was significantly lower than before intervention, and the difference was statistically significant ($F=514.046$ P < 0.05). It was observed that the analgesic effect of duloxetine combined with ozone pain point injection in the treatment of fibromyalgia was better than that of single therapy. There was no significant difference in quality of life among the groups before treatment. After 2 weeks and 4 weeks of treatment, the FIQ of each group was significantly lower than that before intervention, and the difference was statistically significant ($F = 324.365$, $P<0.05$). It was observed that duloxetine combined with ozone pain point injection for fibromyalgia significantly improved the quality of life of patients, especially in terms of improving sleep, compared with treatment alone. At the end of 4 weeks of treatment, HAMD scores for depressive symptoms were significantly lower in all 3 groups than before intervention ($F=1079.961$, $P<0.05$), and

loxetine combined with ozone pain point injection for fibromyalgia had a more significant antidepressant effect (F=5.089, P <0.05).

Conclusion

This study confirmed that duloxetine combined with ozone pain-point injection can effectively relieve pain in patients with FM, significantly improve the accompanying symptoms of sleep disorder and depression, and improve the quality of life of patients, which is worthy of clinical promotion.

Strengths And Limitations Of This Study

Though this study provided clinical evidence for treating FM with combination of duloxetine and ozone trigger point injection, still we were insufficient of study cases and short of follow-up time and research depth. In the following clinical study, more cases and in-depth elucidating of the pathogenesis of FM at the molecular level are needed.

Introduction

Fibromyalgia (FM) is a common clinical chronic disease characterized by widespread chronic muscle ache and discomfort throughout the body, usually accompanied by various emotional disorders such as depression, anxiety, and cognitive and sleeping disorder[1-3]. Many patients also suffer from other physical ailments, such as Irritable bowel syndrome(IBS),excessive sweating and headache[4, 5]. In the United States, FM affects about 5 million people, which account for 1.6% of the total population, and most of them are females[6, 7]. A global investigation conducted in 2013 suggested that the incidence rate of FM in China has reached 0.8%, thereby leading to prominent economic, social and personal pressure[8-10].

Duloxetine is a FDA approved tricyclic reuptake inhibitor, exerting its function through inhibiting the reuptake of 5-HT and NE by neurons, so as to increase their concentration in centrum and spinal cord[11]. It can be applied to acute severe depression, generalized anxiety disorder, peripheral neuropathic pain and FM[12-16]. Ozone is a powerful oxidant that is extremely unstable, and it can break down to monatomic oxygen and hydroxide radical with very strong oxidizing power[17]. Its function mainly focuses on 5 aspects, which are anti-inflammation and infection, abirritation, oxidizing cholesterol, improving immunity, and providing oxygen to ischemic tissues. Ozone is commonly used for atherosclerosis, hyperlipidemia, rheumatoid diseases and other systemic diseases in clinics[18-20].

However, ozone's merits of safe, convenient and green have greatly expanded its clinical applicability[21]. Now, ozone is widely used in patients who need nerve block and local trigger point injection[22, 23]. The treatment of FM is majorly based on amitriptyline, but more and more data suggested that duloxetine-based treatment is more effective with smaller side effects[24, 25]. Patients of FM have more systemic manifestations. Precise and reliable data on the efficiency of combined therapy is absent. To fill this gap

and meet the clinical need, we compared the therapeutic effect of duloxetine, ozone trigger point injection, and the combination of the two on fibromyalgia.

Methods

General data

This study was approved by the ethics committee of the Taihe Hospital(Reference Number:2012KS006), Shiyan, Hubei province. The Participants were recruited from hospitalized patients who were diagnosed with FM by Department of pain treatment. Written consents from 66 patients (4 males and 62 females) to receive drug and ozone trigger point injection were obtained after informed understanding. 60 patients aged 22~57 years with the disease course of 2~8 years finished the study procedure and follow-up.

Patients with the following conditions were excluded: accompanied by psychiatric disorder and severe organic diseases (such as malignant tumor, nervous system disease and other rheumatic diseases); females during gestation or lactation period; digestive ulcer or gastrointestinal bleeding; allergic to the tested drug or ozone; alcohol or drug abuse; dysfunction of vital organs (such as hepatic renal insufficiency); cardiovascular diseases.

