CAT 3. Effective interventions for preventing or reducing falls

Appraised by Kevin Galbraith, December 2016

Update due 2019

Clinical question
Among people with Parkinson’s, what are the most effective interventions for preventing or reducing falls?

Background
Among people with Parkinson’s, falls are both frequent and recurrent, with 45–68% falling annually, and two-thirds of these falling recurrently. Falls, gait impairment, and postural instability increase the risk of mortality and morbidity. Falls in PD can lead to fractures, increased dependency, nursing home admission and poor quality of life. This CAT sought to identify the most effective interventions for preventing or reducing falls among people with Parkinson’s.

Clinical bottom line
Evidence was found from well-conducted randomised controlled trials (RCTs) that progressive resistance strength training and movement strategy training (both combined with fall prevention education), and Tai chi are effective in preventing falls. Rivastigmine has been assessed but has not been subject to a phase 3 trial, and cannot be recommended. There is a continued need for well-conducted RCTs in fall prevention, and for meta-analyses that can detect possible real effects from existing underpowered studies.

Search terms
(Parkinson Disease/ OR Parkinson$) AND (Randomised Controlled Trials as topic/ OR randomi$) AND (Accidental Falls/ OR fall$) AND prevent$.

Search strategy
Ovid Medline, and adapted for Cochrane Library, and CINAHL. All searches 2010 to August 2016, English language.

Evidence
From 31 articles, 10 addressed fall incidence or frequency as a clinically relevant outcome. One additional phase 2 trial, which investigated the effect of rivastigmine on gait stability, was added after discussion with the Evidence Based Practice Themed Working Group, in view of wide publicity.

Summary of evidence
The search conducted in this study yielded intervention studies with fall reduction as an outcome: one meta-analysis of exercise and motor training; three RCTs evaluating balance training specifically; one RCT evaluating two specific physiotherapy interventions (resistance strength training and movement strategy training), both combined with fall prevention education; one systematic review and one trial evaluating sunlight exposure; and three studies evaluating Tai chi – a systematic review, a randomised controlled trial and a commentary on a trial published in Chinese. Two trials were added after discussion among the Evidence-Based Practice Themed Working Group: a phase 2 trial of rivastigmine, and a trial of treadmill training enhanced with virtual reality (VR) technology.
Exercise and motor training
Evidence was from one meta-analysis. It included only two trials of interventions to reduce falls, and failed to demonstrate a reduction in falling. One of the trials did not include highly challenging balance exercises, and did not aim to demonstrate a reduction in falls; the other trial failed to give a clear description of the balance training intervention.

Balance training
Evidence was from three RCTs that included balance training in the intervention. No trials of only balance training were found. Two lacked sufficient power to show real effects, and relied on self-reporting of falls. One was well-conducted overall, but suffered significant attrition: 25 participants (22%) undertook a modified program to account for pain and coexisting conditions, and 24 participants (21%) discontinued the exercise program. This trial identified a lower fall-rate among a lower severity subgroup. Though pre-planned, such a subgroup analysis should be interpreted with caution, particularly as no Bonferroni adjustment was made for multiple analyses. Two trials excluded patients with cognitive impairment, reducing their generalisability to the wider population. One did not employ blinding of assessors to the group allocation.

Resistance strength training and movement strategy training
Evidence was from one RCT, in which 210 patients with Parkinson’s were randomised to receive either progressive resistance strength training plus fall prevention education N=70, or movement strategy training plus fall prevention education N=69, or the control intervention of life skills information N=71. The strength-training group had 84.9% fewer falls than controls (incidence rate ratio [IRR] = 0.151, 95% CI 0.071-0.322, p<0.001. The movement strategy training group had 61.5% fewer falls than controls (IRR = 0.385, 95% CI 0.184-0.808, p=0.012. This was a well conducted RCT. Attention was paid to allocation concealment, assessors were blind to group allocation, and the assessments were standardised. Analyses were conducted according to the intention-to-treat principle. Falls were self-recorded on fall calendars over a long follow-up period of 12 months. The study excluded patients with cognitive impairment, and severe Parkinson’s. This could impair its external validity in the wider population.

Sunlight exposure
Evidence was from one systematic review, which included only one study in patients with Parkinson’s. This study has been retracted, so neither it, nor the systematic review were critically appraised.

Tai Chi
Evidence was from one systematic review, one RCT, and one commentary on a trial published in Chinese, described here in chronological order.

The systematic review of Tai Chi concluded from a search up to 2008 that there was insufficient evidence that it is an effective intervention for Parkinson’s. One included RCT found Tai Chi to be superior to conventional exercise in terms of the Unified PD Rating Scale UPDRS, p=0.026 and frequency of falls p=0.009. A second RCT found no effect on locomotor ability compared with qigong meditation. This examined surrogate outcomes (gait velocity, stride length) rather than the more clinically relevant fall frequency. Two other trials also employed surrogate outcomes. One was a crossover trial, which investigated the effect of Tai Chi versus wait list controls on UPDRS, Parkinson’s Disease Questionnaire 39 (PDQ39), and the Timed Up and Go (TUG) test. After 12 weeks, there were no significant differences for any outcome. The other was a non-randomised trial comparing Tai Chi, a combined exercise program, and no treatment. After 8 weeks, the UPDRS, Schwab and England Activity of Daily Living, and quality of life scores were higher for Tai Chi than for no exercise. No significant difference was found between Tai Chi and the combined exercise program. Other included studies were of poor quality.

