Parkinson’s disease and fall prevention

Colleen Canning

NSW Falls Prevention Network Forum
23 May 2014
Parkinson’s disease overview

Motor impairments
- bradykinesia
- Freezing of gait
- postural instability
- tremor & rigidity
- dyskinesia
- ↓ muscle strength

Non-motor impairments
- ↓ cognition
- fatigue
- sleep disturbances
- pain
- anxiety & depression
- autonomic dysfunction
Falls in PD

› Multi-system neurodegenerative disease
  - Motor and non-motor impairments

› Falls – each year
  - 45% to 68% of people with PD fall
    • over 60% fall recurrently
    • 20% fall ≥ 10 times
Overview

› Evidence for prevention of falls

› Fall risk factors

› Prediction of falls

› Implications for assessment and intervention
Effect on falls (n = 250)
Ashburn, 2007
Nieuwboer, 2007

Effect of Exercise / Motor Training

Study Name | RR | 95% CI
---|----|---
Ashburn, 2007 | 0.1
Nieuwboer, 2007 | 0.5

Meta-analysis
Effect of exercise / motor training

Balance and Falls in Parkinson’s Disease: A Meta-analysis of the Effect of Exercise and Motor Training

Natalie E. Allen, PhD,1* Catherine Sherrington, PhD,2 Serene S. Paul, BAppSc(Hons),1 and Colleen G. Canning, PhD1

1Neurological Rehabilitation Research Group, Faculty of Health Sciences, University of Sydney, Sydney, Australia
2Musculoskeletal Division, George Institute for Global Health, University of Sydney, Sydney, Australia

Randomised controlled trials

- Completed randomized controlled trials (2011 - current)
- PD participants
- Falls as primary or secondary outcome
  - not when monitored for safety/adverse events
- Analysis of rate of falls
Scope

► Completed randomized controlled trials (2011 - current)

► PD participants

► Falls as primary or secondary outcome
  - not when monitored for safety/adverse events

► Analysis of rate of falls

4 trials – exercise interventions
(766 participants)
Summary - recently completed RCTs

Falls as primary outcome – exercise/motor training

› Goodwin (2011), Fletcher (2012)
› Morris (protocol 2008, 2011)
› Canning (protocol 2009)

Falls as secondary outcome – exercise

› Li (2012)

High quality trials
Focus - between group differences
An exercise intervention to prevent falls in people with Parkinson’s disease: a pragmatic randomised controlled trial

Victoria A Goodwin,1 Suzanne H Richards,1 William Henley,2 Paul Ewings,3 Adrian H Taylor,4 John L Campbell1

Fletcher et al. BMC Health Services Research 2012, 12:426
http://www.biomedcentral.com/1472-6963/12/426

An exercise intervention to prevent falls in Parkinson’s: an economic evaluation

Emily Fletcher1, Victoria A Goodwin2, Suzanne H Richards1, John L Campbell1 and Rod S Taylor2

Goodwin et al (2011) JNNP 82:1232,
Fletcher et al (2012) BMC Health Services Res, 12426
Tai Chi and Postural Stability in Patients with Parkinson’s Disease

Fuzhong Li, Ph.D., Peter Harmer, Ph.D., M.P.H., Kathleen Fitzgerald, M.D., Elizabeth Eckstrom, M.D., M.P.H., Ronald Stock, M.D., Johnny Galver, P.T., Gianni Maddalozzo, Ph.D., and Sara S. Batya, M.D.
Published protocols + feasibility

BMC Neurology

Study protocol

Exercise therapy for prevention of falls in people with Parkinson's disease: A protocol for a randomised controlled trial and economic evaluation

Colleen G Canning*1, Cathie Sherrington2, Stephen R Lord3, Victor SC Fung4, Jacqueline CT Close3, Mark D Latt5, Kirsten Howard6, Natalie E Allen1, Sandra D O'Rourke1 and Susan M Murray1
Interventions for preventing falls

› Exercises
› Medication
› Surgery
› Fluid or nutrition therapy
› Psychological
› Knowledge
› Environmental/assistive technology
› Management of urinary incontinence
› Other

Effects of a central cholinesterase inhibitor on reducing falls in Parkinson disease

ABSTRACT

Objective: To investigate if a central cholinesterase inhibitor will reduce falling frequency in subjects with Parkinson disease (PD) with advanced postural instability.

