MANAGEMENT OF DEPRESSION IN THE NURSING HOME

Pharmacotherapy: What to Consider and What to Monitor

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Agenda

- What to Consider
  - Efficacy of antidepressant therapy
  - Which drugs
  - Switching, Combination or Augmentation?
- What to Monitor
  - For efficacy
  - For side-effects

Antidepressants in SNFs

- 2004 National Nursing Home Survey (NNHS) data showed 46.22% (95% CI, 45.16–47.27) of nursing home patients over age 65 were on an antidepressant
- Most antidepressant users were >85 years of age (49.7%), female (75.7%)
- Citalopram (12.92%; 95% CI, 12.21–13.63) was the most prescribed individual antidepressant, followed by mirtazapine (10.19%; 95% CI, 9.55–10.84)

Karkare SU, Bhattacharjee S, Kamble P, Aparasu R. Prevalence and Predictors of Antidepressant Prescribing in Nursing Home Residents in the United States. Am J Geriatr Pharmacother. 2011 Apr. 1;9(2):109-119.

Problems in Evidence-Based Medicine for Antidepressants in Nursing Home Residents

- Very few randomized blinded trials of antidepressants in nursing homes
- The best trials of antidepressant therapies, such as STAR*D, have relatively few elderly participants

Antidepressant Efficacy in the Elderly with depression without Dementia

- Ten trials (4 unpublished) with 2,377 patients who received active drug and 1,788 received placebo met selection criteria – all outpatients > 60 years
- The odds ratio (OR) for response rates with antidepressant and placebo was 1.40 (95% confidence interval [CI] 1.24–1.57, $p < 0.001$)
- OR for remission was 1.27 (CI 1.12–1.44, $p < 0.001$)
- Mean pooled response rates for antidepressant and placebo were 44.4% and 34.7%, respectively → therefore "number needed to treat" [NNT] = 10

Nelson JC, Delucchi K, Schneider LS. Efficacy of second generation antidepressants in late-life depression: a meta-analysis of the evidence. Am J Geriatr Psychiatry. 2008 Jul.;16(7):558-567.

Antidepressant Efficacy in the Elderly with depression & Dementia

- Seven trials with 330 participants met selection criteria - outpatient clinics, inpatient units, residential settings.
- The odds ratio (OR) for six trials reporting response rates with antidepressant and placebo was 2.12 (95% confidence interval (CI) = 0.95-4.70; P=0.07)
- OR for five trials reporting remission rates was 1.97 (95% CI= 0.85–4.55; P=0.11).
- Therefore – no evidence base proving efficacy

Nelson JC, Devanand DP. A Systematic Review and Meta-Analysis of Placebo-Controlled Antidepressant Studies in People with Depression and Dementia. J Am Geriatr Soc. 2011 Mar. 31;59(4):577-585.

“sequenced treatment alternatives to relieve depression” (STAR*D)

- NIH funded, multi-institution study of real world treatment of depression with goal of remission.
- The STAR*D studies found that only 36.8% of patients exhibited remission after treatment with the SSRI, citalopram, and found a cumulative remission rate of 67% after multiple treatments were attempted.

Lessons From STAR*D

- Need for several steps to achieve remission for most patients
- No clear medication "winner" for patients whose depression did not remit after one or more aggressive medication trials
- Both switching and augmenting appeared to be reasonable options when an initial antidepressant treatment failed

Gaynes BN, Warden D, Trivedi MH, Wisniewski SR, Fava M, Rush AJ. What Did STAR*D Teach Us? Results From a Large-Scale, Practical, Clinical Trial for Patients With Depression. Psychiatric Services. 2009 Nov. 1;60(11):1439-1445.

Lessons From STAR*D

- Anxious depressed patients had significantly worse chance of remission with initial (citalopram) treatment and lower chance of remission after switching or augmentation

Fava M, Rush A, Alpert J. Difference in treatment outcome in outpatients with anxious versus nonanxious depression: a STAR* D report. Am J Psychiatry 2008; 165:342–351

- The response rates (47%) and remission rate (28%) after 14 weeks of an SSRI (citalopram) were not significantly different for older adults (approximately 25% of the sample of 2876 was over 51 years of age)

Which Initial Agent?

