SUPPLEMENT 2

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研究成果報告

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心理健康

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Musculoskeletal Disorders
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Health and Health Services Research Fund

Research Dissemination Reports

MUSCULOSKELETAL DISORDERS

Editorial

Dissemination reports are concise informative reports of health-related research supported by funds administered by the Food and Health Bureau, for example, the *Health and Health Services Research Fund* (which was consolidated into the *Health and Medical Research Fund* in December 2011). In this edition, 11 dissemination reports of projects related to mental health, injuries and accidents, neurology, and musculoskeletal disorders are presented. In particular, four projects are highlighted due to their potentially significant findings, impact on healthcare delivery and practice, and/or contribution to health policy formulation in Hong Kong.

Depression is a global health concern and will be the second highest cause of disability by 2020. The prevalence of postnatal depression ranges from 5% to 25%. Leung et al[1] conducted a randomised controlled trial in 164 postnatal Chinese women comparing group cognitive behavioural therapy with usual care (information booklet) in reducing depressive symptoms and the rate of postnatal depression after intervention. The cognitive behavioural therapy intervention significantly reduced depressive symptoms and was well received by postnatal women. The authors suggest further testing cognitive behavioural therapy as an integral part of postnatal care to complement existing services and reduce waiting time.

Fall is the second leading cause of accidental death worldwide and the elderly is particularly at risk. Poor balance control is a major risk factor for falling in the elderly. Tsang et al[2] conducted a randomised controlled trial in 79 elderly Chinese nursing home residents with a history of fall comparing virtual reality exercise (Wii Fit) with conventional balance training. The results showed that playing Wii Fit games can improve standardised measures of balance and enhance the management of fall prevention in older adults (especially for those living in aged care facilities) and may reduce health care costs and suffering in older adults.

Falls and fall-related injuries after stroke are common. Physical rehabilitation can restore balance control, promote functional recovery, and prevent secondary complications, disability, and handicap. Ng et al[3] conducted a randomised controlled trial to test the effectiveness of transcutaneous electrical nerve stimulation plus task-oriented balance training in recovery of balance and motor function after the first sub-acute stroke. The authors found that the experimental intervention was superior to placebo in improving balance performance and motor functions. Future studies should examine the optimal combined training programme in terms of frequency, duration, and intensity.

Spasticity leads to decreased range of motion of joints, increased pain, spasm, functional disability, and contractures. Limb spasticity also increases the burden on carers in the provision of nursing and personal care. Lam et al[4] conducted a randomised controlled trial comparing botulinum toxin A and placebo (saline) as a supplement to conventional physiotherapy and occupational therapy to treat upper limb spasticity in 55 debilitated infirmary patients. Patients receiving botulinum toxin had significant improvement in muscle tone and joint mobility, and caregivers were able to perform basic upper limb care more easily.

We hope you will enjoy this selection of research dissemination reports. Electronic copies of these dissemination reports and the corresponding full reports can be downloaded individually from the Research Fund Secretariat website (http://www.fhb.gov.hk/grants). Researchers interested in the funds administered by the Food and Health Bureau also may visit the website for detailed information about application procedures.

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A brief group intervention using a cognitive-behavioural approach to reduce postnatal depressive symptoms: a randomised controlled trial

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KEY MESSAGES

1. Postnatal women preferred psychotherapy to pharmacotherapy for reduction of postnatal depression.
2. A brief, cognitive-behavioural, group intervention with 6 weekly sessions significantly reduced depressive symptoms and was well received by postnatal women.
3. This brief group intervention could be further tested as an integral part of postnatal care to complement existing services and reduce waiting time.

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Introduction

According to the World Health Organization in 2005, depression is a major health concern and will be the second highest cause of disability by 2020.[1] Postnatal depression (PND) is a global health issue that affects childbearing families. Many pharmacological and psychosocial interventions have been used to prevent and treat PND. Most postnatal women prefer psychotherapy to pharmacotherapy, particularly breastfeeding mothers who fear the effect of the latter on their infants.[2] Individual cognitive behavioural therapy (CBT) and interpersonal therapy have been recommended by the National Institute for Health and Clinical Excellence guidelines for women with PND in the United Kingdom.[3] Group CBT is equally or even more effective than individual CBT, but the optimal length of CBT intervention for PND remains inconclusive. Group CBT is associated with a lower cost, shorter waiting time, reduced therapy time, and more available places. CBT usually comprises eight to 12 sessions. This study aimed to assess the efficacy of six-sessions of group CBT among postnatal Chinese women in reducing depressive symptoms and the rate of PND at 3 months and 6 months after intervention.

Methods

This randomised controlled trial was conducted from December 2010 to June 2013. Informed consent was obtained from each participant. Hong Kong Chinese postpartum women aged ≥18 years at 6 to 8 weeks after delivery, living with their husband, and able to communicate in Cantonese who had an Edinburgh Postnatal Depression Scale (EPDS) score ≥10 and were assessed by Structured Clinical Interview by DSM-IV were recruited between March 2011 and May 2012 from Kwong Wah Hospital, Tsan Yuk Hospital, and Queen Elizabeth Hospital (Fig). Those with major mental illness who required medication, were referred for psychiatric or psychological therapy, or whose baby had died or required intensive care were excluded.

A total of 164 postnatal women were equally randomised to the brief six-session group intervention or control group. Participants in the control group were provided with a booklet that contained comprehensive information and education material about perinatal depression and a list of community resources.

Each group intervention comprised 10 to 12 participants who received a weekly 2-hour session for 6 weeks. The CBT intervention aimed to change cognitions and subsequently reinforce coping skills to enhance psychological resources and responses. CBT-guided participants to proactively respond to stress by reducing their negative thoughts. Participants learned the common postnatal mood changes and were asked to review their own postnatal events that triggered stress as well as

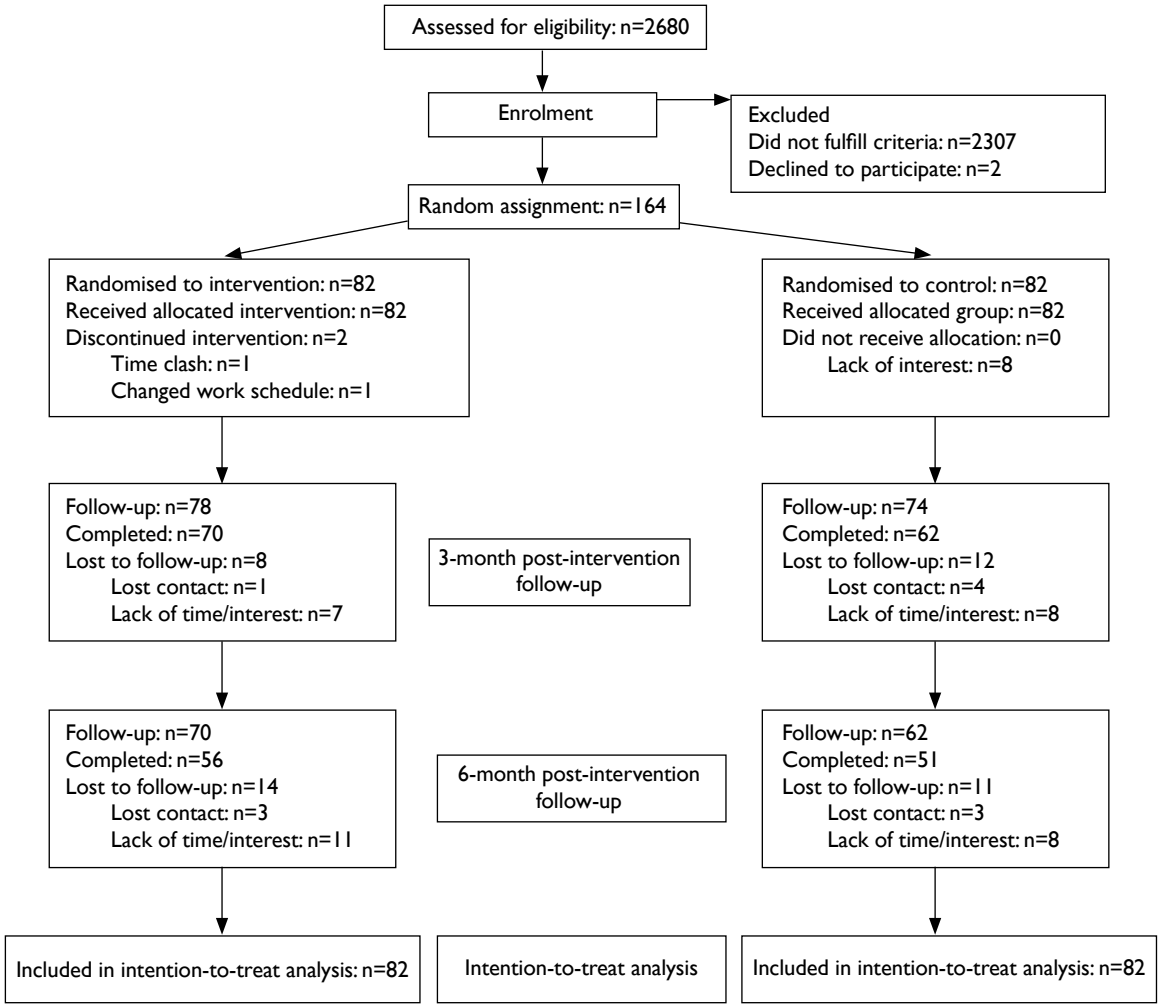

FIG. Flow chart of participants

their emotions and beliefs toward stress. They then learned cognitive techniques such as recognition of automatic thoughts, cognitive re-structuring and scheduling of pleasurable activities. Participants practised replacing their negative or irrational thoughts with positive and rational thoughts. Facilitators assisted them to identify their negative automatic thoughts and to guide them along the cognitive re-structuring process.

In the first session, participants learned the ABC model of CBT. Using the model, participants tried to assess their own physiological, emotional, behavioural, and cognitive responses to activating events. The second session focused on irrational thought patterns. The third session introduced the '5S' coping strategies in applying the cognitive-behavioural model: (1) be alert to the physiological stress signals, (2) stop automatic thoughts immediately, (3) self-questioning for searching positive and rational thoughts to replace the irrational thoughts, (4) use sidetracking small behaviours to divert attention from the stressful event, and (5) create smart card to remind themselves not to fall into the same trap in future stressful situations. The fourth session helped them to identify the underlying restraining beliefs that were linked to the irrational thoughts. In the fifth session, participants learned how to relax those restraining beliefs. In the sixth session, participants consolidated what they had learned and drew up a plan for coping with future emotionally provocative events.

Stressful or conflict scenarios that commonly encountered by postnatal women were identified in the pilot study were used to illustrate and discuss the physiological, emotional, behavioural, and cognitive responses. Group discussion, exercises, and homework assignment were core components of the sessions and emphasised throughout the

six sessions. Participants were assessed at baseline (T1) and at 3 months (T2) and 6 months (T3) after intervention.

The 10-item EPDS was used to measure the level of depressive symptoms after intervention. The 14-item, self-report Hospital Anxiety and Depression Scale (HADS) with two subscales of anxiety and depression was used to assess antenatal anxiety and depression. The 4-item Perceived Stress Scale was used to measure global stress level (how much the respondents find their lives unpredictable, uncontrollable, and overloading). The 40-item Dysfunctional Attitudes Scale (DAS) was used to identify and measure cognitive distortions, particularly distortions that might relate to or cause depression. The items contained seven major value systems based on the Beck's cognitive therapy model: approval, love, achievement, perfectionism, entitlement, omnipotence, and autonomy. The 5-item Family APGAR was used to measure satisfaction with family functioning in five dimensions: adaptation, partnership, growth, affection, and resolve. It was designed to identify individual's perception of the value of the family as a psychosocial resource (high score) or poor social support or possible stressor. The 32-item Dyadic Adjustment Scale was used to measure marital relationship. It comprises four subscales on affectional expression (4 items), dyadic consensus (13 items), dyadic cohesion (5 items), and dyadic satisfaction (10 items).

Results

The participants were aged 21 to 45 (mean±standard deviation, 31.02±4.78) years; 62% and 35.5% had monthly household income of HK$10 000 to $29 999 and HK$30 000 or above, respectively (Table 1). All completed secondary education or above and 40% attended post-graduate school. Demographics between respondents and non-respondents were comparable (all P>0.05).

The intervention group reported a significant reduction in EPDS score at T2 (T2-T1: t=3.86, P=0.03) and T3 (T3-T1: t=4.80, P<0.01), whereas in the control group the reduction in EPDS score was only significant at T3 (T3-T1: t=2.89, P=0.02). Nonetheless, the group differences were not significant ($F_{1, 161}$=3.07, P=0.05 at T2 and 2.71 at T3,

TABLE 1. Demographics of participants at baseline

Demographics	Mean±SD or No. (%) of subjects		t or χ^2 (P value)
	Intervention group (n=82)	Control group (n=82)	
Age (years)	31.56±3.78	30.9±5.7	0.04 (0.97)
Baseline Edinburgh Postnatal Depression Scale score >12	16 (20)	14 (17)	4.80 (0.18)
Education			2.90 (0.36)
Secondary & below	48 (58.5)	50 (61.0)	
Tertiary & above	34 (54.1)	32 (48.7)	
Monthly household income (HK$)			0.76 (0.48)
<20 000	8 (0.05)	18 (15.4)	
20 000-29 999	42 (53.9)	28 (35.9)	
≥30 000	32 (41)	36 (48.7)	
Working status			2.62 (0.70)
Full time work	44 (53.7)	57 (73.1)	
Housewife	22 (28.2)	17 (21.8)	
Other	12 (14.6)	4 (5.1)	
Parity			0.36 (0.93)
Primipara	50 (73)	58 (74)	
Second time	32 (27)	24 (26)	
History of depression			0.47 (0.61)
Yes	14 (17.0)	11 (13.4)	
No	68 (82.9)	71 (86.6)	
Family member had history of depression			0.56 (0.81)
Yes	16 (19.5)	24 (29.3)	
No	70 (85.4)	58 (70.7)	

P>0.05, Table 2). Respectively in the intervention and control group, 20% and 17% at baseline, 12% and 15% at T2, and 10% and 11% at T3 had an EPDS score >12. For the rate of PND, the respective percentages were 10% and 9% at baseline, 7% and 15% at T2, and 10% and 11% at T3.

For the depression subscale of HADS, score reduction in the intervention group was significant at T2 (T2-T1: t=3.00, P=0.04) and T3 (T3-T1: t=3.90, P=0.02), but in the control group the change was not significant at T2 (T2-T1: t=0.87, P=0.06) or T3 (T3-T1: t=0.76, P=0.72). The group differences were not significant ($F_{1, 161}$=1.94 at T2 and 0.23 at T3; P>0.05, Table 2).

The intervention group reported a significant reduction in cognitive distortions at T2 (T2-T1: t=2.79, P=0.03) and T3 (T2-T1: t=2.38, P=0.04), but in the control group, change was not significant at T2 and T3 (P<0.05). The group differences were also not significant ($F_{1, 161}$=3.02 at T2 and 1.33 at T3; P>0.05, Table 2).

The changes at T2 and T3 for both intervention and control groups on perceived stress scores, depression and anxiety scores, satisfaction with family functioning, and marital relationship, as well as the group differences were not significant (Table 2).

In testing the prediction of the depressive

TABLE 2. Outcome measures at baseline (T1), 3-month post-intervention (T2), and 6-month post-intervention (T3)

Outcome measure	Intervention (n=82)	Mean difference from T1	Control (n=8)	Mean difference from T1	Group mean difference*	Cohen *d*†
	Mean±SD	*t* (P value)	Mean±SD	*t* (P value)	$F_{1,163}$ (P value)	
Edinburgh Postnatal Depression Scale						
T1	12.79±2.25		12.10±2.56			
T2	10.71±3.76	3.86 (0.03)	11.56±2.89	0.89 (0.67)	3.07 (0.05)	0.28
T3	9.40±2.78	4.80 (<0.01)	10.00±3.22	2.87 (0.03)	2.71 (0.08)	0.23
Hospital Anxiety and Depression Scale (HADS)						
T1	16.87±7.56		17.20±8.13			
T2	15.63±6.55	0.94 (0.12)	16.73±7.21	0.87 (0.60)	1.94 (0.21)	0.15
T3	15.40±8.03	1.89 (0.10)	17.00±6.87	0.76 (0.72)	0.23 (0.72)	0.16
Depression subscale of HADS						
T1	8.50±5.18		8.32±4.53			
T2	7.50±5.44	3.00 (0.04)	7.81±5.11	1.38 (0.20)	0.54 (0.44)	0.16
T3	7.20±4.75	3.90 (0.02)	7.90±5.56	1.21 (0.24)	1.32 (0.12)	0.16
Perceived Stress Scale						
T1	31.75±6.74		32.79±6.47			
T2	31.07±6.02	0.38 (0.68)	32.43±5.77	0.20 (0.78)	1.06 (0.17)	0.09
T3	32.35±5.95	0.29 (0.71)	31.57±6.52	0.41 (0.54)	0.94 (0.65)	0.14
Dysfunctional Attitudes Scale						
T1	187.50±19.12		178.62±20.41			
T2	153.36±22.41	2.79 (0.03)	184.26±21.56	0.16 (0.88)	3.02 (0.05)	0.26
T3	169.40±36.67	2.38 (0.04)	168.72±33.48	0.18 (0.86)	1.33 (0.90)	0.17
Family APGAR						
T1	7.35±2.62		7.30±2.50			
T2	7.46±2.48	0.60 (0.81)	7.10±3.06	0.98 (0.72)	0.87 (0.69)	0.10
T3	7.29±2.82	0.87 (0.43)	6.98±2.98	1.48 (0.09)	1.22 (0.25)	0.12
Spanier's Dyadic Adjustment Scale						
T1	107±20.78		116±18.16			
T2	112±21.40	0.46 (0.66)	108±22.34	0.43 (0.69)	0.02 (0.80)	0.09
T3	96±25.36	0.72 (0.48)	100±23.94	0.88 (0.40)	0.33 (0.55)	0.17

* Repeated measures ANCOVA controlled for baseline measure

† Cohen *d* effect sizes: 0.20 (small), 0.50 (medium), and 0.80 (large)

symptoms measured by EPDS, the follow-up depressive symptoms at T2 and T3 were set as dependent variable and the change of dysfunctional thoughts from baseline to post-intervention as predictor. Hierarchical multiple regression was conducted controlling for baseline EPDS depressive symptoms and other baseline measures including cognitive distortions, perceived stress, satisfaction with family functioning, marital satisfaction. The change in cognitive distortion significantly predicted depression at T2 ($F_{5, 164}$=2.12, P=0.04) but not at T3 ($F_{1, 161}$=1.61, P>0.05).

Encouraging feedback was received from post-intervention evaluation. All participants were satisfied with the intervention, with 30% rated as excellent. About 92% reported most of the programme materials useful; 89% agreed or strongly agreed that the programme enabled them to think more rationally; 90% agreed or strongly agreed that the programme enhanced their confidence in managing postnatal stress and that they planned to use new strategies to manage the stress.

