DOCTORAL THESIS

Randomized controlled clinical trials for the evaluation of efficacy and safety of Chinese medicine in treatment of neurodegenerative diseases

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ABSTRACT

Background: Neurodegenerative diseases (NDD) are very common in the aging population, of which Parkinson's disease (PD) and Alzheimer disease (AD) are the two most common. Since the etiology of the neuronal death in these diseases remains unclear, currently no curative therapy is available. Traditional Chinese medicine (TCM) has been used to treat certain diseases, which based on their symptoms we now know that they are included PD and AD, for thousands of years. However, our pervious systematic review reports that the quality of current TCM clinical trials related to this area had limited internal validity due to methodological flaws and insufficient data reporting.

Methods: This study includes two add-on double-blinded randomized controlled trials (RCT), PD full-scale study and AD pilot study. It aims to provide evidence for the efficacy and safety of two specific TCM decoctions, Jia-Wei-Liu-Jun-Zi Tang (JWLJZT) and Di-tan decoction (DTD) in treating PD and AD, respectively. These clinical trials follow the Consolidated Standards of Reporting Trials (CONSORT) as well as the International Conference on Harmonization guidelines on Good Clinical Practice (GCP). Also, this two RCT obtained the approval from the Human and Animal Research Ethics Committee of Hong Kong Baptist University before the study and registered on the Chinese Clinical Trial Registry.

Result: In the PD trial, 111 idiopathic PD patients were randomly assigned to receive either JWLJZT or placebo for 32 weeks. Although there was not significant difference in the primary outcome of Movement Disorder Society – Sponsored Revision of Unified PD Rating Scale (MDS-UPDRS) Part I total score ($p = 0.216$), significant improvements was observed in the secondary outcome of Non-motor symptom assessment scale for Parkinson's disease (NMSS) total score ($p = 0.019$), subtype of mood/cognition ($p = 0.005$) and hallucinations ($p = 0.024$). In addition, post-hoc analysis showed a significant reduction in constipation ($p < 0.001$). On the other hand, 40 AD patients were randomly assigned to receive either DTD or placebo for 24 weeks in the AD trial. There was an improvement trend in the primary outcome of the cognitive subscale of Alzheimer's Disease Assessment Scale (ADAS-cog) total score in the DTD group though the difference relative to the placebo group was not statistically significant ($p = 0.315$). No significant difference was found in the secondary outcomes. Adverse events were mild and comparable between treatment and placebo groups in both trials.

Discussion: JWLJZT did show some improvement in non-motor symptoms, including mood, cognition, and constipation, in PD patients, while, DTD did show a reducing trend in the cognitive impairment based on rigorous RCT. Further study focusing on the effective dosage, pharmacologic mechanism of JWLJZT and DTD are needed to give a fuller picture as well as better support for using them in human being as a routine treatment. In fact, JWLJZT and DTD are the only two examples of TCM for treating NDD. These two clinical trials are served as examples of how to evaluate efficacy and safety of TCM for the treatment of various diseases using rigorous RCT methods and standard.

Keywords: Randomized Controlled Trials, Parkinson's disease, Alzheimer disease, Traditional Chinese medicine, Jia-Wei-Liu-Jun-Zi Tang, Di-tan decoction, Efficacy, Safety

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