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A Pilot Study of Acupuncture plus Moxibustion in Treating Major Depressive Disorder

WANG Xue-feng

Abstract: *[Objectives]* To observe the response rate and the remission rate of acupuncture plus moxibustion in treating major depressive disorder(MDD), and to compare them with the SSRI antidepressant citalopram in STAR*D. *[Method]* This is a real world study. The study was carried out in a private practice located in a small city of Switzerland from Nov 2016 to Mar 2018. Any patient who met the criteria of inclusion was observed. Altogether 13 patients, 11 women and 2 men, are included according to the diagnosis of MDD. The age is between 23 and 69, $46.31 \pm SD14.53$. They may have anxiety and different general medical conditions. Acupuncture was used on the points SI19, HT5, HT4, ST25, KI4, ST41, GB35, KI9, and moxibustion was used on the points BL15, BL19, BL20. Every patient had maximal 10 sessions of treatments. The PHQ9 was recorded before and after treatments. GAD7 was recorded to measure the severity of anxiety before and after treatments when patients report anxious symptoms. The response rate and the remission rate were compared with antidepressants citalopram in the first level of STAR*D research. *[Results]* Before the treatment, all patients' scores of PHQ9 are between 10 and 25. After treatment, the scores of ten patients are below 5, one is 50% above the initial score, and two patients dropped out. So both the response rate and remission rate are 76.9%. Comparing with the response rate and remission rate of Citalopram in the first level of STAR*D, 47% and 33% individually, this pilot study shows that acupuncture and moxibustion treatment could approach much higher response rate and remission rate in treating MDD and further research is strongly advised to confirm this result.

Keywords: major depressive disorder; anxiety; citalopram; acupuncture; moxibustion; STAR*D

Introduction

There are 216 million people suffering depression (Major depressive disorder, MDD) in 2015, around 3% of the global population^[1]. Antidepressant is the main choice to treat depression, but the effect is similar to placebo for most of the depression patients^[2], except those with very serious depression^[3]. The largest antidepressant research, Sequenced Treatments Alternative to Relieve Depression (STAR*D), sponsored by NIH, found out that the remission rate and response rate of SSRI antidepressant citalopram in the first level is only 33% and 47%^[4]. Antidepressants have many side effects, including sexual dysfunction, long-term weight gain, insomnia, nausea, and diarrhea, as well as a great

risk to pregnant women^[2]. Some even increase the suicide rate in juvenile^[5].

Acupuncture, on the contrary, has few side effects. Some research found the efficacy of the electric acupuncture is similar to antidepressant^[6]. Others found acupuncture plus antidepressant are more effective than antidepressant alone^[7]. Some research found out the combination of moxibustion, acupuncture and SSRIs is more effective than only SSRIs in treating depression^[8]. But all these researches only compare the response rate but not remission rate. And the mostly used acupoints in reported researches of treating MDD focused in treating brain, which are apparently influenced by western medicine conception. In TCM theory the heart governs the spirit, conscience and happiness.

In ancient Chinese acupuncture books, many acupoints recorded to treat sadness are from heart meridian or related to heart.

In this pilot study, the main purpose is to observe the remission rate and response rate of treating MDD with acupuncture plus moxibustion(AM), and to compare them with SSRI antidepressant Citalopram in the first level of STAR*D. In addition of using response rate, which only means 50% reduction of scale score, the remission requires the score of a healthy person. Remission means normal social and work function and less odds of relapse. That is the reason why the STAR*D uses remission rate, which is also used in this research.

Materials and Methods

Inclusion criteria: The patients must satisfy the criteria of MDD diagnosis. The age is between 18 and 75. The diagnosis is established when the patient's PHQ9 score (Patient Health Questionnaire 9) ≥ 10 , and the score of first or second item of PHQ9 must ≥ 2 . So all the patients included are at least of moderate degree of MDD, some are severe degree.

Exclusion criteria: Psychotic depression, Bipolar patients, patients with bereavement, patients of cancer or hypothyroidism, and other secondary depression.

From Nov 2016 to Mar 2018, totally 13 patients are included in the research according to inclusion criteria and exclusion criteria. Among them, 11 women and 2 men, age between 23 and 69 ($46.31 \pm SD14.53$), 5 patients have the history of taking antidepressants but relinquished because of side effects or no effect, 4 patients are taking antidepressants but still with severe depression, 4 patients have never used antidepressants before. They all are treated by the same TCM therapist, using acupuncture points SI19, HT5, HT4, ST25, KI4, ST41, GB35, and KI9, with no special manipulations. The needles are of 0.25mm \times 25mm, produced by Acuprime Co. The depth of needling is

between 3mm and 10mm. Moxibustion was used on the points BL15, BL19, and BL20, with the method of grain moxibustion, chain of two grains on each acupoint. It took around one hour for each treatment session. Patients might get extra acupuncture, moxibustion or herbal treatment for other medical conditions, such as headache, etc. The PHQ9 was recorded before and after treatments. Every patient had at most 10 sessions of treatment. Some stopped before having had 10 sessions when achieved remission. In the first two weeks the treatment was given twice a week. Later the treatment was given once a week. GAD7 was recorded to measure the severity of anxiety when patients report anxious symptoms before and after treatments. The patients' informed consents are acquired by signed letters or through telephone.

