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Psychiatry and Addictions Case Conference
UW Medicine | Psychiatry and Behavioral Sciences

PROVIDER CONSULTATION LINE:

GOOD QUESTION SERIES

DEPRESSION TREATMENT

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SPEAKER DISCLOSURES

✓ Any conflicts of interest?

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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OBJECTIVES

1. To Review Depression treatment cases from the Provider Consultation Call.
2. Use the cases to develop clinical questions that need to be addressed.
3. Review the evidence base of the clinical questions.

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CASE 1:

83YO F WITH DEPRESSION AND WORSENING KIDNEY FUNCTION

- Patient has a history of depression well-controlled on Venlafaxine ER 150 mg daily for years. She is also on trazodone 50 mg nightly for insomnia, with good results.

- Over time, she had developed chronic kidney disease, now at stage 3b, with substantially lowered creatinine clearance.

- She also has had a 55 lbs unintentional weight loss going from 210 lbs to 155 lbs. She is 5’8”. Overall, she is pleased with it. Extensive workup for this – many labs and tests identify no explanation for the weight loss.

Question: What do you recommend for managing her symptoms?

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CLINICAL QUESTIONS

83YO F WITH DEPRESSION AND WORSENING KIDNEY FUNCTION ON VENLAFAXINE

- What antidepressants do I need to worry about in chronic kidney disease?

- What adjustments in antidepressant treatment do I need to consider in chronic kidney disease?

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ANTIDEPRESSANTS AND CKD

- Antidepressants do not directly harm the kidneys
- Safety concerns emerge
  - Short term SSRI risk
    - Increase risk in upper GI bleeding (platelet function)
    - Hip fracture (bone metabolism)
  - No longer term effect on mortality or CKD progression
  - Mirtazapine
    - Higher risk of mortality (HR, 1.11; 95% CI, 1.00 to 1.22)
  - Starting at a lower than standard dose helped with side effects

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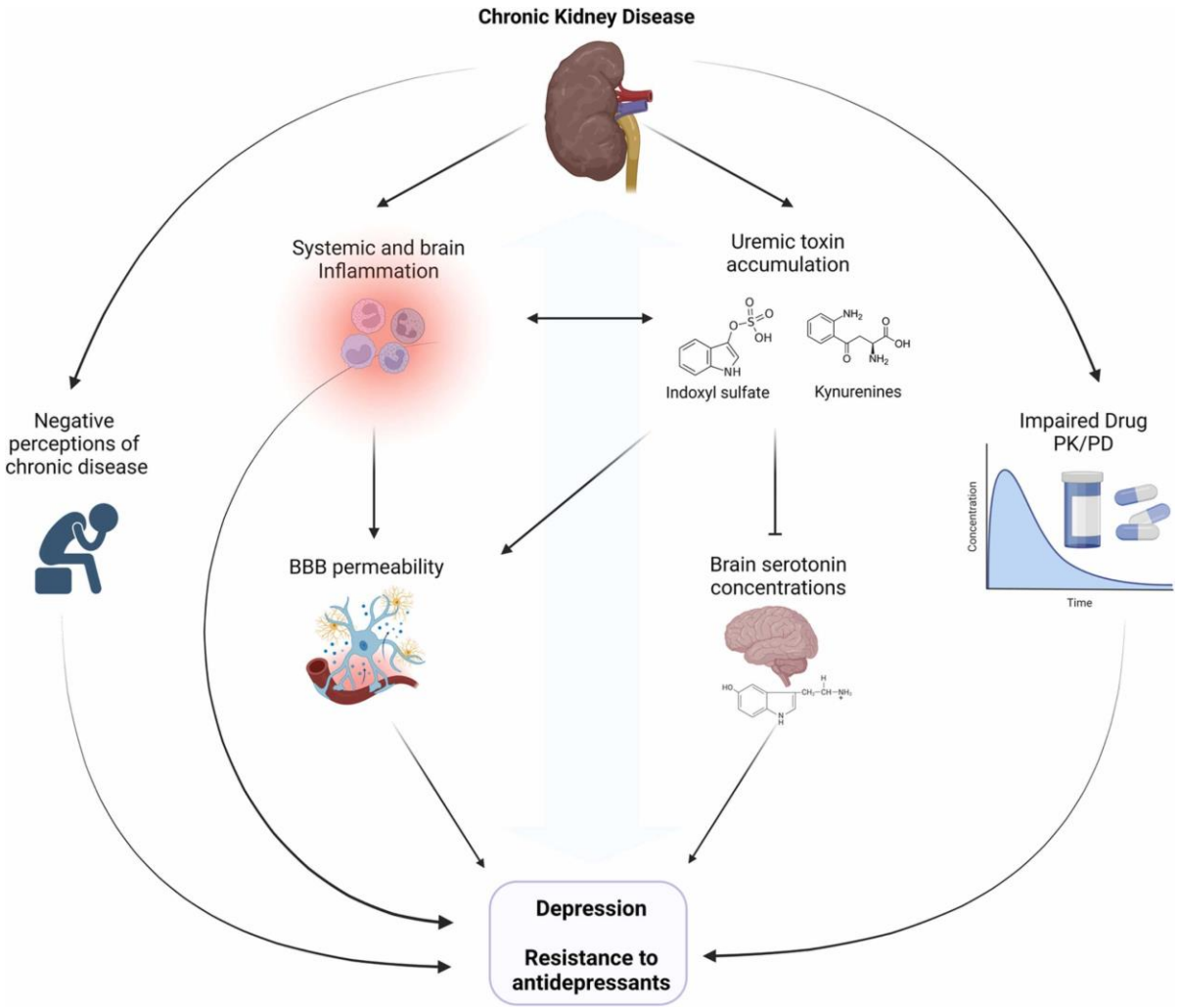
CHRONIC KIDNEY DISEASE & ANTIDEPRESSANTS