Discussion

The brief 6-week postnatal CBT intervention significantly corrected dysfunctional cognition. The change in dysfunctional cognition was predictive of 3-month post-intervention depression. Nonetheless, no significant differences were found between the two groups. The mean Cohen's d of 0.16 was small for the seven outcome measures. The 3-month post-intervention Cohen's d was 0.28 for EPDS and only 0.16 for HADS depression subscore. Both were below the criterion for clinical significance (0.05) recommended by the National Institute for Health and Clinical Excellence guidelines for treatment of depression. This short intervention included exclusively CBT techniques; some studies of CBT intervention have included other components such as structured pharmacology,[4] interpersonal, and psychodynamic strategies.[5]

One limitation of this study was that assessment of a clinical diagnosis of PND was performed by a trained research assistant, not a mental health specialist. Another limitation was the exclusion of postnatal women who could not speak Cantonese or who were not staying in Hong Kong during the postnatal period. Women from Mainland China represented a large proportion of postnatal women in Hong Kong at the time of the study. Although they lived and worked in Hong Kong and many were Hong Kong residents, they often preferred to go back to their hometown for better postnatal care by their parents or extended family. The findings of this study cannot be generalised to this group of women. In addition, a non-directive counselling comparison group and evaluation of the impact on the development of infants was lacking. This affected their participation and hence the impact of the intervention. As CBT demands participants to have a certain level of cognitive ability to reflect their own thoughts and to restructure thinking, their consistent participation is crucial.

Conclusions

This brief group intervention can maximise retention of participants, is of low cost and can be conducted by non-specialists. Although this short intervention was weakly effective, it might enhance clinician efforts to prevent PND. The findings could help inform researchers about further enrichment of the programme content. Rather than focusing mainly on cognitive restructuring, the behavioural component could be further enhanced to include discussion of pleasurable activities with group review. More clinical trials are needed to evaluate the effectiveness of a further enhanced and brief programme. With further enhancement and evaluation, this intervention could be considered complementary to the existing clinical services provided by the Comprehensive Child Development Services. Future studies should include comparison groups with longer follow-up and assessment of infants' health and developmental conditions.

Acknowledgement

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Acupuncture for persistent insomnia associated with major depressive disorder: a randomised controlled trial

KF Chung *, WF Yeung, SP Zhang, ZJ Zhang, MT Wong, WK Lee, KW Chan

KEY MESSAGES

1. Standardised acupuncture has only a mild hypnotic effect for residual insomnia associated with major depressive disorder (MDD). Its efficacy does not differ to that of minimal acupuncture or placebo control.
2. The within-group effect size for the primary outcome measure—sleep-diary-derived sleep efficiency—was 0.4 at 1-week post-treatment, but there was almost no change in actigraphy-derived objective sleep parameters.
3. Standardised acupuncture and minimal acupuncture were well-tolerated, with rates of discontinuation (secondary to adverse events) of 5.0% and 3.3%, respectively.
4. Residual insomnia associated with MDD partially responds to non-specific factors of acupuncture, but it fails to attain full remission. Further studies exploring individualised acupuncture, a longer course of acupuncture and cognitive behavioural therapy for this persistent problem are needed.

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Introduction

Major depressive disorder (MDD) is a common psychiatric condition. A sizable proportion of patients with MDD partially respond to mainstream treatment and are left with residual symptoms, of which insomnia is the most common.[1] Although pharmacological and psychological treatments may help to alleviate residual insomnia, both have limitations. The use of complementary and alternative medicine therapies for insomnia has become more common. Acupuncture is one of the most popular procedures. In 2011, we published the first randomised trial of electroacupuncture for residual insomnia associated with MDD.[2] Electroacupuncture and minimal acupuncture were comparable and more efficacious than placebo control. In the present study, we aimed to enhance the efficacy of acupuncture for insomnia by augmenting essential acupoints. We hypothesised that electroacupuncture was significantly more efficacious than minimal acupuncture and placebo acupuncture for the treatment of residual insomnia in MDD.

Methods

The study was a placebo-controlled, subject- and assessor-blinded, randomised trial. The use of placebo needles was to control for the non-specific effects of acupuncture and the natural course of illness. Using superficial needling at non-therapeutic points could test the relevance of specific acupuncture points, deep needling, and *de qi*. Patients were assessed at baseline, 1-week and 5-week post-treatment. The study was registered at clinicaltrials.gov (identifier: NCT01707706).

Patients were recruited from May 2011 to August 2013 at four regional psychiatric outpatient clinics in Hong Kong. Inclusion criteria were: (1) age 18-70 years, (2) a diagnosis of MDD based on the DSM-IV criteria, (3) insomnia ≥3 nights per week for at least 3 months, (4) Insomnia Severity Index (ISI) score ≥15 at screening and baseline, and (5) taking the same antidepressants at a fixed dose for at least 12 weeks prior to baseline and during the study. Exclusion criteria were: (1) a 17-item Hamilton Rating Scale for Depression (HRSD-17) score >18 at screening and baseline, (2) an apnoea-hypopnoea index ≥10 or a periodic limb movement disorder index ≥15 as assessed by in-laboratory overnight polysomnography, (3) significant suicidal risk according to the HRSD-17 item on suicide (score ≥3). Eligible subjects were randomly assigned to electroacupuncture, minimal acupuncture, or placebo acupuncture in a ratio of 2:2:1.

Intervention was three times per week for three

consecutive weeks. All acupuncture treatments were performed by the same registered Chinese medicine practitioner who had at least 3 years of clinical experience.

For electroacupuncture, subjects were needled at bilateral Ear Shenmen, Sishencong (EX-HN1), Anmian (EX), Neiguan (PC6), Shenmen (HT7), Sanyinjiao (SP6), as well as unilateral Yintang (EX-HN3) and Baihui (GV20). *De qi* was achieved if possible. An electric-stimulator was connected to the needles and delivered a constant-current, 0.4-ms, square-wave, brief-pulse stimulus of 4-Hz frequency to the subjects. The needles were left for 30 minutes and then removed.

For minimal acupuncture, subjects were needled superficially at non-acupoints on the head, ears, wrists, and legs that have no therapeutic effects according to the traditional Chinese medicine (TCM) theory. The points on the limbs included bilateral 'forearm', 1 inch lateral to the middle point between Shaohai (HE3) and Shenmen (HE7); 'upper arm', 1 inch lateral to Tianfu (LU 3); and 'lower leg', 0.5 inch dorsal to Xuanzhong (GB39). For points on the head, they included bilateral 'head', the middle point between Shuaigu (GB8) and Touwei (ST8); 'forehead', the middle point between Touwei (ST8) and Yangbai (GB14); 'neck', the middle point between Tianyou (TB16) and Tianrong (SI17); and 'ear', a point on the helix, inferior to the apex. Other treatment conditions were the same as in the electroacupuncture group.

For placebo acupuncture, subjects were treated by placing placebo needles at sites 1 inch beside the acupoints used in the electroacupuncture group. The needles were connected to an electric-stimulator, but with zero frequency and amplitude.

The primary outcome measure was the sleep-diary-derived sleep efficiency. Secondary outcome measures included other sleep parameters derived from the sleep diary, actigraphy measures, ISI, Pittsburgh Sleep Quality Index (PSQI), HRSD-17, Hamilton Anxiety Rating Scale (HARS), Hospital Anxiety and Depression Scale (HADS), Somatic Symptom Inventory (SSI), Sheehan Disability Scale (SDS), Multidimensional Fatigue Inventory (MFI), Epworth Sleepiness Scale (ESS), 36-item Short Form Health Survey (SF-36), and Credibility of Treatment Rating Scale (CTRS). Dichotomous outcomes were the proportion of subjects who obtained a sleep-diary-derived sleep efficiency of at least 85% or a sleep-onset latency (SOL) or wake time after sleep onset (WASO) of ≤30 minutes. After the sixth treatment, the success of blinding was tested by asking the participants which kind of acupuncture treatment they thought they had received. Adverse events were assessed after the third, sixth, and ninth sessions, using a standardised adverse events form.

The effects of the intervention over time were assessed using the mixed-effects model of group-by-time interaction. Standardised effect size was computed by dividing the difference in means by the pooled standard deviation.

Results

A total of 150 subjects (mean age, 49.3 years) were randomised; 79.3% were female. They had been diagnosed with MDD for a mean of 8.4 years; 84.0% were taking antidepressants (Table 1). The electroacupuncture, minimal acupuncture, and placebo acupuncture groups were comparable in terms of sociodemographics, clinical features, and pharmacotherapy. Sixteen (10.7%) subjects dropped out, and 18 (12.0%) withdrew 5 weeks post-treatment (Fig). The attrition rate among the groups was comparable at 1-week and 5-week post-treatment (χ^2 test, P>0.05).

In mixed-effects model analysis, the between-group difference was not significant in sleep-diary-derived sleep efficiency, SOL, WASO, or sleep quality at 1-week or 5-week post-treatment (Table 2), nor in the ISI and PSQI scores. Nonetheless, a greater reduction in dosage of hypnotics was noted in the placebo acupuncture group compared with the electroacupuncture and minimal acupuncture groups at 5-week post-treatment (group-by-time interaction, P=0.02).

There was no significant group-by-time interaction in actigraphy-derived measures, HRSD-17, HARS, HADS anxiety and depression, SSI, SDS, MFI, or ESS scores. Nonetheless, mixed-effects model showed that electroacupunc¬ture and minimal acupuncture achieved greater improvement in SF-36 physical component summary score than placebo acupuncture at 1-week and 5-week post-treatment (group-by-time interaction, P<0.05).

A higher proportion of subjects in the electroacupuncture group achieved a SOL ≤30 minutes compared with those with minimal acupuncture at 1-week post-treatment (P=0.04), but not those with placebo acupuncture. At 5-week post-treatment, the between-group difference was not significant. There was no significant difference in the proportion of participants who attained a sleep efficiency ≥85% or WASO ≤30 minutes at 1-week and 5-week post-treatment (χ^2 test, all P>0.05).

There was no significant between-group difference in the CTRS score and the proportion of participants who correctly guessed, made a wrong guess, or had no idea which acupuncture treatment they had received (P=0.11).

Electroacupuncture and minimal acupuncture were well-tolerated, with rates of discontinuation (secondary to adverse events) of 5.0% and 3.3%, respectively. No serious adverse events were reported.

TABLE 1. Demographics and clinical characteristics of subjects

Variables	Mean±SD or No (%) of subjects			
	Electro-acupuncture (n=60)	Minimal acupuncture (n=60)	Placebo acupuncture (n=30)	Total (n=150)
Age (years)	48.8±9.9	50.9±9.5	47.4±9.5	49.3±9.7
No. of males:females	14:46	14:46	3:27	31:119
Education attainment (years)	10.7±2.9	10.4±3.4	11.6±3.0	10.8±3.2
Marital status				
Never married	7 (11.7)	10 (16.7)	7 (23.3)	24 (16.0)
Married/cohabiting	33 (55.0)	36 (60.0)	19 (63.3)	88 (58.7)
Divorced/widowed	20 (33.3)	14 (23.3)	4 (13.3)	38 (25.3)
Occupation				
Professional and associate professional	3 (5.0)	4 (6.7)	1 (3.3)	8 (5.3)
Skilled and semi-skilled worker	11 (18.3)	7 (11.7)	3 (10.0)	21 (14.0)
Unskilled worker	8 (13.3)	5 (8.3)	3 (10.0)	16 (10.7)
Retired	9 (15.0)	11 (18.3)	5 (16.7)	25 (16.7)
Unemployed/housework	29 (48.3)	33 (55.0)	18 (60.0)	80 (53.3)
Insomnia duration (years)	8.7±7.1	12.0±11.4	9.2±8.4	10.1±9.3
Chronic medical illnesses	16 (26.7)	13 (21.7)	8 (26.7)	37 (24.7)
Insomnia Severity Index	19.6±3.0	20.2±3.6	19.6±2.7	19.8±3.2
Pittsburgh Sleep Quality Index	14.1±3.0	14.7±2.5	15.0±3.5	14.5±2.9
Age of onset of depression (years)	39.9±10.0	40.9±10.5	38.6±9.2	40.0±10.0
Depression duration (years)	7.5±6.1	8.9±12.9	9.3±15.9	8.4±11.4
17-item Hamilton Rating Scale for Depression	10.4±4.2	9.9±4.1	11.5±4.0	10.4±4.2
Current antidepressant use	51 (85.0)	48 (80.0)	27 (90.0)	126 (84.0)
Selective serotonin reuptake inhibitors	27 (45.0)	16 (26.7)	14 (46.7)	57 (38.0)
Serotonin and noradrenalin reuptake inhibitors	8 (13.3)	5 (8.3)	1 (3.3)	14 (9.3)
Tricyclic antidepressants and others	6 (10.0)	15 (25.0)	5 (16.7)	26 (17.3)
Others	1 (1.7)	2 (3.3)	3 (10.0)	6 (4.0)
Combination	9 (15.0)	10 (16.7)	4 (13.3)	23 (15.3)
Current hypnotics use	27 (45.0)	26 (43.3)	16 (53.3)	69 (46.0)
Benzodiazepines	7 (11.7)	5 (8.3)	5 (16.7)	17 (11.3)
Non-benzodiazepine hypnotics	12 (20.0)	9 (15.0)	5 (16.7)	26 (17.3)
Combination of benzodiazepines and non-benzodiazepine hypnotics	7 (11.7)	9 (15.0)	4 (13.3)	20 (13.3)
Antihistamine	1 (1.7)	3 (5.0)	2 (6.7)	6 (4.0)

Discussion

There was no evidence to support better efficacy of traditional needle acupuncture as an intervention for residual insomnia associated with MDD. Although a within-group effect size of >1.0 was noted in the ISI score, the effect size in sleep-diary-derived sleep efficiency was quite small. Only a few participants could achieve sleep efficiency ≥85% on completion of the 3-week acupuncture treatment, and there was almost no change in actigraphy-derived sleep parameters. These suggest that the TCM-style standardised acupuncture attained a response mostly by its non-specific effects; the mean sleep-diary-derived sleep efficiency post-treatment was 71.4%, indicating that acupuncture is not likely to be an adequate monotherapy for residual insomnia associated with MDD.

Our previous studies showed that electroacupuncture had slightly better efficacy than placebo acupuncture.[2,3] Despite an enhanced acupuncture regimen, the hypnotic efficacy of electroacupuncture did not improve much in the current study. In addition, there was a greater placebo response that narrowed down the group difference. Some factors may have reduced the effectiveness of the traditional acupuncture.

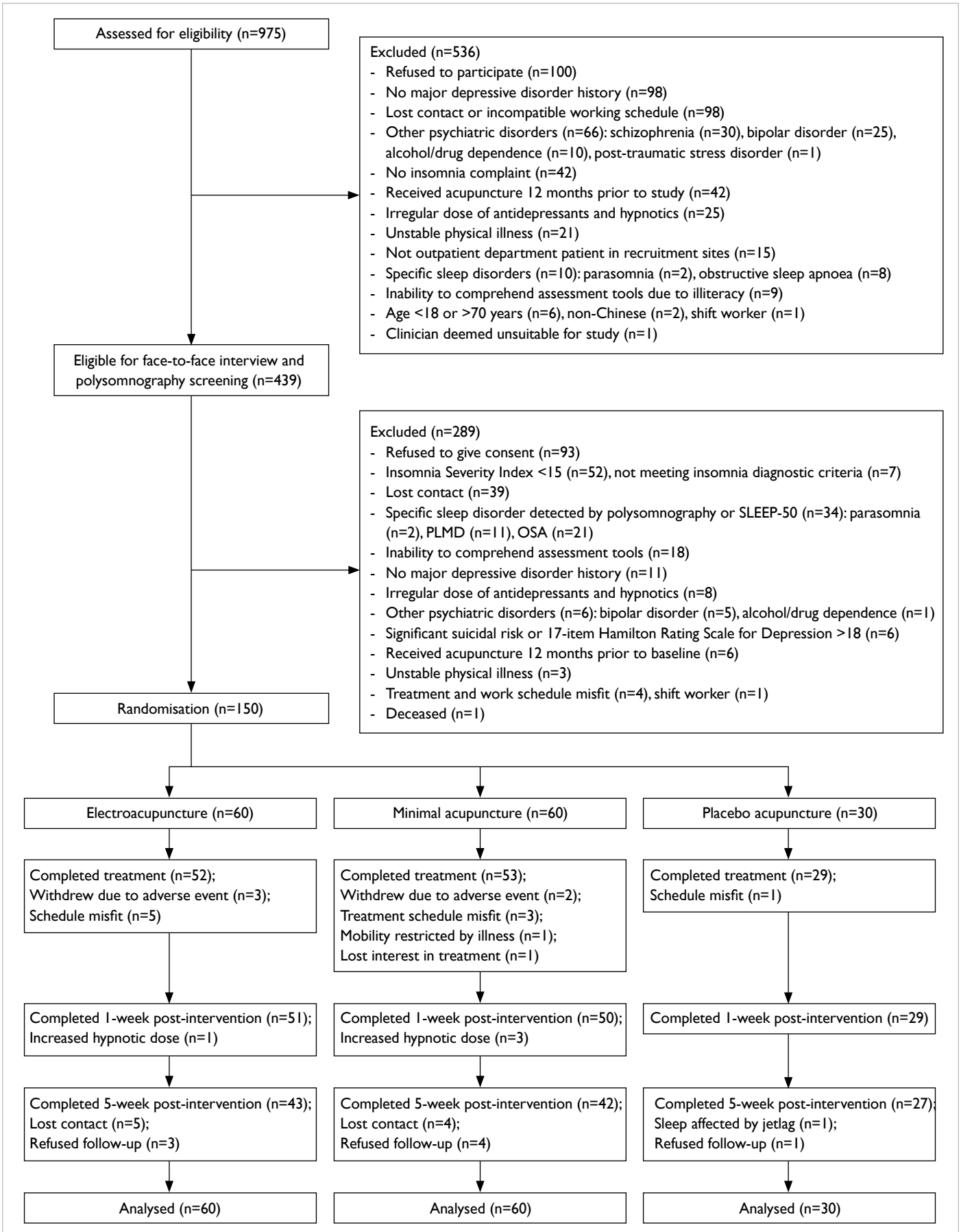

FIG. Flowchart of the subjects

TABLE 2. Sleep diary and actigraphy measures across study time points

Outcome measure	Electroacupuncture (n=60)		Minimal acupuncture (n=60)		Placebo acupuncture (n=30)		P value (group-by-time interaction)
	Mean±SE	Within-group effect size	Mean±SE	Within-group effect size	Mean±SE	Within-group effect size	
Sleep diary							
Sleep onset latency (mins)							
Baseline	58.9±5.5		69.0±5.6		69.0±7.8		
1-week post-treatment	47.5±5.6	0.27	48.5±5.8	0.46	54.9±7.8	0.33	0.33
5-week post-treatment	46.4±6.1	0.28	44.9±6.3	0.52	50.4±8.2	0.42	0.52
Total sleep time (mins)							
Baseline	318.7±10.3		314.6±10.4		338.6±14.5		
1-week post-treatment	345.5±10.5	-0.33	364.1±10.8	-0.60	369.5±14.5	-0.39	0.24
5-week post-treatment	352.9±11.6	-0.40	367.8±12.0	-0.61	382.2±15.3	-0.53	0.47
Wake time after sleep onset (mins)							
Baseline	62.8±6.7		62.2±6.8		48.7±9.5		
1-week post-treatment	46.3±6.9	0.31	43.4±7.1	0.35	48.2±9.5	0.01	0.16
5-week post-treatment	48.5±7.5	0.26	46.1±7.7	0.29	41.6±10.0	0.13	0.41
Sleep efficiency (%)							
Baseline	64.6±2.0		62.4±2.0		64.0±2.8		
1-week post-treatment	71.4±2.0	0.44	72.8±2.1	0.65	68.3±2.8	0.20	0.13
5-week post-treatment	71.1±2.3	0.39	72.3±2.3	0.59	74.0±3.0	0.44	0.09
Equivalent dose of hypnotics in diazepam (mg/d)*							
Baseline	9.9±1.7		8.3±1.8		5.4±2.4		
1-week post-treatment	8.6±1.7	0.10	5.3±1.9	0.21	4.0±2.4	0.11	0.60
5-week post-treatment	9.5±1.7	0.03	7.9±1.9	0.03	2.6±2.4	0.21	0.02†
Actigraphy							
Sleep onset latency (mins)							
Baseline	31.2±4.1		30.1±4.0		29.2±5.7		
1-week post-treatment	33.9±4.1	-0.08	29.8±4.1	0.01	35.1±5.8	-0.13	0.57
5-week post-treatment	33.4±4.5	-0.07	27.4±4.5	0.08	24.2±6.0	0.11	0.43
Total sleep time (mins)							
Baseline	387.3±13.5		390.7±13.4		396.8±18.9		
1-week post-treatment	395.1±13.8	-0.07	415.0±13.6	-0.23	391.2±19.4	0.05	0.47
5-week post-treatment	392.9±14.2	-0.05	389.1±14.3	0.01	398.1±19.4	-0.01	0.72
Wake time after sleep onset (mins)							
Baseline	53.4±4.3		70.3±4.2		76.4±6.0		
1-week post-treatment	60.6±4.3	-0.22	65.9±4.3	0.13	74.5±6.1	0.06	0.03‡
5-week post-treatment	55.3±4.6	-0.06	67.0±4.7	0.10	81.9±6.2	-0.16	0.05
Sleep efficiency (%)							
Baseline	78.8±1.4		76.0±1.3		76.9±1.9		
1-week post-treatment	78.3±1.4	0.05	76.2±1.4	-0.02	76.5±1.9	0.04	0.88
5-week post-treatment	78.7±1.4	0.01	77.7±1.4	-0.16	77.3±1.9	-0.04	0.65

