Depression in Post-Acute and Long-Term Care

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I do not intend to discuss any off-label, investigative use of commercial products or devices.

Objectives

Discuss prevention of depression in post-acute and long-term care (PALTC) populations

Discuss suicide prevention strategies in PALTC populations

Discuss non-pharmacological and pharmacological interventions for depression in PALTC populations

Prevention

Target population: Older adults with subsyndromal depression

Interventions: Education, behavior activation, exercise training, family intervention, psychotherapy (cognitive behavioral therapy, problem solving therapy, interpersonal psychotherapy).

- American Psychological Association Clinical Practice Guidelines for Treatment of Depression. 2019.

Prevention

Interventions to reduce loneliness and or social isolation

Examples: reminiscence therapy, group physical exercise programs, video conferences with family, horticulture therapy, gender-based social groups.

Social prescribing (volunteering, teaching, book clubs)

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Prevention

Stepped care approach

Watchful waiting, cognitive behavioral therapy (CBT), CBT-based bibliotherapy, problem solving therapy, and final step of referral to PCP for antidepressants.

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Prevention

Instilling of hope and positive thinking

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Suicidal ideation

Suicidal ideation is prevalent in PALTC population but death by suicide is rare.

- Barak and Gale. Suicide in long-term care facilities: the exception or the norm? JAMA Network Open 2019.

Suicide prevention

Columbia Suicide Severity Rating Scale

Stanley Brown Safety Plan

Case Presentation

Geriatric Depression

Older adults tend to endorse a lack of emotions rather than depressed mood

Older adults endorse feelings of irritability and fearfulness rather than sadness.

- Gallagher-Thompson et al. Late life depression. Practical strategies in geriatric mental health. American Psychiatric Association Publishing 2020.

Assessment tools

Patient Health Questionnaire -9 (contains suicide item that is more relevant)

Geriatric Depression Scale - 15

Cornell Scale for Depression in Dementia

- Gallagher-Thompson et al. Late life depression. Practical strategies in geriatric mental health. American Psychiatric Association Publishing 2020.

Diagnostic workup

Depression secondary to other causes (e.g., hypothyroidism, B12 deficiency, pain).

Medication induced depression

Substance-induced depression

- Veterans Administration DoD Clinical practice guidelines for management of major depressive disorder. 2022.

Testing

CBC, CMP

B12, Folate, D, Magnesium

TSH

CRP

- Jacobson and Wilde. Laboratory testing and neuroimaging studies in psychiatry. The APA Publishing Textbook of Psychiatry, 7th Ed. 2019.

Psychotic depression

Patient with psychotic depression should always be referred to a psychiatrist for urgent review.

Combination of an antidepressant with an antipsychotic is recommended.

- ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Clinical tips

Medicalization of human suffering

Adjustment disorders misdiagnosed as Major depression

Grief and Prolonged Grief Disorder misdiagnosed as Major depression

Bipolar depression misdiagnosed as unipolar major depression

Depression as part of PTSD misdiagnosed as major depression

Best Practice

Strong recommendation to use collaborative / integrated care models

- Veterans Administration DoD Clinical practice guidelines for management of major depressive disorder. 2022.

Mild depressive episode

For mild depressive episodes (Beck depression inventory [BDI-II] score 14-19), psychotherapy or psychoeducation are alternatives to antidepressants. If antidepressants are chosen, SSRIs are first-choice medication.

- ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Non-pharmacological treatments

Behavior Activation Therapy

Psychotherapy

Exercise therapy

Mindfulness based Cognitive Behavioral Therapy

Bright light therapy

Gratitude-based interventions

Lifestyle medicine-based interventions

Individualized pleasant activity schedule (IPAS)

Psychotherapy

First line for mild episode (CBT [cognitive behavioral therapy] has best evidence).

In combination with antidepressants for moderate to severe symptoms.

Partial response to antidepressants

Problems with adherence to antidepressants

Patient prefers it

- ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Meaning-centered psychotherapy

Advanced cancer patients struggling with despair, hopelessness and desire for hastened death.

- William Breitbart. Memorial Sloan-Kettering Cancer Center, New York, NY. Meaning-centered psychotherapy for advanced cancer patients. *Logotherapy and Existential Analysis* 2016.

