Pharmacological Treatment of Behavioural and Psychological Symptoms of Dementia (BPSD)

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with thanks to Jonathan Cavan for his input
Aims

✓ Define BPSD and common symptoms
✓ State the considerations for treatment of BPSD and outline the main treatment options
✓ Describe the risks versus benefits associated with the use of antipsychotics in BPSD
✓ Discuss the management & review of patients on antipsychotics
Dementia

What is it?
A syndrome including loss of memory, mood changes, and problems with communication and reasoning.

Associated with?
Chronic, organic brain disorders - mostly progressive over years. Incidence increases with age. Main types are Alzheimer’s and vascular dementia.

Ref: Clinical Knowledge Summaries accessed Nov 2011
BPSD?

- AGITATION
- DISINHIBITION
- AGGRESSION
- IRRITABILITY
- PERSISTANT QUESTIONING
- PERSISTANT VOCALISATION
- DELUSIONS
- HALLUCINATIONS
- PARANOIA
- REDUCED APPETITE
- APATHY
- ANXIETY
- SLEEP DISTURBANCES
Prevalence & Time Course

- Agitation
- Diurnal rhythm
- Irritability
- Wandering
- Aggression
- Hallucinations
- Delusions
- Sexually inappropriate behavior
- Accusatory behavior
- Suicidal ideation
- Depression
- Social withdrawal
- Paranoia
- Anxiety
- Mood change
- Mood change

Consequences?

BPSD

CARER BURDEN

INSTITUTIONALISATION
NICE recommends that “People with dementia who develop non-cognitive symptoms or behaviour that challenges should be offered a pharmacological intervention in the first instance only if they are severely distressed or there is an immediate risk of harm to the person or others.”
Use of Antipsychotics in UK?

Key findings (2009)

- 180,000 people with dementia treated with antipsychotics per year
- Up to 36,000 may derive some benefit from treatment
- Results in additional 1,800 deaths and 1,620 cerebrovascular events
- Up to two-thirds of prescriptions unnecessary with appropriate support?

Key Recommendations

11 key recommendations including:

**Recommendation 4:** People with dementia should receive antipsychotic medication only when they really need it. To achieve this, there is a need for clear, realistic but ambitious goals to be agreed for the reduction of the use of antipsychotics for people with dementia. Explicit goals for the size and speed of this reduction in the use of antipsychotics in dementia, and improvement in their use where needed, should be agreed and published locally following the completion of the baseline audit. These goals should be reviewed yearly at primary care trust, regional and national level, with information published yearly on progress towards them at each level.

**Recommendation 11:** Specialist older people’s mental health services and GPs should meet in order to plan how to address the issue of people with dementia in their own homes who are on antipsychotic medication. Using practice and patient-level data from the completed audits on the use of these medications, they should agree how best to review and manage existing cases and how to ensure that future use follows best practice in terms of initiation, dose minimisation and cessation.
National Dementia & Antipsychotic Prescribing Audit 2012

• Published by NHS Information Centre
• WHAT? Analysis of collected demographic and prescribing information for people with a diagnosis of dementia from primary care clinical systems, over a six year period (2006 to 2011).

• KEY FINDINGS?
• The number of people newly diagnosed each year with dementia in the participating practices has increased by 67.7% from 2006 to 2011
• The majority (94.7%) of people diagnosed with dementia are ≥ 65 years and there is a higher prevalence in women than in men
• The number of people with dementia receiving prescriptions for antipsychotic medication decreased from 17.05% in 2006 to 6.80% in 2011 (~10%)
National Dementia & Antipsychotic Prescribing Audit 2012

- The number of people with dementia receiving prescriptions for antipsychotic medication decreased from 17.05% in 2006 to 6.80% in 2011
- The number of people with dementia receiving a prescription of antipsychotic medication halved (reduction of 51.8%) over two yrs (2008 to 2011)
- When looking at the results by SHA, the decrease in the prescription of an antipsychotic ranges from 5.48% to 11.98%
- Prescriptions for donepezil, galantamine, rivastigmine and memantine show little variation across the audit period, varying between 9.7% and 10.3% over the six audit years
Antipsychotic OR NOT?