* Only subjects taking hypnotics and completed the study were analysed: electroacupuncture (n=27), minimal acupuncture (n=23), and placebo acupuncture (n=14)

† Post hoc group-by-time interaction: electroacupuncture vs placebo acupuncture (P=0.01), minimal acupuncture vs placebo acupuncture (P=0.06), electroacupuncture vs minimal acupuncture (P=0.69)

‡ Post hoc group-by-time interaction: electroacupuncture vs placebo acupuncture (P=0.09), minimal acupuncture vs placebo acupuncture (P=0.76), electroacupuncture vs minimal acupuncture (P=0.02)

In terms of TCM theory, acupuncture should be customised according to TCM diagnoses and clinical response to acupuncture treatment. We are uncertain whether individualised acupuncture would achieve better efficacy. Another potential factor is the length of treatment. The 3-week treatment period may be too short, and a difference between 'real' and 'placebo' acupuncture might have emerged if the treatment had been longer. The other potential factor relates to the biophysiologic mechanism of acupuncture.[4] Previous studies have shown that acupuncture can enhance a sympatho-inhibitory effect, opioid-dependent analgesic effect, and nocturnal melatonin secretion. It is uncertain whether these acupuncture-induced biophysiologic effects failed to occur in most of our subjects who were using antidepressants, sedatives, or hypnotics.

Nonetheless, the current study included a well-documented screening process, proper randomisation, placebo acupuncture needles, validated subjective scales, objective measures, and comprehensive adverse event monitoring. In addition, the sample size is the largest to date among other published studies.[5] Almost all subjects were unable to tell the kind of acupuncture they had received, so the blinding was successful.

Conclusion

The effectiveness of acupuncture as an intervention for residual insomnia in MDD was mild at best, mainly owing to its non-specific effects. After 3 weeks of thrice-weekly acupuncture treatment, a high proportion of patients remained significantly affected by insomnia. It is uncertain whether TCM pattern-based individualised acupuncture or acupuncture treatment of longer duration can improve its effectiveness for insomnia. Further studies are needed to explore treatments for this debilitating and persistent problem, which could affect the long-term outcome of MDD. Cognitive-behavioural therapy is a promising treatment for insomnia and its applicability as an intervention for patients with residual insomnia associated with MDD should be explored.

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Integrated supported employment plus cognitive remediation training for people with schizophrenia

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KEY MESSAGES

1. Integrated supported employment plus cognitive remediation training (ISE+CRT) or ISE alone produced positive therapeutic effects for people with schizophrenia.
2. More improvement trends in vocational, clinical, and cognitive outcomes were noted in the ISE+CRT group, and a more positive trend for the psychological and functional outcomes was noted in the ISE group.
3. The hypothesis that ISE effect would be augmented by the addition of CRT is not well supported in vocational, clinical, and cognitive domains.
4. Further comparative studies are required to determine whether the addition of CRT to an ISE programme enhances vocational and clinical outcomes in the long term.

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Introduction

Helping people with schizophrenia to gain competitive employment is a key to improving their quality of life and facilitating their recovery.[1] Through a combination of individual placement and support, work-related social skills training, and cognitive remediation training (CRT), our earlier studies demonstrated that 78.8% of people with severe mental illness succeeded in getting competitive employment; the longest job tenure was 24 weeks using the integrated supported employment (ISE) model that combines individual placement and support and work-related social skills training.[2] ISE outperformed other vocational rehabilitation services in Hong Kong. Cognitive ability is a predictor of employment outcomes including work success, skills acquisition, and independent living among those with severe mental illness.[3] This study aimed to test whether helping people with schizophrenia to restore their neurocognitive functions by CRT enhances the effects of ISE programme. We hypothesised that better vocational and clinical outcomes would be achieved with this model that combines three evidence-based rehabilitation components.

Methods

This study was conducted from January 2011 to March 2014. A total of 90 eligible participants aged ≥18 years with a diagnosis of schizophrenia or schizoaffective disorder from the psychiatric service units of the Baptist Oi Kwan and United Christian Hospital were recruited from April 2011 to April 2013. Those who had moderate or greater cognitive impairment (based on the 30-item Mini-Mental State Examination score of >18) were excluded.

Participants were randomly assigned to the ISE+CRT (n=45) or ISE (n=45) group. For ISE, intervention followed the protocol described in our previous study.[1] For ISE+CRT, in addition to ISE, 6 hours (2-hour session, 3 sessions) per week of individualised computer-assisted cognitive exercises with two cognitive remediation software systems (Strong Arm System and Captain's Log) per week for 12 weeks were included. Recreational activities were added to the ISE group as control to neutralise the effect of additional time and therapist contact in the ISE+CRT group.[4]

Participants were assessed before and after completion of the 3-month service, and at 7-month, 11-month, and 15-month follow-up by independent, trained, and blinded assessors. Only 70 participants were followed up at 15 months.

The primary outcome measures were vocational outcome (as measured by the employment outcome checklist) and clinical outcome (as measured by the 18-item Brief Psychiatric Rating Scale). Secondary measures included the Global Assessment of Functioning, executive functioning

measured by Wisconsin Card Sorting Test, and five cognitive domains measured by MATRICS Consensus Cognitive Battery. Verbal learning and working memory was measured in three stages of information processing by the Hong Kong List Learning Test 2nd Edition.

Baseline variables were compared using ANOVA or Chi-square test to detect group differences. Repeated ANOVA measures with post-hoc analysis were used to determine whether significant differences occurred at different stages of the study. The employment rate reported at different follow-up periods was the cumulative rate. Job tenure was defined as the longest duration of a job held. All

TABLE 1. Baseline characteristics and outcomes of the Integrated supported employment plus cognitive remediation training (ISE+CRT) and ISE alone groups

Variable	Mean±SD or No. (%) of subjects		χ^2 or *t*	P value
	ISE+CRT (n=45)	ISE (n=45)		
Age (years)	35.38±9.2	36.89±9.4	-0.771	0.443
Gender			0.05	0.827
Male	28 (62.22)	29 (64.44)		
Female	17 (37.78)	16 (35.56)		
Recruitment sites			0.41	0.523
Baptist Oi Kwan	21 (46.67)	18 (40.00)		
United Christian Hospital	24 (53.33)	27 (60.00)		
Marital status			2.35	0.672
Single	40 (88.89)	39 (86.67)		
Married	1 (2.22)	2 (4.44)		
Divorced	3 (6.67)	3 (6.67)		
Widowed	0 (0.00)	1 (2.22)		
Separated	1 (2.22)	0 (0.00)		
Education since K1 (years)	15±2.71	14.89±2.48	0.203	0.840
Diagnosis			1.64	0.286
Schizophrenia	29 (64.44)	23 (51.11)		
Schizoaffective disorder	16 (35.56)	22 (48.89)		
Age at diagnosis (years)	24.04±7.51	25.8±9.58	-0.968	0.336
Age of first hospitalisation (n=35)	24.1±7.29	25.97±9.18	-0.974	0.333
Duration of illness (years)	11.33±8.87	11.08±6.62	0.148	0.883
No. of hospital admissions (n=45 vs n=44)	2.38±2.28	2.25±2.37	0.259	0.796
Mini-Mental State Examination (range, 0-30)	28.0698±1.75	27.58±2.37	1.074	0.286
Brief Psychiatric Rating Scale (range, 0-126)	23.78±3.25	23.71±4.42	-0.082	0.935
Global Assessment of Functioning (range, 0-100)	60.64±7.34	61.47±8.53	-0.49	0.625
Employment history			0.35	0.557
Yes	44 (97.78)	43 (95.56)		
No	1 (2.22)	2 (4.44)		
Living condition			2.5	0.475
Family	34 (75.56)	35 (77.78)		
Alone	8 (17.78)	6 (13.33)		
Relatives	3 (6.67)	2 (4.44)		
Hostel	0 (0.00)	2 (4.44)		
Income (n=45 vs n=44)			1.94	0.585
Family	14 (31.11)	11 (24.44)		
Disability allowance	17 (37.78)	24 (53.33)		
Comprehensive Social Security Assistance	8 (17.78)	6 (13.33)		
Others (alimony, training compensation)	5 (11.11)	4 (8.89)		

analyses followed the principle of 'intent-to-treat'. The 'last observation carried forward' method was used to replace the missing data. Significance level was set at P<0.05 with Bonferroni adjustment.

Results

The ISE+CRT participants attended a mean of 25 (70%) of 36 sessions of CRT, whereas the ISE participants attended a mean of 28 (78%) of 36 TV watching sessions (P=0.405). The programme attrition rate was 11.11% with no significant between-group difference at the 11-month follow-up (χ^2=0.45, *df*=1, P=0.502). The two groups were comparable in baseline demographics and clinical outcomes (Table 1).

At 15-month follow-up, 20 (60.6%) ISE+CRT participants and 23 (62.2%) ISE participants obtained competitive employment (Table 2). Most worked at entry-level jobs such as security guard, cleaner, shop assistant, clerk, or delivery worker. The ISE+CRT participants had a trend to work longer (but not significantly) in a job than the ISE group at 7 months (P=0.780) and 11 months (P=0.591). Both groups were paid an hourly wage greater than the minimum hourly wage of HK$30. The number of job terminations was low for both groups throughout the period.

For clinical symptoms, the time-by-group difference up to 11 months was not significant [F(3, 264)=0.429, P=0.70]. Both groups showed a gradual downward trend of the total Brief Psychiatric Rating Scale score up to 11 months but no significant time effect (P=0.262, Table 1, Fig). At 15 months, the ISE group elicited more psychotic symptoms than the ISE+CRT group but not significantly (P=0.065). For the Global Assessment of Functioning, there was significant group-by-time interaction effect up to 11 months [F(3, 264)=3.05, P=0.05]. There was a significant upward time trend in global functioning for both groups throughout the 15-month period (P<0.05, Table 1, Fig). The two groups did not differ significantly in terms of psychological, social, or occupational functioning at any of the time intervals (all P>0.01 with Bonferroni correction).

For executive functioning, both groups improved significantly in categories completed score and conceptual level response throughout the 15-month period (P<0.01). Both groups improved significantly in perseverative errors (P<0.001) and non-perseverative errors (P<0.001).

TABLE 2. Employment rate of the Integrated supported employment plus cognitive remediation training (ISE+CRT) and ISE alone groups

Employment rate	ISE+CRT	ISE	χ^2	df	P value
At 7 months	22.2% (10/45)	28.9% (13/45)	0.526	1	0.468
At 11 months	44.4% (20/45)	55.6% (25/45)	1.110	1	0.292
At 15 months*	60.6% (20/33)	62.2% (23/37)	0.018	1	0.894

* 20 participants were not followed up due to recruitment delay

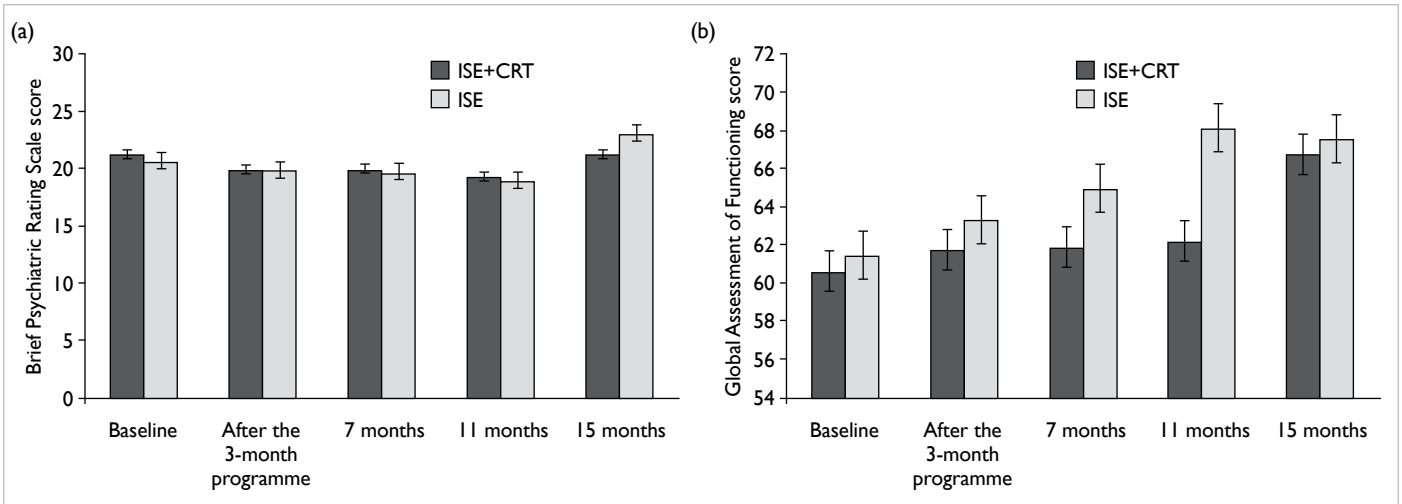

FIG. The mean scores of the (a) Brief Psychiatric Rating Scale and (b) Global Assessment of Functioning for the Integrated supported employment plus cognitive remediation training (ISE+CRT) and ISE alone groups at various time intervals

The interaction effects of group over time were not significant for the five neurocognitive domains. Both groups improved significantly in attention/vigilance and visual learning immediately after the 3-month programme (all P<0.001). Both groups showed better performance in reasoning and problem solving since the 7-month follow-up (P<0.001) and speed of processing starting at the 11-month follow-up (P<0.01). Nonetheless, a slight decrease in social cognition performance was noted for both groups over the 15-month period (P<0.05). Post hoc t-test on the simple effect of group showed no significant difference in any domain at any interval, with the exception of visual learning. The significant group difference was noted in the visual learning domain immediately after the intervention, with higher scores in the ISE+CRT than ISE group (P<0.025 with Bonferroni correction).

For verbal learning and memory and the three information processing stages (acquisition, retention, and retrieval), a positive time trend was significant for the stage of acquisition (P<0.001), while the negative time trend was significant for retention (P<0.001). No significant time trend was noted at the retrieval stage. The CRT+ISE group appeared to learn and memorise more words than the ISE group, but performed relatively poorly in the retrieval stage at the 15-month follow-up (all P>0.01 with Bonferroni correction). Nonetheless, no significant interaction for group effect over time or group difference was found at any of the three stages.

Discussion

Both the ISE+CRT and ISE groups demonstrated sustained improvement in vocational, clinical, psychological, and neurocognitive outcomes. Nonetheless, there was no evidence that cognitive remediation facilitated improvement in these aspects above and beyond the gains associated with ISE alone. In addition, ISE and CRT had different effects across the spectrum of outcomes. The augmenting effect of CRT on ISE is more complicated than the simple equation of 1+1=2.

The improved employment rate of 60-62% is comparable with that from western countries that focused on adding CRT to an individual placement and support programme.[4] In our study, more ISE+CRT participants worked full-time jobs, worked longer in a job, and received a higher hourly wage than ISE participants at the 7- and 11-month follow-up, but the effect was not sustained at the 15-month follow-up. In clinical aspects, the ISE group elicited more psychotic symptoms than the ISE+CRT group at the 15-month follow-up, but this effect was not detected immediately after the interventions. Further comparative studies are required to determine whether the addition of CRT to an ISE programme enhances vocational and clinical outcomes in the long term.

Given that our study excluded participants with moderate or severe cognitive impairment, addition of CRT components targeting them might result in a larger group difference that poorer cognitive functioning along with more clinical symptoms at baseline may be associated with better cognitive improvements.[5] On the contrary, a decreasing performance was noted in the social cognition domain for the ISE+CRT group. Further analysis of the addition of social cognition training in the vocational context is recommended.

This study had a number of limitations. Many outcome measures did not differ significantly between the two groups. This might have been due to the plateau effect induced by the work-related social skills training that had already pushed the effects to the upper limit. Adding CRT may not have caused significant further improvement. In the absence of work-related social skills training, adding CRT may significantly improve the outcome of an individual placement and support programme.[4] The insignificant results might be due to the small sample size.

Acknowledgements

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Virtual reality exercise to improve balance control in older adults at risk of falling

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KEY MESSAGES

1. Playing Wii Fit games can improve the Berg Balance Scale score and stability limits of institutionalised and frail older adults with a history of fall.
2. The Wii Fit balance training was more effective than conventional balance training in this regard.
3. The Wii Fit balance training can enhance the management of fall prevention in older adults (especially for those living in aged care facilities) and may reduce health care costs and suffering in older adults.

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Introduction

It is estimated that 28% to 35% of older adults (age 65 years) experience at least one fall each year; fall is the second leading cause of accidental death worldwide.[1] Risk factors of fall include intrinsic and extrinsic factors. Balance control is intrinsic and modifiable. Virtual reality (VR) simulates daily life activities by presenting an illusion of three-dimensional vision and direct visual and auditory feedback.[2] Interventions using the Nintendo Wii Fit force-sensing platform and its built-in VR games for balance, yoga, aerobic, and strength training have been reported.[2]

The effectiveness of Wii Fit exercise versus conventional exercise on balance control has been studied. In a study of 36 community living older adults, the Wii Fit balance training group achieved better balance control post intervention, based on the Tinetti test and the Wii Fit centre of gravity test.[3] In another study of 32 community living older adults, the Wii-fit group, the traditional exercise group, and the control group achieved significant but comparable improvement in Berg Balance Scale (BBS) score of 3.55, 3.45, and 2.99, respectively.[4] However, scientific evidence on the effects of VR exercise using Wii Fit on balance control among institutionalised older adults with a fall history is still lacking. Hence, this randomised clinical study aimed to compare Wii Fit balance training with conventional balance training in this group of older adults.