Light therapy

For seasonal affective disorder (winter / fall depression)

Protocol adherence needs to be ensured (10,000 lux at 5 feet distance for 20-40 minutes daily in morning for 2-4 weeks; 2,500 lux for 2 hours per day)

- ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Complementary and Alternative Treatments

- Omega 3 fatty acids
- L-methyl folate
- SAMe
- Mindfulness based stress reduction (MBSR)
- Tai Chi
- Arts and cultural activities
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.
  - Merrill D, Payne M, Lavretsky H. Complementary and alternative medicine approaches for treatment and prevention of late-life mood disorders. *Late-life Mood Disorders*. Oxford University Press 2013; pp 432-447.
  - Noguchi et al. Arts and cultural engagement and depressive symptom onset among older adults: A longitudinal study from the Japanese Gerontological Evaluation Study. International Journal of Geriatric Psychiatry 2022, March.

Pharmacogenetic testing

Not recommended

Exception: recurrent severe side effects to several antidepressants

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Pharmacogenetic testing

CYP2C19 rapid metabolizers should avoid escitalopram, citalopram, sertraline and consider antidepressants not metabolized by this enzyme (e.g., paroxetine, venlafaxine).

- Clinical Pharmacogenetics Implementation Consortium CPIC. CYP2C19 prescribing guidelines.
- *Precision Medicine*. Leanne Williams and Laura Hack. American Psychiatric Association Publishing, 2022.

Pharmacotherapy in PALTC populations

Depression due to pain prevalent.

Lithium may carry higher risks in this population.

Dose adjustments based on renal function often needed (e.g., reducing dose of duloxetine in patients with low GFR).

High prevalence of adverse drug-drug interactions – recommend involvement of a consultant pharmacist

- Desai and Grossberg. Chapter 5. Major depressive disorder, other mood disorders, and suicide. *Psychiatric Consultation in Long-Term Care: A guide for healthcare professionals*. 2nd Edition. Cambridge University Press. 2017.

Selecting antidepressants

Sertraline and duloxetine as first line

Citalopram and escitalopram as alternatives but concerns over QTc prolongation may limit their dosage to subtherapeutic levels.

Venlafaxine, bupropion, mirtazapine and vortioxetine are reasonable as second line agents.

Avoid fluoxetine because of its long half-life

Avoid paroxetine due to higher anticholinergic effects

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Partial response to antidepressant

No change for another 4 weeks.

Augment with another antidepressant, lithium, atypical antipsychotic (e.g., aripiprazole) or specific psychotherapy (CBT, PST).

Switch to another antidepressant (same or another class)

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Monitoring adverse effects

Hyponatremia

Falls

Bleeding risk

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Discontinuation

High rate of discontinuation symptoms if not done judiciously

ADS: antidepressant discontinuation syndrome (FINISH: flu like symptoms, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal [paresthesias, brain zaps, mood fluctuation, dizziness, headache])

- Zweibel and Viguera. Discontinuing antidepressants: Pearls and Pitfalls. Cleveland Clinic Journal of Medicine Jan 2022.

Resources

Older adults and depression: Knowing when to get help. National Institute of Aging at NIH.

2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Desai and Grossberg. Chapter 5. Major depressive disorder, other mood disorders, and suicide. *Psychiatric Consultation in Long-Term Care: A guide for healthcare professionals*. 2nd Edition. Cambridge University Press. 2017.

Resources

American Psychological Association Clinical Practice Guidelines for Treatment of Depression. 2019.

One Day Mindfulness Millionaire: Living Mindfully – A light-hearted primer for the uninitiated. Book Baby

Resources

Depression and Bipolar Support Alliance https://www.dbsalliance.org

Anxiety and Depression Association of America https://adaa.org

Resources: High-quality apps for Meditation, Mindfulness and Relaxation exercises

Healthy Minds Program app https://hminnovations.org/meditation-app

Cleveland Clinic Mindful Moments app https://clevelandmagazine.com/health/articles/get-fit-cleveland-clinic's-mindful-moments-app-is-comforting

UCLA Mindful app https://www.uclahealth.org/programs/uclamindful/free-guided-meditations/guided-meditations

Resources: High-quality apps for insomnia and PTSD

CBT-i Coach app https://mobile.va.gov/app/cbt-i-coach

PTSD Coach app https://mobile.va.gov/app/ptsd-coach

Namaste

Efficacy plateaus for antidepressants in adults

- Sertraline 75-100mg
- Citalopram 30-40mg
- Escitalopram 10-15mg
- Mirtazapine 30mg
- In general, increasing the dose further may not yield greater efficacy.