Results

As shown in the table, before AM treatments, all 13 MDD patients' PHQ9 score are between 10 and 25, average $15.54 \pm SD4.48$. After AM treatments, ten patients achieved remission when their scores are under 5. One patient's score was above 10 and over 50% of the original score. Two patients dropped out because of the burden of the cost or being classified as no remission and no response, although they reported feeling much better. 11 patients' average PHQ9 score is $3.18 \pm SD1.94$. Both of the response rate and the remission rate are 76.9%. Comparing with Citalopram in the first level of STAR*D research, of which the response rate and remission rate are 47% and 33% individually, AM treatment achieved much better results.

Discussion:

Just like STAR*D, this is a real world research rather than a controlled clinical trial. It has very broad inclusion criteria and very few exclusion criteria. Among 13 patients, 70% have chronic and recurrent MDD. Most of the patients showed improvements after 4 sessions of treatment, normally in less than two weeks.

General profile of patients and the result

Features	Statistics
Gender	Male (2), Female (11)
Age (y)	46.31±SD14.53
MDD (PHQ9 score) before treatment	≥20(2,15.3%), ≥15, <20(6,46.1%), ≥10,<15(5,38.5%), Average score 15.54±SD4.48
Antidepressant	Taking (4/30.8%), Taken but stopped (5/38.5%), Never taken (4 /30.8%)
Anxiety (GAD score ≥10)	Yes (3), No(10)
Remission	Yes (10,76.9%),No(1/7.7%), Dropped out(2/15.3%), Average PHQ9 score 3.18±SD1.94
Response	Yes (10/76.9%), No (1/7.7%), Dropped out (2/15.3%)

It is observed that in contrast to MDD patients without anxiety, those with anxiety are a little difficult to achieve response and remission. GAD7 is a self-report questionnaire to measure the severity of anxiety. Scores of 5, 10, and 15 are taken as the cut-off points for mild, moderate and severe anxiety respectively. Among 13 patients, three patients' scores were over 10. After treatment, these three patients have an unsatisfied outcome, one remission, one no response and one dropped out. The remission of MDD combined with anxiety is only 33.3%. But when the other ten patients have no anxiety or have mild anxiety, which means their GAD7 is under 10, the remission rate is 90%.

The SSRI antidepressant citalopram used in the first level of STAR*D showed the frequency and intensity of side effect are both around 85% while AM treatment in this study showed no side effect.

The response rate and remission rate of AM treatment on MDD in this research are much higher than any other previous research. The difference of the result can be contributed to the difference of acupoints. The most frequently used ten acupoints according to archives of treating MDD are Baihui(D20), Yintang (EX-HN3), Neiguan (PC6),

Sanyinjiao (SP6), Taichong(LR3), Shenmen(HT7), Zusanli(ST36), Sishencong (EX-HN1), Hegu(LI4), and Shenting(Du24) [9]. All these 10 acupoints were not selected in this research. Instead, most of acupoints used in this research have never been reported to treat MDD before. The acupoints selected are Tinggong(SI19), Tongli(HT5), Lingdao(HT4), Dazhong(KI4) Tianshu(ST25), Yangjiao(GB35), Zhubin(KI9), Jiexi(ST41), Xinshu(BL15), Danshu(BL19), and Pishu(BL20). Among them, six points was recorded in ancient Chinese acupuncture essay "One Hundred Symptoms(百症赋)". The author is unknown. It was first published in the book "Zhen Jiu Ju Ying(《针灸聚英》)", which was compiled in 1537 by Gao Wu. The essay has it that "Tinggong and Pishu can relieve the sadness of the heart", "Choose the points Tongli and Dazhong for tiredness and sleeping too much", and "For panic and palpitation, not to forget Yangjiao and Jiexi". All the symptoms described here can be found in MDD.

The other five acupoints are selected according to Dr. Zhou Meisheng's Book "Zhen Jiu Jing Dian Chu Fang Bie Cai (《针灸经典处方别裁》)" in treating psycho diseases [10]. These acupoints can

also be found to treat mental disease in other ancient acupuncture books, such as “*Zhen Jiu Jia Yi Jing* (《针灸甲乙经》)”, “*Zhen Jiu Zi Sheng Jing* (《针灸资生经》)”, “*Qian Jin Yao Fang* (《千金要方》)”. The moxibustion on the back are applied in view of the Japanese acupuncturist Bunshi Shiroda’s book “*Zhen Jiu Lin Chuang Zhi Liao Xue* (《针灸临床治疗学》)”, in which four cases of depression patients were reported cured using moxibustion^[11]. He believes that comparing with acupuncture, moxibustion can enhance the vigor better.