- No good comparative study suggests one drug better than another

Thakur M, Blazer D. Depression in long-term care. J Am Med Dir Assoc. 2008 Feb. 1;9(2):82-87.

- SNRIs no more efficacious than SSRIs

Schneider LS. Venlafaxine offers no benefit over sertraline and is less well tolerated in depressed nursing home residents. Evidence-Based Mental Health. 2004 May 1;7(2):47-47.

- Choice based on side-effect profile, drug-drug interactions, cost, formulary

Psychotic Depression

- At least one recent randomized controlled trial confirmed that combination therapy with an antipsychotic and antidepressant improved outcomes

Wijkstra J, Burger H, van den Broek WW, Birkenhäger TK, Janzing JGE, Boks MPM, et al. Treatment of unipolar psychotic depression: a randomized, double-blind study comparing imipramine, venlafaxine, and venlafaxine plus quetiapine. Acta Psychiatrica Scandinavica. 2010 Mar.;121(3):190-200.

SSRIs and NSAIDs

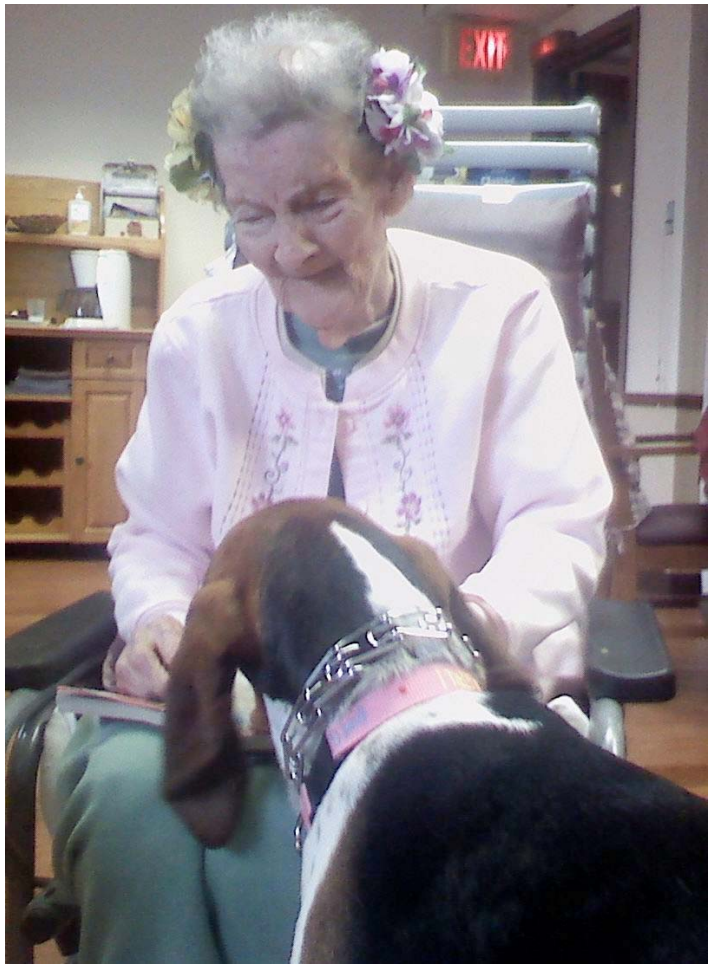
- Antiinflammatory drugs antagonize both biochemical and behavioral responses to selective serotonin reuptake inhibitors.
- Specific to the SSRIs and not a general effect on all classes of anti-depressants
- STAR*D dataset used to determine whether nonsteroidal antiinflammatory drugs (NSAIDs) could play a role in the treatment outcome of depressed individuals taking SSRIs.

Warner-Schmidt JL, Vanover KE, Chen EY, Marshall JJ, Greengard P. Antidepressant effects of selective serotonin reuptake inhibitors (SSRIs) are attenuated by antiinflammatory drugs in mice and humans. Proceedings of the National Academy of Sciences. 2011 Jan. 25;

Regulatory Changes

- In December, 2006, the Centers for Medicare & Medicaid Services (CMS) released an update of its “F329 - Unnecessary Drugs” guidelines for surveyors.
- This added antidepressants as a class of medication to be considered for tapering with a “Gradual dose reduction” (GDR)

Response to Regulatory Changes



- Agree to utility of CONSIDERING GDR for antidepressants, but acknowledging that many require lifetime antidepressant therapy

Long Term Care Professional Leadership Council, American College of Health Care Administrators, American Medical Directors Association, American Society of Consultant Pharmacists, National Association Directors of Nursing Administration/Long Term Care. Use of antidepressants in nursing home residents. A joint statement of the members of the Long Term Care Professional Leadership Council (LTCPLC). Consult Pharm. 2008 Mar.;23(3):231-234.

