A Community Clinician Led Review of Antidepressant Drugs in a Scottish Nursing Home

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Abstract

\textit{Background:} Prevalence rates for depression are consistently high in patients with dementia and it is known to increase morbidity and mortality levels. Management with antidepressant drugs, often viewed as innocuous medication, may have numerous adverse drug reactions (ADRs).

\textit{Objective:} The implementation of a clinician led review process of all antidepressant medications in a nursing home would reduce ADRs specifically related to antidepressant medications.

\textit{Methods:} All 49 patient records in a Dundee nursing home were reviewed. All patients who were >65-years-old with dementia and a diagnosis of unipolar depression treated with a single antidepressant agent were eligible for the study. Patients were excluded if they were on any other psychoactive medications or on \( \geq 5 \) general medications. In total 12 patients were included in the study. ADRs were recorded by antidepressant drug-class for a 2-month period before and after a general practitioner (GP) review of antidepressant drugs.

\textit{Results:} Twelve of 49 patients (25\%) received treatment with antidepressant drugs including SSRIs, SNRIs or TCAs. Various ADRs including hyponatremia (n=1), worsening of hypertension (n=1), increasing falls (n=3) and prolonged bleeding (n=2) were documented. The number of documented ADRs reduced from 5 in the control period to 2 in the study period, although this did not reach statistical significance (\( p = 0.06 \)). Prescription of TCAs ceased after GP review with patients switched to SSRIs.

\textit{Conclusions:} Antidepressant drugs are commonly prescribed for residents in nursing homes. A clinician led antidepressant drug review resulted in treatment changes and a trend to reduced ADRs. Importantly, TCAs (high risk drugs associated with falls) were immediately stopped after review despite being prescribed on repeat prescriptions for months. The authors feel reviewing all psychoactive drug prescriptions and avoiding repeat prescriptions in nursing home residents may be beneficial in reducing ADRs.

Keywords: Behavioural and Psychological Symptoms of Dementia (BPSD), Community Geriatrics, Nursing Homes, Adverse Drug Reactions
Introduction

Approximately 750,000 people in the United Kingdom (UK) have a confirmed diagnosis of dementia with many being cared for in care and nursing homes. Work by Robert et al noted that up to 90% of these patients exhibit behavioural and psychological symptoms of dementia (BPSD), including depression. Importantly, prevalence rates for depression are consistently high in patients with dementia when compared to the general population, particularly in the early stages of the disease or shortly after nursing home admission. This relationship is crucial for clinicians to be aware of as a diagnosis of depression increases patients’ overall morbidity and mortality levels. Work by Nicholson et al showed that a depressive disorder is associated with an 80% increased risk in the development and mortality associated with coronary heart disease. In addition, the UK based National Institute of Clinical Excellence (NICE) states that it is common for patients with depression to have psychiatric and physical co-morbidity. Importantly, older patients are disproportionately likely to develop a depressive disorder and commit suicide than age-matched controls. The reasons for this are multi-factorial with long standing health problems, a reduced sense of purpose, loneliness and social isolation commonly quoted as the underlying causes. In addition, older patients have an increased exposure to commonly used medications that have mood disorders as a side-effect (including statins, oestrogens, steroids, H2-receptor antagonists and β-blockers).

Treatment for depression managed in primary care is often classified into two categories, drug therapy and non-drug therapy. Importantly, adverse drug reactions (ADR) relating to antidepressant medication are more common in older patients (≥65 years) in line with age-related reductions in hepatic and renal functions. Therefore, British guidelines recommend that non-drug options should be pursued as first line if possible. British guidelines recognize the association between dementia and depression, and advocate regular depression screening in dementia patients (structured assessments such as Beck or Hamilton reviews) and psychosocial therapies including reminiscence therapy and multi-sensory stimulation. However, there are clear challenges in attempting to deliver non-drug treatments for depression in patients with a co-morbid diagnosis of dementia. Indeed, NICE care guidelines question the clinical efficacy of some of these non-drug approaches, suggesting that patients even with early stages of dementia may struggle to engage in structured talking therapies such as cognitive behavioral therapy.

