More than 90% of patients with dementia will experience at least one behavioural and psychological symptom of dementia (BPSD) during the course of their condition. The most common BPSDs are delusions, hallucinations, agitation and aggression. They cause significant distress to people with dementia and their caregivers, increase the likelihood of institutionalisation and represent a considerable clinical challenge for clinicians. The management of BPSDs is extremely challenging. Best practice guides emphasise the assessment and treatment of contributing medical conditions, appropriate analgesia for pain relief and the efficacy of simple non-pharmacological interventions. Despite these measures, however, there remains an important role for pharmacological management.

The challenge of treating BPSD

It has been established through robust placebo-controlled clinical trials that the antipsychotics risperidone, olanzapine and aripiprazole confer modest but significant benefits in the clinical trials that the antipsychotics risperidone, olanzapine and aripiprazole confer modest but significant benefits in the treatment of aggression and psychosis over 6–12 weeks in people with dementia.1 The most common BPSDs are delusions, hallucinations, agitation and aggression. They cause significant distress to people with dementia and their caregivers, increase the likelihood of institutionalisation and represent a considerable clinical challenge for clinicians. The management of BPSDs is extremely challenging. Best practice guides emphasise the assessment and treatment of contributing medical conditions, appropriate analgesia for pain relief and the efficacy of simple non-pharmacological interventions.2 Despite these measures, however, there remains an important role for pharmacological management.

The paper from Gerhard and colleagues9 addresses several of these key issues. The study examined 180-day non-cancer mortality in a...
large retrospective cohort of 136 000 adults over the age of 65 living in the community and treated with antipsychotic medication. Approximately a third of the individuals had dementia and the other two-thirds did not. Patients with a diagnosis of schizophrenia, bipolar disorder or cancer during the 180-day period preceding the prescription of antipsychotics were excluded. As all patients included in the analysis were prescribed antipsychotic medication, the aim was to examine the specific risk of individual antipsychotics compared with risperidone, and to evaluate the relationship between mortality risk and dose. Inclusion of people with and without dementia also enabled the authors to comment on the broader mortality risk associated with antipsychotic prescribing.

When combining outcomes with all antipsychotics, there was a clear relationship between dose and mortality risk. When examining individual antipsychotics, the mortality risk was substantially increased for haloperidol and decreased for quetiapine compared with risperidone. After controlling for dose and other major confounding factors, the mortality risk, although reduced, was still significantly higher for haloperidol than for risperidone. Of particular note in this analysis, olanzapine, aripiprazole and quetiapine all had significantly reduced mortality risk compared with risperidone. The relative mortality risks of different agents and by dose were similar in patients with and without dementia.

Implications for clinical practice and research

The study is the first to carefully examine the relationship between antipsychotic dose and mortality risk, showing a clear stepwise increase in risk from low to medium and from medium to high doses. This is potentially extremely important in guiding clinical practice, although it is still important that treatments are prescribed within the therapeutic window shown to be effective. For example, the placebo-controlled randomised controlled trials of risperidone clearly show that a dose of 0.5 mg daily does not confer benefit in the treatment of aggression or psychosis, and that 1 mg/day is the lowest effective dose. Gerhard et al’s study also confirms several other reports indicating that haloperidol is associated with higher mortality risk and quetiapine with lower mortality risk than risperidone in patients with dementia. Although the mortality risk is slightly lower for quetiapine, this is of limited clinical utility given the consistent evidence from randomised controlled trials in people with Alzheimer’s disease and Parkinson’s disease dementia that quetiapine is ineffective in treating psychosis, aggression or agitation. In addition, quetiapine appears to have a more substantial detrimental impact on cognition than other atypical antipsychotics in patients with Alzheimer’s disease. Of more interest are the findings that olanzapine and aripiprazole may be associated with lower mortality risk than risperidone when adjusting for dose. The findings do however have to be interpreted cautiously as there were a smaller number of patients treated with these agents, particularly with aripiprazole. Of note, both drugs have been shown to have comparative efficacy to risperidone in previous meta-analyses of randomised controlled trials. A further meta-analysis of cohort studies reporting mortality associated with individual drugs is now urgently needed to determine whether olanzapine or aripiprazole could be an equally effective and slightly safer alternative to risperidone for the treatment of aggression and psychosis in patients with dementia.

What does the study tell us about the risks of antipsychotic use in older people without a dementia diagnosis – in particular those with functional psychoses for whom management with a non-drug treatment or alternative class of psychotropic would not be an option? Gerhard and colleagues acknowledge that dementia may have been underdiagnosed in their sample, but it is just as likely that patients with schizophrenia and bipolar disorder would also have been underdiagnosed and consequently would have been inadvertently included among the two-thirds of participants without a dementia diagnosis. In the absence of an untreated comparison group it is of course impossible to comment on the absolute increase in mortality associated with antipsychotic use in patients with functional psychoses. But the demonstration of a dose–response relationship with mortality risk that was independent of dementia diagnosis is strongly suggestive of similar risks to those seen in people with dementia. It would be important for Gerhard and colleagues to re-examine their data-set, looking specifically at patients who did have a diagnosis of schizophrenia or bipolar disorder to confirm this. It is probably already established practice to use the lowest effective antipsychotic dose and to avoid haloperidol for older patients with functional psychoses, and this study hints at the potential dangers of not following these principles.

Acknowledgements

The authors would like to thank the NIHR Mental Health Biomedical Research Centre and Dementia Unit at South London and Maudsley NHS Foundation Trust and (Institute of Psychiatry) King’s College London in supporting their time in producing this editorial.

Clive Ballard, MD, MRCPsych, Anne Corbett, PhD, Wolfson Centre for Age-Related Diseases, King’s College London; Robert Howard, MD, MRCPsych, Institute of Psychiatry, King’s College London, UK

Correspondence: Clive Ballard, Professor of Age-Related Diseases, Wolfson Centre for Age-Related Diseases, Guy’s Campus, King’s College London, London SE1 1UL, UK. Email: clive.ballard@kcl.ac.uk

First received 29 Apr 2014, accepted 1 May 2014

References

Prescription of antipsychotics in people with dementia
Clive Ballard, Anne Corbett and Robert Howard
BJP 2014, 205:4-5.
Access the most recent version at DOI: 10.1192/bjp.bp.113.128710

References
This article cites 7 articles, 1 of which you can access for free at:
http://bjp.rcpsych.org/content/205/1/4#BIBL

Reprints/permissions
To obtain reprints or permission to reproduce material from this paper, please write to permissions@rcpsych.ac.uk

You can respond to this article at
/letters/submit/bjprcpsych;205/1/4

Downloaded from
http://bjp.rcpsych.org/ on September 30, 2017
Published by The Royal College of Psychiatrists