Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial

Jane Fossey, Clive Ballard, Edmund Juszczak, Ian James, Nicola Alder, Robin Jacoby, Robert Howard

Abstract

Objective To evaluate the effectiveness of a training and support intervention for nursing home staff in reducing the proportion of residents with dementia who are prescribed neuroleptics.

Design Cluster randomised controlled trial with blinded assessment of outcome.

Setting 12 specialist nursing homes for people with dementia in London, Newcastle, and Oxford.

Participants Residents of the 12 nursing homes; numbers varied during the study period.

Intervention Training and support intervention delivered to nursing home staff over 10 months, focusing on alternatives to drugs for the management of agitated behaviour in dementia.

Main outcome measures Proportion of residents in each home who were prescribed neuroleptics and mean levels of agitated and disruptive behaviour (Cohen-Mansfield agitation inventory) in each home at 12 months.

Results At 12 months the proportion of residents taking neuroleptics in the intervention homes (23.0%) was significantly lower than that in the control homes (42.1%): average reduction in neuroleptic use 19.1% (95% confidence interval 0.5% to 37.7%). No significant differences were found in the levels of agitated or disruptive behaviour between intervention and control homes.

Conclusions Promotion of person centred care and good practice in the management of patients with dementia with behavioural symptoms provides an effective alternative to neuroleptics.

Introduction

A large proportion of nursing home residents with dementia receive major tranquillisers for behavioural symptoms, despite evidence of only modest efficacy, high placebo response, and serious adverse events. Good practice guidelines recommend that psychological or environmental management options should be the first line approach and that drugs should be stopped after symptoms have been absent or minimal for three months. Individually tailored interventions based on antecedent behaviour consequence assessments and the “tool box” approach are effective at the patient level. Liaison and staff training interventions have short term benefits, although a review of 48 studies showed limited evidence for the sustained implementation of knowledge.

We carried out a cluster randomised controlled trial to determine whether behavioural symptoms in people with severe dementia could be safely managed with an intervention package (focused intervention training and support) to reduce the proportion being treated with neuroleptics.

Methods

We used a cluster trial design primarily to avoid contamination (because care staff receiving extra training and support could not be expected to treat individual residents differently) but also for practical purposes. The intervention was aimed at changing clinical practice in the nursing home, and hence the home was the unit of randomisation and analysis.

Sample size

We estimated that about 55% of residents would be taking neuroleptics at the start of the trial and that we could reduce this to 30% in the intervention arm by 12 months. For a conventional trial with randomisation of individual patients to be able to detect such a reduction, a minimum of 69 patients would need to be recruited to each arm of the trial (138 patients in total), for a significance level of 5% (two sided), a power of 85%, and equal allocation. As we used cluster randomisation for the purposes of our study, the implications of this are reduced efficiency and loss of power. We therefore required a larger sample size to compensate for this design effect (the ratio of the total number of patients required using cluster randomisation to the number required using individual randomisation). The formula 1+[(m−1)×r1] where r1 = s^2b/(s^2b+s^2w), the intracluster correlation coefficient, is used where s^2b is the variance between clusters and s^2w is the variance within clusters. Based on the additional assumptions of an estimated intracluster correlation coefficient of 0.05 and an average of 30 eligible and consenting patients in each cluster: 1+(30−1)×0.05 = 2.45 we would need 2.45×69 = 170 eligible patients per arm, which is in the order of six clusters (nursing homes) per arm, or 12 clusters in total.

Participants and randomisation

We recruited residents within 12 nursing homes, four each in London, Newcastle, and Oxford. Eligible homes were those registered to accept elderly mentally impaired people and with a minimum of 25% of residents with dementia who were taking neuroleptic drugs.