Challenges in providing non-drug approaches to this patient group may go someway to explaining the fact that drug treatments for depression are commonly prescribed by health practitioners. Work by Guthrie et al showed that up to one in six patients with dementia are currently prescribed antidepressants, the majority of which are on long-term repeat prescription. Management with antidepressant drugs, often viewed as innocuous drugs by clinicians, have a wide array of ADRs (see table 1). Indeed, the risks associated with these drugs has been incorporated by NICE suggesting clinicians avoid tricyclic antidepressants (due to the risk of cognitive decline and increasing falls), commence therapy at the lowest clinically efficacious dose and provide regular monitoring for all patients.
The importance of reviewing and avoiding repeat prescriptions in relation to neuroleptic drugs has become clear over the last few years. Indeed, studies have shown that clinician review of medications can improve prescribing patterns in both community and hospital settings, although improvements can be hard to sustain.

The authors feel regular clinical review should be indicated for all psychoactive medications, including antidepressants. One such community clinician review programme noted that a single visit by a GP to a nursing home to commence a comprehensive prescribing review reduced the number of prescribed medications, lead to cost saving for health systems and may be associated with lower iatrogenic side-effects.

This clinical study has reviewed the efficacy of a clinician led (general practitioner (GP)/Family Doctor) monthly review of all antidepressant medications for nursing homes residents with dementia upon ADRs. The researchers hypothesised that the implementation of a GP led review process would reduce ADRs specifically related to antidepressant medications.

Table 1. Common Drug Cautions of Anti-Depressant Medications.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Side Effect</th>
<th>Additional Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective serotonin reuptake inhibitor [SSRI]</td>
<td>Increased risk of bleeding</td>
<td>Significant risks in elderly and patients on drugs known to damage gastric mucosa or interfere with clotting.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>I. Avoid SSRI drug class if possible and use safer alternative (such as Trazodone or Mirtazapine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>II. Prescribe gastro-protective drug.</td>
</tr>
<tr>
<td>Serotonin-norepinephrine reuptake inhibitor [SNRI]</td>
<td>Venlafaxine at high dose may exacerbate cardiac arrhythmias Worsening of hypertension on venlafaxine and duloxetine</td>
<td>Avoid in patients with high risk of suicide. Regular BP monitoring required.</td>
</tr>
<tr>
<td>Tricyclic Antidepressants [TCA]</td>
<td>Postural hypotension, falls, cognitive impairment and arrhythmias are more common in &gt;65.</td>
<td></td>
</tr>
</tbody>
</table>

Methods

The study was undertaken in a Dundee (Scotland) nursing home, specialised for patients with severe dementia (Mini Mental State Examination (MMSE) score ≤9 points on admission), between August and November 2010. The MMSE is useful in establishing whether a patient has a degree of cognitive impairment. The MMSE takes around 5-10 minutes to administer and assesses orientation in time and place.
points), registration (3 points), attention and calculation (5 points), recall (3 points), language (2 points) repetition (1 point) and interpreting complex commands (6 points).\textsuperscript{18,20} Scores below 25 out of 30 indicate a degree of cognitive impairment and scores ≤9 suggest severe dementia.\textsuperscript{18,19,20} Ethical approval was granted from Four Seasons Healthcare Management as this study was part of a care home development programme. In addition, informed consent obtained from all patient families.

The unit was home to 49 Caucasian British residents throughout the study with an age range of 69 - 92 years [27 females & 22 males]. All patients who were >65-years-old with a confirmed diagnosis of both dementia and unipolar depression being treated with a single antidepressant agent were eligible for the study. Patients were excluded if they were on any other psychoactive medications or on ≥5 prescription medications. Psychoactive medications were defined according to the recently developed and validated central nervous system drug model, which included benzodiazepine receptor agonists, conventional & atypical neuroleptics and opioid receptor agonists.\textsuperscript{21}

All 49 patient records were reviewed and inclusion and exclusion criteria applied accordingly, leaving a total of 12 patients in the study. All 12 patients had their antidepressant drug class and dose recorded at the start of the study. Baseline measurements were obtained by the research team and repeated weekly. These measurements included blood pressure (BP), electrolyte blood results and body mass index.