The RCT published in 2012 however, found the incidence of falls to be lower with an individualised programme of Tai Chi than with stretching (incidence rate ratio, 0.33; 95% CI, 0.16 to 0.71) or resistance training (incidence rate ratio, 0.47; 95% CI, 0.21 to 1.00), though the latter did not achieve significance. After follow-up for 3 months, patients who received Tai Chi had fewer falls than those in the stretching group (incidence rate ratio, 0.31; 95% CI, 0.14 to 0.67; p=0.003) and those in the resistance–training group (incidence rate ratio, 0.40; 95% CI, 0.18 to 0.88; p=0.02). The study was well conducted. Assessors were blind to group allocation, analysis was conducted according to the intention-to-treat principle, and losses...
to follow up were minimal. Falls were self-reported however, and patients with cognitive impairment (itself a risk factor for falls) were excluded.

The commentary described a single-blind RCT published in 2014 of Tai Chi (three sessions per week for 12 weeks) versus no Tai Chi, among Parkinson’s patients drawn from hospital and local communities in China. The risk of falls in the intervention group was significantly lower than among controls (relative risk 0.44, 95% CI 0.22 to 0.89). Falls were self-reported using a falls diary, but checked by monthly phone calls. The commentator noted that the intervention was not clearly described, and that replication in other settings might require an experienced instructor, which might be difficult in some countries. It was helpfully calculated that for every four people (95% CI 2 to 18) who undertake Tai Chi, one person avoids a fall who otherwise would have fallen.

**Rivastigmine**

Evidence from a single phase 2 pilot trial, in which 130 patients with moderate Parkinson’s were randomised to receive the anticholinesterase inhibitor rivastigmine (n=65) or placebo (n=65). The primary outcome was a surrogate marker of fall risk (reduction in step time variability). After 32 weeks, compared to the placebo group, patients on rivastigmine had improved on normal walking (ratio of geometric means 0.72, 95% CI 0.58 to 0.88) and on a simple dual task (0.79, 95% CI 0.62 to 0.99). On a complex dual task, improvements did not differ significantly (0.81, 95% CI 0.60 to 1.09). Sensitivity analyses to account for missing data resulted in an upper limit of the 95% CI for simple walking of 0.97 (just below the null value of 1.0), and the difference for the simple dual task failed to reach significance. No correction was made for multiple testing, rendering the findings for the simple dual task susceptible to Type I error. More participants in the rivastigmine group correctly guessed their allocation than would be expected by chance, signaling possible failure of blinding, and potential ascertainment bias. Participants in the rivastigmine group suffered more gastrointestinal side effects (31% versus 5% for nausea, and 17% versus 5% for vomiting). Among secondary outcomes, patients in the rivastigmine group suffered fewer falls (adjusted IRR 0.55; 95% CI 0.38 to 0.81), but there was no significant difference for disease severity or quality of life.

**Virtual-reality-enhanced treadmill training**

A multicentre, single-blinded randomised controlled trial was conducted among adults aged 60–90 years with a history of two or more falls in the previous 6 months. They were randomly allocated to either treadmill training enhanced by virtual reality (VR) technology (n=154) or treadmill training alone (n=148). The VR component involved digital capture of foot movements and projection of these onto a visual simulation, complete with obstacles, multiple pathways and distractors necessitating continual adjustment of steps. Randomisation was stratified in each clinical site by sex and by 3 subgroups: (1) history of idiopathic falls (n=109); (2) mild cognitive impairment (n=43); and Parkinson’s (n=130). Among the participants with Parkinson’s, the fall incidence after training was lower in the treadmill training plus VR group than in the treadmill training group (IRR 0.45, 95% CI 0.24 to 0.86; p=0.015). After adjusting for disease severity, the IRR was 0.47 (95% CI 0.25 to 0.89; p=0.021). The other subgroups did not experience a similar between-group reduction of fall incidence. The following should be noted:

- As a subgroup analysis, this finding should be treated with caution. However, the analysis was pre-planned, it was one of a small number of subgroup analyses, and the magnitude of effect was large.

- The study was not powered to detect differences in effect between study groups. As the authors point out, we can therefore only hypothesise that the benefit was greatest among those with Parkinson’s, and such a hypothesis will need to be tested in further studies.

- Falls were self-reported. The study was therefore susceptible to recall bias among participants, aware that they were allocated to the ‘training plus VR’ arm of the study rather than treadmill training alone.

- Overall, this study provides moderate strength of evidence that treadmill training plus VR is effective in preventing falls among people with Parkinson’s.
Conclusion

In summary, the best evidence gleaned by this CAT was for (i) progressive resistance strength training in combination with fall prevention education, (ii) Tai Chi, and (iii) virtual-reality-enhanced treadmill training. Common methodological problems among studies were the use of surrogate outcomes, exclusion of Parkinson's patients with cognitive impairment, and lack of power to demonstrate a real effect (Type II error). There is a continued need for well-conducted RCTs, and for meta-analyses that can detect possible real effects from existing underpowered studies.

References


This Critically Appraised Topic, the others in the series, and the related clinical summary are the work of the Evidence-Based Practice Theme Working Group:

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