All cases ruled out conditions of inflammation, infection, tumor and autoimmune disease. Dignostic criteria: 1. widespread symmetrical specific tender point (11 or more out of 18) throughout the body; 2. sleeping disorder; 3. irritableness; 4. intestinal disorder; 5. excessive sweating; 6. the course of the disease is over a year without other organic diseases. (Figure1).

Treating strategy

According to the final treatment plan selection of patients, the patients was enrolled in accordance with the order of hospitalization, and each group was terminated after 20 patients were enrolled. They were divided into duloxetine group (D group), ozone injection group (O group) and duloxetine-ozone injection group (D+O group) with 20 cases in each group. All participants were treated for 1 month. Subjects in D group were given a daily dose of duloxetine 60mg qd, according to the FDA-recommended dosage. O group received an O_3 trigger point injection which ozone (at a concentration of 30 ug/mL and a volume of 2 mL) was injected into each trigger point once every three days, twice a week, 8 times in total. D + O group received all the treatment mentioned above. During the treatment, participants were not allowed to take other anti-depression drugs, opioid analgesics and non-steroidal drugs.

Therapeutic effect evaluation

VAS, FIQ and tender point count were done prior, 2 weeks and 4 weeks after treatment. A psychiatrist was invited to perform HAMD and PSQI scoring to evaluate the therapeutic effect of each group on FM. A higher VAS score indicates greater pain intensity. The higher the FIQ, the worse the quality of life. A higher HAMD score is recognized to be a higher risk factor for depression. Participants with high PSQI scores

have poor sleep. Tender point: press the diagnosis-involved 18 tender areas with approximately 4 kg pressure and count the number of tender points.

Statistical analysis

All data was represented as average ± standard deviation (`x ± SD), and SPSS 23.0 was used for statistical analysis. Homogeneity test of variances was adopted to compare the means of multiple groups. ANOVA was applied in the intergroup comparison. Intra-group comparisons were performed using repeated measures ANOVA, and SNK is used to test whether there is a significant difference between the groups. Define that a = 0.05 and P < 0.05 indicated statistical significance.

Patient and Public Involvement

This study according to the patient's own will and family economic conditions, some patients choose their own treatment plan. According to the treatment effect, the doctor will also help the patient to choose the best and appropriate treatment plan, and the final result shall prevail. Since this was a retrospective study, patients were not informed before the study, and the group design was made according to the results of the selected plan. Patients are not involved in the recruitment to and conduct of the study. Study results are confidential to patients. The burden of the intervention assessed by patients themselves, we will appropriately offer certain economic compensation.

Results

（1）No significant difference was observed in general characteristics among the three groups (Table 1).

Table 1 The general data of the three groups were compared before treatment

Group	*n*	Age	Gender		Course
			Male	Female	
D	20	38.70±10.584	1	19	4.00±1.298
O	20	39.20±9.666	2	18	3.90±1.518
D+O	20	39.05±8.721	1	19	3.80±1.609

(2) In terms of pain There was no significant difference between groups prior treatment. 2 weeks and 4 weeks after treatment, the VAS score of each group was significantly lower than that prior treatment (F=324.365, P < 0.05), and there is difference among groups with statistical significance (F=4.735, P < 0.05). Trigger point count was apparently reduced than that prior treatment (F=514.046, P < 0.05), the difference between the groups was statistically significant (F=9.452, P < 0.05). These results suggested that the analgesic effect of the combination of duloxetine and ozone injection was better than either one of them (Table 2).

Table 2 The VAS score and pain point count were compared among three groups before and after treatment

Group		*n*	VAS	Pain points count
D				
	Before	20	5.20±1.152	14.35±2.303
	2w	20	3.30±1.129	10.35±2.700
	4w	20	4.20±1.056	7.85±2.720
O				
	Before	20	5.45±1.234	13.85±2.41
	2w	20	4.30±1.218	12.25±2.53
	4w	20	4.45±1.146	9.25±2.149
D+O				
	Before	20	5.40±1.314	14.35±2.254
	2w	20	2.00±1.124*△	7.35±1.631*△
	4w	20	2.80±0.894*△	5.35±1.531*△

Note: * P <0.05,Compared with pre-intervention group, compared with pre-intervention group; △ P < 0.05, Compared with group D and group O