Background: Falling due to postural instability is a significant problem in advancing PD, and is minimally impacted by dopaminergic therapy. Anticholinergic medications increase falling in the elderly. Further, CNS cholinergic neuron loss occurs in PD. We hypothesized that acetylcholine augmentation may reduce frequent falling in subjects with PD.

Methods: We enrolled 23 subjects with PD who reported falling or nearly falling more than 2 times per week. In a randomized, placebo-controlled, crossover design, subjects were given 6 weeks of donepezil or placebo with a 3-week washout between phases. The primary outcomes were daily falls and near falls reported on postcards. Secondary outcomes included scores on the Activities of Balance Confidence Scale, Berg Balance Scale, Clinical Global Impression of Change, Folstein Mini-Mental State Examination, and the motor section of the Unified Parkinson's Disease Rating Scale.
Randomised, crossover, double-blind trial of donezepil

Inclusion criteria

› Idiopathic PD (n=23)
› ≥ 2 falls or near falls/week
› Independently mobile at home with or without a walking aid

Exclusion criteria

› Freezing
› Non-CNS contributors to falls (eg, orthostatis, neuropathy)
› Currently using anticholinesterase inhibitors
› Anticholinergic or sedative drugs
› MMSE<25
### Primary outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Donepezil (6 weeks)</th>
<th>Placebo (6 weeks)</th>
<th>Between-group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall frequency (falls/day)</td>
<td>0.13 (0.03 SE)</td>
<td>0.25 (0.08 SE)</td>
<td>0.12 (-0.09 to 0.33)</td>
</tr>
<tr>
<td>Near fall frequency</td>
<td>2.50 (4.1 SE)</td>
<td>2.04 (2.08 SE)</td>
<td></td>
</tr>
</tbody>
</table>

### Secondary outcomes

- Participant impression of improvement: NS
- Balance confidence (ABC scale): NS
- BBS: NS
- UPDRS III: NS
- MMSE: NS

Once-weekly risedronate for prevention of hip fracture in women with Parkinson’s disease: a randomised controlled trial

Yoshihiro Sato,¹ Jun Iwamoto,² Yoshiaki Honda¹

ABSTRACT

Background Incidence of a fracture, particularly in the hip joint, is high in Parkinson’s disease (PD), owing to the immobilisation-induced bone resorption and vitamin D deficiency with reduced bone mineral density (BMD). The authors previously demonstrated the lowered incidence of hip fractures in PD by daily administration of risedronate and vitamin D.

Methods This randomised, double-blind, placebo-controlled study was conducted to determine the efficacy of 17.5 mg once-weekly risedronate in the prevention of hip fracture in women with PD. Patients were randomly assigned to 17.5 mg risedronate once a week (n=136) or a placebo (n=136) combined with daily 1000 IU of ergocalciferol. Incidence of hip fractures was compared between the two groups during the

PD.⁵ Recent studies outside Japan have shown the effectiveness of once-weekly risedronate 35 mg in women with postmenopausal osteoporosis.¹⁰ A weekly dosage of 17.5 mg risedronate is now approved by the Japanese insurance system and may have better compliance than a daily dosage.¹¹

We conducted a double-blind trial to evaluate the efficacy of once-weekly risedronate and ergocalciferol in older women with PD in reducing hip fractures.

MATERIALS AND METHODS

We selected 272 female outpatients (mean age 74 years, range 65–86) who had been examined at the Mitate Hospital. Patients with impairment of renal, hepatic, cardiac or thyroid function or those
Randomised controlled trial of risedronate vs placebo (n = 272)

Inclusion criteria
- Women with PD
- Mobile with or without assistance

Intervention
- 17.5 mg risedronate vs placebo once/wk
- 24 month follow up

Outcome
- Hip fractures: risedronate group = 3, placebo group = 15
- Falls: no significant difference between groups (numbers not reported)
Interventions for preventing falls

› Exercises
› Medication
› Surgery
› Fluid or nutrition therapy
› Psychological
› Knowledge
› Environmental/assistive technology
› Management of urinary incontinence
› Other

https://www.healthtap.com/topics/actonel-vs-fosamax
Amelioration of osteoporosis and hypovitaminosis D by sunlight exposure in Parkinson’s disease☆

Yoshihiro Sato a,*, Jun Iwamoto b, Yoshiaki Honda a

a Department of Neurology, Mitate Hospital, 3237 Yugeta, Tagawa 826-0041, Japan
b Institute for Integrated Sports Medicine, Keio University School of Medicine, Tokyo 160-8582, Japan

