

ANTIDEPRESSANTS AND DEMENTIA

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With thanks to Dr Bev Rayers

Overview

- Neuropsychiatric symptoms in dementia
- Depression and diagnosis
- Why to treat, when to treat
- Why we try to avoid prescribing psychotropic drugs- the downfalls

Neuropsychiatric symptoms in dementia

- Agitation
- Aggression
- Delusions
- Hallucinations
- Wandering
- Apathy
- Disinhibition
- Sleep disturbance
- Depression

Depression;

Depression is a mood disorder causing persistent feelings of sadness and loss of interest. It affects how people feel, think and behave and can lead to a variety of emotional and physical problems including suicidal thoughts. Loss of productivity and carer stress can result in significant economic burden to a family and society

Risk factors;

- Past history
- Family history
- Secondary to life changes (loss, grief, adjustment)
- Organic/neurological degenerative process
- Chronic pain
- Disability
- Medications
- Trauma history

Depression (continued)

- Depression is the most common mental health problem in the elderly
- Prevalence studies suggest 14% to 20% of the elderly living in the community experience depressive symptoms (but clinically diagnosed occurrence lower than in younger adults)
- Higher rates among the elderly in hospital (12% to 45%)
- Even higher rates in long-term care facilities (an estimated 40%)

Treatment of depression in the Elderly- the evidence

- Most depression studies have been conducted on younger populations
- When mixed-aged groups have been studied older adults have been underrepresented
- Often elderly or those with comorbid conditions are excluded from studies
- Limits the ability to generalize from these study findings when treating the elderly but increasing body of literature specific to the elderly
- Pharmacological and non pharmacological strategies are both usually helpful

It can be difficult to diagnose depression in a person with dementia. Some characteristic signs are:

- Loss of interest and pleasure in previously enjoyed activities (anhedonia)
- Lack of energy
- Poor sleep
- Loss of appetite and weight
- Expressing feelings of worthlessness and sadness
- Being unusually emotional, crying, angry or agitated
- Increased confusion

Agitation or aggression may be the primary manifestation of depression

Therapeutic trial of antidepressant medication may be only diagnostic strategy possible

Attributing cognitive impairment to the dementia or the depressive disorder may be difficult until an adequate trial of treatment for depression has occurred.

Challenges in Diagnosis

- Communication difficulties caused by hearing or cognitive impairment,
- Absence of depressed mood or other classic diagnostic features
- Comorbidities with physical symptoms similar to mental disorder
- Stigma associated with mental illness that can limit the self-reporting of depressive symptoms.
- Tendency for people to see their symptoms as part of the normal aging process, which they are not.
- Typically a major depressive episode develops over weeks to a few months, and is a significant new impairment for the person. Conversely, the dementia alone may develop insidiously over months or years and be slow in progression

Geriatric Depression Scale

- The Geriatric Depression Scale (GDS) is a validated screening tool for depression in the elderly that comes in two common formats: the 30-item (long form) and 15-item (short-form) self-rating scale. its reliability decreases with increasing cognitive impairment.
- If there is significant cognitive impairment, the Cornell Scale for Depression in Dementia (CSDD) is the gold standard. Scores are determined by a combination of prior observation and two interviews: 20 minutes with the carer and 10 minutes with the patient.

Patient _____ Examiner _____ Date _____

Directions to Patient: Please choose the best answer for how you have felt over the past week.
Directions to Examiner: Present questions VERBALLY. Circle answer given by patient. Do not show to patient.

1. Are you basically satisfied with your life? **yes** (1) **no** (1)
2. Have you dropped many of your activities and interests? **yes** (1) **no**
3. Do you feel that your life is empty? **yes** (1) **no**
4. Do you often get bored? **yes** (1) **no**
5. Are you hopeful about the future? **yes** **no** (1)
6. Are you bothered by thoughts you can't get out of your head? **yes** (1) **no**
7. Are you in good spirits most of the time? **yes** **no** (1)
8. Are you afraid that something bad is going to happen to you? **yes** (1) **no**
9. Do you feel happy most of the time? **yes** **no** (1)
10. Do you often feel helpless? **yes** (1) **no**
11. Do you often get restless and fidgety? **yes** (1) **no**
12. Do you prefer to stay at home rather than go out and do things? **yes** (1) **no**
13. Do you frequently worry about the future? **yes** (1) **no**
14. Do you feel you have more problems with memory than most? **yes** (1) **no**
15. Do you think it is wonderful to be alive now? **yes** **no** (1)
16. Do you feel downhearted and blue? **yes** (1) **no**
17. Do you feel pretty worthless the way you are now? **yes** (1) **no**
18. Do you worry a lot about the past? **yes** (1) **no**
19. Do you find life very exciting? **yes** **no** (1)
20. Is it hard for you to get started on new projects? **yes** (1) **no**
21. Do you feel full of energy? **yes** **no** (1)
22. Do you feel that your situation is hopeless? **yes** (1) **no**
23. Do you think that most people are better off than you are? **yes** (1) **no**
24. Do you frequently get upset over little things? **yes** (1) **no**
25. Do you frequently feel like crying? **yes** (1) **no**
26. Do you have trouble concentrating? **yes** (1) **no**
27. Do you enjoy getting up in the morning? **yes** **no** (1)
28. Do you prefer to avoid social occasions? **yes** (1) **no**
29. Is it easy for you to make decisions? **yes** **no** (1)
30. Is your mind as clear as it used to be? **yes** **no** (1)