(3) Participants' quality of life There was no significant difference between groups before treatment. 2 weeks and 4 weeks after treatment, the FIQ score of each group was significantly reduced when compared to that before treatment (F=324.365, P < 0.05). Significant differences exist among groups (F=4.73, P < 0.05). PSQI of each group was significantly lower than that prior treatment (F=121.349, P < 0.05), and the difference between the groups was statistically significant (F=12.304, P < 0.05). These results suggested that combination of duloxetine and ozone injection performed better in improving participants' quality of lives, especially their sleeping, than either one of them. Evaluation of depressive symptoms At the end of 4-weeks treatment, scores of 3 groups were significantly reduced compared to that before treatment (F=1079.961, P < 0.05), and the D + O group exhibited a more remarkable effect on anti-depression (F=5.089, P < 0.05),(Table 3).

Table 3 The FIQ, PSQI and HAMD of three groups were compared before and after treatment

Group		*n*	FIQ	PSQI	HAMD
D					
	before	20	50.35±7.118	12.20±3.518	25.55±5.610
	2w	20	36.30±7.406	10.35±2.907	16.50±4.149
	4w	20	28.05±7.119	10.75±2.633	11.30±2.958
O					
	before	20	49.70±7.399	11.90±2.918	26.00±4.531
	2w	20	31.55±6.030	7.30±2.716	15.10±4.734
	4w	20	24.00±5.731	7.40±2.371	10.25±3.370
D+O					
	before	20	51.15±6.885	12.00±3.197	25.10±5.340
	2w	20	21.25±6.680*△	4.70±2.055*△	10.35±3.066*△
	4w	20	17.40±5.614*△	4.15±2.139*△	6.95±2.502*△

Note: * $P < 0.05$,Compared with pre-intervention group, compared with pre-intervention group; △ $P < 0.05$, Compared with group D and group O

Discussion

In this study, a combination of duloxetine and ozone trigger point injection was used for treating FM patients for the first time. Results indicated that the D + O group performed better in relieving pain, improving sleeping, and promoting the quality of life of participants than the D group or O group. FM is characterized by muscle stiffly pain and discomfort with obvious specific tender points throughout the body. Someone put forward a hypothesis of “vasomotor abnormalities in local tissue”, which suggested that muscle aches can be effectively relieved by increasing blood supply in local tissues[26]. Another research found that the mean oxygen saturation of FM patients was lower than 90% at night[27, 28]. We asked whether deficiency of blood supply in local tissue can cause the upregulation of IL-1 and P substance in local tissue and muscle, and further make the patients suffer from chronic and durable aches. While ozone injection can remarkably improve oxygen supply in local tissue, recover cell function and enhance oxygen metabolism of cells, thus we proposed that for FM which encompasses a wide profile of symptoms, ozone local injection can significantly alleviate the ache of patients.

The results proved our hypothesis. Relevant researches data were reported that the pathogenesis of FM involves disciplines of central nervous system, automatic nervous system, neurotransmitter, hormone secretion, immune system, genetics and psychiatry[29–34]. Among them, neurotransmitter of 5-HT and cytokines such as IL-6 and IL-8 were closely related to the development of FM[35–42]. Though this study provided clinical evidence for treating FM with combination of duloxetine and ozone trigger point injection, still we were insufficient of study cases and short of follow-up time and research depth. In the following clinical study, more cases and in-depth elucidating of the pathogenesis of FM at the molecular level are needed.

In conclusion, our research proved that combination of duloxetine and ozone trigger point injection can effectively alleviate the pain of FM patients, significantly improve the accompanied sleeping disorder and depression, so it is worth promoting in clinical use. Compared with traditional anti-depression drug

amitriptyline, duloxetine has smaller side effects but higher prices, therefore its clinical promotion within FM patients is somehow limited. Ozone trigger point injection is welcomed in clinical patients as it is safe, effective and side effect absent.

FM patients suffer from chronic aches, which dropped their quality of life, reduced their social activities and lowered their sense of self-value and decreased their implementation capability. Our research indicated that after 4 weeks of combined treatment, not only the ache of FM patients was remarkably alleviated, but also the depression and sleeping disorder were improved. Therefore, the combination of duloxetine and ozone injection therapy has practical significance of further popularization.