The trial’s manager enrolled the nursing homes. Consent was obtained from the management of the homes, and the family carers of residents were asked to give consent for involvement of their relatives. Research assistants carried out baseline assessments before randomisation. As neuroleptic prescribing levels varied between the groups, the trial’s statistician (blind to the identity of the homes) classified two homes in each region as having low neuroleptic use and two as having high use. The stat-
involved the philosophy and application of person centred skills training, behavioural management techniques, and clinicians started and supported the use of activities through environmental, care practice, and attitudinal factors. The trial's staff did not identify the intervention homes to the residents who had not been employed during the intervention period. Assessments at 12 months were carried out by a psychology research assistant. Despite these efforts, because the package was designed to influence the whole care approach of staff, it is likely that the research assistant would have been able to detect which homes had received the intervention.

**Data analysis**

Primary outcomes (at the cluster level) were the proportion of patients receiving neuroleptic treatment at 12 months and the mean dose of neuroleptic. Secondary outcomes were agitation, patient level quality of life, proportion of patients taking other psychotropic drugs, adverse events (including documented falls), and incidents involving irritable behaviour directed at staff or other residents.

Analysis followed a prespecified plan based on an intention to treat basis; all clusters with available data were analysed in the groups to which they were allocated. With only six clusters in each group, it was not possible for us to carry out analyses at individual level, since the large sample approximations underlying these procedures are questionable. All primary analyses were therefore carried out at the cluster level using a weighted two sample t test, weighted by the number of patients in each home. Although the test assumes no severe departures from normality, it is remarkably robust to violations of the underlying assumptions, especially when there are equal numbers of clusters assigned to each intervention group. The assumptions of the test are also more likely to be satisfied if a weighted analysis is carried out. With only six clusters in each group, the Shapiro-Wilk test for normality will have low power, and a histogram may be difficult to interpret. We therefore used the non-parametric Wilcoxon signed rank test as a sensitivity analysis to test for differences between the groups. In principle, a stratified design should be accompanied by a stratified analysis, but with such a small number of clusters and two stratification variables it is unlikely that the gain in precision would outweigh the loss in degrees of freedom. For primary outcomes we used a weighted linear regression analysis (weighted by cluster size) as a sensitivity analysis, to adjust for the stratification factors. For the primary outcome, the proportion of patients receiving neuroleptics at 12 months, we present results for each cluster (nursing home) graphically in a bubble plot, where the size of the bubble is proportional to the size of the cluster, and for each intervention group, equivalent to the weighted mean of the cluster specific proportions for each randomised group. We express the treatment effect as the difference between the two weighted means, along with a 95% confidence interval, P value, and intraclass correlation coefficient. Subsequent analyses for the coprimary and secondary outcomes were based on the 12 cluster specific proportions for dichotomous outcomes, and the means or medians, depending on normality, for continuous outcomes. We used the weighted t test to compare the appropriate summary measures obtained for each cluster. Treatment effect sizes are expressed as the difference between the treatment groups, along with 95% confidence intervals, P values, and intraclass correlation coefficients. All analyses were carried out using Stata version 8.

**Results**

Six care homes were randomised to the training and support intervention and six to treatment as usual (control homes; fig 1). All residents, not just those present, were analysed at each time point. This did not affect the primary analyses, carried out on the follow-up data at 12 months only.

Personal and clinical characteristics of the residents in both arms were similar at baseline (table 1).
Neuroleptic use

At 12 months’ follow-up, 40 of 174 (23.0%) residents in the intervention homes were taking neuroleptics compared with 69 of 164 (42.1%) in the control homes: average reduction 19.1% (95% confidence interval 0.5% to 37.7%). With one exception, little or no overlap was found in the proportion of residents using neuroleptics in each home across the treatment groups (figs 2 and 3). To examine the robustness of this result, a sensitivity analysis was carried out excluding residents with conditions that precluded the withdrawal of neuroleptics (for example, residents with a primary diagnosis of schizophrenia, bipolar disorder, or psychotic depression who are increasingly placed in nursing homes registered for dementia care). After exclusion of these residents from analysis, 28 of 161 (17.4%) residents in the intervention group were taking neuroleptics at 12 months compared with 60 of 155 (38.7%) in the control group: average reduction 21.3% (4.3% to 38.3%; P = 0.02). A further sensitivity analysis, adjusting for stratification variables (baseline neuroleptic use and region), gave an average reduction in neuroleptic use of 19.4% (−3.0% to 41.7%; P = 0.08).