TOTAL: Please sum all bolded answers (worth one point) for a total score. _____

Scores: **0 - 9 Normal 10 - 19 Mild Depressive 20 - 30 Severe Depressive**

Source: www.stanford.edu/~ yesavage

Cornell Scale for Depression in Dementia

Name	Age	Sex	Date	
<input type="checkbox"/> Inpatient <input type="checkbox"/> Aged care home resident <input type="checkbox"/> Outpatient				
SCORING SYSTEM				
A = unable to evaluate 0 = absent 1 = mild or intermittent 2 = severe				
Ratings should be based on symptoms and signs occurring during the week prior to interview. No score should be given if symptoms result from physical disability or illness.				
A. Mood related signs				
1. Anxiety: anxious expression, ruminations, worrying	A	0	1	2
2. Sadness: sad expression, sad voice, tearfulness	A	0	1	2
3. Lack of reactivity to pleasant events	A	0	1	2
4. Irritability: easily annoyed, short tempered	A	0	1	2
B. Behavioural disturbance				
5. Agitation: restlessness, hand wringing, hair pulling	A	0	1	2
6. Retardation: slow movement, slow speech, slow reactions	A	0	1	2
7. Multiple physical complaints (score 0 if GI symptoms only)	A	0	1	2
8. Loss of interest: less involved in usual activities (Score only if change acutely, ie. in less than 1 month)	A	0	1	2
C. Physical signs				
9. Appetite loss: eating less than usual	A	0	1	2
10. Weight loss (score 2 if greater than 5 lb in 1 month)	A	0	1	2
11. Lack of energy: fatigues easily, unable to sustain activities (Score only if occurred acutely, ie. in less than 1 month)	A	0	1	2
D. Cyclic functions				
12. Diurnal variation of mood: symptoms worse in the morning	A	0	1	2
13. Difficulty falling asleep: later than usual for this individual	A	0	1	2
14. Multiple awakenings during sleep	A	0	1	2
15. Early morning awakening: earlier than usual for this individual	A	0	1	2
E. Ideational disturbance				
16. Suicide: feels life is not worth living, has suicidal wishes or makes suicide attempt	A	0	1	2
17. Poor self esteem: self blame, self depreciation, feelings of failure	A	0	1	2
18. Pessimism: anticipation of the worst	A	0	1	2
19. Mood congruent delusions: delusions of poverty, illness or loss	A	0	1	2

Principles of treatment: considerations

- Previous response to treatment; what has worked in past?
- Type of depression- psychotic depression will likely not respond to antidepressant monotherapy, bipolar depression will require a mood stabiliser.
- Anxiety component will likely respond better to SSRI
- Other medical problems: caution not to worsen the condition or cause adverse events. eg anticholinergics in dementia, cardiovascular problems, diabetes, and Parkinson's disease.
- Other medications: minimise drug- drug interactions
- Risk of overdose· Tricyclic antidepressants are lethal in overdose and are often avoided for this reason.

Suicide Risk

- A person is at increased risk of suicide during the initial phase of treatment
- They will require increased monitoring and regular risk assessments
- Consider hospital admission if risk is high or there are no identified protective factors
- Risk usually diminishes after 2-3 weeks but varies

Drugs to avoid

- Benzodiazepines of limited value in dementia
- AND have adverse effects
 - Worsening gait
 - Paradoxical agitation & disinhibition
 - Physical dependence
 - Increased confusion

May be useful in temporary stress (e.g. change in residence, medical event, titration of other psychotropic medication)– use those with short half life- e.g. Lorazepam.

Choice of antidepressant

- Several antidepressants are efficacious in elderly patients with a major depressive episode without psychotic features.
- Selection should be based on the best side effect profile and lowest risk of drug-drug interactions.
- SSRI's SNRI's Mirtazapine and Moclobemide are all *relatively* safe in the elderly with similar efficacy
- Fluoxetine has a long half-life and greater drug interactions
- Paroxetine greater anticholinergic effect can be problematic

SSRI and SNRI- Adverse Effects

- Common side effects of SSRIs : nausea, dry mouth, insomnia, somnolence, agitation, diarrhoea, sweating, and sexual dysfunction
- Hyponatraemia secondary to a syndrome of inappropriate antidiuretic hormone secretion. It affects 10% of patients taking antidepressants
- Hypertension; dose dependent (SNRI)
- Liver effects: Cholestatic jaundice Raised transaminase enzyme activities
- Falls
- GI Bleeds