Monitoring For Efficacy

- MDS incorporating PHQ-9
- GDS
- Cornell
- QIDS

- Sleep, weight, participation in activities, etc.

Monitoring for Side-effects

- Symptoms
  - Suicidality
  - Sedation
  - Dizziness
  - Confusion
  - Anorexia
  - Diarrhea
  - Anything else
- EKG – before TCAs and with titration of TCAs
- BP – especially for SNRIs

Monitoring for Side-effects

- Laboratory Tests
  - CYP genotyping not yet indicated
  - Therapeutic drug monitoring – not yet indicated
  - Baseline work-up for medical causes of depression symptoms likely would include CBC, transaminases, electrolytes, thyroid testing, calcium levels
  - Duloxetine: 1% alanine transaminase (ALT) elevation
    - Consider ALT after starting
  - Monitoring for hyponatremia with SSRIs and SNRIs:

Hyponatremia

- Reported with all SSRIs and SNRIs
- Can be as severe as 110 mmol/L
- Elderly at higher risk
- Risk highest in patients taking diuretics or otherwise volume depleted
- CNS impairments most common effect

- What should be your monitoring strategy?

Hyponatremia

- Prospective study in elderly (using paroxetine)
- 12% incidence of hyponatremia
- Hyponatremia developed a mean of 9 days after paroxetine was started (range 1-14 days). It was not dose related and did not correlate with plasma concentrations of paroxetine.

- Recommendation - before initiating treatment with paroxetine or other SSRIs and at 1 and 2 weeks after initiation of treatment. Recheck if CNS symptoms develop e.g. lethargy, confusion

Arch. Intern. Med. 164[3]:327-32, 2004

Additional Monitoring for Augmentation Drugs

- Antipsychotics
  - Baseline and yearly fasting blood sugar (FBS) or hemoglobin A1c – more often if BMI > 25
  - Consider baseline and yearly lipid panel (total and HDL and LDL cholesterol, triglycerides)
- Lithium
  - Prior to initiation of lithium treatment, the following baseline laboratory data should be assessed: electrolytes, creatinine, and thyroid function (e.g., TSH)
  - Plasma lithium level frequently monitored on initiation, periodic e.g. q6 mos lithium level, Cr, TSH afterwards

Additional Monitoring for Augmentation Drugs

- Divalproex
  - Baseline CBC with platelets, liver enzymes
  - Liver enzymes, CBC with platelets tests should be assessed at one and two months following initiation of divalproex and every 6-12 months afterwards. Coags, Bleeding time if planning surgery.

Consensus Guidelines:

- VPA level**:** 2 levels to establish therapeutic dose – then VPA level "as clinically indicated"
- Every 3 months for one year then annually: LFTs, CBC w/diff and plt.

Ng F et al. The International Society for Bipolar Disorders (ISBD) consensus guidelines for the safety monitoring of bipolar disorder treatments. Bipolar Disorders. 2009;11:559-595.

And now from left field

- Forty-six depressed female nursing home in Pavia, Italy residents with depression, aged 66-95 years
- Two-months, randomized, double-blind, placebo-controlled trial.
- Intervention group received 2.5 g/day of fish oil, with 1.67 grams of EPA and 0.83 grams of DHA
- Geriatric Depression Scale score was 3.2 points lower in treatment group ($p=0.017$)
- SF-36 physical function score significantly better in treatment group ($p<0.001$)

Rondanelli M, Giacosa A, Opizzi A, Pelucchi C, La Vecchia C, Montorfano G, et al. Long chain omega 3 polyunsaturated fatty acids supplementation in the treatment of elderly depression: effects on depressive symptoms, on phospholipids fatty acids profile and on health-related quality of life. J Nutr Health Aging 2011;15(1):37-44.