Methods

Approval was obtained from the nursing homes prior to the study. Ethical approval was obtained from the ethics committee of the nursing home and The Hong Kong Polytechnic University. Informed consent was obtained from each participant. A total of 79 older adults aged over 65 years who were nursing home residents with a functional ambulatory category (FAC) of 2 (walking with one person assistance) or 3 (walking without assistance but needed a standby guard for safety) were recruited in this single-blinded, randomised clinical trial. Subjects were randomised to a Wii Fit balance training group or a conventional balance training group. Each group received three 1-hour sessions of training per week for 6 weeks. The Wii Fit balance training games included Soccer Heading, Table Tilt, and Balance Bubble. The conventional balance training regimen was led by a physiotherapist and included leg strengthening exercises, tandem standing exercise in parallel bars, tandem walking in parallel bars, sideways walking and turning around in parallel bars, stepping exercises, sit-to-stand exercises, and mini-squats.[5] Outcome measures included BBS, timed-up-and-go test, and limits of stability test.

Independent t-test was used to compare the two groups in terms of age, height, weight, body mass index, and number of falls in the previous year. Chi-squared test was used to compare the distribution of genders and functional ambulation categories. Two-way repeated measures analysis of variance was used to test the group and time effects and any interaction of group and time with intent-to-treat. Post-hoc analysis was conducted using the independent *t*-test to compare between-group measurements and the paired *t*-test to compare within-group measurements. The alpha level was set at 0.05 with Bonferroni correction.

Results

Of the 79 subjects, 39 were randomised to Wii Fit

balance training and 40 to conventional balance training. All subjects completed the 6 weeks of training and post-intervention assessment. The two groups were comparable in terms of gender distribution, age, height, weight, body mass index, FAC, and number of falls in the previous year (Table 1).

Repeated measures analysis of variance was used to assess the group-by-time interaction, which was significant in the BBS score, and two of the four balance components in the limits of stability test (the end-point excursion and the maximum excursion).

Pre-test values of the two groups were comparable, but post intervention the Wii Fit

TABLE 1. Demographics of the Wii Fit and conventional balance training groups

Parameter	Wii Fit balance training (n=39)	Conventional balance training (n=40)	P value
Mean±SD age (years)	82.3±3.8	82.0±4.3	0.806
No. of males:females	16:23	15:25	0.820
Mean±SD height (m)	1.54±0.1	1.57±0.1	0.139
Mean±SD weight (kg)	52.6±4.6	55.9±8.5	0.183
Mean±SD body mass index (kg/m^2)	22.3±2.1	22.8±2.8	0.625
No. of subjects in the functional ambulatory category 2:3	22:17	20:20	0.654
Mean±SD No. of falls in the previous year	2.4±1.0	2.2±1.1	0.312

TABLE 2. Outcome measures of the Wii Fit and conventional balance training groups

Outcome measures	Mean±SD				P value		
	Wii Fit balance training (n=39)		Conventional balance training (n=40)				
	Pre-test	Post-test	Pre-test	Post-test	Pre-test (group effect)	Post-test (group effect)	Group-by-time effect
Berg Balance Scale score	37.0±3.0	40.7±3.2*	37.1±1.8	37.8±1.8*	0.804	<0.001†	<0.001‡
Timed-up-and-go time (s)	19.7±3.1	17.0±2.8*	18.9±3.1	18.2±2.4*	0.290	0.061	0.434
Limits of stability reaction time (ms)							
Anterior	696.3±166.9	605.8±144.2	716.0±137.6	706.9±133.0	0.599	0.003†	0.145
Posterior	703.1±165.1	648.9±139.3	667.4±155.8	646.5±137.3	0.412	0.710	0.540
Left	635.3±245.2	658.5±225.7	577.4±238.2	651.9±196.4	0.286	0.976	0.483
Right	640.2±282.2	772.2±273.4	697.8±299.9	710.4±266.0	0.318	0.382	0.258
Limits of stability end-point excursion (mm)							
Anterior	93.1±27.0	121.2±29.1*	90.3±24.8	78.8±13.4	0.667	<0.001†	<0.001‡
Posterior	87.3±30.2	103.3±23.9*	81.8±20.3	70.7±11.5	0.391	<0.001†	0.001‡
Left	93.6±29.7	105.3±28.4*	88.6±24.6	82.6±19.2	0.467	<0.001†	0.048‡
Right	92.4±37.5	113.0±32.6*	87.1±29.5	76.1±19.8	0.532	<0.001†	0.007‡
Limits of stability maximum excursion (mm)							
Anterior	121.8±26.0	158.8±22.1*	118.4±21.8	102.3±12.4	0.572	<0.001†	<0.001‡
Posterior	112.6±27.7	136.1±18.9*	108.3±26.4	91.7±11.4	0.524	<0.001†	<0.001‡
Left	123.4±30.8	135.8±25.7*	116.5±25.1	105.1±15.9	0.330	<0.001†	0.011‡
Right	118.5±31.8	142.3±34.7*	108.9±27.7	97.5±15.5	0.200	<0.001†	0.001‡
Limits of stability directional control (%)							
Anterior	89.8±1.9	91.0±3.5	90.2±2.4	88.2±6.0	0.389	0.026	0.055
Posterior	86.5±3.5	86.7±4.3	86.6±3.8	84.8±5.5	0.967	0.136	0.212
Left	90.3±4.0	89.0±5.5	90.8±3.8	90.6±4.7	0.620	0.220	0.538
Right	90.2±4.7	89.2±5.5	89.9±5.4	90.8±4.0	0.812	0.190	0.292

* P≤0.01 after Bonferroni correction (0.05/4=0.0125) within group (time effect)
† P≤0.01 after Bonferroni correction (0.05/4=0.0125) between groups (group effect)
‡ P≤0.05 between and within groups (group-by-time effect)

balance training group achieved better balance performance than the conventional balance training group, namely a significantly better BBS score, faster reaction time in the anterior direction, and further end-point excursion and maximum excursion in all four directions of the limits of stability test (P≤0.01, Table 2).

Within the Wii Fit balance training group, the BBS score, timed-up-and-go test, end-point and maximum excursions in all four directions in the limits of stability test improved significantly (Table 2). Within the conventional balance training group, only the BBS score and the timed-up-and-go test improved significantly (Table 2).

Discussion

The improvement in BBS score was significantly more in the Wii Fit than the conventional balance training group (3.7 vs 0.7). This may be attributed to the real-time performance feedback and cuing stimuli in the VR training to support error-free learning. The results of this study are comparable with other studies conducted in community in which Wii Fit intervention significantly improved older adults' BBS score.[6-8]

The improvement in the timed-up-and-go test for the Wii Fit and conventional balance training groups was 2.7 and 0.7 seconds, respectively. Both groups focused on training standing balance and neither the Wii Fit nor the conventional balance training emphasised walking speed. Nonetheless, the static balance training could enhance a more dynamic balance control in our institutionalised and frail (FAC 2 or 3) subjects as reflected by the timed-up-and-go test.

The reaction times of the limits of stability test of the two groups were comparable. In a cross-sectional study, experienced Tai Chi practitioners achieved significantly better reaction time than non-Tai Chi practitioners.[9] In contrast, another study by the same research group in 2004 reported that there was no significant difference in reaction time between subjects who received 8 weeks of Tai Chi training and controls who received health education.[10] One possible explanation for these contrasting results is that it may require a longer training period to improve the reaction time in older adults, particularly those who are institutionalised and with low mobility status (FAC 2 or 3). Thus, the training duration may need to be longer than the present protocol.

Only the Wii Fit group achieved significant improvement in end-point (20.8%) and maximum (20.3%) excursion in all four directions of the limits of stability test (P≤0.01), and was significantly better than the conventional balance training group (P≤0.01). In a study measuring the functional reach test (also known as the voluntary limits of stability - anterior direction) in 16 older adults without a history of fall,[11] Wii Fit intervention for 4 weeks achieved a significant increase of 2.48 inch (from 10.92 to 13.40 inch); the percentage change was 22.7%. The Wii Fit balance training resembles the body movements of the limits of stability test, which quantifies the maximum distance by which a person can intentionally displace their centre of gravity by leaning without assistance, losing their balance or stepping. Such body-weight-shifting practice was not included in the control balance training. In this connection, Tai Chi practitioners had significantly better reaction time, maximum excursion and directional control than non-Tai Chi practice controls.[9] Such enhanced balance performance as reflected by the limits of stability test might be due to the weight-shift involved in Tai Chi practice, which is similar to the Wii Fit training.[12,13] Better end-point and maximum excursion may be related to the better performance of functional activities, which might, in turn, minimise the risk of fall.

The directional control of the limits of stability test of the two groups was comparable. In the balance control perspective, Tai Chi training seems more effective in improving directional control than Wii Fit balance exercises, as Tai Chi practitioners improved more than controls after 8 weeks of Tai Chi practice.[10] This might be due to the nature of the exercise. The Wii Fit balance training required the individual to shift body weight to random target positions. This constantly challenged the balance control system to maintain the body's centre of mass within the base of support. However, such erratic movements might not develop smooth and coordinated weight shifting. Yet, to prevent falls, smoothness and continuous weight shifting is less important than a quick response to perturbation. Therefore, further kinematic and kinetic study of centre of mass movement during falls and during Wii Fit training is warranted.

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Adverse events and poisoning from over-the-counter traditional Chinese medicine: a population-based survey

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KEY MESSAGES

1. Adverse events related to over-the-counter (OTC) traditional Chinese medicine (TCM) use are much more prevalent in Hong Kong than previously suggested from hospital-based data.
2. Widespread misperceptions among users, and the use of unreliable OTC TCM information sources (such as magazines) present major challenges for safe OTC TCM use.
3. In addition to greater consumer education, OTC drug safety can be improved with more stringent labelling regulations, up-to-date OTC TCM product safety websites for consumers and health professionals, and improved surveillance of adverse events in an outpatient setting.

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Introduction

In Hong Kong, self-medication with traditional Chinese medicine (TCM) is a common practice for conditions ranging from the common cold to chronic health conditions.[1] Approximately one-seventh of Chinese herbal medicine poisoning cases reported from accident and emergency departments have been attributed to over-the-counter (OTC) TCM products.[2] The majority of TCM users were reported to have self-prescribed OTC products without prior consultation of a TCM practitioner.[3] There is concern about the potential misuse of these products, particularly given that most OTC TCM users are of lower educational status.[3]

As of January 2012, only 188 (1.8%) of the 10 518 OTC TCM products available in Hong Kong have completed formal registration required for proprietary TCM products; the remaining are in the process of transitional registration.[4] This study aimed to examine knowledge, attitude, and behaviour of OTC TCM users in Hong Kong and their association with adverse events.

Methods

This study was conducted from January 2011 to January 2012. Ethical approval was obtained from the Survey and Behavioural Research Ethics Committee of The Chinese University of Hong Kong. A population-based telephone survey targeting Chinese residents of Hong Kong aged over 18 years was conducted. For unanswered calls, at least four further calls were made before considering the number to be invalid. If more than one eligible person were available, the 'last birthday method' was used to select the participant. The study sampled 1100 respondents (response rate, 70.1%).

Respondents were asked about their background (age, gender, household income level, educational attainment, marital status, employment status, self-reported general health, and presence of health insurance), the conditions for which they used OTC TCM (whether the condition was self-diagnosed or by a medical professional, whether the product labels had clear information about dosage and contraindications), and any adverse events in the past year (rash, nausea, vomiting, fever, dizziness, heart/blood pressure problems, systemic allergic reactions, sleep problems, and all others). Those who experienced adverse events were asked about the type of OTC TCM used, source of product use information, and where they sought professional medical help for the adverse event.

In addition, their beliefs and knowledge about the safety, effectiveness, potential harms, potential drug interactions, and potential benefits of the OTC TCM were recorded, as were their perception of current OTC TCM labels, their beliefs about the likelihood of side effects, drug interactions and adverse events after OTC use and the perceived severity of these effects. Respondents were questioned about what they perceived as the main barriers to better-informed OTC TCM use (financial barriers, lack of convenient access to TCM practitioners, lack of published information on the internet, unclear written instructions, lack of information at the retail establishments, lack of knowledge among western doctors and pharmacists), and whether they had

ever received any warnings about OTC TCM drug safety and how confident they were of being able to find reliable OTC TCM information.

Chi-square test and t-test were used to assess associations between predictors (eg demographic variables) and outcome variables (ie adverse events, knowledge levels, information-seeking behaviours). Variables with a P value <0.15 in the unadjusted analyses were used as candidate variables for stepwise multivariable logistic regression models to examine whether the respondent experienced an adverse drug reaction and whether the respondent sought OTC information from reliable sources (package labels, health professionals, and TCM retailers).

Results

Of the 1100 respondents, 789 (71.7%) reported past-year OTC TCM use. The most common conditions for which OTC TCM was used were cold/influenza symptoms (54.0%), gastrointestinal/digestive problems (44.0%), musculoskeletal pain (43.9%), 'qi' imbalance (23.7%), general health enhancement (13.7%), and sleep problems (5.3%) [Table 1]. OTC TCM users were comparable with non-users except that the former were more likely to be of middle income (15 000-29 999/month) and less likely to report 'very good' or 'good' health status. Of the entire sample, 2.3% (3.2% of users, n=25) reported at least one past-year adverse event. Only 56.8% of respondents reported exposure to warnings about safe OTC TCM use from any source.

Comparing OTC TCM users who did or did not report an adverse event in the past year, the former surprisingly reported greater information-seeking practice and were more likely to be exposed to drug safety warnings (Table 1). The multivariable logistic regression analysis revealed that occurrence of a past-year adverse event was associated with lower educational attainment (P=0.01) and seeking OTC information from unreliable sources such as television (P<0.05), popular magazines (P<0.05), or books (P<0.10). Respondents who were less educated, male, and those with less self-efficacy in obtaining reliable OTC information were less likely to seek OTC use information from the package, TCM retailers, or health professionals (Table 2).

TABLE 1. Comparison of over-the-counter (OTC) traditional Chinese medicine (TCM) users who did or did not report adverse events

Parameter	Mean±SD or % of users			P value
	All users (n=789)	Adverse events (n=25)	No adverse events (n=764)	
Read OTC Labels				0.005
Always	48.3	84.0	47.1	
Often	18.5	0.0	19.1	
Sometimes	16.5	4.0	16.9	
Seldom	7.5	8.0	7.5	
Never	9.3	4.0	9.4	
Read OTC package inserts				0.031
Always	35.4	64.0	34.4	
Often	20.5	20.0	20.5	
Sometimes	20.7	8.0	21.1	
Seldom	11.3	4.0	11.5	
Never	12.2	4.0	12.4	
Asks OTC information from retailers				0.410
Always	3.8	4.0	3.8	
Often	9.4	12.0	9.3	
Sometimes	19.9	28.0	19.6	
Seldom	15.8	24.0	15.6	
Never	51.1	32.0	51.7	
Search online OTC information				0.342
Always	1.0	4.0	0.9	
Often	2.9	0.0	3.0	
Sometimes	7.1	12.0	6.9	
Seldom	8.5	12.0	8.4	
Never	80.5	72.0	80.8	

TABLE 1. (cont'd)

Parameter	Mean±SD or % of users			P value
	All users (n=789)	Adverse events (n=25)	No adverse events (n=764)	
Ask medical doctors or pharmacists about OTC use				0.030
Always	0.4	4.0	0.3	
Often	2.9	4.0	2.9	
Sometimes	3.9	8.0	3.8	
Seldom	8.5	4.0	8.7	
Never	84.2	80.0	84.4	
Tell their medical doctors of TCM use				0.285
Always	20.9	32.0	20.6	
Often	12.3	20.0	12.1	
Sometimes	11.2	8.0	11.3	
Seldom	9.4	12.0	9.3	
Never	46.2	28.0	46.8	
Ask TCM practitioner about OTC?				0.186
Always	2.9	0.0	3.0	
Often	5.2	12.0	5.0	
Sometimes	14.4	16.0	14.3	
Seldom	7.6	16.0	7.3	
Never	69.9	56.0	70.3	
Practice score (max=28)	9.22±5.00	9.12±5.0	12.20±5.8	0.002
OTC knowledge score (max=6)	3.52±1.45	3.64±1.60	3.52±1.45	0.712
Perceived benefits score (max=12)	6.67±2.99	6.76±2.40	6.67±3.01	0.851
Perceived OTC adverse event severity (max=6)	4.71±1.25	4.48±1.61	4.72±1.24	0.467
Perceived adverse event susceptibility (max=8)	3.50±1.97	3.46±1.95	3.50±1.95	0.937
Perceived OTC info barriers (max=12)	7.23±2.21	7.36±2.31	7.24±2.20	0.801
Usual source(s) of OTC information				
TV	8.1	24.0	7.6	0.003
Retailers	22.8	40.0	22.2	0.037
Internet	5.6	4.0	5.7	0.724
Newspapers	7.6	16.0	7.4	0.109
Health professionals	11.6	8.0	11.7	0.570
Friends and family	43.4	52.0	43.1	0.377
Magazines	5.3	20.0	4.9	0.001
Drug labels/inserts	56.7	66.7	56.4	0.387
Other sources (books)	7.6	16.0	7.1	0.092
Conditions for past year OTC use				
Cold/flu	54.0	64.0	53.7	0.308
Gastrointestinal/digestive problems	44.0	44.0	44.0	0.971
Musculoskeletal pain	43.9	76.0	42.7	0.001
'Qi' imbalance	23.7	32.0	23.4	0.321
General health enhancement	13.7	20.0	13.5	0.351
Sleep problems	5.3	20.0	4.8	0.001
Skin and hair problems	4.3	8.0	4.1	0.333
Treating open wounds	4.1	8.0	3.8	0.287
Chronic respiratory problems	3.5	0.0	3.5	0.339
Slimming/weight loss	1.1	8.0	0.9	0.001
Blood pressure/heart conditions	0.5	4.0	0.4	0.012
Improving mental functioning/memory	0.3	8.0	0.0	<0.0001
Sexual health/reproductive conditions	0.4	0.0	0.4	0.754
Vision problems	0.3	0.0	0.3	0.798
All other conditions	1.8	4.0	1.7	0.392

TABLE 2. Correlates of adverse events and seeking reliable information (including package labels and inserts, health professionals, and retailers) in over-the-counter (OTC) traditional Chinese medicine (TCM) users (n=789)

Parameter	% with adverse events	P value	OR (95% CI)		% seeking reliable OTC information	P value	OR (95% CI)	
			Sociodemographic factors	All factors			Sociodemographic factors	All factors
Total OTC TCM users	3.2							-
Gender		0.146				0.076		
Male	2.2		Not significant	-	66.6		1.00	1.00
Female	4.0				72.4		1.38 (1.01-1.87)*	1.53 (1.07-2.20)*
Age (years)		0.043				0.816		
18-44	1.9		Not significant	-	69.3		-	-
45+	4.4				70.1			
Educational level		0.002				0.010		
F6 and higher	0.7		1.00	1.00	75.0		1.00	1.00
Up to F5 (grade 11)	4.8		7.43 (1.74-31.8)†	9.64 (2.20-42.3)†	66.3		0.64 (0.46-0.88)†	0.64 (0.44-0.94)*
Household income (HK$/month)		0.291				0.794		
≥15 000	4.3		-	-	71.2		-	-
0-14 999	2.7				70.3			
Health Insurance		0.100				0.740		
Insured	4.3		Not significant	-	70.3		-	-
Uninsured	2.2				69.3			
Employment		0.008				0.263		
Employed or full-time student	1.8		Not significant	-	71.3		-	-
All else	5.1				67.6			
OTC knowledge level		0.307				0.003		
High knowledge score (>IQR)	6.0			-	82.1			Not significant
Score in IQR	2.9				69.6			
Low knowledge score (<IQR)	2.9				58.6			
Perceived benefit		0.141				0.628		
High benefit score (>IQR)	2.2				69.3			-
Score in IQR	4.2				71.0			
Low benefit score (<IQR)	0.9				65.1			
Perceived barrier		0.472				0.835		
Low barrier score (<IQR)	3.2			-	69.9			-
Score in IQR	2.8				69.3			
High barrier score (>IQR)	4.9				70.9			
Perceived severity of OTC adverse event		0.101		Not significant		0.249		
High severity score (>IQR)	2.7				100.0			-
Score in IQR	4.3				70.3			
Low severity score (<IQR)	7.7				65.4			
Perceived susceptibility to OTC adverse event		0.674				0.338		
High susceptibility score (>IQR)	2.9			-	68.4			-
Score in IQR	2.6				69.2			
Low susceptibility score (<IQR)	4.1				75.3			