Prior to the commencement of the clinical study, a one-hour seminar was run by the research team for all nursing staff at the care home that outlined the key ADRs associated with antidepressant medication. Key ADRs associated with antidepressants were defined as those explicitly discussed in the NICE clinical care guidelines. These included nausea, indigestion, dry mouth, slight tremor, fast heartbeat, constipation, sleepiness, and weight gain.

Throughout the study period nursing staff recorded all clinical sign(s) that might be attributed to the patients’ antidepressant medication. All nurses had been employed at the home for a minimum of 1.5 years and the research team assumed that they knew the residents baseline behaviour and general medical condition. Each claim was investigated by the research team (using clinical history and recorded BP/BMI) and after discussion with a local GP/family doctor (with specialist interest in old age psychiatry). They would then decide if the sign could be solely attributed to the antidepressant medication.

ADRs were recorded according to antidepressant drug-class for a 2-month period before and after (the control and study period respectively) a GP review of antidepressant drugs. In the control period the patients had their prescription collected and dispensed without any difference from normal practice. In the study period at the beginning of each month, three local GPs reviewed all antidepressant medications in the care home and made changes to drug class when they deemed clinically appropriate. Results were analysed with the non-parametric Mann Whitney U test.

The research team would manage potentially confounding factors as appropriate. Staffing levels were maintained at consistent skill mix and gross number throughout the control and study periods.
Results

Twelve of the 49 nursing home residents (25%) received treatment with antidepressant drugs for their unipolar depression and matched inclusion criteria. Patients were prescribed three different classes of antidepressants in the control period: SSRIs, SNRIs and TCAs. The name and dosage of each antidepressant are noted in Table 2.

Table 2. Breakdown of Drug Name & Dose at Start of Study [N =12 patients]

<table>
<thead>
<tr>
<th>SSRI</th>
<th>SNRI</th>
<th>TCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Patients</td>
<td>2 Patients</td>
<td>2 Patients</td>
</tr>
<tr>
<td>Sertraline 100mg (od)</td>
<td>Duloxetine 20mg (bd)</td>
<td>Amitriptyline 50mg (od) *</td>
</tr>
<tr>
<td>3 Patients</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Citalopram 10mg (od)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2 Patient</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fluoxetine 60mg (od)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* Patients on 50mg (od) Amitriptyline were both changed to Citalopram 10mg (od)

There were significant changes in the drug classes prescribed between the control and study period (Table 3). Interestingly, prescription of TCAs ceased immediately after GP review with both patients on amitriptyline being switched to citalopram. Crucially, the GPs established that there was no other indication for these patients to be prescribed the higher risk drug class (e.g.- neuropathic pain). Amitriptyline had been continued on repeat prescriptions for at least 3 and 6 years (for each resident respectively), after drug charts from nursing home admission were reviewed.

Table 3. Drug treatment pre- and post-review

<table>
<thead>
<tr>
<th>SSRI</th>
<th>SNRI</th>
<th>TCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-review</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Post-review</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

Over the four-month period nursing staff recorded a total of 19 occasions where a clinical sign(s) could have been attributed to the patients’ antidepressant medication. Using clinical history and recorded data (BP, BMI & blood results) each claim was investigated by the research team and after discussion with a local GP, a total of 7 ADRs were noted to be specifically related to prescribed antidepressant medication.

Various forms of ADRs were documented including hyponatraemia, prolonged bleeding, worsening of hypertension and falls (Table 4). Analysis of the proportion of patients in each drug group affected by ADRs during the study revealed a reduction from 5 ADRs in the control period to 2 ADRs in the study period. However, despite the trend towards a reduction after the GP drug review it did not reach statistical significance (Fig 1). It should be noted that throughout the study no residents developed acute disease or were admitted to hospital. None of the 12 patients had any prescription medications changed by their GP, excluding their antidepressant medication.
Table 4. Nature of Documented ADRs

<table>
<thead>
<tr>
<th></th>
<th>SSRI</th>
<th>SNRI</th>
<th>TCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-review</td>
<td>2 (↓Na⁺, ↑bleeding)</td>
<td>0</td>
<td>3 (falls)</td>
</tr>
<tr>
<td>Post-review</td>
<td>1 (↑bleeding)</td>
<td>1 (↑BP )</td>
<td>0</td>
</tr>
</tbody>
</table>