- 20% to 25% of patients with CKD have depression.
- SSRIs (sertraline) do not consistently improve depressive symptoms or quality of life vs placebo in patients with non-dialysis CKD
  - Caveat: 12 week study
- Limited efficacy of antidepressants?
  - Uremic toxin accumulation
  - Chronic inflammation
  - Medication adherence



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DOSING AND CKD

- SSRIs
  - Most are renally cleared
  - Reduced renal function→Increased drug exposure/risk of side effects
  - Guideline: start at lowest possible dose and titrate slowly
    - Can reduce risk of bleeding
    - Reduce dose for severe CKD (eGFR < 30/mL/min/1.73m^2)
  - Sertraline: best studied in dialysis with dose ranges 25-200mg
  - Avoid: Paroxetine and fluvoxamine
    - More renally cleared

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DOSING AND CKD

- SNRIs
  - More extensively renally cleared and metabolic products accumulate, increasing the risk for hypertension and other side effects
  - Easier to just avoid
    - Duloxetine: avoid in severe renal impairment
  - If used, keep doses low and monitor for side effects carefully

- Mirtazapine
  - Clearance reduced by 30% in moderate impairment and 50% in severe impairment.
  - Dose reduction required

- Bupropion
  - 80% excretion in urine, active metabolite
  - Dose reduction needed in severe CKD

- **Summary: review need for dosing reductions in chronic kidney disease**

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CASE RECOMMENDATIONS

83YO F WITH DEPRESSION AND WORSENING KIDNEY FUNCTION ON VENLAFAXINE AND UNEXPLAINED WEIGHT LOSS

- Although venlafaxine is first extensively hepatically metabolized, metabolic products are eliminated in the urine, and decreased renal clearance may be causing elevated levels of venlafaxine and metabolites that could possibly be contributing to anorexia.
- It is also true that, CKD aside, hepatic metabolism and overall metabolism slow with age, and people need and tolerate better lower doses of most medications as they age. Seeing how she does on half the dose of venlafaxine seems wise. It could be halved again to 37.5 mg.

CASE 2:

63YO M WITH A RETURN OF DEPRESSIVE SYMPTOMS

- Patient is a 63 year old male patient who has a history of well managed anxiety and depression, who has recently begun to struggle with low mood and amotivation.

- He'd been on Duloxetine 60mg BID and Lexapro 20mg BID for many years. In the context of this recent relapse, you've been discussing medication options with him. A cross taper from Lexapro to Fluoxetine was attempted but the patient felt more restless and experienced intrusive thoughts before self-discontinuing.

- He reports a history of childhood seizure disorder, so he declines a trial of Bupropion. He is also able to recall a prior, failed trial of Citalopram.

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CLINICAL QUESTIONS

63YO M WITH A RETURN OF DEPRESSIVE SYMPTOMS ON BOTH DULOXETINE AND ESCITALOPRAM

- Is there ever a role for two serotonergic meds to treat depression?

- What is the best way to improve this regimen?