Tricyclic Adverse Effects

- Tricyclic's no longer considered first-line agents due to adverse effects but many older people have been taking them for decades
- Postural hypotension, which can contribute to falls and fractures
- Cardiac conduction abnormalities
- Anticholinergic effects- delirium, urinary retention, dry mouth, and constipation.
- If chosen as a second-line medication, then nortriptyline often best choice- less anticholinergic
- ECG and postural blood pressure prior to tricyclic antidepressant and after increasing the dose
- Tricyclic antidepressant blood levels should be monitored

Mirtazapine, Moclobemide and MAOI adverse effects

- Mostly as for SSRI's
- Dyscrasias; (disorder of the blood)
- Given high rates of drug-drug interactions, and dietary restrictions, monoamine oxidase inhibitors (MAOIs) are usually reserved for treatment resistant depression

Dosing

- Starting dose should be half that prescribed for a younger adult
- “Start low and go slow” Increase the dose regularly as tolerated at 1- to 2-week intervals in order to reach an average therapeutic dose more quickly
- Average therapeutic dose is typically lower but much individual variability
- If no improvement after 2 to 4 weeks on an average therapeutic dose, increase
- Regular follow-up visits to monitor efficacy, tolerance and compliance and titrating accordingly
- Monitor for any worsening of depression, agitation or anxiety, and suicide risk, especially in the early stages of treatment.

Maintenance

- Treat to remission
- If no improvement after 8 weeks change treatment
- Consider wash out period, cross titration possible with some combinations
- Sudden cessation (venlafaxine and paroxetine) can lead to a withdrawal syndrome that includes anxiety,
- If some improvement but not full remission consider augmentation (antidepressant of a different class, another agent such as lithium, psychotherapy such as cognitive-behavioral therapy or interpersonal therapy- Limited efficacy in cognitive decline
- If a second antidepressant is added, monitor for the emergence of serotonin syndrome,

Lithium; a special case

- Lithium is the gold standard when it comes to mood stabilisers
- Lithium requires diligent monitoring otherwise it may lead to kidney damage
- Lithium can affect thyroid & calcium levels
- NSAIDS should not be used
- The patient should ensure adequate fluid intake
- Diuretics should be used with cautious monitoring of levels & electrolytes
- Vomiting, diarrhoea or other causes of dehydration may risk toxicity

ACUTE LITHIUM TOXICITY

- Symptoms include:
 - Diarrhoea
 - Dizziness
 - Nausea
 - Stomach pains
 - Vomiting
 - Weakness
 - Hand tremors
 - Lack of coordination of arms and legs
 - Muscle twitches
 - Seizures
 - Slurred speech
 - Uncontrollable eye movement

- Check bloods, reduce or cease lithium, urgent psychiatric review

Augmentation

- Atypical antipsychotics used as add-on therapy in the treatment of depression shows some promise.
- 2010 study showed efficacy for the use of adjuvant aripiprazole in older adults with an incomplete response to standard antidepressant treatment, both in terms of a significant reduction of depressive symptoms and improvement in remission rates.
- Risperidone, olanzapine or quetiapine are other options
- In severe cases of treatment resistant depression ECT maybe indicated

On the importance of monitoring

- Regular pathology because of the risks of hyponatraemia - (U&E) , blood dyscrasia, GI bleeds (FBC) and liver dysfunction (LFT).
- These should be done at commencement (baseline), once stable on medication and then every 3 months or at any change in presentation, in particular confused state
- Lithium should be done more often- after any change in circulating volume (D&V etc), infection, change of other meds as well as every 3 months along with renal function and TFT every 6 months.
- Baseline ECG as all psychotropics can affect cardiac function

Antipsychotic Treatment

- Older (first generation) more Extrapyramidal Side Effects
- Risperidone for BPSD (PBS restriction)
- Quetiapine likely to be safest in Parkinson's
- Very low dose

Adverse effects of antipsychotics in elderly

- Metabolic syndrome (Endocrine effects)- Weight gain, Diabetes mellitus
- Cardiac (ECG) changes prolonged QT interval and risk of arrhythmias
- Postural hypotension
- Movement disorders: EPSE, Akathisia, Acute dystonia, Tardive dyskinesia
- Anticholinergic effects
- Hypersalivation
- GI effects Nausea, Constipation, Diarrhoea
- Altered liver function

Atypical Antipsychotics in Dementia

- Absolute mortality risk increase of 1% over about 10 to 12 weeks of treatment
NNH 100 when antipsychotics were compared with placebo in patients with dementia
- 1 in 20 (NNH) over a 12 month period
- 3.5 x increased risk of stroke

Summary

- Exclude medical cause for neuropsychiatric symptoms
- Try environmental behavioural and non pharmacological therapies first
- Exercise caution with all psychotropic drugs
- Most antidepressants increase the risk of hyponatraemia, falls, GI bleeds, and ECG changes
- Antipsychotics can cause strokes and shorten life expectancy (in 1 in 20 people treated for one year)
- Risk v benefit analysis in all cases- aim is usually to improve quality of life & reduce distress- discuss openly with guardian the associated risks.

Thank You. And don't forget.....

- *“Management of depression in a person with dementia should be enthusiastic with an aim to optimise quality of life”* (Dr. David Kitching, Senior psychiatry specialist, Concord Hospital, Sydney)