An observational study of acupuncture and complementary treatments for major depression: Case series from a preliminary study of proposed collaborative care model

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1. Introduction

Depression is one of the leading causes of disability in the world, the main characteristics of which are low mood and anhedonia, and it may include sleep architecture disturbance, nutritional state impairment, chronic fatigue, and disrupted social interactions. MDD has a complex physiopathology (it is a psycho-immune-endocrine disorder) and can have many comorbidities; it is also
considered a life-threatening disease, as 10–15% of patients with depression die from suicide, and 90% of suicides are related to a depressed mood. The lifetime prevalence in adults is estimated at 12%, with a continuously increasing rate. MDD may become the second most prevalent global burden of disease by 2030, according to the World Health Organization (WHO). This dynamic is reflected in Taiwan’s epidemiology, where the prevalence doubled between 1990 and 2010, and the rate of depression in the population is nearly 25%.

There are many challenges in treating depression, which also impact epidemiology, as available treatments are less than satisfactory (only 40% of patients respond to treatment), and one of the main complaints about medications is intolerable side effects. For this reason, we wanted to create an outpatient model using an integrated approach and a multidisciplinary understanding of human physiology that incorporates multiple medical sciences and a teaching mechanism for patients.

We considered the novelty of our study as there is a gap in the literature regarding an integrated treatment method with a multitarget mechanism that successfully can be translated into clinical practice, as well as the use of CCMQ (constitution Chinese medicine Questionnaire) as a tool for personalized treatment in the psychiatric field.

We present a case series based on CARE guidelines of 15 participants who were involved in a diversified and integrated treatment created to evaluate the effectiveness of a multidisciplinary treatment to decrease symptoms and improve health and quality of life.

2. Materials and methods

2.1. Participants

Participants included in the study were between 18 and 65 years old and had a diagnosis of major depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (diagnosis codes 296.21–296.30, 300.4). The participants all had moderate cognitive impairment (21-item Hamilton depression rating [HAM-D 21] ≥14 points). Patients with other mental diagnoses (including substance abuse), serious suicidal ideation, the antecedent of taking antipsychotic or antiepileptic drugs in the last six months, or severe medical pathologies (cerebral, renal, cardiac, hepatic diseases) were excluded.

Eighteen patients who met the criteria were recruited from the Ambulatory Psychiatric Department of Western Medicine and the Traditional Chinese Medicine Department of China Medical University Hospital in Taichung, Taiwan and were included in the study after signing the informed consent. The protocol registration number IRB is CMUH109-REC3-041; trial registration number NCT04469608; supported by the Department of Chinese Medicine and Pharmacy, Ministry of Health and Welfare (M09G1025). And The practitioners underwent a Western psychiatric examination and were included in the study only if their health status was suitable for participation.

2.2. Evaluation

Response to treatment was evaluated by comparing data collected at baseline, two months after the treatment began (week 8), and one week after treatment concluded (Week 9). The main outcomes were a reduction in depression severity assessed by self-reporting on questionnaires. These included the HAM-D 21[11] and the Beck Depression Inventory (BDI).[12] Sleep disruption was evaluated using the Pittsburgh Sleep Quality Scale (PSQS).[13] and the Quality of Life Scale (QOLS)[14] instrument screened for quality of life perception.[15] The Constitution in Chinese Medicine Questionnaire (CCMQ)[16] was used to determine constitution imbalance based on traditional Chinese medicine (TCM) theory.

Heart rate variability (HRV) was tested twice: once at baseline and once at week 8, each time for about 2 min. This was a non-invasive method of obtaining information about the body’s autonomic nervous system. We used a handheld HRV analyzer (pressing the thumb and index finger). Additionally, blood sample analysis was performed with about 15 ml each time, evaluating white blood cell (WBC) count with differential, liver function (AST, ALT), kidney function (blood urea nitrogen [BUN] and creatinine), and inflammation markers (high sensitivity C-reactive protein [hs-CRP]).

2.3. Intervention

Our outpatient model was based on multidisciplinary team cooperation among complementary medicines. All participants continued Western psychiatric treatment while they underwent an eight-week outpatient clinic program with integrated treatment consisting of four main interventions: acupuncture, nutrition education, acupressure instruction, and movement meditation (Table 1).

2.3.1. Acupuncture

The acupuncture protocol was based on standards for reporting interventions in clinical trials of acupuncture (STRICTA) guidelines. Traditional acupuncture treatment with 0.35 mm × 25 mm filiform needles was performed two times per week for 20 min in each session for a total of eight weeks, with an interval of more than 48 h between each session. All participants received scalp acupuncture at eight points following TCM standards (Baihui, Sishencong (EX-HN1), Yin Tang (Ext-2), and Fajit), and individualized acupoints were selected along the 12 meridians according to practitioner experience and participant constitution. Needle manipulation was allowed until the “de-Qi” sensation was determined by the practitioner and participant. The intervention was carried out by a physician-certified acupuncturist with eight years of work experience.