* P<0.05
† P<0.01
‡ Comparison with those not reporting those behaviours

TABLE 2. (cont'd)

Parameter	% with adverse events	P value	OR (95% CI)		% seeking reliable OTC information	P value	OR (95% CI)	
			Sociodemographic factors	All factors			Sociodemographic factors	All factors
Preventive practice		0.008						
High practice score (>IQR)	6.0			1.00	-			-
Score in IQR	2.4			0.40 (0.17-0.96)*				
Low practice score (<IQR)	1.0			0.16 (0.03-0.72)*				
Exposed to any TCM warnings		0.650				0.002		Not significant
Yes	2.9			-	73.8			
No/can't recall	3.5				63.2			
Self-efficacy for obtaining reliable OTC information?		0.123				<0.001		
Yes, have self-efficacy	2.4			Not significant	78.1			1.00
No/not sure	4.4				58.2			0.52 (0.36-0.76)†
Usual source of OTC information								
Package labels	3.1	0.387‡		-	80.9	<0.001		
Retailers	5.6	0.037‡		Not significant	83.7	<0.001		
Health professionals	2.2	0.570‡		-	74.7	0.268		
Internet	2.3	0.724‡		-	77.3	0.249		
TV	9.4	0.003‡		2.93 (1.01-8.50)*	62.5	0.198		
Newspapers	6.7	0.109‡		NS	65.0	0.415		
Magazines	11.9	0.001‡		3.32 (1.03-10.7)*	69.0	0.924		
Family & friends	3.8	0.377‡		-	65.1	0.014		
Books	6.9	<0.001‡		2.74 (0.84-8.90)	82.8	0.025		

There were 27 adverse events reported by 25 respondents; they were most commonly caused by pills/capsules (37%), followed by plasters/dressings (25.9%), ointments/creams (18.5%), and ingestible powders (11.1%) [Fig]. There were no reported adverse events from syrups or tinctures. Allergic reactions, dizziness/disorientation, and gastrointestinal symptoms (such as diarrhoea, stomach ache and cramping) comprised nearly three-quarters of all adverse events reported. Respondents who used OTC TCM for musculoskeletal pain, sleep problems, blood pressure/heart conditions, weight loss, or improving mental functioning were more likely to report adverse events (Table 1).

Professional medical treatment was sought in only one-third of the adverse events (n=8): allergic reaction (n=2), severe nausea (n=1), dizziness (n=1), sleep problems (n=1), stomach ache (n=1), fever (n=1), and exacerbation of influenza-like symptoms (n=1) caused by pill/capsules (n=4), ingestible powders (n=3), and topical ointment/cream (n=1).

Discussion

The majority of OTC TCM users who experienced adverse events did not seek any professional medical treatment indicating that these adverse events were an underappreciated public health issue in Hong Kong. Nonetheless, since only one-third of respondents with adverse events sought medical treatment, most adverse events were likely to be mild and self-limiting.

Despite existing labelling regulations, over one third of respondents still found OTC labels to be unclear. This is partly because many of the listed drug actions, such as 'normalising the gall-bladder', require advanced understanding of TCM pathology. Most OTC TCM users self-medicated without consulting a TCM practitioner or seeking OTC information. Unlike western over-the-counter drugs that offer symptom-based treatment, TCM treatment relies upon holistic diagnosis of the underlying syndrome, and the prescribed treatment for a particular symptom may vary greatly between individuals. Given the lower educational status of TCM users in Hong Kong,[4] there is a potential for inappropriate OTC use of TCM.

The use of an unreliable source of OTC information (eg mass media, magazines) was the primary behavioural risk factor for OTC TCM–related adverse events, rather than lower information-seeking behaviours. In view of the pervasiveness

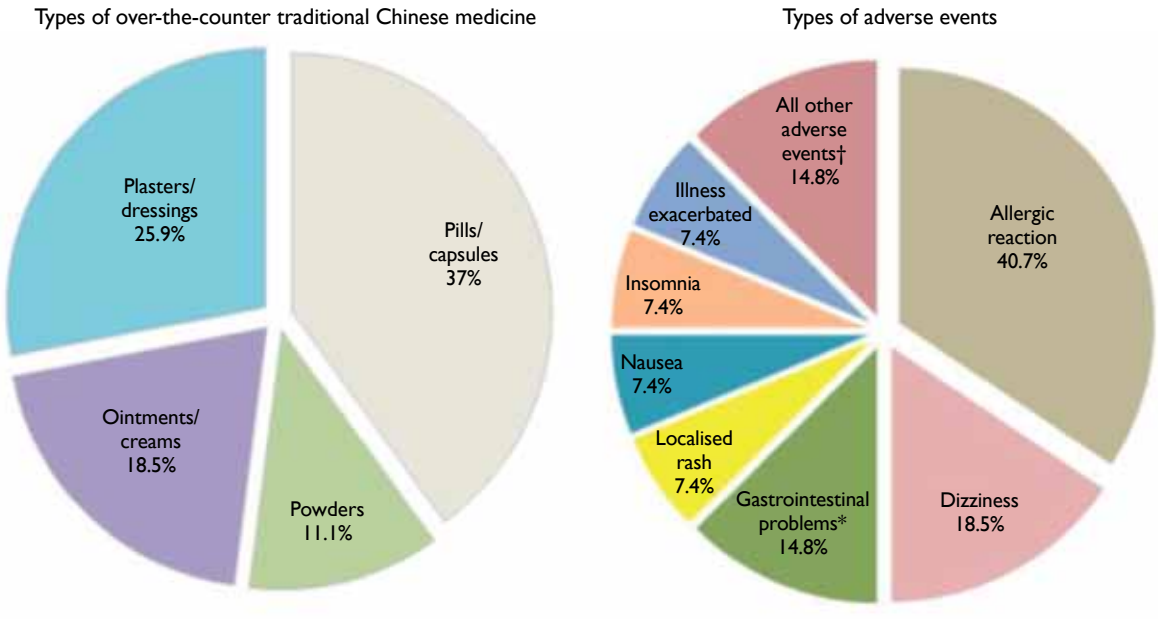

FIG. Types of over-the-counter traditional Chinese medicine and types of adverse events (n=27)

* Including diarrhoea, stomach ache, abdominal cramping

† Including one case each of blistering, heart problems, high fever, coughing spasms

of low-risk perceptions, these findings suggest that reliance on improved labelling regulations is unlikely to address all OTC-related adverse effects. Strategies for promoting safe OTC TCM drugs use should be included to raise public awareness of drug safety.

The main limitation of this study was the lack of clinical validation of self-reported adverse events; some of which may have been unrelated to their medication use, or simply symptoms of the disease itself. It was also possible that some OTC TCM–related adverse events may not have been recognised as such by users. Even among the valid cases of adverse events that were reported, it was not possible to determine whether poor drug quality, product misuse, or drug interaction was the underlying cause of the adverse event. Moreover, detailed product information was also not obtained from respondents who reported adverse events.

Nonetheless, our study can inform drug policy for governments to implement stricter regulation of alternative medicine. Increased global trade has enabled rapid growth in the availability of OTC products worldwide.[5] The total output of China's TCM manufacturing industry was US$13 billion in 2002.[5] In addition to addressing pervasive OTC TCM misconceptions, there is a need to reduce barriers to reliable drug safety information. Better communication between the TCM manufacturers, retailers, TCM practitioners, and western health professions is required to develop effective safety measures for OTC TCM. The trend towards greater alternative medicine use necessitates not only stringent labelling regulations and better consumer risk communication, but also improved surveillance of adverse events.

Acknowledgement

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Functional outcome in patients sustaining moderate and major trauma

TH Rainer *, CA Graham, HH Yeung, WS Poon, HF Ho, CW Kam, GN Cattermole, P Cameron

KEY MESSAGES

1. Compared with the Hong Kong norm, initial survivors of moderate and major trauma had reduced mean SF-36 physical component score persisting for at least a year.
2. The SF-36 physical component score is most reduced and slowest to recover in patients with spinal and extremity injury.
3. Compared with the Hong Kong norm, initial survivors of moderate and major trauma had reduced mean SF-36 mental component score initially but it exceeded the norm by 6 months after injury.
4. Hong Kong possibly lags behind Australia in terms of potential improvement in 6- and 12-month post-injury functional outcome, but a larger study is required to confirm this.

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Introduction

Implementation of a trauma system may improve survival and functional outcome in trauma patients.[1] In 2003, the Hospital Authority in Hong Kong designated five hospitals as trauma centres. The potential survival rate in Hong Kong still lags behind that in Australia,[2] and survivors of trauma patients often experience late sequelae that affect their everyday life.[3]

This study aimed to (1) evaluate physical and mental health status and functional outcome in adult patients following moderate and major trauma in Hong Kong, and (2) compare functional outcome in the Hong Kong Registry with the Victoria State Trauma Outcome Registry (VSTR) in Australia.

Methods

This study was conducted between 1 January 2010 and 30 November 2011. Ethical approval was obtained. Patients aged ≥18 years with moderate or major trauma (defined as an injury severity score [ISS] ≥9) who survived the first 48 hours of injury in three regional hospitals (the Prince of Wales Hospital, Queen Elizabeth Hospital, and Tuen Mun Hospital) were included.

The VSTR is a population-based registry for all major trauma patients in Victoria. Patients aged ≥18 years who sustained an injury between 1 July 2009 and 30 June 2010 with an ISS >15 were selected for comparison.

The physical and mental health status of trauma patients was evaluated using the physical component summary (PCS) and mental component summary (MCS), respectively, of the Short-Form 36 (SF-36) health questionnaire and Glasgow Outcome Scale-Extended (GOSE).[4,5] The Hong Kong norm for the PCS is 52.83 and for the MCS is 47.18. This is comparable with the United States norm (50 for both PCS and MCS). For comparison between Hong Kong and VSTR, the Short-Form 12 was used.

Demographic data including age, sex, and mechanism of injury, ISS, Revised Trauma Score, probability of survival, Glasgow Coma Scale (GCS), and hospital and intensive care unit length of stay were recorded. Isolated injury was defined as a single abbreviated injury scale (AIS) ≥3. Multiple injury was defined as ≥2 regions with AIS ≥3. Working status was defined as a GOSE ≥5.

The end point was 12 months post injury. The primary outcome was post-traumatic SF-36 score at 30 days, 6 months, and 12 months. The secondary outcomes were GOSE score and return to work.

A univariate analysis was conducted to identify predictors of 12-month functional outcome and quality of life. Significant parameters ($P<0.05$) were then entered into a multiple logistic regression model.

Results

A total of 400 patients (69.5% male) aged 18 to 106 (mean, 53.3) years were recruited. In patients with isolated or multiple injury, the mean PCS gradually increased with time and peaked at 12 months but

was still lower than the Hong Kong norm; none of the subgroup injuries reached the level of the Hong Kong norm at 12 months. Nonetheless, the mean MCS exceeded that of the Hong Kong norm at 6 months; the mean MCS in subgroups of primary extremity and abdominal injury reached the level of the Hong Kong norm by 1 month, and that in all subgroup injury exceeded the Hong Kong norm by 6 months (Figs 1 and 2).

In terms of the GOSE score, only 16.5% of patients achieved upper good recovery by 12 months; 56% achieved a GOSE of ≥5 by 12 months

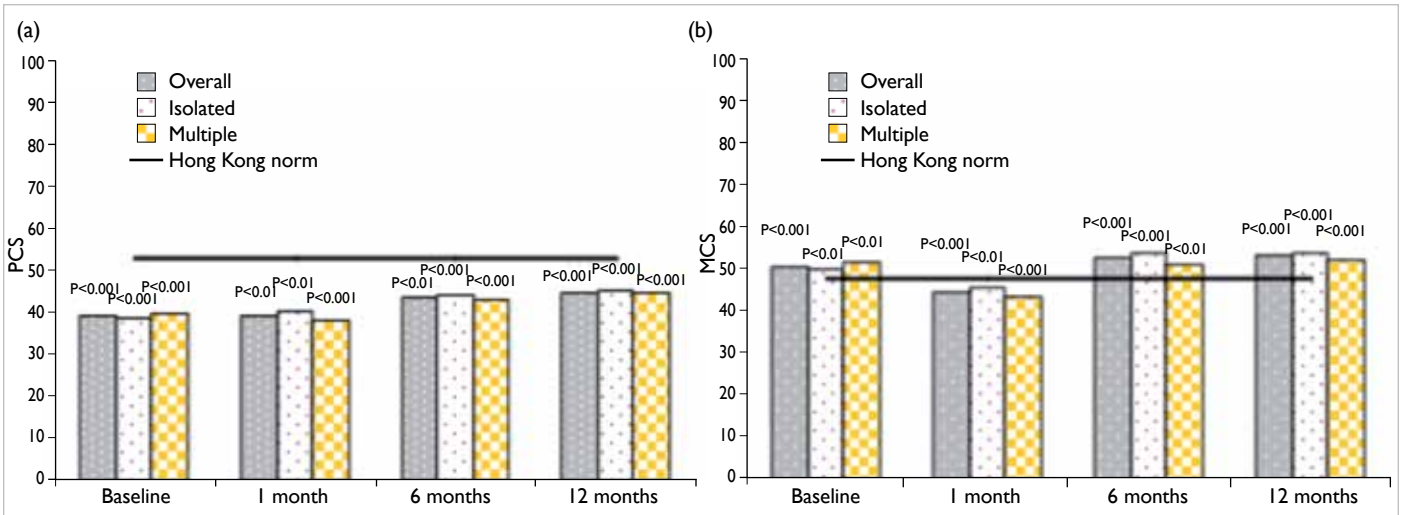

FIG 1. (a) Physical component summary (PCS) and (b) mental component summary (MCS) scores over 12 months after trauma in patients with isolated or multiple trauma

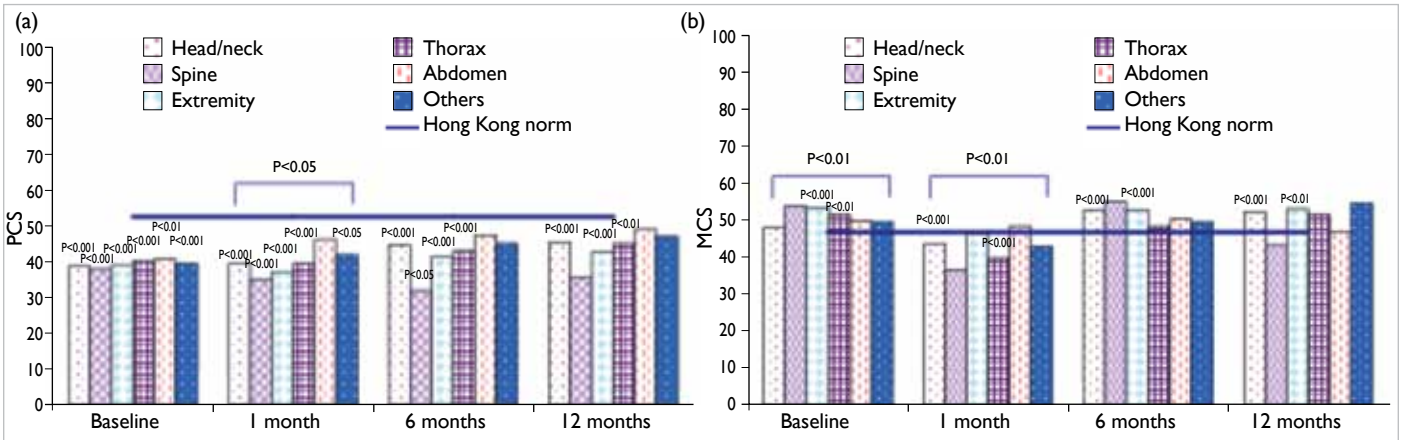

FIG 2. Recovery in (a) physical component summary (PCS) and (b) mental component summary (MCS) scores over 12 months after trauma in terms of principal body part.

TABLE 1. Post-injury Glasgow Outcome Scale-Extended outcome in Hong Kong patients

Glasgow Outcome Scale-Extended (score)	No. (%) of patients (n=400)			
	Baseline (n=398)	1 month (n=341)	6 months (n=280)	12 months (n=237)
Upper good recovery (8)	14 (3.5)	33 (9.7)	45 (16.0)	39 (16.5)
Lower good recovery (7)	7 (1.8)	23 (6.7)	40 (14.3)	37 (15.6)
Upper moderate disability (6)	9 (2.3)	16 (4.7)	24 (8.6)	25 (10.5)
Lower moderate disability (5)	26 (6.5)	46 (13.5)	62 (22.1)	36 (15.2)
Upper severe disability (4)	128 (32.3)	115 (33.7)	31 (11.1)	23 (9.7)
Lower severe disability (3)	145 (36.3)	49 (14.4)	22 (7.9)	16 (6.8)
Vegetative state (2)	68 (17)	22 (6.5)	1 (0.4)	1 (0.4)
Death (1)	1 (0.3)	37 (10.9)	55 (19.6)	60 (25.3)

indicating independent activities of daily living and partial return to work (Table 1).

Respectively in the VSTR and Hong Kong, 1955 and 261 patients were compared, 10.4% and 13.9% of them were in-hospital deaths, and 89.6% and 85.1% were survivors. With the VSTR patients as a reference, the adjusted odds of a better functional outcome in Hong Kong patients was 0.88 (95% confidence interval [CI]=0.66-1.17) at 6 months and 0.83 (95% CI=0.60-1.12) at 12 months (Table 2).

Respectively in the VSTR and Hong Kong, valid SF-12 scores were recorded in 855 and 102 patients at 6 months and 861 and 76 patients at 12 months. The VSTR and Hong Kong patients were comparable in terms of the mean PCS-12 score at 6 months (mean difference=1.1, 95% CI= −1.3-3.4, P=0.39) and at 12 months (mean difference= −0.3, 95% CI= −3.1-2.5, P=0.82) and the mean MCS-12 score at 6 months (mean difference=1.3, 95% CI= −1.1-3.6, P=0.29) and at 12 months (mean difference=1.9, 95% CI= −0.7-4.6, P=0.15) [Fig 3].