- Furukawa T et al. Optimal dose of SSRIs, mirtazapine, and venlafaxine in major depression: a systematic review. Lancet Psychiatry 2019;6:601-609.

Monitoring adverse effects

- If SSRI or SNRI chosen, inquire about history of hyponatremia as part of consent process.
- Check sodium levels if there is history of hyponatremia.
- Check serum sodium levels within 2-4 weeks of initiating a SSRI or an SNRI (2 weeks if patient on diuretics or history of hyponatremia)
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Monitoring adverse effects

- Falls risk (high dose citalopram [40mg] and escitalopram [20mg] have higher risk of falls compared to dose of sertraline above 75mg [Haddad et al 2022]).
- Insomnia
- Agitation and anxiety
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.
  - Haddad YK et al. A comparative analysis of selective serotonin reuptake inhibitors and fall risk in older adults. J Am Geriatr Soc Feb 8, 2022.

Augmentation with aripiprazole

- Average dose 7mg
- NNT 6
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Combination of two antidepressants

- Combining a reuptake inhibitor (SSRI, SNRI) with a presynaptic alpha 2 autoreceptor antagonist (mirtazapine, trazodone) was superior to monotherapy, both for first line treatment and for nonresponders and drop out rates did not differ.
- Combination antidepressant therapy may be a potential option as first line for treatment of severe depression and for nonresponders to monotherapy.
  - Henssler et al. Combining antidepressants vs antidepressant monotherapy for treatment of patients with acute depression – a systematic review and meta-analyses. JAMA Psychiatry Feb 16, 2022.

Efficacy of antidepressants questioned

- Benefits of antidepressants over placebo on average may be minimal or non-existent for mild to moderate depression (Hamilton Depression Rating Scale scores below 23). For patients with very severe depression, the benefits of antidepressants over placebo is substantial.

- Fournier JC et al. Antidepressant drug effects and depression severity. A patient-level meta-analysis. JAMA 2010; 303(1):47-53.

Efficacy of antidepressants questioned

- Antidepressants are marginally superior to placebo in both moderate and severe depression. The clinical significance of this small drug-placebo effect is questionable, even in the most severe forms of depression. In addition, the modest efficacy if likely an overestimation of true efficacy given the systematic method biases. Recommendations from guidelines are in contradiction with the current evidence.

  - Ploderl M, Hengartner MP. Guidelines for the pharmacological acute treatment of major depression: conflicts with current evidence as demonstrated with the German S3-guidelines. BMC Psychiatry 2019; 19:265.

Selecting antidepressants in patients with developmental disabilities

- Citalopram associated with irritability
- Sertraline associated with diarrhea
- Venlafaxine associated with nausea, vomiting

- Integrated Mental Health Treatment Guidelines for Prescribers in Intellectual and Developmental Disabilities. The Center for Start Services. Institute on Disability / UCED 2021. University of New Hampshire

Moderate to severe depression in epilepsy patients

- For moderate to severe depression (Beck depression inventory [BDI-2] score 20 or more), SSRIs are first-choice medication.

- ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Severe depression

- Offer combination of antidepressant therapy and psychotherapy.

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Duration of antidepressant trial

- 10-12 weeks were needed for older adults to achieve a response.
- NNT 6.7

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Close follow up initially

- Every 1-2 weeks (in person or virtually) to assess response, side effects and to titrate the dose.
- Provide supportive psychosocial interventions, monitor for suicide risk, agitation, and worsening of depression.