Dose of neuroleptic

Data on dose of neuroleptics did not follow the normal distribution. The median was therefore the appropriate summary statistic for each cluster, and the mean of the medians between groups was compared. At 12 months the mean dose was 107.1 in the control group and 102.1 in the intervention group: average difference 4.9 (−20.0 to 29.9; P = 0.67: table 2). Adjusting for stratification variables (baseline neuroleptic use and region), gave an average reduction in neuroleptic use of 19.4% (−3.0% to 41.7%; P = 0.08).

Table 1 Baseline personal and clinical characteristics of residents of care homes assigned to focused training and support package or usual care (control). Values are numbers (percentages) of residents unless stated otherwise

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control homes (n=6; 168 residents)</th>
<th>Intervention homes (n=6; 181 residents)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range) age (years)</td>
<td>82 (53-101)</td>
<td>82 (60-98)</td>
</tr>
<tr>
<td>Men</td>
<td>102/168 (61)</td>
<td>117/181 (65)</td>
</tr>
<tr>
<td>Taking neuroleptics</td>
<td>83/187 (45)</td>
<td>85/181 (47)</td>
</tr>
<tr>
<td>Median (range) dose of neuroleptic in chlorpromazine equivalents (No of patients)</td>
<td>100 (12.5-630) (n=83)</td>
<td>100 (10-1200) (n=84)</td>
</tr>
<tr>
<td>Taking other psychotropics</td>
<td>89/168 (53)</td>
<td>98/181 (54)</td>
</tr>
<tr>
<td>A least one fall in past 12 months</td>
<td>98/168 (58)</td>
<td>101/169 (60)</td>
</tr>
<tr>
<td>Median (range) Cohen-Mansfield agitation inventory*</td>
<td>37 (29-119) n=163</td>
<td>39 (29-114) n=167</td>
</tr>
<tr>
<td>At least one episode of aggression in past 12 months</td>
<td>29/168 (15.5)</td>
<td>11/169 (6.5)</td>
</tr>
<tr>
<td>Clinical dementia rating:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None, questionable, or mild</td>
<td>37/163 (22)</td>
<td>25/170 (15)</td>
</tr>
<tr>
<td>Moderate</td>
<td>32/163 (20)</td>
<td>46/170 (27)</td>
</tr>
<tr>
<td>Severe</td>
<td>94/163 (58)</td>
<td>99/170 (58)</td>
</tr>
<tr>
<td>Median (range) well-being† (No of patients)</td>
<td>0.9 (-2.5 to 2.5)</td>
<td>0.8 (-1.7 to 2.5)</td>
</tr>
<tr>
<td>Spending some (&gt;0%) time asleep‡</td>
<td>111/145 (77)</td>
<td>124/160 (78)</td>
</tr>
<tr>
<td>Spending some (&gt;0%) time withdrawn‡</td>
<td>98/145 (68)</td>
<td>103/160 (64)</td>
</tr>
</tbody>
</table>

*Range 29-203; higher scores mean more agitation (scores >40 usually accepted as clinically significant).
†Range -5 to 5.
‡Estimated using dementia care mapping.

Neuroleptic use

At 12 months’ follow-up, 40 of 174 (23.0%) residents in the intervention homes were taking neuroleptics compared with 69 of 164 (42.1%) in the control homes: average reduction 19.1% (95% confidence interval 0.5% to 37.7%). With one exception, little or no overlap was found in the proportion of residents using neuroleptics in each home across the treatment groups (figs 2 and 3). To examine the robustness of this result, a sensitivity analysis was carried out excluding residents with conditions that precluded the withdrawal of neuroleptics (for example, residents with a primary diagnosis of schizophrenia, bipolar disorder, or psychotic depression who are increasingly placed in nursing homes registered for dementia care). After exclusion of these residents from analysis, 28 of 161 (17.4%) residents in the intervention group were taking neuroleptics at 12 months compared with 60 of 155 (38.7%) in the control group: average reduction 21.3% (4.3% to 38.3%; P = 0.02). A further sensitivity analysis, adjusting for stratification variables (baseline neuroleptic use and region), gave an average reduction in neuroleptic use of 19.4% (−3.0% to 41.7%; P = 0.08).