TABLE 2. Multivariate analysis of the association between trauma characteristics and Glasgow Outcome Scale-Extended at 6 months (n=1853) and 12 months (n=1840)

Covariate	Adjusted odds ratio (95% CI)	
	6 months (n=1853)	12 months (n=1840)
Setting		
Victoria (reference)	1	1
Hong Kong	0.88 (0.66, 1.17)	0.83 (0.60, 1.12)
Sex		
Male (reference)	1	1
Female	0.87 (0.72, 1.06)	0.80 (0.66, 0.98)
Age (years)	0.972 (0.967, 0.976)	0.967 (0.963, 0.972)
Injury Severity Score	0.95 (0.90, 1.01)	0.96 (0.95, 0.97)
Mechanism		
Fall (reference)	1	1
Motor vehicle	1.23 (0.96, 1.58)	1.11 (0.87, 1.42)
Motorcycle	1.37 (1.01, 1.84)	1.49 (1.10, 2.01)
Pedal cyclist	2.03 (1.33, 3.10)	2.97 (1.89, 4.65)
Pedestrian	1.20 (0.85, 1.69)	1.11 (0.79, 1.56)
Other	1.17 (0.89, 1.53)	1.25 (0.95, 1.64)
Glasgow Coma Scale		
13-15 (reference)	1	1
9-12	0.44 (0.32, 0.59)	0.51 (0.38, 0.70)
3-8	0.12 (0.09, 0.17)	0.13 (0.10, 0.18)
Comorbid status		
Healthy	1	1
Pre-existing condition	0.90 (0.75, 1.07)	0.87 (0.73, 1.04)

Discussion

For all trauma patients, the mean MCS exceeded that of the Hong Kong norm by 6 months. This may be due to the positive effect of an awareness of surviving trauma, with a greater sense of well-being. The mean PCS improved gradually but did not reach the level of the Hong Kong norm. Compared with the VSTR patients, the trend in functional recovery

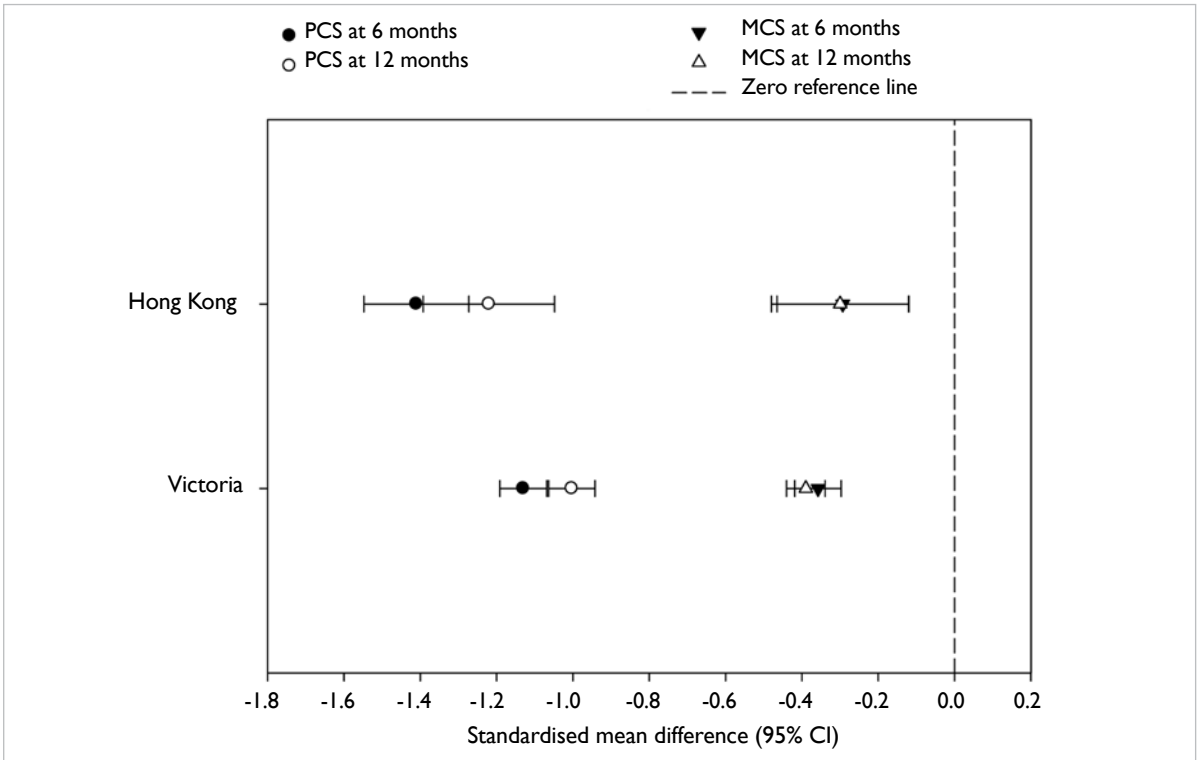

FIG 3. Adjusted standardised mean difference for the physical component summary (PCS) and mental component summary (MCS) scores of the SF-12 at 6 months and 12 months

at 12 months in Hong Kong was less favourable (but not significantly). The successful follow-up rate at 12 months in Hong Kong was only 44%.

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Cutaneous electrical stimulation to improve balance performance in patients with sub-acute stroke: a randomised controlled trial

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KEY MESSAGES

1. In subjects with sub-acute stroke, rehabilitation that combined transcutaneous electrical nerve stimulation (TENS) with task-oriented balance training (TOBT) was superior to placebo stimulation with TOBT in improving balance performance and motor functions.
2. In subjects with sub-acute stroke, TENS is particularly useful as a complementary therapy to TOBT.

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Introduction

Falls and fall-related injuries after stroke are common and include fractures, fear of falling, and the consequent restriction of activity. Physical rehabilitation can restore balance control, promote functional recovery, and prevent secondary complications, disability, and handicap.

In chronic stroke patients, electric somatosensory stimulation can augment the effects of task-related training in improving lower limb strength and walking capacity.[1,2] The anatomic connections between the somatosensory cortex and motor cortex have been shown to provide the anatomic substrate through which electrical stimulation-induced somatosensory inputs can enhance motor cortical reorganisation following stroke.[3] The greatest improvement in motor function occurs between 3 and 6 weeks post-stroke, and plateaus at 90 days.[4] The first 8 weeks after stroke are the best time to enhance motor recovery.

The null hypothesis was that transcutaneous electrical nerve stimulation (TENS) plus task-oriented balance training (TOBT) did not differ significantly to placebo-stimulation (P-STIM) plus TOBT in recovery of balance and motor function after the first sub-acute stroke.

Methods

This single-blinded, randomised, placebo-controlled study was conducted from February 2011 to March 2013. It was approved by the local ethics committee. Informed consent was obtained from each subject. According to two clinical studies of sub-acute stroke patients using Berg Balance Scale (BBS) scores and distance covered in 6-minute walk test (6MWT), the weighted effect size was 0.75. Therefore, a sample of 68 subjects was necessary to achieve 80% chance (beta level=0.2) of detecting 20% difference (alpha level=0.05) in changes among the two treatment groups. Anticipating a possible dropout, the sample size was increased from 68 to 76.

Subjects were included if they had a single stroke within 3 to 11 weeks of the first onset of stroke, were able to stand upright unsupported for 1 minute, and had moderate gait deficit (Functional Ambulatory Category >II). Those with medical comorbidity, receptive dysphasia, or cognitive impairment denoted by scoring <7 of 10 on the Abbreviated Mental Test were excluded.

Subjects were randomised to receive TENS+TOBT or P-STIM+TOBT. They were required to attend twice per week for 8 weeks (16 sessions). The TENS+TOBT group received 60 minutes of TENS from a TENS stimulator. Electrodes were placed over the common peroneal nerve and sural nerve of the paretic leg. The P-STIM+TOBT group received 60 minutes of placebo stimulation from an identical-looking TENS device with the electrical circuit disconnected inside. Concurrently, all subjects had 60 minutes of TOBT that included six exercises: (1) stepping up and down exercise, (2) heel-raising exercise, (3) gait re-education, (4) walking exercise across obstacles, (5) standing exercise on balance board, (6) kicking exercise with alternate legs, (7) partial squatting exercise, and (8) transitional training between sit-to-stand and walking tasks. Standardised progression was made by the physiotherapist.

All subjects received 2.5 hours of conventional rehabilitation that involved 60 minutes each of standardised physiotherapy and occupational

therapy, followed by 30 minutes of speech therapy and/or health talks arranged by the geriatric day hospitals as usual practice.

Subjects were assessed at four time points by an assessor blinded to treatment allocation: before treatment (baseline), after eight sessions, after 16 sessions, and 3 months after treatment. Primary outcomes included BBS and 6MWT. Secondary outcomes included modified Rivermead Mobility Index (MRMI), timed up and go test (TUG), incidence of falls, and Short Form General Health Questionnaire (SF-36).

Multiple analysis of covariance incorporating all outcome measures at all time points was used to test the time-by-group effect of the intervention. The post-hoc analysis was conducted using univariate two-way analysis of covariance to indicate at which time point significant difference between two groups occurred, with the significance level set at 5%. Intention-to-treat analysis was performed, and missing values for any drop-outs were imputed using the last observation carried forward method.

Results

A total of 76 subjects (age, 70.1±9.9 years) were included at 6.2±2.8 weeks after stroke. Seven (9.2%) subjects dropped out during the 8-week intervention period, and 17 (22.4%) subjects dropped out 3 months after treatment. The TENS+TOBT and P-STIM+TOBT groups were comparable in terms of demographics and baseline outcomes (Table 1).

Both groups generally showed improvement in all outcomes at all time points, compared with baseline values. Compared with P-STIM+TOBT group, the TENS+TOBT group achieved significantly greater improvement in BBS and MRMI scores after eight sessions, as well as in BBS and TUG scores, and physical function subscale in SF-36 after 16 sessions (Tables 2 and 3). The effect on BBS and SF-36 was maintained 3 months after treatment. The two groups did not differ significantly in 6MWT distance, and did not report any fall 3 months after treatment.

Discussion

The effects of spontaneous recovery on outcome observed mostly in acute and sub-acute stroke must be considered when evaluating clinical trials of exercises, as the spontaneous gain makes between-group effects more difficult to detect because controls are also improving.

Both groups' training involved repetitive strengthening exercises of muscles relating to balance control and functional tasks that challenged

TABLE 1. Subject characteristics and baseline outcome between the transcutaneous electrical nerve stimulation (TENS) plus task-oriented balance training (TOBT) group and placebo-stimulation (P-STIM) plus TOBT group

Variable	Mean±SD or No. (%) of subjects		P value
	TENS+TOBT (n=37)	P-STIM +TOBT (n=39)	
Age (years)	72.6±97	69.3±100	0.145
Gender			
Male	24 (64.9)	24 (61.5)	
Female	13 (35.1)	15 (38.5)	
Hemiparetic side			
Left	18 (48.6)	20 (51.3)	
Right	19 (51.9)	19 (48.7)	
Time post-stroke (weeks)	6.1±2.7	6.3±2.9	0.783
Type of stroke			
Ischaemic	31 (83.8)	34 (87.2)	
Haemorrhagic	6 (16.2)	5 (12.8)	
Height (cm)	160.1±8.6	159.1±8.4	0.627
Weight (kg)	59.5±10.3	57.7±10.1	0.455
Body mass index (kg/m^2)	23.1±3.0	22.7±3.1	0.570
No. of stroke	1.0±0.00	1.05±0.223	0.167
No. of subjects having falls in previous 4 weeks	5	7	
No. of falls in previous 4 weeks	0.3±0.9	0.2±0.5	0.704
Abbreviated Mental Test	9.1±1.1	9.0±1.1	0.829
Modified Functional Ambulatory Category	5.6±0.6	5.4±0.8	0.218

TABLE 2. Comparison of outcome measures between the transcutaneous electrical nerve stimulation (TENS) plus task-oriented balance training (TOBT) group and placebo-stimulation (P-STIM) plus TOBT group

Outcome measure	Mean±SD			
	Baseline	After 8 sessions	After 16 sessions	3 months after treatment
Berg Balance Scale				
TENS+TOBT	37.78±7.59	44.7±6.63*	47.68±5.69†	49.05±6.78*
P-STIM+TOBT	35.41±10.95	40.62±9.38	44.23±7.40	46.08±5.79
Distance covered in 6-minute walk test (m)				
TENS+TOBT	127.27±73.10	174.78±79.98	197.16±82.88	210.59±92.04
P-STIM+TOBT	107.56±59.20	148.56±76.84	171.56±95.36	199.51±99.64
Modified Rivermead Mobility Index				
TENS+TOBT	31.51±2.93	34.73±3.06*	36.27±2.99	36.84±3.98
P-STIM+TOBT	30.31±4.72	32.74±4.08	34.97±3.83	36.56±3.15
Timed up and go test (s)				
TENS+TOBT	42.89±27.06	30.38±17.75	22.82±10.75†	21.33±10.75
P-STIM+TOBT	45.60±23.67	34.27±18.52	31.68±22.08	19.41±21.18

* P<0.05 compared with P-STIM+TOBT group
† P<0.01 compared with P-STIM+TOBT group

TABLE 3. Comparison of sub-scores of SF-36 between the transcutaneous electrical nerve stimulation (TENS) plus task-oriented balance training (TOBT) group and placebo-stimulation (P-STIM) plus TOBT group

SF-36 Subscales	Mean±SD		
	Baseline	After 16 sessions	3 months after treatment
Physical function			
TENS+TOBT	39.86±19.38	62.84±22.56*	68.92±17.60*
P-STIM+TOBT	38.46±20.59	50.38±22.98	57.05±23.53
Role physical			
TENS+TOBT	46.35±20.09	63.2 0± 25.50	66.22±25.04
P-STIM+TOBT	45.19±31.75	66.92±25.82	67.82±21.20
Bodily pain			
TENS+TOBT	71.96±26.37	75.20±24.26	77.43±23.37
P-STIM+TOBT	71.73±31.75	75.19±26.57	75.19±27.83
General health			
TENS+TOBT	52.70±20.97	54.73±18.41	62.57±21.90
P-STIM+TOBT	52.31±21.91	56.41±19.73	61.92±21.63
Vitality			
TENS+TOBT	58.92±17.68	68.63±17.86	68.57±14.95
P-STIM+TOBT	56.92±13.61	64.87±16.68	66.28±19.73
Social functioning			
TENS+TOBT	56.58±22.85	67.51±19.64	67.74±16.15
P-STIM+TOBT	58.79±20.65	64.17±16.69	64.65±20.77
Role functioning-emotion			
TENS+TOBT	77.16±22.13	80.86±18.92	77.61±17.85
P-STIM+TOBT	73.47±22.59	80.51±18.40	76.75±19.51
Mental health			
TENS+TOBT	68.49±22.35	70.93±15.75	68.92±17.23
P-STIM+TOBT	68.62±22.35	69.97±20.76	70.89±19.35

* P<0.05 compared with P-STIM+TOBT group

dynamic balance. Both groups demonstrated improvement in MRMI, BBS, and TUG scores after 8 sessions of intervention compared with baseline. The mechanism underlying improvement in motor functions following TOBT appears multi-factorial, and could be attributed to enhancement of descending voluntary commands to the paretic muscles, reduced agonist-antagonist co-contraction, improved gross motor efficiency induced by exercise-mediated neuromuscular adaptations, and reorganisation of synapses and cortical representation following repetitive practice of functional tasks.[1,2]

The TENS+TOBT group was superior to P-STIM+TOBT group in improving balance performance and motor functions. This finding is consistent with that in studies in which TENS applied to areas supplied by the common peroneal nerves improved walking functions in patients with chronic stroke.[1,2] TENS can be a useful complementary therapy to TOBT. Possible mechanisms underlying the motor improvements following TENS could be disinhibition of descending voluntary commands to the motoneurons of paretic muscles and decreased co-contraction of the spastic antagonist.[1,2] In addition, TENS sent afferent input to the sensorimotor cortex that in turn enhanced output from the primary motor cortex, thereby improving motor function. The anatomic connections between somatosensory cortex and motor cortex have been shown to provide the anatomic substrate through which electrical stimulation can enhance motor cortical reorganisation after stroke.[3]

A BBS score <45 has been reported as a threshold of fall risk.[5] All our subjects had attained a BBS score >45 after 16 sessions of treatment and 3 months after treatment.

The TUG test includes a series of motor tasks that demand balance control in addition to muscle strength and movement coordination.[6] Older adults who were able to complete the TUG task in <20 seconds were more likely to be independent in the transfer tasks needed for the activities of daily living, whereas those who required ≥30 seconds tended to be more dependent in their activities of daily living and require assistive devices for ambulation. In the TENS+TOBT group, the TUG time was 42.89±27.1 seconds at baseline and improved to 21.3±10.8 seconds after 16 sessions of treatment.

Task-related exercise played a main role in increasing the 6MWT distance in both groups. Physical exercise might modify any physical deconditioning, and might improve gross motor efficiency by inducing exercise-mediated neuromuscular adaptations, thus improving walking endurance in subjects with sub-acute stroke.

One limitation of the study was the absence of an independent task-orientated balance training group to delineate the effects of exercise. Due to time and resource constraints, treatment effectiveness was assessed only up to 3 months after treatment. Whether greater improvement in motor functions can be attained with longer treatment remains unknown.

Conclusion

In patients with sub-acute stroke, TENS+TOBT was generally more effective than P-STIM+TOBT in improving balance and motor functions. Improvement in balance was maintained even 3 months after treatment. Future studies should examine the optimal combined training programme in terms of frequency, duration, and intensity.

Acknowledgements

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Validation of selective attention and memory measures as early markers for Alzheimer's disease

CS Tse *, LCW Lam, DA Balota, GTY Leung, KT Hau, JF Chang

KEY MESSAGES

1. The measures of prospective memory (ie the ability to remember what one has to do when a specific event occurs in the future) and selective attention (ie the ability to maintain the task goal over time and resolve the conflict between incongruent information) can discriminate between healthy older adults and those who are in the earliest stage of Alzheimer's disease.
2. Prospective memory and selective attention performance declined as a function of Alzheimer's disease severity, after taking into account age and number of years of education.
3. The discriminative power of prospective memory and selective attention measures for early-stage Alzheimer's disease is comparable with that of other psychometric measures. These cognitive abilities should be incorporated into standard Alzheimer's disease assessment.

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Introduction

It is important to diagnose people with Alzheimer's disease at the earliest possible stage and discriminate these individuals from healthy older adults. This study aimed to develop prospective memory and selective attention measures to enable detection of individuals with the earliest stage of Alzheimer's disease. Three groups of community-dwelling older adults were recruited: healthy older adults (mean age, 75.06 years), older adults in the earliest stage of Alzheimer's disease but not yet clinically diagnosed (mean age, 78.66 years), and older adults clinically diagnosed with Alzheimer's disease (mean age, 80.20 years). Informed consent was obtained from each individual. Participants were screened for colour-blindness, depression, untreated hypertension, reversible dementia, and other disorders that could potentially produce cognitive impairment. Prospective memory and selective attention tasks were conducted using a laptop computer at place of residence or regional social centre.