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Severe depression

- For severely depressed patient (BDI-2 score 30 or more), consider risk of overdose when antidepressants are prescribed.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Suicidal thoughts or intent

- If the patient has suicidal thoughts or intent, patient should be referred to a psychiatrist for urgent review.
- Hospital admission without patient consent may be necessary.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Quetiapine monotherapy

- One study found it effective for geriatric depression.
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Drug-Drug Interaction in epilepsy patients

- Enzyme inducing antiepileptics (e.g., carbamazepine) reduce levels of bupropion by 90%.
- Fluoxetine, fluvoxamine and to a lesser extent sertraline can raise levels of phenytoin and to a lesser extent valproate through inhibition of CYP2C9.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Duration of treatment

- At least 6 months following remission from the first depressive episode; 9 months in patients with long previous episode, even longer for severe depression and for those with residual symptoms.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Remission, Response, Recovery, Relapse

- Remission: Disappearance of all depression symptoms.
- Response: 50% or more reduction of symptoms.
- Recovery: remission for 6 months or more.
- Relapse: recurrence of symptoms before recovery.
- Recurrent: return of symptoms after recovery.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Discontinuation

- Over 1-4 weeks.
- Close monitoring and re-starting the antidepressant if relapse of symptoms.

- ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Discontinuation

- May last days to months
- Different symptoms have different duration
- Slow antidepressant taper or cross-taper
- Slow taper over weeks to months as necessary

- Zweibel and Viguera. Discontinuing antidepressants: Pearls and Pitfalls. Cleveland Clinic Journal of Medicine Jan 2022.

Combination of two antidepressants

- SSRI with mirtazapine can be considered if monotherapy failed.
- Venlafaxine plus mirtazapine may be accompanied by worsening of side effects.

- ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Lithium augmentation in epilepsy patients

- Adding lithium to an antidepressant is recommended if monotherapy has failed.
- Lithium should be prescribed only by psychiatrists.
- Target lithium levels: 0.6-1.0 for acute mania; 0.4-0.8 for prophylaxis
- Consider drug-drug interaction (e.g., increased risk of thyroid toxicity, especially in combination with carbamazepine; topiramate may reduce lithium clearance)
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Antipsychotic augmentation in epilepsy patients

- Adding quetiapine or aripiprazole to an antidepressant represents and alternative to lithium and is recommended if monotherapy has failed.
- Risks: sedation (quetiapine), weight gain (quetiapine and to a lesser extent aripiprazole), akathisia (aripiprazole).
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Antipsychotic augmentation in epilepsy patients

- Carbamazepine can reduce quetiapine levels to “undetectable.”
- Olanzapine and quetiapine use are associated with slightly increased risk of seizures but other antipsychotics (e.g., risperidone) are not.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Methylphenidate augmentation

- Methylphenidate may be added to an SSRI if monotherapy fails.
- Methylphenidate should be used short term (but a minimum of 8 weeks).
- Weight loss was not a common side effect.
  - Smith et al. Methylphenidate in geriatric depression: a systematic review. Geriatric Psychiatry 2021.

Pramipexole

- There is some evidence for treatment of major depression.
- Due to its selective D3 dopamine receptor agonist effect, it may activate reward networks (e.g., ventral tegmental area) and improve anhedonia (inability to take pleasure in activities that usually bring joy and provide a sense of purpose).
  - Tundo et al. Pramipexole in the treatment of unipolar and bipolar depression: systematic review and meta-analysis. Acta Psychiatr Scand. 2019; 14(2):116-125.
  - *Precision Medicine*. Leanne Williams and Laura Hack. American Psychiatric Association Publishing, 2022.

Depression in patients with hypothyroidism

- Target TSH of around 2 is recommended. 2 case reports of patients with depression and TSH around 3.2 to 3.3: depression improved when thyroid supplementation dose was increased to bring the TSH level to below 2.5 (preferably 2 or lower). The repeat TSH levels were between 1-2 and there was significant improvement in depression and Case 1 was able to lower antidepressant dose without any worsening of depression.
  - Cohen BM et al. Antidepressant-resistant depression in patients with comorbid subclinical hypothyroidism or high normal TSH levels. American Journal of Psychiatry 2018; 175(7):598-604.