ABSTRACT

A high incidence of fractures, particularly of the hip, represents an important problem in patients with Parkinson’s disease (PD), who are prone to falls and have osteoporosis. We previously showed that 25-hydroxyvitamin D (25-OHD) deficiency due to sunlight deprivation with compensatory hyperparathyroidism causes reduced bone mineral density (BMD) in elderly patients with PD. The present study was undertaken to address the possibility that sunlight exposure may maintain BMD and reduce the inci-
Randomised controlled trial of sunlight vs usual lifestyle (n = 324)

Inclusion criteria
› Diagnosis of PD
› Mobile with or without assistance
› > 65 years (mean age 75)

Intervention
› 15 mins sunlight exposure outdoors/day vs placebo
› 24 month follow up

Outcome
› Hip fractures: sunlight group = 3, usual lifestyle group = 11
› Fallers: sunlight group = 64 (40%), usual lifestyle group = 61 (38%)
Interventions for preventing falls

› Exercises
› Medication
› Surgery
› Fluid or nutrition therapy
› Psychological
› Knowledge
› Environmental/assistive technology
› Management of urinary incontinence
› Other
Emerging evidence of efficacy of interventions in preventing falls

Cochrane systematic review

Interventions for preventing falls in people with Parkinson’s disease

Colleen Canning, Natalie Allen, Cathie Sherrington (University of Sydney, Australia)
Alice Nieuwboer, Geert Verheyden (KU, Leuven, Belgium)
Bastiaan Bloem, Samyra Keus, Marten Munneke (UMC Radboud, Netherlands)
### Fall risk factors in PD

<table>
<thead>
<tr>
<th>Generic</th>
<th>PD-specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - older</td>
<td>Fall history</td>
</tr>
<tr>
<td>Gender - female</td>
<td>Disease severity</td>
</tr>
<tr>
<td>Medication – chronic use of sedatives</td>
<td>PD medication</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>↓ mobility</td>
</tr>
<tr>
<td>Postural hypotension</td>
<td>Shuffling and short stepped gait</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>Freezing of gait</td>
</tr>
<tr>
<td>Arthrosis</td>
<td>Flexed posture</td>
</tr>
<tr>
<td>Use of assistive device</td>
<td>Postural instability</td>
</tr>
<tr>
<td>Fear of falling</td>
<td>Transfers</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>Cognitive impairment</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>Axial rigidity</td>
</tr>
<tr>
<td>Daily use of alcohol</td>
<td>Dyskinesia</td>
</tr>
<tr>
<td>Environmental hazards</td>
<td>Deep Brain Stimulation</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td>Dual tasking</td>
</tr>
<tr>
<td>Depression</td>
<td>Urinary incontinence</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
</tr>
</tbody>
</table>

Van der Marck et al (2014) Park Rel Disord 20:360
Explaining falls in PD

Prospective cohort study of people with PD

N=205

125 participants (59%) fell during the 6 mth follow-up period

Potential predictor variables were
- cognition
- balance and mobility
- leg muscle strength
- Freezing of gait (FOG)
- dyskinesia
- abnormal posture
- fear of falling

Explaining falls in PD

<table>
<thead>
<tr>
<th>Independent risk factors*</th>
<th>Additional risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freezing of gait</td>
<td>Dyskinesia</td>
</tr>
<tr>
<td>Impaired anticipatory balance</td>
<td>Lower limb weakness</td>
</tr>
<tr>
<td>Impaired reactive balance</td>
<td>Impaired proprioception</td>
</tr>
<tr>
<td>Impaired orientation</td>
<td></td>
</tr>
<tr>
<td>Impaired executive function</td>
<td></td>
</tr>
</tbody>
</table>

* Multivariate model not including fall history or disease severity

Impulsiveness as a risk factor

- Prospective cohort study of people with PD
- N = 388
- 6 mth follow-up period
- Non-fallers (n=237) compared to recurrent fallers (>1 fall, n=78)
- Attentional impulsivity* – tendency to be more sensitive to distraction
- Attentional impulsivity is an independent contributor to fall risk (when gender, disease severity, medication, cognition, postural instability are entered into multiple regression models)

Prospective cohort study of people with PD

N = 205

125 participants (59%) fell during the 6 mth follow-up period

Potential predictor variables were

- falls history
- disease severity
- cognition
- balance and mobility
- leg muscle strength
- FOG
- dyskinesia
- abnormal posture
- fear of falling