Prospective memory

Many cognitive tasks tap older adults' memory abilities but most focus almost exclusively on their retrospective memory, eg studying a list of unrelated words and then recalling them. In contrast, prospective memory, which refers to the ability to remember what one has to do in the future,[1] has received much less attention, despite its connection with activities of daily living. In a prospective memory task, older adults were instructed to spontaneously perform an intended action when a specific event occurs, while engaging in a concurrent attention-demanding task. In each trial, they were asked to respond to a highlighted arrow by pressing the left or right key. The top and bottom bars varied in colours (red, blue, yellow, or green) across trials (Figs 1a and 1b). In one-fifth of trials (24 out of 120 trials), the top and bottom bars were the same colour, and the participants were told to press an alternative key instead of judging the arrow direction. They were reminded to keep this instruction in mind because they would not be told again. That is, throughout the task older adults were not reminded with the prospective memory instruction. At the end, older adults were asked to recall what they had been asked to do during the task. Only those participants who were able to recall the prospective memory instruction were included in the following analyses. This retrospective memory report ensured that older adults' failure to respond on the prospective memory trial was due to their inability to initiate the intended action at the right moment, rather than having forgotten the prospective memory instruction. The task took about 12-15 minutes to complete. As the task does not involve verbal materials, it is suitable for Hong Kong older adults whose education level is generally low. This laboratory task may simulate daily-life situations, eg remembering to take a medicine before sleep or watching the news programme on TV. Older adults with Alzheimer's disease often demonstrate prospective memory failure in their activities of daily living, which poses a great challenge for their caregivers. Hence,

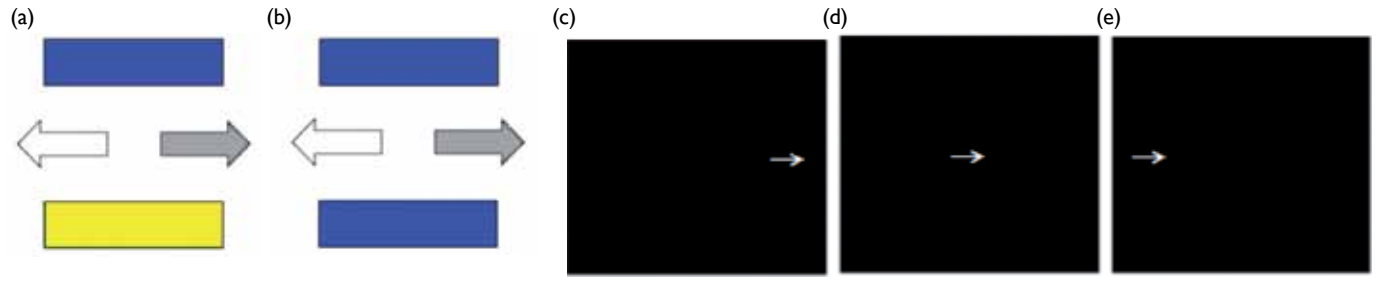

FIG 1. Displays of the prospective memory and selective attention task: (a) typical trial of the prospective memory task, (b) prospective memory trial of the prospective memory task, (c) congruent trial of the selective attention task, (d) neutral trial of the selective attention task, and (e) incongruent trial of the selective attention task

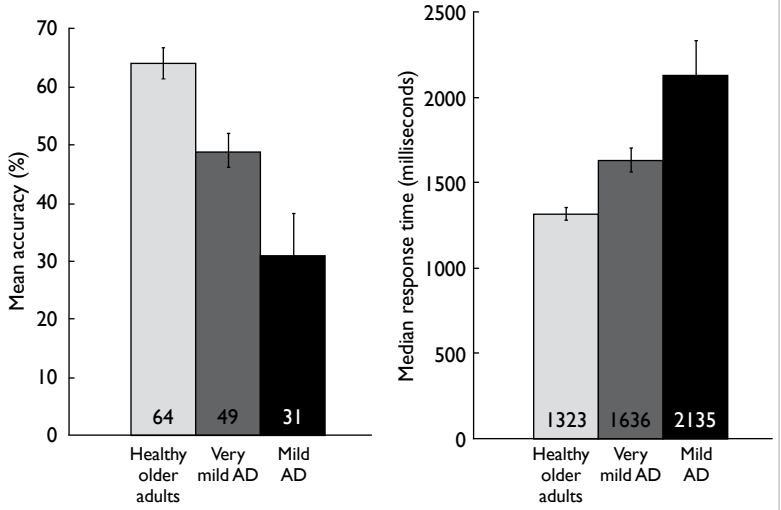

FIG 2. Accuracy and response time in the prospective memory trials as a function of Alzheimer's disease (AD) severity in the prospective memory task

prospective memory performance of older adults may have some implications for their ability to maintain independence in everyday life. Although the current task may not be directly related to older adults' prospective memory in activities of daily living,[2] it is more objective and relies less on older adults' self-reported data. Older adults' accuracy (and response time) in responding to the prospective memory trials is expected to decrease (and be slower) as a function of Alzheimer's disease severity.[1]

After taking into account the differences in age and education level across groups, the accuracy in the prospective memory trials decreased as a function of Alzheimer's disease severity, indicating that older adults with more severe Alzheimer's disease were less able to spontaneously press the alternative key in the prospective memory trials (ie when the top and bottom colour bars were in the same colour). The response time data were congruent with the accuracy data, with older adults with more severe Alzheimer's disease responding more slowly in the prospective memory trials (Fig 2). Hence, prospective memory performance was sensitive to Alzheimer's disease at the earliest detectable stages. This suggests that those with early-stage (very mild) Alzheimer's disease were less able to track the target events and spontaneously trigger the intended action than healthy older adults. This is consistent with our hypotheses and previous findings.[1]

Selective attention

Although memory loss has been considered the first clinical manifestation of Alzheimer's disease, recent evidence also shows a decrease in attentional control as a function of Alzheimer's disease severity.[3] Selective attention was studied via a simple task, in which older adults were told that an arrow pointing to either left or right would appear on the left half, right half, or centre of the screen. They were instructed to ignore the arrow location and judge the arrow direction by pressing either left or right key that corresponded to the arrow direction (Figs 1c to 1e). In congruent trials, the arrow direction (eg pointing right) corresponded to the arrow location (eg at the right). In incongruent trials, the arrow direction (eg pointing right) was opposite to the arrow location (eg on the left). In neutral trials, the arrow appeared in the centre of the screen. The three types of trial were randomly intermixed within the task. A deficit in attentional control could lead to an impaired performance in this task, especially when the arrow location was incongruent with its direction. Specifically, to properly respond to an incongruent trial, one must maintain the task goal (responding to arrow direction, but not arrow location) and resolve the conflict by inhibiting task-irrelevant location information and accessing task-relevant direction information. In contrast, there was no conflict between direction and location information in congruent trials. Previous studies showed that older adults in the earliest stage of Alzheimer's disease made far more errors in incongruent trials (relative to congruent trials) than healthy older adults, suggesting that Alzheimer's disease could influence one's attentional control abilities.[4] The task took about 10-12 minutes to complete. Because the task does not involve verbal materials, it is suitable

for Hong Kong older adults whose education level is generally low. We predicted that older adults' errors in incongruent trials (relative to congruent trials) would increase as a function of their Alzheimer's disease severity.

After taking the differences in age and education level across groups into account, the accuracy in both congruent and incongruent trials decreased as a function of Alzheimer's disease severity. Nonetheless, the drop in performance in incongruent trials (93% → 85% → 68%) was sharper than that in congruent trials (97% → 94% → 82%) [Fig 3], indicating that older adults with more severe Alzheimer's disease were less able to maintain the task goal and resolve the conflict between incongruent information. This is consistent with our hypotheses and previous studies.[4]

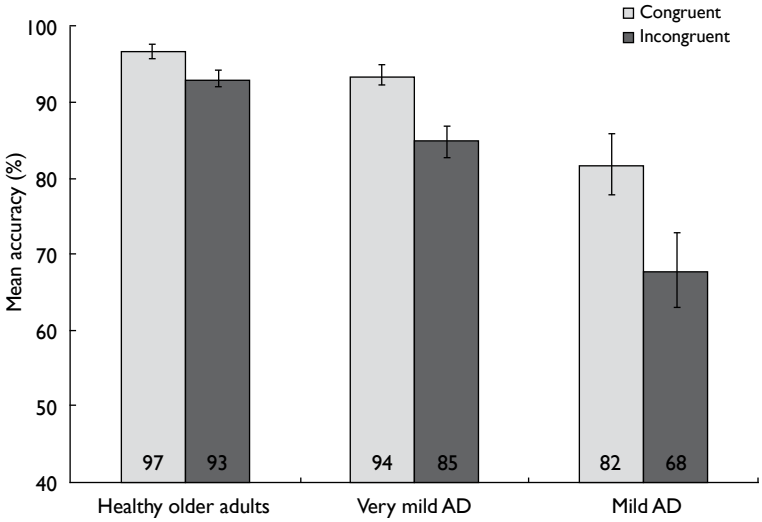

FIG 3. Accuracy in the incongruent and congruent trials as a function of Alzheimer's disease (AD) severity in the selective attention task

Predictive utility and reliability of prospective memory and selective attention measures

We also tested whether the prospective memory and selective attention measures could discriminate between healthy older adults and those at the earliest stage of Alzheimer's disease after taking into account their general cognitive functioning, which could be reflected by these older adults' performance in the psychometric assessment. After controlling for the variance explained by each of the psychometric measures, accuracy and response time in prospective memory trials and errors in the incongruent (vs congruent) trials in the selective attention task still significantly predicted Alzheimer's disease severity (ie healthy old *or* very mild Alzheimer's disease) in most cases, suggesting that the constructs measured by our two tasks did not completely overlap with those measured by standard psychometric measures. To test the reliability of our measures, about one-third of our healthy old and very mild Alzheimer's disease individuals were invited to repeat the task. The reliability of most of the measures in the two tasks was acceptable and quite comparable with most of the psychometric measures.

Conclusion

This study identified measures of prospective memory and selective attention tasks that can discriminate an individual who is at the earliest detectable stage of Alzheimer's disease from healthy older adults in a Hong Kong Chinese population. Most of these measures demonstrated moderate reliability and comparable discriminative power for Alzheimer's disease severity to most standard psychometric measures. The findings are consistent with those reported in previous studies, although the mean education level of our samples was lower than that of previous studies (6 vs 14 years). This suggests that the prospective memory and selective attention measures could be sensitive to the decline due to early-stage and mild Alzheimer's disease for older adults with a lower education level. Future studies should determine whether our prospective memory and selective attention measures can predict older adults' everyday functioning (such as remember to lock the main door before bedtime) or examine the influence of individual differences (such as education level) on the discriminative power of various cognitive measures.[5]

Acknowledgements

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Detection of amyloid plaques in patients with post-stroke dementia

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KEY MESSAGES

1. Using ^{11}C-Pittsburgh Compound B (PiB) positron emission tomography (PET), Alzheimer's disease pathology was found in one-fifth of patients with post-stroke dementia.
2. Patients with Alzheimer's disease pathology had a more progressive cognitive decline over 3 years after stroke or transient ischaemic attack.
3. In patients with post-stroke dementia, PiB PET may be used to guide treatment decision, as those with significant Alzheimer's disease pathology may be more responsive to anti–Alzheimer's disease drugs than those without.

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Introduction

Cognitive impairment is a common sequel to stroke; the rate of post-stroke dementia is 6% to 30%. As a predictor of long-term mortality and functional disability (independent of physical impairment), post-stroke dementia poses a huge economic and social burden in developed countries. Cerebrovascular disease may not be the only factor responsible for the cognitive decline following stroke/transient ischaemic attack. Alzheimer's disease pathology may also play a role in post-stroke dementia. Amyloid plaques are a pathological hallmark of Alzheimer's disease. Cerebrovascular lesions and amyloid frequency co-exist with ageing. ^{11}C-Pittsburgh Compound B (PiB) positron emission tomography (PET) can detect amyloid plaques in Alzheimer's disease patients with high sensitivity and specificity.[1] Alzheimer's disease treatment (eg acetylcholinesterase inhibitors) may be more beneficial in patients with mixed dementia than in those with pure vascular dementia. Therefore, determining the presence of concurrent Alzheimer's disease among patients with post-stroke dementia has clinical implications.

This study aimed to determine the frequency of amyloid plaques in patients with post-stroke dementia, and whether the cognition of post-stroke dementia patients with amyloid plaques declines faster than those without.

Methods

This study was conducted from January 2010 to June 2013. A total of 75 patients with stroke or transient ischaemic attack 3 months after hospital admission were recruited and followed up annually for 3 years.[2] Patients underwent PiB PET at 3 months and were classified as PiB+ (characteristic of Alzheimer's disease) or PiB-. Cognition was assessed yearly using the Mini-Mental State Examination (MMSE) and Alzheimer's Disease Assessment Scale Cognitive subscale (ADAS-cog).

Results

Of the 75 patients, 14 (18.7%) were PiB+. At baseline (3 months after stroke), three patients could not complete the ADAS-cog assessment. After 1 year, eight patients died, and nine patients could not complete the ADAS-cog assessment due to poor health, and two patients refused further follow-up. Eventually, 53 subjects completed serial ADAS-cog assessments at year 1. Overall, subjects who withdrew had more impaired cognitive function than those who completed the study. The PiB+ patients had a lower education level but a higher rate of having a genotype of the APOEε4 allele (a genetic risk factor for Alzheimer's disease) [Table 1].

The PiB+ and PiB- groups did not differ significantly in ADAS-cog score (P=0.069) at different time points (P=0.562) after adjustment for education level and genotype of ApoE, or in the cognitive decline rate at 1 year (P=0.499), or in MMSE score at 1 year.

In 60 patients, cognitive change over 3 years was assessed using MMSE. The PiB+ and PiB- groups were comparable in the rates of lost to follow-up (7.1% vs 24.2%, P=0.277) and death (7.1% vs 16.1%, P=0.678). Overall, subjects who withdrew had comparable clinical characteristics with those who completed the study. The PiB+ patients were older (P=0.037) and had a lower education level

(P=0.013) and a higher rate of genotype of ApoE ε4 allele (P=0.023). Because the age and education level had potential effects on cognition, they were treated as covariates in longitudinal analysis to evaluate changes between the two groups.

During 3 years of follow-up, cognition declined over time in the PiB+ and PiB- groups (Table 2 and Fig). The change in MMSE score at different stages differed significantly between PiB+ and PiB- groups (P=0.025, Table 2). In the PiB+ group, the MMSE score continued to decline over time at a relatively consistent rate. In contrast, the score in the PiB- group declined initially from baseline to year 1, but levelled off during the following 2 years (Fig). The rate of decline of MMSE score in the PiB+ and PiB- groups was comparable between baseline and year 1 (P=0.324), but the PiB+ group had a faster rate of decline between year 1 and year 2 (P=0.068), and significantly greater between year 2 and year 3 (P=0.005). Therefore, the mean MMSE score at 3 years was lower in PiB+ than PiB- patients (11.8±5.9 vs 17.2±6.8, P=0.049), and the total decline in MMSE score at 3 years was greater in PiB+ than PiB- patients (-5±6 vs -1.8±4.3, P=0.044).

Discussion

Abnormal amyloid deposits may play a role in determining the long-term progression of cognitive impairment in patients with stroke or transient ischaemic attack. In the early stage after stroke, cognition of both PiB+ and PiB- patients declined. Yet, cognition of PiB+ patients continued to decline in the long term, while that of PiB- patients remained relatively stable. In addition, the prevalence of concurrent amyloid deposits in post-stroke dementia patients was 18.7%.

The use of PiB PET enables valid diagnosis in living persons and overcomes the limitations of post-mortem studies with their retrospective nature, long time lag from dementia onset, and uncertainty about the temporal relationship between the development of brain lesions and dementia onset.

Limitations of this study included a high attrition rate during the 1-year study period. There were 22 (29.3%) patients who failed to return for

TABLE 1. Demographic and clinical characteristics of patients with positive or negative PiB positron emission tomography outcome at 1 year

Parameter	Mean±SD or No. (%) of patients		P value
	PiB+ (n=12)	PiB- (n=41)	
Age (years)	78.7±3.8	75.7±8.3	0.084
No. (%) of females	5 (41.7)	18 (43.9)	0.891
Education (years)	1.7±2.1	4.9±4.7	0.026
With APOEε4 allele*	7 (58.3)	4 (11.4)	0.003
Mortality	1/14 (7.1)	6/61 (9.8)	1
Dropout rate	2/14 (14.3)	20/61 (32.8)	0.21

* Data were not available for six subjects

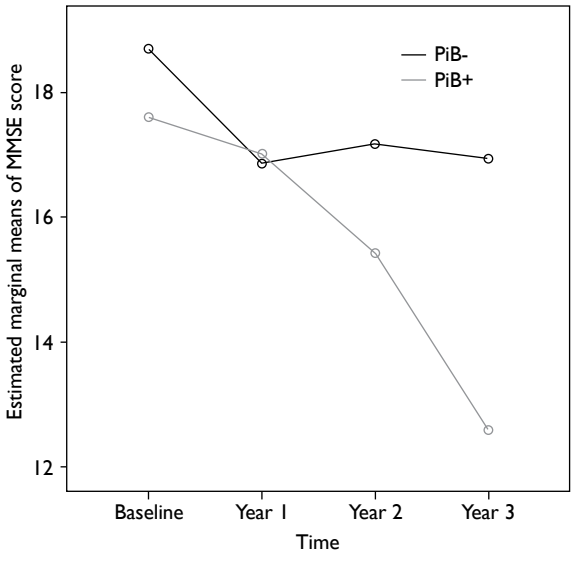

FIG. Cognitive decline over 3 years in terms of Mini-Mental State Examination (MMSE) score in patients with positive or negative PiB positron emission tomography outcome

TABLE 2. Change in Mini-Mental State Examination (MMSE) score in patients with positive or negative PiB positron emission tomography outcome

MMSE score	Mean±SD (adjusted mean±SD)		P value
	PiB+ (n=13)	PiB- (n=47)	
Baseline	16.7±5 (17.6±6.5)	19±6.6 (18.7±6.3)	0.599
Year 1	16.1±5 (17±5.9)	17.1±6.1 (16.9±5.7)	0.934
Year 2	14.5±5.8 (15.4±6.6)	17.4±6.6 (17.2±6.4)	0.406
Year 3	11.8±5.9 (12.6±6.8)	17.2±6.8 (16.9±6.6)	0.049
Change			
Baseline to year 1	-0.6±4.5 (-0.6±4)	-1.8±3.6 (-1.8±3.8)	0.324
P value	1	0.006	
Year 1 to year 2	-1.6±2.3 (-1.6±3.2)	0.3±3.2 (0.3±3.1)	0.068
P value	0.211	1	
Year 2 to year 3	-2.7±2.5 (-2.8±2.8)	-0.3±2.7 (-0.2±2.7)	0.005
P value	0.028	1	
Baseline to year 2	-2.2±5.3 (-2.2±4.4)	-1.5±3.8 (-1.5±4.3)	0.64
P value	0.872	0.059	
Year 1 to year 3	-4.3±2.9 (-4.4±3.6)	0.04±3.6 (0.08±3.5)	<0.001
P value	0.002	1	
Baseline to year 3	-5±6 (-5±5)	-1.8±4.3 (-1.8±4.8)	0.044
P value	0.078	0.045	

a second ADAS-cog assessment. We could not infer the cognitive progression of the 19 patients who did not attend follow-up. It is probable that their cognitive symptoms were too severe to communicate, but the possibility of other physical pathology causing aphasia could not be omitted. In addition, because the prevalence of PiB+ was lower than our preliminary estimation, the final number of PiB+ patients was small. Hence, a larger study is needed to verify the findings of our study.

Conclusions

Concurrent amyloid pathology is found in about one-fifth of patients with stroke or transient ischaemic attack and dementia; it can exert a negative long-term impact upon cognitive progression. The use of PiB PET enables detection of amyloid plaques in patients with post-stroke dementia. In those with concurrent amyloid plaques, Alzheimer's disease treatment may help to slow cognitive decline in the long term.

Acknowledgements

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Use of botulinum toxin to improve upper limb spasticity and decrease subsequent carer burden in long-term care residents: a randomised controlled study

K Lam *, KK Lau, KK So, CK Tam, YM Wu, G Cheung, KS Liang, KM Yeung, KY Lam, S Yui, C Leung

KEY MESSAGES

1. Infirmary patients who were treated with intramuscular injection of botulinum toxin A for upper limb spasticity had significant improvement in muscle tone and joint mobility, and caregivers were able to perform basic upper limb care more easily.
2. A basic stretch programme was also beneficial in improving joint mobility, or at least prevented further deterioration of limb contracture in such patients.

