Research Snapshots

Hsiewe Ying (Amy) Tan BAppSc
RMIT University, Melbourne, Australia
Research Snapshots Section Coordinator

Anna Hyde BAppSc
RMIT University, Melbourne, Australia

Dawn Wong Lit Wan BAppSc
RMIT University, Melbourne, Australia

Nancy Lee BHSc (Acupuncture) (in progress)
Endeavour College of Natural Health, Gold Coast, Australia

EFFICACY AND TOLERABILITY OF RISPERIDONE, YOKUKANSAN, AND FLUVOXAMINE FOR THE TREATMENT OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA: A BLINDED, RANDOMIZED TRIAL

BACKGROUND: Behavioural and Psychological Symptoms of Dementia (BPSD) refer to a range of non-cognitive symptoms seen in dementia patients, including psychosis, agitation, aggression, anxiety, depression and sleep disturbance. Current treatment options for BPSD in elderly patients are limited and can involve the use of antipsychotics, which can produce severe adverse effects.

OBJECTIVES: To compare the efficacy and tolerability of three pharmacological interventions for the treatment of BPSD, using a randomised, head-to-head, rater-blinded trial design. The interventions were the atypical antipsychotic risperidone, the selective serotonin reuptake inhibitor (SSRI) fluvoxamine and the Japanese Kampo formula *Yokukansan* which is also known as *Yi Gan San*.

The aim was to help establish a reliable BPSD treatment strategy.

METHODS: All participants were inpatients at a psychiatric hospital in Japan. All had been admitted to the hospital due to the severity of BPSD. Informed written consent regarding the trial was gained from each participant where possible, and a legal representative of each participant was also consulted, in accordance with the relevant ethics committees and the Declaration of Helsinki.

Initially all participants underwent a washout period of at least one week, during which all psychotropic medications were discontinued. The trial consisted of an eight-week treatment period where 82 participants were randomly assigned to receive oral risperidone (0.5 – 2.0 mg/d), *Yokukansan* (2.5 – 7.5 g/d) or fluvoxamine (25 – 200 mg/d). The dosages were flexible and were adjusted throughout the trial at the discretion of the trial investigator, who also administered the drugs. The dosages were within the normal ranges for elderly patients with psychotic disorders.

Yokukansan formula is typically prepared as extract granules and contains *Atractylodes Lancea Rhizome* (*Baizhu*), *Poria Sclerotium* (*Fulling*), *Cnidium Rhizome* (*Chuanxiong*), *Uncaria Hook* (*Gouteng*), Japanese Angelica Root (*Danggui*), Bupleurum Root (*Chai Hu*) and *Glycyrrhiza* (*Gancao*), as registered in the *Japanese Pharmacopoeia*.

There were 27 participants in the risperidone group (mean age 80.72 years), 27 participants in the Yokukansan group (mean age 83.50 years) and 28 participants in the fluvoxamine group (mean age 83.20 years).

A blinded rater assessed the participants at weeks 0, 2, 4, 6 and 8 (end point), primarily using the Neuropsychiatric Inventory-Nursing Home version (NPI-NH) outcome measure to assess efficacy in terms of psychopathology. Secondary outcome measures were the Mini-Mental State Exam (MMSE) to assess cognitive function, Functional Independence Measure (FIM) to assess daily life function, and the Drug Induced Extra-Pyramidal Symptoms Scale (DIEPSS) to assess severity of uncontrolled movement caused by taking antipsychotic drugs.

RESULTS: Seventy-six (76) out of 82 patients completed the trial. The study team found that overall the three interventions had equal efficacy in reducing BPSD in elderly patients, but risperidone was less well tolerated. The total NPI-NH scores were significantly reduced from 26.20 (SD 15.77) to 17.72 (SD 11.49). Severe, moderate and mild adverse effects occurred more frequently in the risperidone group. Cognitive function and daily life function did not change significantly over the eight weeks in any group.

CONCLUSION: It was concluded that the three interventions had equal efficacy in the treatment of BPSD in elderly patients, but *Yokukansan* and fluvoxamine were better tolerated and therefore should be recommended over risperidone.