2.3.2. Nutritional assessment

Each participant received personalized nutritional guidance and dietary advice during the first week of enrollment from a nutritionist in a 30-min session, followed by Chinese constitutional theory and patient needs. The intervention also included goal setting and motivational interviews to support adherence to the recommended diet. Participants received a food hamper that provided examples of serving sizes, a list of recommended foods and the main components for meal plans.

2.3.3. Acupressure

Based on the patient’s main constitution according to the CCMQ, eight possible groups of points were set according to meridian theory and acupuncture points. Participants learned to identify and locate these points for daily self-care massage (Table 2).

2.3.4. Tai chi, mindfulness and yoga

Movement meditation was performed during weekly 1-h sessions of tai chi taught by a physician, and once a month, mindfulness, breathing meditation, and yoga were taught by a psychologist. Each class was 1 h long. A video recording of instruction was provided to the class to practice at home. A weekly register was asked to follow up on the outpatient adherence.
2.4. Data analysis

Statistical analysis data obtained in this study were analyzed using the SPSS software, version 20.0. Descriptive statistics were used for the calculation of the data, min, max, and Mean. Intra-group comparison of data with normal distribution was made by using paired t-test. And for the data with non-normal distribution Wilcoxon rank-sum test.

3. Results

The mean age of the participants was 40 years, and 72% of the participants were women. The mean severity according to HAM-D 21 was 21 ± 5. The average number of years since depression was diagnosed was 7 ± 3 years, and 80% were undergoing antidepressant medication prescribed by the Department of Psychiatry. Fifteen of the original 18 participants completed treatment; two abandoned the study for personal reasons, and one patient was excluded based on inclusion criteria. No adverse effects were registered during treatment. (Table 3).

Table 1

| Collaborative model Schedule | W1  | W2  | W3  | W4  | W5  | W6  | W7  | W8  |
|-----------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| Acupuncture                 | •   | •   | •   | •   | •   | •   | •   | •   |
| Nutritional assessment      | •   | •   | •   | •   | •   | •   | •   | •   |
| Acupressure                 | •   | •   | •   | •   | •   | •   | •   | •   |
| Qi cong                     | •   | •   | •   | •   | •   | •   | •   | •   |
| Yoga                        | •   | •   | •   | •   | •   | •   | •   | •   |
| Mindfulness                 | •   | •   | •   | •   | •   | •   | •   | •   |

According to the CCMQ, there was a heterogeneous distribution between constitutions. The main constitution (highest score) was Qi stagnation, followed by blood stagnation. These were also calculated and analyzed, as a higher score reflects a greater imbalance (except for gentleness) (Fig. 2).

Blood sample results showed no differences between baseline and one week post-treatment (Table 5). HRV results showed decreased baseline values of high frequency (HF), low frequency (LF), and LF/HF ratio variables, with no significant change after treatment (see Table 6).

4. Discussion

The complex nosogenesis of depression as a condition of multifactorial causation due to multisystem abnormalities creates limitations in primary treatment. An integrative and multidisciplinary medical intervention is necessary as a pathway for understanding human physiology according to the different spheres: mental, physical, emotional and sociocultural. Our outpatient model included two main branches: Western medicine and traditional Chinese medicine. The response rate was 80% (12/15 patients).
participants) according to HAM-D 21, with a significant difference in response rates for the self-rated scales of BDI and QOLS. Of the 12 participants, three experienced remission and nine had reductions in more than 50% of their symptoms. These outcomes correlate to meta-analysis report rates, in which the success of the synergistic treatments of acupuncture and antidepressants range from 18% to 100% (mean of 76.8%), compared with 4.2%—93.6% (mean of 50.83%) with antidepressants alone.18

We used acupuncture as part of traditional Chinese medicine, which has been widely studied and shown to be safe and effective for symptoms of depression. Among mental health conditions, depression has the highest evidence-based acupuncture effects in quality studies. Decreases in severity compared to placebo have been documented19, with even more significant effects when combined with Western medicine20 as it decreases antidepressant dosage requirements and, therefore, side effects.21 In specific phenotypes, such as women in perimenopause and menopause, it is a viable alternative for reducing symptoms.24 Additionally, Nutritional assessment (with solid epidemiological evidence that poor nutrition leads to depression25—27) and movement meditation based on the benefits of mindfulness and Qigong28,29 practice were included in the collaborative intervention model (Fig. 3).