A model including 8 predictors had high discrimination in identifying fallers (AUC 0.83, 95% CI 0.77–0.88):

- history of falls
- FOG
- impaired postural sway
- gait speed
- sit-to-stand
- standing balance with narrow base of support
- coordinated stability
- knee extensor muscle strength
A simple three step clinical tool (AUC = 0.80)

<table>
<thead>
<tr>
<th>Assessing the probability of falling in people with Parkinson’s disease</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1 Ask your patient: Have you fallen in the past twelve months?</td>
<td></td>
</tr>
<tr>
<td>Yes = 6</td>
<td></td>
</tr>
<tr>
<td>No = 0</td>
<td></td>
</tr>
<tr>
<td>Step 2 Ask your patient: Have you experienced freezing of gait in the past month?</td>
<td></td>
</tr>
<tr>
<td>Yes = 3</td>
<td></td>
</tr>
<tr>
<td>No = 0</td>
<td></td>
</tr>
<tr>
<td>Step 3 Time your patient walking over the middle 4 m of a 6 m walkway at their self-selected comfortable pace:</td>
<td></td>
</tr>
<tr>
<td>&gt; 3.6 s to walk 4 m = ‘Yes’.</td>
<td></td>
</tr>
<tr>
<td>Yes = 2</td>
<td></td>
</tr>
<tr>
<td>No = 0</td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total score</th>
<th>Probability of falling in next six months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Low (17%)</td>
</tr>
<tr>
<td>2 – 6</td>
<td>Moderate (51%)</td>
</tr>
<tr>
<td>8 – 11</td>
<td>High (85%)</td>
</tr>
</tbody>
</table>

**FIG. 1.** The 3-step clinical prediction tool for assessing the probability of falling in people with Parkinson’s disease.
Implications for assessment and intervention

- Establish risk of falls

![Assessment Table](image)

**FIG. 1.** The 3-step clinical prediction tool for assessing the probability of falling in people with Parkinson’s disease.

Implications for assessment and intervention

High Risk

› Assessment
  - fall history,
  - medical review,
  - assessment of potentially remediable fall risk factors (FOG, anticipatory and reactive balance, muscle strength, cognition, fear of falling, impulsiveness)

› Intervention
  - Consider avoidance of high-risk activities
  - Targeted single interventions (introduced sequentially) addressing remediable fall risk factors

Canning et al (in press) Neurodegenerative Disease Management
Implications for assessment and intervention

Low Risk  *(strongest evidence for efficacy of single interventions)*

› Assessment
  - Key risk factors to be targeted

› Intervention
  - Group or minimally-supervised exercise program including challenging balance exercises
  - Targeted interventions addressing remediable fall risk factors
Implications for assessment and intervention

Moderate Risk

› Assessment

1. Brief fall history to identify evidence of multiple falls, injurious falls or falls associated with dizziness or syncope

2. Brief screening for evidence of key significant risk factors (FOG, impaired cognition, impaired balance, impulsiveness)

› Intervention

- If evidence of 1 or 2 above, approach intervention as high risk

- If no evidence of 1 or 2 above, approach intervention as low risk
Implications for interventions

› Interventions which deliberately target both physical and cognitive processes, and are individually-tailored

› Novel methods of delivery, utilizing technology to enhance engagement, provide cues and feedback, systematic increase in challenge
V-TIME: a treadmill training program augmented by virtual reality to decrease fall risk in older adults: study design of a randomized controlled trial

Anat Mirelman¹,²,⁸*, Lynn Rochester³, Miriam Reelick⁴, Freek Nieuwhof⁴, Elisa Pelosin⁵, Giovanni Abbuzzese⁵, Kim Dockx⁶, Alice Nieuwboer⁶ and Jeffrey M Hausdorff¹,⁷,⁸
PD-Step pilot study underway

Home-based stepping training using interactive videogame versus usual care

Based on modified Dance-Dance Revolution videogame, shown to improve balance in the elderly. (Schoene, PLoS One 2013;8:e57734)

Canning et al, in progress, ACTRN 12613000688785, www.anzctr.rog.au
Participants
Physiotherapists

NHMRC
Parkinson’s NSW
Harry Secomb Foundation

Natalie Allen
Jacqui Close
Inez Farag
Victor Fung
Gillian Heller
Stephane Heritier
Kirsten Howard
Mark Latt
Stephen Lord
Susan Murray
Christine O’Brien
Sandra O’Rourke
Serene Paul
Cathie Sherrington
Jooeun Song