NICE states (03/2011) “...severe non-cognitive symptoms (psychosis and/or agitated behaviour causing significant distress) may be offered treatment with an antipsychotic drug after the following conditions have been met...”

- full discussion with the person with dementia and/or carers about the possible benefits and risks of treatment

- cerebrovascular risk factors should be assessed and the possible increased risk of stroke

- possible adverse effects on cognition discussed and assessed at regular intervals

- alternative medication should be considered if necessary

- target symptoms should be identified, quantified and documented

- changes in target symptoms should be assessed and recorded at regular intervals
Antipsychotics - General Principles

- an atypical antipsychotic is to be preferred over a typical one
- lowest possible effective dose, for the shortest possible time, ideally less than 12 weeks
- continuation should be reviewed regularly (2 weekly); at review, reduction or cessation of the medication should be actively considered
- ensure baseline and follow-up physical health e.g. blood tests

Varying side-effect profile – guide choice?

Risperdal® licensed “for the short-term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer’s dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others.”

No other antipsychotics licensed for use in Alzheimer’s dementia therefore “off-label use”
Choice of antipsychotic?

- **JAMA** featured a meta-analysis of trials assessing the efficacy and safety of atypical antipsychotic medications for off-label indications.

- **Conclusions:** For symptoms of psychosis, agitation, and global behavioural symptoms in elderly patients with dementia, small but statistically significant benefits were observed for *risperidone*, *aripiprazole* & *olanzapine*.

- **Quetiapine** failed to show any statistically significant benefits and therefore, should *not* be routinely used for the treatment of BPSD. It also has anticholinergic properties.

Central and North West London Good Practice Checklist

At Initiation
• Define target symptom(s), including history, severity and frequency
• Exclude possible underlying cause(s), e.g. pain, infection, drug-induced
• Consider aggravating or alleviating factors
• Consider non-pharmacological approaches, if appropriate
• Document reason(s) for pharmacological management, e.g. severe distress
• Consider cardiovascular risk factors, when initiating antipsychotics
• Ensure baseline physical health monitoring, including relevant blood tests
• Discuss with service user/carers, i.e. risks versus benefits, & if “off-label” use
• Document details of treatment, i.e. medicine name, dose and frequency
• Confirm next review, ideally within two weeks

At Review
• Assess changes in target symptom(s), including severity and frequency
• Assess for any side-effects, including any necessary management
• Ensure physical health monitoring completed, including obs & blood tests
• Consider medication cessation or reduction, if appropriate and rationale
Lorazepam

- is licensed for short-term use in managing agitation and anxiety. It may be used short-term when a calming or sedative effect is appropriate
- Usual dose prescribed in older adults is 0.5mg-1mg up to twice daily
- Caution: Hx of benzodiazepine tolerance or misuse or significant respiratory distress

“Plan B” - Promethazine 25-50mg a day; Sedating antihistamine.
NICE states that AChEIs should be considered for “…people with mild, moderate or severe Alzheimer’s disease who have [BPSD]…causing significant distress or potential harm to the individual if a non-pharmacological approach is inappropriate or has been ineffective, and an antipsychotic drugs are inappropriate or have been ineffective”

Alternative options to manage BPSD: Acetylcholinesterase inhibitors (AChEI)

- Most effective for depression, dysphoria, apathy and anxiety
- Not effective for clinically relevant aggression or agitation in short-term
- Many now available as generics eg. donepezil and rivastigmine oral
Alternative options to manage BPSD: **Antidepressants**

- **SSRIs** have been used since 1980s but limited. Preferred 1st line treatment for depression
- **RCT evidence-base in BPSD**
  - RCTs for both sertraline & citalopram vs placebo in agitation
  - One RCT suggests *comparable efficacy* between citalopram and risperidone over 12 weeks for agitation

Note: maximum dose of citalopram in older people is **20mg** daily from 2011
Alternative options to manage BPSD: **Antidepressants**

- **Trazodone** is a tricyclic-related antidepressant with sedative effects.
- Cochrane Review (Apr 2008) states *insufficient* RCT evidence but anecdotally effective.
- Doses initiated at 50mg nocte and titrated slowly to 300mg nocte.
- CNWL Trust approved for agitation where also sleep disturbances “off-label” use.
Alternative options to manage BPSD: Carbamazepine

- LIMITED good quality evidence for carbamazepine for agitation and aggression in AD

- Initiate at 100-200mg daily and increasing by 100-200mg daily every 2 wks to maintenance dose of 200-600mg daily

- Mixed reviews for how tolerated (falls etc); improved by prescribing modified-release preparation

- Ensure physical health monitoring i.e. baseline and follow-up bloods tests

- Always check for drug-drug interactions!