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Introduction

Spasticity leads to decreased range of motion of joints, increased pain, spasm, functional disability, and contractures. Limb spasticity also increases the burden on carers in the provision of nursing and personal care. The use of botulinum toxin to treat spasticity has increased. It blocks acetylcholine release at the neuromuscular junction, thereby inhibiting muscle contraction and decreasing spastic muscle tone. Its antispastic effect usually lasts approximately 3 months. It is safe, with few (usually transient and localised) adverse effects. Since 2008, the American Academy of Neurology has recommended that botulinum neurotoxin be offered as a treatment option for spasticity in adults and children. Nonetheless, its effect on immobile infirmary patients has not been studied. This study aimed to evaluate the role of botulinum toxin A for treating upper limb spasticity in debilitated infirmary patients and the decrease in carer burden when given as a supplement to conventional physiotherapy and occupational therapy.

Methods

This double-blind, placebo-controlled study was conducted from November 2009 to March 2011. The sample size calculation was based on the proportion of subjects in each group attaining a clinically significant four-point improvement in carer burden scale at 6-week post injection. Based on the data from a pilot study, the total sample size was calculated to be 70.

Patients aged >16 years who had (1) upper limb spasticity for >1 year, (2) shoulder adductor, finger flexor, or elbow flexor spasticity >2 on the Modified Ashworth Scale (MAS),[1] (3) at least moderate difficulty with two out of four items defining carer burden scale,[1] and (4) were able to tolerate limb stretching exercises and limb splints for treating spasticity were recruited from four infirmary units and five care and attention homes in Hong Kong. Patients were excluded if they had (1) functionally useful movement in the spastic limb, (2) rigid affected elbow and finger joints that were unlikely to respond to botulinum toxin injection, (3) severe swallowing difficulties and no tube-feeding support, (4) unstable medical conditions, or (5) peripheral motor neuropathic diseases or neuromuscular junctional disorders.

Patients were randomised to receive botulinum toxin or saline injection by a clinician. The maximum total dose of intramuscular botulinum toxin type A (Dysport) used was 1000 units for one patient. Dose selection for individual muscles was based on clinical judgment of spasticity by the injection team. Electrical stimulator-guided or ultrasound-guided method was used for deep muscles in the region of the forearm. All patients received concurrent standardised physiotherapy of passive limb stretching exercises twice a week, in addition to splinting of the affected upper limb for 3 hours/day, 5 days/week. The assessor, patients, and their care-givers were blinded to the injection material.

The primary outcome was carer burden scale at 6 weeks post intervention. Secondary outcomes included Goal Attainment Scaling, degree of spasticity using the Tardieu scale and MAS, resting angular positions of the shoulder and elbow joints using a plastic goniometer with a 360º scale, passive range of movement of shoulder abduction, elbow extension, finger position at rest and at maximal passive finger extension as recorded by a five-point scale, pain assessment using the Pain Assessment

in Advanced Dementia (PAINAD) Scale[2] observed while performing carer burden scale, and incidence of osteoporotic fracture, pressure sores and skin infections in the affected limb. Serial assessments were made at baseline and 2, 6, 8, 12, 16, 20, and 24 weeks post injection.

Results

A total of 21 males and 34 females (mean±standard deviation age, 69±18 years) were randomised to the botulinum toxin A or saline injection group. The two groups were comparable in baseline demographics (Table 1). The mean Charlson's comorbidity index was 3.5, indicating a high number of comorbidities. More than 90% of patients were bedbound or chairbound; all had chronic spasticity, and the mean duration of spasticity was >9 years. Most patients already had some degree of joint contractures at baseline; the mean passive range of movement in the affected joints was less than half that of the normal value.

TABLE 1. Baseline characteristics of the botulinum toxin and saline groups

Characteristics	Mean±SD or No. (%) of patients	
	Botulinum toxin (n=30)	Saline (n=25)
Age (years)	68.5±18.1	69.0±19.2
No. of males	12 (40.0)	9 (36.0)
Severe spasticity	12 (40.0)	9 (36.0)
Baseline carer burden score	10.9±1.7	10.3±1.9
Charlson's co-morbidity index	3.9±2.0	3.1±1.5
Duration of spasticity (years)	9.5±4.2	9.8±4.6
Spasticity caused by brain problem	30 (100)	25 (100)
Taking oral antispasticity medications	12 (40.0)	8 (32.0)
Rancho cognitive functioning ≥level V	11 (36.7)	11 (44.0)
Modified Functional Mobility Categories of lier or sitter	30 (100)	24 (96.0)
Received baseline limb stretching exercise	6 (22.0)	4 (16.0)
Received baseline splinting	4 (13.3)	2 (8.0)

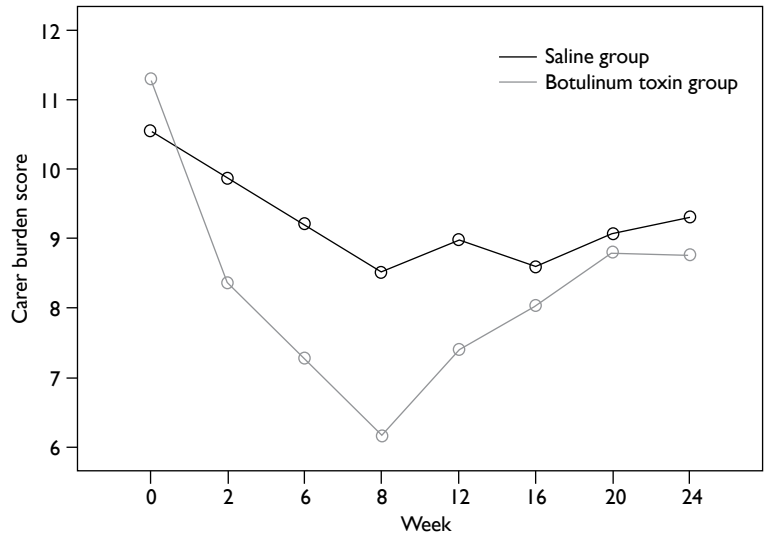

FIG. Carer burden score of the botulinum toxin and saline groups (P<0.001)

At 6 weeks post injection, compared with the placebo group, the botulinum toxin group had a significant decrease in the carer burden scale (2/25 (8%) vs 18/30 (60%) patients had a four-point reduction, P<0.001, Fig) and simultaneous improvement in resting PAINAD (-1.0, P=0.013), PAINAD during basic care procedures (-1.8, P<0.001), MAS of shoulder adductors (-1.47, P<0.001), MAS of elbow flexors (-1.63, P<0.001), and MAS of finger flexors (-0.83, P<0.001), as well as passive range of movement for shoulder abduction (+15°, P<0.001), elbow extension (+19°, P<0.001), and finger extension (+0.47 as recorded by a five-point scale, P=0.006). The trend in improvement in carer burden scale, PAINAD, passive range of movement, and MAS scores in the botulinum toxin group peaked or plateaued at week 8; thereafter improvements gradually diminished in magnitude.

Compared with the saline group, the botulinum toxin group had a significantly greater magnitude of improvement in their Goal Attainment Scaling score (12.65, P=0.001). Most goals pertained to improving the resting position of the limbs (40%) and the range of movement of the joints (32%), followed by decreasing pain during limb stretching (16%) and promoting healing of skin (11%). The botulinum toxin group patients had a significantly greater magnitude of improvement in all four goals, particularly for decreased pain during limb stretching (38% vs 100%, P=0.007).

The botulinum toxin group had clinically significant improvement in muscle spasticity of the affected upper limb (as measured by Tardieu scale and MAS) over the 24-week study period, as well as in the upper limb position (resting angles of both shoulder and elbow joints) The botulinum toxin group also had a trend of improvement in joint mobility in terms of shoulder abduction and elbow extension.

In the saline group, one patient had spasticity in both arms with the right arm being more severely affected, and only the right arm was given interventions including passive stretching and splinting. This patient developed a humeral fracture in his left upper arm (Table 2). In the botulinum toxin group, three patients died of pneumonia: two at week 13 and one at week 20 (Table 2). The two groups did not differ significantly in the cumulative incidence of pneumonia, fever, soft tissue swelling, pressure points, or death.

Discussion

Infirmary patients with limb spasticity seldom receive appropriate treatment, despite its high prevalence and great impact on daily care and quality of life. In our study, only 18% and 11% of patients received limb stretching and splinting, respectively, at baseline, and only 36% were given oral anti-spastic drugs.

Botulinum toxin significantly improved the rating on the carer burden scale in patients

with moderate-to-severe upper limb spasticity, mainly due to its effect on reducing limb spasticity and improving the joint range of movement. In patients with severe cognitive impairment and high dependence on carers for activities of daily living, the carer burden has been shown to be an indicator of patient prognosis and well-being. For totally dependent infirmary patients who are unable to communicate, the carer burden is an objective measure of how severely the patient is disabled by limb spasticity and contractures. The carer burden also indirectly reflects the patient's quality of life. If the carer burden is high, the patient will likely be subjected to difficult and possibly painful care procedures on a daily basis, sometimes more often. The results of our study are in accordance with previous studies showing that botulinum toxin effectively decreases disability and carer burden in patients with post-stroke arm spasticity.[1,3]

The botulinum toxin and saline groups did not differ significantly in pain level (as measured by the PAINAD scale). Pain relief after botulinum toxin treatment may be due to a decrease in severe spasticity of the affected muscles and increased joint mobility. Botulinum toxin may also act as an analgesic by blocking the effect of neurotransmitters that have been implicated in the pain pathway.[5] Nonetheless, the results of previous studies with patients who were able to communicate varied with regard to pain improvement after botulinum toxin injection for upper limb spasticity.[1,3,4] Our study evaluated the impact of botulinum toxin in patients who were unable to communicate, so an observation scale for pain (PAINAD) was used. Nevertheless, it cannot differentiate pain from discomfort or negative affect in such patients. Apart from pain, a high PAINAD scale may indicate that the patient is resistant to care, or is experiencing negative emotions or anxiety.[2] Other external factors could have simultaneously affected the patients' pain level, so it would be difficult to determine degree of pain relief directly due to relief of spasticity.

It should be noted that the saline group also showed improvements in spasticity and passive range of movement of the affected joints, with a mean reduction in carer burden scale score of 1.2 (P=0.002) at 24 weeks post-intervention. This implies that passive stretch and splinting alone can improve joint mobility, or at least prevent further deterioration of the limb contracture.

One patient in the saline group with bilateral upper limb spasticity developed a spontaneous humeral fracture in his left upper arm, although he only received passive stretch and splinting in his right upper arm. It is likely that this humeral fracture was related to difficult basic care procedures due to the bilateral upper limb spasticity. During passive transfer or lifting of bed-bound infirmary patients, their joint contractures act as a supporting point of leverage to exert any external force on the nearby fragile bone, thereby causing the fracture.

Three patients in the botulinum toxin group died of pneumonia at least 3 months post injection when the effects of botulinum toxin had already begun to fade; these deaths were not considered to be related to botulinum toxin type A treatment.

TABLE 2. Cumulative incidence of complication in the botulinum toxin and saline groups at week 24

Complication	No. (%) of patients	
	Botulinum toxin (n=30)	Saline (n=25)
Pneumonia	4 (13.3)	2 (8.0)
Fever	8 (26.7)	6 (24.0)
Soft tissue swelling	4 (13.3)	1 (4.0)
Skin breakdown at pressure points	5 (16.7)	6 (24.0)
Long bone fracture	0	1 (4)
Death	3 (10.0)*	0

* Two patients died at week 13 and one patient died at week 20 due to pneumonia

Conclusions

Infirmary patients who were treated with intramuscular injection of botulinum toxin A for upper limb spasticity had significant improvement in muscle tone and joint mobility, and carers were able to perform basic upper limb care more easily. The treatment was also associated with improved scores for patient-centred outcome measures. The dosage of 1000 U was safe in these frail infirmary patients.

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Prevalence of bisphosphonate-related osteonecrosis of the jaw in Hong Kong

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KEY MESSAGES

1. The prevalence of bisphosphonate-related osteonecrosis of the jaw (BRONJ) was higher in Hong Kong than other parts of the world.
2. Clinicians and dental surgeons should educate patients more about the risk of BRONJ.
3. Policy makers should formulate local guidelines for the prevention and management of BRONJ.

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Introduction

Osteoporosis is a major public health problem in Asia. In 2050, >50% of hip fractures are projected to occur in Asia.[1] Osteoporotic fracture poses a great burden to both the patient and society, as it increases morbidity and mortality. In Hong Kong, there were approximately 6000 hip fractures in 2006. Osteonecrosis of the jaw has been reported in patients with long-term bisphosphonate or high-dose intravenous bisphosphonate therapy for metastatic bone disease. It has also been reported in post-menopausal women prescribed oral bisphosphonate for the treatment of osteoporosis. Risk factors related to osteonecrosis of the jaw include previous radiotherapy to the head and neck region, chronic steroid use, pre-existing dental infections, poor oral hygiene, and smoking.

According to the Task Force of The American Society of Bone and Mineral Research, the incidence of osteonecrosis of the jaw in patients prescribed oral bisphosphonate is estimated to be one in 10 000 to 100 000 patient-years of bisphosphonate exposure.[2] But a more recent larger scale study in the USA suggested that the prevalence was as high as one in 1537 with a frequency of 28 per 100 000 person-years of bisphosphonate exposure.[3] In Hong Kong, the incidence may be higher, because older people in Hong Kong have poorer dental health and a higher prevalence of diabetes mellitus, both of which are risk factors for bisphosphonate-related osteonecrosis of the jaw (BRONJ). In addition, based on ad hoc reports from outpatients of the osteoporosis clinic at the Jockey Club Centre for Osteoporosis Care and Control, four confirmed cases of BRONJ have been identified (unpublished data).

With the inclusion of oral bisphosphonate in the funded drug formulary of the Hong Kong Hospital Authority for patients with a fracture history, the number of patients on oral bisphosphonate is expected to increase. It is therefore important to ascertain the prevalence of BRONJ in Hong Kong.

Methods

This study was conducted from January 2012 to December 2012. Records of patients who attended the self-financed clinic of the Jockey Club Centre for osteoporosis care and control from 2002 to 2012 were reviewed. Those who had taken bisphosphonates for ≥3 years were contacted by a research assistant via telephone for interview. A questionnaire designed by a dental surgeon experienced in managing BRONJ was administered to screen for dental symptoms and history. History of bisphosphonate usage, chemotherapy, or radiotherapy for malignancy, risk factors for osteonecrosis of the jaw (smoking, diabetes mellitus) were also obtained.

Results

Of 2046 patients who met the inclusion criteria, 1284 completed the questionnaire screening (response rate, 62.8%). Of the non-respondents, 99 (4.8%) had died at the time of calling, 116 (5.7%) refused to participate, and 547 (26.7%) could not be contacted (no one answered >3 times or wrong telephone number).

Of the 1284 patients whose mean±standard deviation age was 74.6±7.9 years, 1224 (95.3%) were female. The total duration of exposure to oral bisphosphonate was 5440 person-years; 758 (59%) patients had taken alendronate for 3.9±1.5 years, 566 (44.1%) had taken risedronate for 4.0±1.4 years (Table 1). About 23% of respondents had regular dental visit and 32% had never visited a dentist; 30% had a history of dental extraction after taking oral bisphosphonate for osteoporosis.

After screening, 103 patients had symptoms suspicious of BRONJ. After further questioning by a clinician via the telephone, four cases of BRONJ were identified (Table 2). The diagnosis was confirmed by dental case records (n=3) or dental examination by a dental surgeon (n=1). All BRONJ patients were female and three of them had a history of dental extractions before the onset of BRONJ. All had taken bisphosphonates for ≥5 years. None visited the dentist regularly. None was a smoker nor had been exposed to radiotherapy or chemotherapy.

The prevalence of BRONJ in our study population was 0.31% (95% CI=0.01%-0.62%), with a

frequency of 73.53 per 100 000 person-years of oral bisphosphonate treatment (95% CI=1.58-145.47). In a study of a United States population, the prevalence was 0.1% with a frequency of 28 per 100 000 person-years of treatment.[3] The prevalence of BRONJ in our population was three times that in the United States (P=0.089, Chi-square test).

TABLE 1. Baseline characteristics of the respondents

Characteristic	Respondents (n=1284)
Mean±SD age (years)	74.6±7.9
% of women	95.3
Mean±SD bisphosphonate duration (years)	4.2±1.2
Bisphosphonate type (%)	
Alendronate	758
Risedronate	566
Ibandronate (oral)	57

TABLE 2. Characteristics of the four patients with bisphosphonate-related osteonecrosis of the jaw

Sex	Age at diagnosis (years)	History of dental extraction	Diabetes mellitus	Smoking	Regular dental check	Duration of bisphosphonate use (years)
F	69	Yes	No	No	No	5
F	74	Yes	No	No	No	6
F	78	Yes	Yes	No	No	5
F	84	No	No	No	No	5

Discussion

The first few case reports of BRONJ were published in 2003-2004. Since then, dental surgeons and clinicians have become more alert to this condition. In 2007, the incidence of BRONJ was estimated to be one in 10 000 to 100 000 person-years of exposure.[2] In a South Korean study in 2010, the estimated prevalence of BRONJ was 0.05-0.07%. In a more recent larger study in the USA, the prevalence of BRONJ was reported to be as high as one in 1537, with a frequency of 28 per 100 000 person-years of bisphosphonate exposure.[3] The prevalence of BRONJ in our population was even higher; the response rate was 62.8%, and the non-responders did not differ significantly to responders in age, gender, or duration of bisphosphonate use.

The exact mechanism of BRONJ remains unknown; its risk factors may include poor dental condition before starting bisphosphonate, dental extraction, diabetes mellitus, smoking, and irradiation to the head and neck region.

With the inclusion of oral bisphosphonate in the funded drug formulary of the Hong Kong Hospital Authority for patients with a fracture history, the number of patients on oral bisphosphonate is expected to increase. More disabled older patients with limited financial resource will receive bisphosphonate treatment. Although this may help reduce their fracture risk, the risk of BRONJ is likely to increase, as they have less access to dental care, which is not publicly funded. Clinicians should therefore be more cautious about prescribing anti-resorptive drugs in this at-risk population.

Full recovery from BRONJ is feasible with good care by a dental specialist, but sometimes the recovery can be long and necessitate many dental manipulations. As BRONJ occurs more frequently in Hong Kong, both clinicians and dental surgeons should be more aware of this complication. Patients are usually not well informed about the possible complications associated with chronic use of bisphosphonates.[4] They should be made aware of the importance of regular dental checks and good oral hygiene, especially before taking bisphosphonate in order to minimise the risk of BRONJ. Dental surgeons should adopt international guidelines on the prevention and management of BRONJ. The American Dental Association has published a guideline on how to manage patients who are on anti-resorptive treatment. Regular dental visits and maintaining excellent oral hygiene are essential. Routine dental treatment generally should not be modified solely due to the use of anti-resorptive agents. Patients with active dental or periodontal disease should be treated in spite of the risk of anti-resorptive agent-induced osteonecrosis of the jaw, because the risks and consequences of no treatment likely outweigh the risks of developing osteonecrosis of the jaw.[5]

There are many international guidelines published by osteoporosis experts and dental surgeons regarding the long-term use of bisphosphonate and the management of osteonecrosis of the jaw.[5] Local health service providers should follow these guidelines in the management of patients with chronic bisphosphonate use to minimise the risk of developing BRONJ. Both clinicians and dental surgeons should liaise closely in the management of suspected cases of BRONJ to facilitate full recovery. In complicated cases, early detection and referral to a specialist is warranted.

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