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Acupuncture and Herbal Medicine for Depression from Traditional Empiricism to Research Evidence

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Mental diseases have become a very serious issue in public health not only in Hong Kong but also in Mainland China. The types of mental diseases that we concerned may include insomnia, depression, anxiety disorders, bipolar disorders, suicide, substance addiction, senile dementia, schizophrenia and children psychiatry (such as ADHD and autism).

Pharmacotherapy is the mainstream treatment for major psychiatric problems, but there are many shortcomings, for examples, limited efficacy, development of drug tolerance, the issues of addiction and dependence, as well as other adverse side effects [1-5]. Common examples of such adverse side effects of pharmacotherapy are metabolic diseases (such as body weight gain, hyperprolactinemia, amenorrhoea), extrapyramidal symptoms, tardive dyskinesia (as induced by typical anti-psychotic drugs), hyper-salivation, leucopenia, constipation and digestive dysfunction.

Actually, there is a long history in applying Traditional Chinese Medicine (TCM) in treating emotional and mental problems, as well as for the wellbeing. Herbal medicine and acupuncture are the most commonly used ones in the Chinese community. Also, moxibustion, cupping, scraping, massaging and dietary therapy have also been applied. The application of TCM psychological therapy that similar to CBT has also been recorded in TCM literatures. In addition to the above, there are also aromatic therapy, bathing therapy, exercise therapy (tai-qi), meditation and mindfulness therapy (qi-gong), laughter and humor therapy, folk music therapy. All of above can be applied to deal with mental and emotional problems in TCM.

TCM has very huge potentials to develop its roles in mental healthcare. For examples, in the population without or with mild mental-emotional problems, TCM has a lot of approaches for the wellbeing and prevention for "sub-health" in this population. For the population with "curable" or moderate mental-emotional problems, the acupuncture and herbal medicine can serve as monotherapy in treatment. For "refractory" or severe psychiatric illness (like schizophrenia, bipolar disorders), TCM such as acupuncture and herbal medicine can be applied as an adjunctive therapy to enhance efficacy of conventional treatment and to reduce the side effects. Our long-term research direction is to explore novel treatment strategies particularly from herbal medicine and acupuncture for major neuropsychiatric disorders. For examples, neurodegenerative diseases, mood disorders, anxiety disorders, psychotic disorders and cognitive disorders.

Over the past 5 years, we have several clinical trials of herbal medicine and acupuncture for mood disorders. In a work

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joining The University of Hong Kong, we developed new novel acupuncture stimulation treatment, called Dense Cranial Electroacupuncture Stimulation (DCEAS). In our clinical practice for mental problems, 13 or even 14 needles will always be used in DCEAS. Following the putative neural pathways for acupuncture signals [6], we put many needles in the forehead. It is because the pathways go to the brainstem which contains many kinds of important neurotransmitters that relate to the cortical and subcortical modulation [6].

There was a clinical trial for DCEAS for major depression in Kowloon Hospital with objective to determine whether patients with Major Depressive Disorder (MDD) in DCEAS combined with Selective serotonin re-uptake inhibitors (SSRIs) could produce significantly greater clinical improvements compared to sham acupuncture [7]. The inclusion criteria for the trial were people aged 25 to 65 years, have a diagnosis of MDD according to Diagnostic and Statistical Manual of Mental Disorders (4th Edition) (DSM-IV), scored more than 18 points in 17-item Hamilton Depression Rating Scale (HAMD 17), and scored above 4 points in Clinical Global Impression-Severity (CGI-S) as moderately ill. A total of 73 patients were randomized to receive 9 sessions of DCEAS or noninvasive electroacupuncture control procedure (n-EA) combined with fluoxetine for 3 sessions per week in 3-week duration. Clinical outcomes were measured using the HAMD-17, CGI-S, and Self-rating Depression Scale (SDS) as well as the response and remission rates. The credibility of n-EA and DCEAS was also evaluated. After the completion of 9-session treatment, patients were asked: 'As we informed you that you had an equal chance of receiving sham or active acupuncture treatment, which do you think you had received?' No significant difference was found in the baseline characteristics and the result of credibility also found that there was not significant different between the two groups.