Declarations

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The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

X Chen, CQ Ai, JP Mu, XY Xie attended to the patient. X Chen wrote the manuscript. X Wang, CH Wang, HM Chen, LZ Liu and L Pan gave conceptual advice. Patient advisers also be thanked in the contributorship.All authors read and approved the final manuscript.

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Availability of data and materials

The datasets analyzed in this case report are available from the corresponding author on request.

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Taihe Hospital, Shiyan City, Hubei Province [Reference Number:2012KS006].

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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Figures

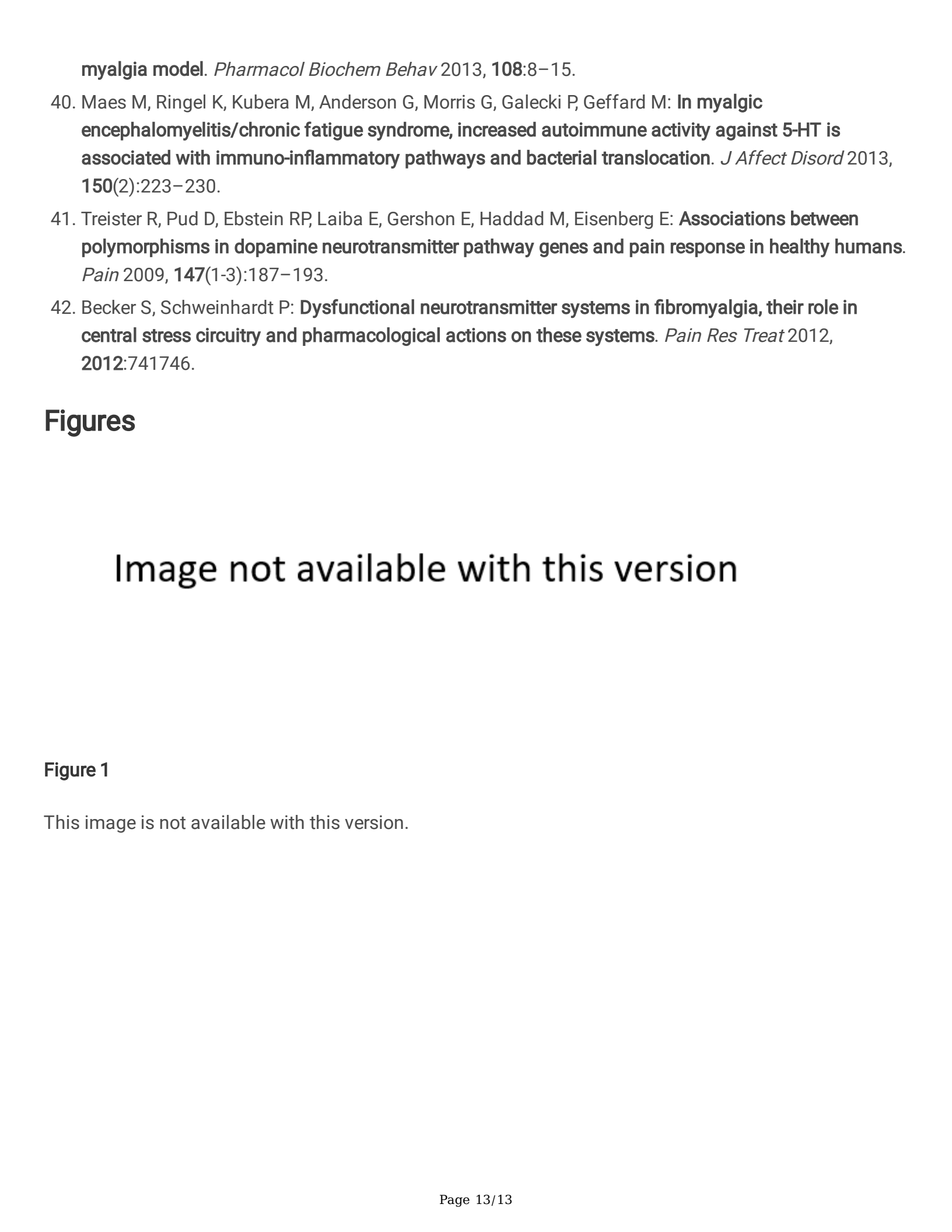

Figure 1

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