COMMENTS: Designing a clinical trial for elderly patients with cognitive

impairment and neuropsychiatric symptoms requires careful consideration regarding ethics. Involving a placebo group may not be appropriate. As the authors mentioned, the lack of a control group was a limitation of the study as environmental or other influences may have played a role in the improvements of the participants' symptoms.

Although the MMSE and FIM scores did not change significantly in any group, it might have been useful to know the rate at which they had previously been declining, in case the interventions had affected the rate of decline. Similarly, a follow up study showing any changes in outcome measure scores after the treatments had been discontinued might have provided useful information.

Teranishi, M, Kurita, M, Nishino, S, Takeyoshi, K, Numata, Y, Sato, T, et al. Efficacy and Tolerability of Risperidone, Yokukansan, and Fluvoxamine for the Treatment of Behavioral and Psychological Symptoms of Dementia: A Blinded, Randomized Trial. J Clin Psychopharmacol. 2013:33(5);600–7. doi: 10.1097/JCP.0b013e31829798d5

Anna Hyde

A LONGITUDINAL STUDY OF THE RELIABILITY OF ACUPUNCTURE DEQI SENSATIONS IN KNEE OSTEOARTHRITIS

OBJECTIVE: This study investigated the reliability of measuring *deqi* sensations and its relationship with clinical outcomes in a population of knee osteoarthritis (OA) patients.

METHODS: Thirty knee OA patients were randomly divided into three groups: the high-dose acupuncture group, the low-dose acupuncture group and the sham acupuncture group. Verum acupuncture was administered to six acupoints in the high-dose acupuncture group and to two acupoints in the low-dose group. The sham acupuncture consisted of the Streitberger placebo needles at six non-acupoints. The deqi sensations were measured using the Massachusetts General Hospital Acupuncture Sensation Scale (MASS). Each participants were asked to rate the sensations twice during each treatment on a scale of 0 to 10, where 0 is no sensation and 10 the most unbearable. The clinical outcomes were measured before the first acupuncture session and at the last acupuncture session using the Knee injury and Osteoarthritis Outcome Score (KOOS). The participants had six sessions of acupuncture over a period of four weeks.

RESULTS: Thirty participants completed the study. It was found that the feeling of soreness and aching were significantly stronger in the real acupuncture group when compared with the sham acupuncture group. Heaviness was the most reliably rated sensation, whereas coldness was the least reliably rated. When compared to sham acupuncture, real acupuncture significantly improved the KOOS subscales scores for pain (p = 0.025), function in sport (p = 0.049) and quality of life (p = 0.039).

CONCLUSION: It was concluded that real acupuncture produced stronger *deqi* sensation and better clinical outcomes. *Deqi* can be reliably measured using the MASS in knee OA patients.

COMMENTS: This study suggests that the strength of *deqi* sensations affect the therapeutic effects of acupuncture and that *deqi* can be reliably measured. As *deqi* sensation is subjective, the study could have also looked at its relationship with psychological factors. Quantifying *deqi* sensations may enable researches to investigate the strength of *deqi* sensations and the type of sensation that will produce optimal therapeutic effects in different conditions. Further, previous studies have found that stimulating the muscles, nerves and blood vessels can evoke sensations such as soreness, aching, numbness, heaviness and distension. These sensations are also associated with *deqi* sensations. Therefore, research on *deqi* sensations may give a better understanding of acupuncture mechanisms.

Spaeth, R.B., et al., A longitudinal study of the reliability of acupuncture deqi sensations in knee osteoarthritis. Evid Based Complement Alternat Med. 2013;2013:204259.

Dawn Wong Lit Wan

AUSTRALIAN FEASIBILITY STUDY FOR ACUPUNCTURE AND STANDARD EMERGENCY DEPARTMENT CARE FOR PAIN AND/OR NAUSEA AND ITS IMPACT ON EMERGENCY CARE DELIVERY

OBJECTIVE: To evaluate the feasibility of delivering acupuncture in an emergency department (ED) to patients presenting with pain and/or nausea.