Dose of neuroleptic

Data on dose of neuroleptics did not follow the normal distribution. The median was therefore the appropriate summary statistic for each cluster, and the mean of the medians between groups was compared. At 12 months the mean dose was 107.1 in the control group and 102.1 in the intervention group: average difference 4.9 (−20.0 to 29.9; P = 0.67: table 2). Adjusting for strati-
fication variables confirmed this result (average difference 4.0, −22.0 to 29.9; P = 0.73). After excluding those residents for whom withdrawal of neuroleptics would have been contraindicated, this difference increased to 19.5 (−7.0 to 45.7; P = 0.13), with a mean dose of 114.5 in the control group and 94.9 in the intervention group.

Other psychotropic drugs and falls
At 12 months the average proportion of residents taking other psychotropics was 109 of 174 (62.6%) in the intervention group and 92 of 162 (56.8%) in the control group: a non-significant difference (5.9%, −27.2% to 15.5%; P = 0.56) suggesting that neuroleptics were not simply replaced with other psychotropic drugs. Similar proportions of residents had at least one fall in the past 12 months—91 of 175 (52.0%) in the intervention group and 90 of 165 (54.6%) in the control group: average difference 2.6%, −18.7% to 23.8%.

Agitation and aggression
No significant differences were found between the intervention and control groups in levels of agitation at 12 months (mean difference 0.3, −8.3 to 8.9; P = 0.94).

At least one episode of aggression was recorded for 14 of 173 (8.1%) residents in the intervention group compared with 16 of 165 (9.7%) in the control group: average difference 1.6% (−12.7% to 15.8%; P = 0.25).

Quality of life and wellbeing
Rates for wellbeing in residents in the intervention group were similar to those in the control group (1.1 vs 0.9, mean difference −0.2, −0.5 to 0.2; P = 0.29). A marginal advantage was shown for the intervention group in the proportion of residents spending at least some time withdrawn during the six hour observation period (37.6% vs 46.4%, average difference 8.8%, −25.2% to 42.8%; P = 0.58). The proportion of residents who spent at least some time asleep was similar between the groups: 110 of 149 (73.8%) for the intervention arm vs 114 of 153 (74.5%) for the control arm.

Discussion
An intervention offering support with individualised psychological intervention as part of a programme promoting person-centred care and good practice provides a viable alternative to neuroleptics for treating behavioural symptoms in patients with dementia.

In both intervention and control homes in our study, psychiatrists reviewed the prescriptions of the residents and recommended withdrawal of neuroleptics in accordance with best clinical practice, yet significantly fewer residents in the intervention homes remained taking these drugs. The percentage of residents (after excluding those with schizophrenia or other psychotic disorders) who were still prescribed neuroleptics at the end of 12 months was less than half that in the control homes. Levels of agitation and episodes of aggressive behaviour did not increase in homes with reduced prescribing of neuroleptics.