According to Chinese medicine theory, acupuncture regulates the Shen (spirit) by fixing the imbalance between internal organs, Qi and blood, and clearing the meridians and blood stasis—all of which leads to emotional stability. Also, the physiology behind its mechanism of action has resulted in neurotransmitter modulation,30—32 inhibition of the tryptophan-Kynurenine pathway,33 reduced cortisol and ACTH levels34—36 and regulation of the

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Table 3
Patients with depression Baseline Characteristics N = 18, HAMD-21 Hamilton depression scale; BDI, Beck Depression Inventory scale; PSQI, Pittsburgh Sleep Quality Scale, QOLS, Quality of life scale.

| Characteristics                                      | N = 18 | Ages (years, mean ± SD) | 40 ± 11.10 | Gender            | Male (n, %) | 5 (27.7%) | Female (n, %) | 13 (72.3%) | BMI Body Mass Index (kg/m2, mean ± SD) | 23.6 ± 4 | MDD history (years, mean ± SD) | 7.12 ± 8.54 | HAMD-21 (mean score ± SD) | 21 ± 5.1 | BDI-II (mean score ± SD) | 29 ± 9.6 | Pittsburgh (mean score ± SD) | 12.9 ± 3.7 | Qol (mean score ± SD) | 41.4 ± 6.9 |
|------------------------------------------------------|--------|-------------------------|------------|-------------------|-----------|-----------|-------------|-----------|-----------------------------|-----------|---------------------------|-------------|-------------------------|-----------|-------------------------|-----------|-------------------------|-------------|-------------------------|-----------|

Main Constitution (CCMQ, mean score ± SD)
- Blood stagnation
- Qi stagnation
- Wetness heat
- Qi deficiency
- Phlegm-wetness
- Gentleness

Taking only prescribed antidepressants (n, %)
Taking only prescribed TCM herbal medicine (n, %)
Taking combine TCM and antidepressants (n, %)

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Table 4
Change in Symptom severity of MDD patients that before and after 8 weeks of treatment N = 15; HAMD-21 Hamilton depression scale; BDI, Beck Depression Inventory scale; PSQI, Pittsburgh Sleep Quality Scale, QOLS, Quality of life scale.

| Variable | Baseline Mean(SD) | 8 weeks Mean(SD) | 9 weeks Mean(SD) | Difference Mean(SD) | T value | P value |
|----------|-------------------|------------------|------------------|---------------------|---------|---------|
| HAMD-21  | 19.5 (4.89)       | 11.26 (5.77)     | 11 (5.61)        | 8.53 (6.06)         | 5.45    | <0.001  |
| BDI      | 28.46 (10.3)      | 18.13 (12.3)     | 18.13 (11.1)     | 10.33 (10)          | 3.99    | 0.0014  |
| PSQI     | 12.1 (3.73)       | 10.13 (3.99)     | 10.13 (3.94)     | 2.00 (3.6)          | 2.11    | 0.0530  |
| QOLS     | 42.97 (6.81)      | 49.39 (9.4)      | 48.935 (8.28)    | −5.95 (5.39)        | −4.28   | 0.0008  |

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Fig. 2. CCMQ constitutions means comparison at baseline and after treatment N = 15, Threshold 40 points. It was observed a significant mean change in Qi deficiency 12.93 (17.6SD, p < 0.01); yin deficiency 7.8 (10.46SD, p < 0.01); Wetness-heat 18.6 (22.05SD, p < 0.006); Qi stagnation 19.73 (31.8SD p < 0.003). As well of a significant increase of Gentleness constitution 11,867 (13.9SD, p < 0.005).
Mechanism of action of multitarget integrated treatment for depressed patients: GI tract: gastrointestinal tract. CNS: central nervous system. BBB: blood brain barrier. HPA: Hypothalamus –pituitary – adrenal axis.

5. Limitations
One of our most significant limitations was the lack of a control group. Additionally, we found difficulty in measuring adherence to the assessment recommendations: nutrition, massage and daily practice of movement meditation. It is difficult to assure outpatient practice. During each medical appointment, doubts were resolved, and adherence was checked. Our study focused on the effectiveness of an integrated intervention, so all participants were followed by psychiatric medical care. However, we did not monitor medication compliance or psychopharmacology efficacy. Finally, we recommend a longer follow-up of participants to evaluate adherence to healthy lifestyle development, continuity and relapsing rate.

6. Conclusion
An integrated outpatient treatment method of Chinese and Western medicine, including acupuncture, nutrition, mind training, and physical activity, can be combined with pharmacological treatment effectively and could reduce depression symptoms when applied successfully in clinical practice. As a preliminary study, future research is needed in multitarget treatments to confirm the implication of this network medicine model for MDD patients; the confirmation of our findings can lead to patient-centralize treatments, thus improving recovery outcomes.
Declarations of competing interest

The authors declare that there are no conflicts of interest.

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