ECT as first line treatment

- Severe major depression with psychotic features
- Severe major depression with psychomotor retardation
- “True” treatment resistant major depression
- Rapid relief is needed (e.g., refusal of food intake, severe suicidality)
- Medication contraindicated (e.g., in pregnancy)
- Previous positive response to ECT
- Patients who prefer ECT for a specific reason
  - Espinoza and Kellner. Electroconvulsive therapy. NEJM 2022; 386:667-672.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

ECT as first line treatment

- Also recommended for older adults with high rates of poor outcomes (e.g., severe physical illness).
- Useful for continuation / maintenance therapy.
- ECT if combination of antidepressant and antipsychotic therapy for psychotic depression fails after 4-8 weeks, earlier if combination therapy is poorly tolerated.
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Exercise training

- As adjunct to medication for mild to moderate depression
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Vagal nerve stimulation (VNS) in epilepsy patients

- An option if insufficient response to trials of pharmacotherapy.
- Parameters different than VNS for epilepsy treatment.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Transcranial magnetic stimulation (TMS)

- Recommended if one failed trial with an antidepressant.
- Not recommended if patient has failed ECT trial or there is history of seizures.
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Transcranial magnetic stimulation (TMS)

- Accelerated form of TMS may improve depression within one week.
- TMS is found to ameliorate altered connectivity involving the default mode network.
- Hypoconnectivity within the DMN associated with lack of response to first- and second-line antidepressants.
  - *Precision Medicine*. Leanne Williams and Laura Hack. American Psychiatric Association Publishing, 2022.

Transcranial magnetic stimulation (TMS) in epilepsy patients

- An option if insufficient response to trials of pharmacotherapy.
- Parameters different than for epilepsy treatment.
- Data about safety and efficacy in people with epilepsy and depression are lacking.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Avoid sleep deprivation therapy in epilepsy patients

- Sleep deprivation may trigger seizures.
  - ILAE clinical practice guidelines for the treatment of depression in adults with epilepsy. International League Against Epilepsy. October 2020.

Biomarkers for Major Depression

- 4 proteins: C-Reactive Protein (CRP), antithrombin III (ATIII),vitamin D binding protein (VDP), inter-alpha trypsin heavy chain 4 (IATHC4) correlated with Major depression but not with Schizophrenia or Bipolar disorder.
- Combination of all four had higher specificity for Major Depression and specificity in distinguishing Major Depression from Bipolar disorder.
  - Shi Y et al. Identifying plasma biomarkers with high specificity for major depressive disorder: a multi-level proteomics study. Journal of Affective Disorder 2020.

Biomarkers for Major Depression

- 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Innovative programs

- Lay health counselors (piloted in India)
- Collaborative psychiatric care with a geriatric psychiatrist via telepsychiatry
- Optimizing visit with video conferencing
- Internet based psychotherapy
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.
  - American Psychological Association Clinical Practice Guidelines for Treatment of Depression. 2019.

Parkinson’s disease

- SSRI as first line
- SNRI as second line
- TCAs not tolerated well
- CBT
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Vascular depression / Post-stroke depression

- SSRI as first line (even for hemorrhagic stroke)
- SNRI as second line
- Methylphenidate if apathy is significant
  - 2021 Canadian guidelines for prevention, assessment and treatment of depression among older adults.

Depression in patients with Kidney Disease

- CBT, SSRIs (no controlled data)
- Pharmacist input for adjusting dose of certain antidepressants (e.g., duloxetine)
  - Hedayati SS et al. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. *Kidney International* 2012; 81(3):247-255.
  - Desai and Grossberg. Chapter 5. Major depressive disorder, other mood disorders, and suicide. *Psychiatric Consultation in Long-Term Care: A guide for healthcare professionals*. 2nd Edition. Cambridge University Press. 2017.

Depression in patients with Dementia

- Individualized pleasant activity schedule (IPAS) intervention did better than placebo.
- Antidepressants have not done better than placebo in general.
  - Desai and Grossberg. Chapter 5. Major depressive disorder, other mood disorders, and suicide. *Psychiatric Consultation in Long-Term Care: A guide for healthcare professionals*. 2nd Edition. Cambridge University Press. 2017.

Namaste

Shukriyaa