Cohen-Mansfield et al carried out a placebo controlled cross over trial of neuroleptic withdrawal in patients with dementia and found no significant worsening of behavioural symptoms when drugs were replaced with a tailored psychological intervention. In another study, 89 people with dementia from a large community nursing home were randomised to receive either a complex intervention including activities, guidelines for drug use, and educational rounds, or treatment as usual. Patients who received the active intervention showed a significant

Table 2 Main outcomes at 12 months. Values are numbers (percentages) of nursing home residents unless stated otherwise

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control homes (n=6; 170 residents)</th>
<th>Intervention homes (n=6; 176 residents)</th>
<th>Weighted mean difference (95% CI)*</th>
<th>P value‡</th>
<th>Intracluster correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taking neuroleptics</td>
<td>69/164 (42)</td>
<td>48/174 (28)</td>
<td>19.1 (0.5 to 37.7)</td>
<td>0.045</td>
<td>0.00</td>
</tr>
<tr>
<td>Mean (SD) median dose in chlorpromazine equivalents (No of patients)</td>
<td>107.1 (15.4) (n=69)</td>
<td>102.1 (23.1) (n=40)</td>
<td>4.9 (−20.0 to 29.9)</td>
<td>0.87</td>
<td>0.07</td>
</tr>
<tr>
<td>Taking other psychotropics</td>
<td>92/162 (57)</td>
<td>109/174 (63)</td>
<td>−5.9 (−27.2 to 5.5)</td>
<td>0.56</td>
<td>0.080</td>
</tr>
<tr>
<td>At least one fall in past 12 months</td>
<td>90/165 (55)</td>
<td>91/175 (52)</td>
<td>2.6 (−18.7 to 23.8)</td>
<td>0.27</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean (SD) Cohen-Mansfield agitation inventory § total (No of patients)</td>
<td>42.0 (15.9) (n=162)</td>
<td>41.6 (17.2) (n=172)</td>
<td>0.3 (−8.3 to 8.9)</td>
<td>0.84</td>
<td>0.077</td>
</tr>
<tr>
<td>At least one episode of aggression in past 12 months</td>
<td>16/165 (10)</td>
<td>14/173 (8)</td>
<td>1.6 (−12.7 to 15.8)</td>
<td>0.25</td>
<td>0.10</td>
</tr>
<tr>
<td>Mean (SD) wellbeing¶** (No of patients)</td>
<td>0.9 (0.35) (n=153)</td>
<td>1.1 (0.04) (n=149)</td>
<td>−0.2 (−0.5 to 0.2)</td>
<td>0.29</td>
<td>0.075</td>
</tr>
<tr>
<td>Spending some time (% of) asleep**</td>
<td>114/153 (73)</td>
<td>110/149 (74)</td>
<td>0.7 (−8.5 to 9.8)</td>
<td>0.87</td>
<td>0.00</td>
</tr>
<tr>
<td>Spending some time (% of) withdrawn**</td>
<td>71/153 (46)</td>
<td>56/149 (38)</td>
<td>8.8 (−25.2 to 42.6)</td>
<td>0.58</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Adjusted for clustering (estimated from weighted t-test).
†Mean of medians (data skewed, therefore median appropriate as summary statistic for each cluster).
‡Truncated at zero.
§Range 29-293; higher scores mean more agitation (scores >40 usually accepted as clinically significant).
¶Range −5 to 5.
**Estimated using dementia care mapping.
improvement in behaviour and a trend towards a reduction in neuroleptic use.

Failure of the training and support intervention to have a significant effect on any of the secondary outcome measures may reflect difficulties inherent in affecting the culture of care within a nursing home enabling change to be measured in such a small scale trial.

In March 2004 the Committee on Safety of Medicines wrote to all doctors in the United Kingdom to advise against the prescription of risperidone and olanzapine in patients with dementia. The effect of this communication, which might have been expected to result in discontinuation of neuroleptics in a large number of participants in both arms of the trial, was only modest. Differences in the proportion of patients receiving neuroleptics at each review (fig 4) between the groups were sustained over the year, and similarly affected by the ruling of the Committee on Safety of Medicines.

The training and support of care home staff reduced neuroleptic use in intervention homes without worsening behavioural symptoms of dementia. The effect of this communication, which might have reflected difficulties inherent in affecting the culture of care within a nursing home enabling change to be measured in such a small scale trial.

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Amendment

This is Version 2 of the paper. In this version, figure 2 has been amended to include all nursing homes [one was missing from the previous version].