- Trust approved but remains “off-label” use
Alternative options to manage BPSD: Sodium Valproate

- Cochrane Review (Oct 2008) highlights with valproate (CNWL approved):
  - Failed to show improvements with agitation
  - Higher rate of harmful effects
  - Current evidence does not support its use
Alternative options to manage BPSD:

**Memantine**

- Memantine was recommended by NICE for treating moderate to severe dementia but **NOT FOR stand** – alone BPSD!!!

- However, incidence of BPSD greater with disease progression – “covered anyway”

- CNWL memory service – mixed reviews of benefit for dementia and actual BPSD

- **Not approved** for combined use with AChEIs

- **SWITCHING?** Manufacturer suggests abrupt or cross-taper eg. 2/52
Consider use of Shared Care Protocols
Points to consider when antipsychotics are prescribed for inpatients with BPSD

- Obtain patient’s full medical & psychiatric history
- Rule out any acute medical underlying causes
- Ensure psychiatric differential diagnoses considered: Schizophrenia, psychosis, dementia?
- Define key symptoms team being treated
- Review “ABC” chart
- All other non-drug treatments considered
- Consider patient’s cardiovascular risk factors
- Develop a plan for treatment and review and discuss with team
- Communicate with mental health team, GP and carers (as appropriate) at discharge and review
Key Considerations

- Assessment and identification of target symptoms
- Individualise treatment and assess risk factors
- Informed decision-making with individual and carers
- Frequent review with consideration of discontinuation or consideration of a non-antipsychotic ALTERNATIVE
References 1:

- Rivastigmine (Exelon®) summary of product characteristics, last updated 11/03/09. Accessible via: http://emc.medicines.org.uk/medicine/1284/SPC/Exelon/
- Donepezil (Aricept®) summary of product characteristics, last updated 28/05/09 accessible via: http://emc.medicines.org.uk/medicine/577/SPC/Aricept/
- Galantamine (Reminyl®) summary of product characteristics, last updated 15/10/09 Accessible via: http://emc.medicines.org.uk/medicine/10335/SPC/Reminyl Tablets/
- Memantine (Ebixa®) summary of product characteristics, last updated 18/02/11. Accessible via: http://emc.medicines.org.uk Direct link is: http://www.medicines.org.uk/EMC/medicine/10175/SPC/Ebixa+5mg+pump+oral+solutio n%2c+20mg+and++10+mg+Tablets+and++Treatment+Initiation+Pack/
References 2:

- Bhasin M, Rowan E, Edwards K et al. Cholinesterase inhibitors in Dementia with Lewy Bodies - which one to use? Int J Ger Psych 2007; 890-895
- Treatment protocol by NHS Medway: Treatment of Behaviour That Challenges,
References 3:

• Antipsychotic prescribing resource library - Resources site by West Midlands NHS; accessible via:


• Tegretol ® retard tablets. Novartis. Electronic Medicines Compendium. (Date of last revision of text 24th of December 2010). Available at: www.emc.medicines.org.uk

References 4:


- Epilim chrono ® tablets. Sanofi Aventis. Electronic Medicines Compendium. (Date of last revision of text 14th of March 2011). Available at: www.emc.medicines.org.uk

- Personal communication via email with Older Adult Consultants at CNWL NHS Foundation Trust.

- Risperidone (Risperdal®) summary of product characteristics, last updated 17/03/09. Accessible via: http://emc.medicines.org.uk/medicine/12818/SPC/Risperdal%20Tablets,%20Liquid%20&%20Quicklet/