Mean Changes from baseline in score on HAMD-17, CGI-S, and SDS over time were reviewed. DCEAS-treated patients exhibited greater improvement on depressive symptoms, as indicated with the significant greater reduction of HAMD-17 and SDS.

There was another randomized controlled trial with 4-week follow-up of acupuncture with paroxetine in patients with major depressive disorder [8]. We divided patients into 3 groups. The first group was the paroxetine (PRX) alone, the second group was paroxetine combined with manual acupuncture (MA-PRX) and the third group was paroxetine combined with electrical acupuncture (EA+PRX). It was not a surprise that the result was similar to the clinical trial in Hong Kong. The clinical response was markedly greater in MA and EA groups than the group with PRX alone. More importantly, at 4 weeks follow-up after completion of treatment, there was still greater improvement in the EA groups comparing to the group treated with PRX alone. However, the clinical response of the MA group was declined to the similar response level of the group with PRX alone. These are very important findings with two implications. The first one was electrical acupuncture may have a long-lasting effect in enhancing the antidepressant effects. The second important one was that the effect of acupuncture is not a placebo effect. If the effect of acupuncture is a placebo effect regardless of manual or electrical acupuncture, the effect should decline after 4 weeks. Also, both MA and EA have higher therapeutic responses and can reduce the dose of paroxetine use. There are also pilot control trials on DCEAS for postpartum depression [9], post-stroke depression [10] and refractory obsessive-compulsive disorder [11].

For the important herbal medicine in TCM, we have one retrospective controlled study in collaboration with the Tongde Hospital in Zhejiang Province in Hangzhou [12]. In this

trial, five herbal medicine formulas were designed that based on traditional Chinese medicine (TCM) diagnoses. Of 1,672 patients who were admitted to the Department of Psychosomatics between 2009 and 2013, we identified 68 patients who have very severe depression episodes and only received conventional psychotropic drugs. Another 78 received combination of anti-depressant and herbal medicine. The study would like to compare the outcomes with or without herbal medicine. With survival analysis, the result was clearly showed that the people with the herbal medicine had 2.179 times higher chance in achieving a clinical response and almost 6 more times higher chance in achieving remission compared to those without herbal medicine. Comparing to treatment with psychotropic drugs alone, the group with additional herbal medicine has less reported incidences of physical tiredness, headache, palpitations, dry month and constipation. It indicated herbal medicine reduces the incidence of adverse events.

Several years ago, we have grants from USA to support clinical trials on Free and Easy Wanderers Plus (FEWP) and two academic papers have been published in Journal of Psychiatric Research [13, 14]. FEWP is a well-known TCM formula which is often used for mood symptoms, such as mood swings, anxiety, depression, menstrual-related mood syndromes. We divided patients into 3 groups for treatment with carbamazepine (CBZ) alone, CBZ plus FEWP, or equivalent placebo for 12 weeks. Compared to CBZ monotherapy, adjunctive FEWP with CBZ resulted in significantly better outcomes on the three measures of depression at week 4 and week 8 and significantly greater clinical response rate in depressed subjects, but failed to produce significantly greater improvement on manic measures and the response rate in manic subjects. There was a lesser incidence of side effect in the combination therapy compared to CBZ monotherapy.

In conclusion, messages from our clinical studies are 1) both acupuncture and herbal medicine are beneficial in treating depressive disorders, 2) depressed patients on acupuncture and herbal medicine had lesser incidence of adverse events, and 3) TCM is an effective approach for the prevention and treatment of depression. Hong Kong is become a very important area in providing health care, TCM can play important role in the new industry of health care.

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