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EVIDENCE FOR SSRI+SSRI, SSRI+SNRI OR SNRI+SNRI

- There is no evidence to support these combinations except for a few case reports
- Concern for serotonin syndrome and other side effects has limited the practice

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POTENTIAL RISKS OF REMAINING ON BOTH SNRI AND SSRI

- Serotonin syndrome
  - Exists on a continuum and can present with anxiety, RLS, tremor that leads to more prescribing
  - Can be brought on by the addition of meds that inhibit the metabolism of antidepressants (cimetidine, ketoconazole, erythromycin)
  - While it usually present early in treatment, it can arise later on, especially as patients age and may not be able to clear drug as effectively

RECOMMENDATIONS

63YO M WITH A RETURN OF DEPRESSIVE SYMPTOMS ON BOTH DULOXETINE AND ESCITALOPRAM

- Patient is coming in on this regimen, current PCP did not start it and thus can't speak to efficacy
- Given that he is on very high doses of two serotonergic antidepressants with similar mechanisms of action and is symptomatic, it makes most sense to reduce polypharmacy and try a more evidence-based approach:
- Augmentation with a presynaptic α2-adrenergic antagonist (mirtazapine), second-gen antipsychotic (aripiprazole), lithium or T3, switch to tricyclic (nortriptyline), referral for neuromodulation or ketamine, referral for psychotherapy

CASE 3:
20 YO F WITH H/O ADHD AND DEPRESSION

- Current Meds: Adderall for ADHD and sertraline for depression
- Sertraline 50mg started ~ 2 mo ago for worsening depression, but the patient recently noted that her depression was worsening with some passive SI, and her dosage was increased to 75 mg.
- About a week later, the patient reported feeling very tired and experiencing nightmares since increasing the dose. Her dose has been reduced back down to 50 mg.
- PCP discussed possible med change, patient is interested in something that is more activating, contemplating fluoxetine.
- Recommended cross-taper from sertraline to fluoxetine:
  - Sertraline to be decreased by 25 mg approximately weekly until discontinued
  - Start the fluoxetine (while still on the sertraline) at 10 mg and titrate to 20 mg in approximately a week. The dose can be further titrated to 30 or 40 mg in about a week or two as needed and as tolerated.

CLINICAL QUESTIONS

20 YO F SWITCHING FROM SERTRALINE TO FLUOXETINE FOR DEPRESSION

- What is the best way to switch antidepressants?

SWITCHING ANTIDEPRESSANT MEDICATIONS

- Consider the following:
  - Specific drug properties
    - Adverse effects
    - Elimination half-life (e.g. fluoxetine has long half-life)
    - Pharmacodynamics (how quick will medication take effect)
    - Risk for discontinuation symptoms (e.g. venlafaxine, paroxetine, imipramine)
  - Drug-drug interactions
    - E.g. fluoxetine and paroxetine inhibit CYP2D6, which metabolizes duloxetine and venlafaxine, thus increased the SNRI serum concentrations
  - Relapse of depression

CROSS-TAPERING

- Standard approach (preferred)
- Process:
  - Lower the dose of current antidepressant gradually while concurrently starting new antidepressant
  - Usually done over 1-3 weeks, but might be slower if patient has h/o sensitivity to discontinuation or side effects
- Prevents both discontinuation symptoms and worsening of depressive symptoms (due to drug withdrawal)
- Cross-tapering contraindicated when switching to or from a MAOI

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DIRECT SWITCHING

- Abruptly stopping one medication and starting the new drug at the equivalent dose (can look up approximate dose equivalent tables)
- Consider direct switching when:
  - There are severe adverse reactions
  - Antidepressants are in same/similar class (SSRI to SSRI, SSRI to SNRI)
  - Antidepressant has been used for a relatively short period of time
- Caution:
  - Discontinuation symptoms could be mistaken as adverse side effects of the new drug

RECOMMENDATIONS

20 YO F SWITCHING FROM SERTRALINE TO FLUOXETINE FOR DEPRESSION

- Cross-taper (most often)
- KEEP IT SIMPLE!
  - Take into account how well the patient can follow cross-taper instructions, if too complex consider direct switch
  - Usually make changes week by week (easier to remember compared to lowering doses q3 days), can go faster or slower if needed
  - Write it out for patients
- Case: switching sertraline 50mg to fluoxetine

  1. Cross-taper: Lower sertraline to 25mg for one week and then start fluoxetine 10mg, and then keep titrating up on fluoxetine

  2. Direct switch to fluoxetine 10mg

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QUESTIONS

Provider Consultation Line

Prescribing providers call anytime, 24/7

Non-prescribing providers call Mon-Fri, 8-5 (excluding holidays)

877-WA-PSYCH (877-927-7924)

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