In the research of STAR*D, the questionnaire 16-item Quick Inventory of Depressive Symptomatology, Self-Report (QIDS-SR) were used to evaluate the severity of depression. In QIDS-SR, 0-5 is normal, 6-10 is mild, 11-15 is moderate, 16-20 is severe, 21-27 is very severe. In this preliminary research, the PHQ9 questionnaire was used, with 0-4 is normal, 5-9 is mild, 10-14 is moderate, 15-19 is moderate to severe, 20 or above is very severe^[12]. As both are self-report system, the remission rate of PHQ9 (0-4) can be regarded as equal to the remission rate of QIDS-SR (0-5). Many America medical institutes recommend PHQ9 to make diagnosis, assessment and supervision of the patients^[13].

Besides STAR*D research, some other research also found in chronic MDD patients the remission rate of antidepressant in 12 weeks treatment is 22%-30%^[14]. So the 33% remission rate of the first level of STAR*D is a representative result. In contrast to other RCT studies, the STAR*D is a real world research. Every patient come from primary or psych clinic, often accompanied with other chronic deceases, and this is unacceptable in any antidepressant RCT clinic trial. This pilot study is also a real world research, patients often have other chronic disease, just like the similar condition of STAR*D. This study is carried out in a private clinic in a small city of Switzerland. The study will continue with more patients observed.

In the past researches of acupuncture treating MDD, one meta analysis shows that AM is not better than antidepressants^[15]. But this study involved heart focused acupoints and found a completely different result that advises AM is much more effective than antidepressant SSRI Citalopram in treating MDD.

What could be the mechanism that AM can treat MDD in this research?

In this research, totally five acupoints are to treat heart disorder directly, and the other six points from other meridians are to help with concentration, energy and courage. In TCM theory the heart governs the spirit and conscience, and the happiness comes from the normal function of the heart. When the heart is impaired, the person will be sad. It is also observed that the weak pulse was quite common in MDD patients before the treatment. When the depression was getting better, the pulse also got stronger. In some patients, the heart points (BL15, D11) on the back can be painful when pressed gently. And this pain may disappear when the patients get remission. This is compatible with lots of reports that MDD is related with heart disease and sudden death. So here is the hypothesis: The low cardiac output, caused by heart impairment, is the key factor in the development of MDD. As thyroxine can increase the cardiac output, so it can also treat depression^[16]. Calcium antagonist and β blocker can increase the risk of MDD, maybe by reducing the cardiac output^[17]. During pregnancy healthy women often have a reversible adaptive cardiac hypertrophy, which will recover to normal after giving birth^[18]. When the cardiac hypertrophy reduces the cardiac output and is slow to recover, it is possible for women to develop perinatal or postpartum MDD. The patients of depression in chronic heart failure sufferers are about 2 to 3 times of the rate in the general population. When the ejection fraction <40%, nearly 50% of them scored as depression^[19]. And low systolic blood pressure can indicate the depression on those juvenile who are the offspring of depressive parents^[20]. All these researches show that it is the low cardiac

output that causes depression. The AM treatment can improve the function of heart qi and blood by showing their pulse getting stronger after treatment. It is noticed that once the patients' pulse get stronger, the depression symptom will also reduce. Usually the etiology of depression is believed in the brain which is lack of enough neurotransmitter. The heart impairment can be caused by mental stress, which can lead to coronary microvascular dysfunction and ischaemia^[21], and sometimes strong mental stress can lead to acute stress cardiomyopathy^[22]. And large quantities of medical literature show that stress is the strongest risk factor for MDD^[23]. Evidence shows stress is also linked to inflammation in the body^[23]. The hypothesis believes that inflammation is the mediator of stress and heart impairment, which lead to low cardiac output and MDD.

Conclusions

This pilot study shows that AM has much higher response rate and remission rate in treating depression than SSRI antidepressant Citalopram in STAR*D. The combination of heart focused acupoints seems to produce better effect than brain focused points in treating MDD. It worth it to carry out further studies widely in large groups to solidify the claim.

Disclosure Statement: No competing financial interests exist.

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● 临床经验 ●

Chinese Herbal Powder for Eczema with Asthma:

A Report of Three Successful Cases

PENG Xiao-ying, FAN Xin-sheng

Abstract: Clinically eczema often combines with asthma. According to the clinical practice of the author, Chinese herbal powder has been used in the treatment of eczema with asthma and achieved