METHODS: This study took place at the Northern Hospital ED in Melbourne, Australia, between January and August 2010. Two hundred people presenting to triage with pain measured on the VAS scale of 1–10 and/or nausea measured on the Morrow Index of 1–6 gave consent to participate as the acupuncture group. The people were screened chronologically from earliest to most recent triage and then again by their physician in charge to assess their suitability for acupuncture. The control was a usual care group of two hundred people whose retrospective data from ED electronic health records closely matched those in the acupuncture group. After patient consent was received, acupuncture treatment prescriptions were developed for each patient individually. Manual acupuncture was performed at the bedside in the ED cubicle or treatment room using Chinese manufactured 0.25mm gauge, 30mm or 40mm needles

and *deqi* was obtained. Acupuncture was delivered by emergency medical physicians with medical acupuncture qualifications, acupuncturists registered with the Chinese medicine registration board of Victoria or final year RMIT university acupuncture students under supervision of registered acupuncturists. The ED doctor was free to assess and consult the patients at any stage and pharmacotherapy was permitted as necessary. Needle retention time was 20 minutes. Immediately after needle removal the acupuncturist recorded patient-reported pain and/or nausea scores, adverse events, and participant's acceptability of a) the ED visit, b) the acupuncture treatment and c) their willingness to repeat acupuncture in the future for a similar condition. Demographic data, adverse events and time management were also recorded.

RESULTS: 89% of patients were interested in acupuncture before or after their medical consultation, with 69% consenting to and completing treatment. 98.5% of patients in the acupuncture group reported a satisfaction score between 5 and 10, with more than half willing to repeat acupuncture, and 57% reporting a satisfaction score of 10. Musculoskeletal pain, pain in the abdomen or flank region, headache or vertigo were among the most common presenting symptoms considered to be suitable for acupuncture treatment by the physicians. There were statistically significant differences in pain scores before (mean = 7.01, SD = 2.02) and after acupuncture (mean = 4.72, SD = 2.62) (t (193) = 14.81, $p < 0.001$) and nausea scores before (mean = 2.6, SD = 2.19) and after acupuncture (mean = 1.42, SD = 1.86, $p < 0.001$) in the acupuncture group. There was no significant difference between waiting times for both groups; however those who received acupuncture before consultation with a medical doctor (n = 55) had a significantly shorter waiting time (66 ± 10 min, SE) than those who received acupuncture after their medical consultation (n = 145, 134 ± 4.95 min, SE, $p < 0.0001$). There was also a considerable difference ($p < 0.0001$) between the time staff took to manage patients who received acupuncture before (mean = 182, SD = 99 min) and after (mean = 273, SD = 152 min) medical consultation. There were four patients in the acupuncture group who reported adverse events, two with slight bleeding and two with mild pain at needling site, but no major adverse events were reported.

CONCLUSION: The study suggests acupuncture to be a safe and acceptable treatment for ED patients. In combination with usual medical care, acupuncture may reduce pain and nausea symptoms among ED patients. Careful planning is required for future studies to achieve recruitment targets within the complex ED environment. Future research should develop high quality, large scale RCTs with specific inclusion/exclusion criteria and evaluation of cost-effectiveness. Patients with musculoskeletal conditions were most commonly suitable for acupuncture, suggesting it would be a practical area for future ED acupuncture research. Acupuncture did not delay conventional care. Continuing ED staff education is recommended on basic acupuncture theory and knowledge of future study protocols.

COMMENTS: Until now the possible advantages of acupuncture in hospital EDs have been relatively unknown and untested in Australia. This feasibility study was appropriately designed for an ED where the range of conditions of patients presenting with pain or nausea is vast. The quality of this study was high with aims, ethics approval, patient consent, selection criteria and adverse events stated. The study stayed true to traditional acupuncture protocol via allowing the acupuncturist to evaluate patients and devise practical acupuncture treatment prescriptions for each individual. Also, the analysis of acupuncture's impact on ED staff and time management was a thoughtful inclusion and results in these areas were significant. This pilot has attracted media and public attention and brought about community awareness. The study was funded by the Department of Health Victoria and provides another positive step towards acupuncture's integration into the mainstream healthcare system, a united effort to maximise outcomes for patients.

Zhang AL, Parker SJ, Smit DV, et al. Acupuncture and standard emergency department care for pain and/or nausea and its impact on emergency care delivery: a feasibility study. Acupunct Med. 2014, Feb;(0):1–7.

Nancy Lee