Non-parametric Mann Whitney U test: p-value = 0.06

Figure 1. Proportion of Patients in Each Drug Treatment Group Exhibiting ADRs (p>0.05)

Discussion

Unipolar depression is a disabling mental health condition that adversely affects a patient’s life in multiple domains (family, work or school life). In line with the high prevalence of depression in dementia patients and challenges in providing non-drug treatments, antidepressant medications are commonly prescribed for residents in nursing homes. These drugs are known to have an array of class dependent and class independent side-effects explicitly discussed in UK care guidelines.\(^7,8,9\) Prescribing of multiple drug classes in nursing homes has recently been an area of intense discussion\(^22,23,24\) as age-related reductions in efficiency of elimination and metabolism of drugs and higher rates of poly-pharmacy (≥ 5 prescription medications) place older patients at an increased risk of ADRs.\(^25\)

This study found that a GP led program of antidepressant review led to a 60% reduction in ADRs (from 5 to 2) associated with antidepressant medications as well as the cessation of tricyclic antidepressant prescription. The study appears to have similar findings to the literature noting that the review process is beneficial for the overall medical care of residents.\(^15,16,17\) However, in contrast to Khunti et al this study noted that the net number of prescribed medications remained the same in the pre and post intervention period.\(^17\) It should be noted that calculating cost savings in terms of prescribed medications and management of ADRs was beyond the scope of this report.

Guthrie et. al stressed the importance of reviewing and avoiding repeat prescriptions of neuroleptic (antipsychotic) drugs in nursing home residents due to an increased
risk of developing or worsening of cardiovascular and cerebrovascular disease.14 The authors feel that this approach is valid for other psychoactive medications including antidepressant drugs.

There are a number of limitations to this research that should be noted when interpreting the findings. Firstly, this is only a single centre study with a homogenous study population (Caucasian group of severely demented patients in deprived area of Scotland). The small sample size meant that results highlighted a trend towards reduction of ADRs without statistical significance. Studies in other centers are required to determine if these findings can be reproduced in other UK nursing homes with different ethnic and socio-economic groups. In addition, larger more comprehensive studies are important to assess whether ADR reduction associated with clinician review can be statistically significant. However, as this study found similar results to previous work in the field15,16,17 the researchers strongly feel that this would be the case or at the very least stop the prescription of higher risk medications.

Secondly, the study was only 4 month long and only focused upon antidepressant medication ADRs. The researchers would have ideally liked to increase the follow-up period to assess whether the improvements are long lasting and review ADR reductions in multiple classes of psychoactive drugs. Thirdly, there are significant challenges associated with diagnosing some subtle ADRs in patients with dementia. The study attempted to address this challenge by reviewing all nursing staff suggestions of ADRs using clinical history, lab results and the experience of a long standing GP with a specialist interest in old age psychiatry. Although the research team attempted to fully assess each potential ADR with experienced clinicians before deciding that an ADR could be attributed to the antidepressant medications and all patients remained on the same medications for the entire study, it is possible that some of the side-effects were related to other medications. Finally, and perhaps most importantly in this current political climate, the economic cost of the long-term implementation of our clinician led review needs to be ascertained.

However, despite these limitations this research project highlights the pivotal role that a once monthly review of medication can have upon ADRs and antidepressant drug prescription. Patients prescribed high-risk TCA agents had their medication stopped after the first drug review by local GPs despite these medications previously being prescribed on repeat prescription for years. The study also noted a trend towards reduction of ADRs and an increase in nursing staff satisfaction associated with increased contact with local clinicians. It is hoped that this study provides the starting point for further research in this topical area.

**Competing Interest Declaration**

LDH and GR were employees of Four Seasons throughout this project. CN has no interests to declare.

**Ethical Approval**

Ethical approval was granted from Four Seasons Healthcare Management as part of a care home development programme and informed consent obtained from all families of the patients involved.
**Funding sources**

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**Acknowledgements**

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