UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

Overview of Strategies to Switch Antidepressants

Background:

Antidepressants have been used for many years to treat mental health conditions such as depression and anxiety (not an all-inclusive list). Several classes of antidepressants exist: tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs) and atypical antidepressants. Their mechanisms are somewhat unique to the class of antidepressant and guide our pharmacologic selection depending on the symptom we are treating. For instance, we use tricyclic antidepressants (TCAs) or serotonin norepinephrine reuptake inhibitors (SNRIs) for neuropathic pain potentially due to their ability to bind to sodium channels and voltage-gated calcium channels, and interfere with the pain pathway through neurotransmitter modulation respectively.[1]

Importance:

Our patients take antidepressants for a myriad of reasons. It is not uncommon in clinical practice to switch between antidepressants, if efficacy is questionable or if trying to target an additional symptom such as neuropathic pain. Palliative care clinicians should be familiar with general strategies used when considering switching antidepressants.

Reference Guides:

You can use the following documents as a *general guide* when considering switching from one antidepressant to another:

- Switching and Stopping Antidepressants. Aust Prescr. 2016 Jun;39(3):76-83.
- Switching Antidepressants: British Columbia Guidelines. 2013

Overview:

- Why switch?
  - Intolerance to first antidepressant (ie. side effect, safety concerns such as QTc)
  - Non-response to first antidepressant for depression or anxiety
  - Targeting new or worsening neuropathic pain
- Common switching strategies:
  - **Taper and switch:**
    - **Without wash-out**: gradually taper the first antidepressant, then start the new antidepressant immediately after discontinuation
    - **With wash-out**: gradually taper the first antidepressant, then start the new antidepressant after 5 half-lives of first antidepressant
      - Most conservative methods of switching, least likely to have withdrawal or drug interactions
      - Not always feasible in palliative care practice given lag time to benefit for antidepressants. It may not be clinically appropriate to "start over" with a new antidepressant
  - **Cross-taper**: Taper the first antidepressant over 1-2 weeks, and start/gradually increase the new antidepressant simultaneously
    - Typically, reduce dose of first antidepressant and start low dose of new antidepressant at same time, continue both for 1-2 weeks, stop first antidepressant and increase new antidepressant to target dose
    - Used in patients with high risk from illness relapse or when targeting symptomatic improvement as quickly as possible
    - Increased risk of drug interactions and adverse effects from combined use of medications
  - **Direct-switch:** stop the first antidepressant and start new antidepressant the next day (typically at "equivalent" dose)
    - This strategy has highest risk for withdrawal, depending on pharmacokinetics of new antidepressant
    - Use of this method when switching within the same class of antidepressant preferred (e.g. SSRI to SSRI)
    - Might be "easiest" for patients at high risk for medication adherence misadventures, so benefit of adherence may outweigh risk of discontinuation syndrome in select clinical scenarios

Antidepressant*	Class	Half-life (hrs)	Dose (mg)[2]
Fluoxetine	SSRI	4-16	40mg
Citalopram	SSRI	1.5	n/a
Escitalopram	SSRI	1.5	20mg
Paroxetine	SSRI	1.0	30-35mg
Sertraline	SSRI	1.1-1.3	100mg
Duloxetine	SNRI	0.5	n/a
Venlafaxine	SNRI	0.6	150mg
Amitriptyline	TCA	0.2-1.9	100-125mg
Nortriptyline	TCA	0.8-2.3	100mg
Bupropion	Atypical	0.8-1.8	~350mg
Mirtazapine	Atypical	0.8-1.6	~45mg
Trazodone	Atypical	0.2-0.4	350-400mg

*MAOIs not included given strict guidelines to be followed;
[2]Doses are approximate based on data sited

- Other considerations:
  - Withdrawal possibility
    - Venlafaxine associated with the most severe withdrawal effects
    - Least likely with fluoxetine, due to long half-life
  - Relapse and exacerbation
    - A risk for relapse and/or exacerbation exists with reduction or cessation of antidepressant
    - Slowly reducing the dose prior to discontinuation reduces risk of relapse of psychiatric symptoms or exacerbation
- **Appropriateness of these strategies depend on the indication for antidepressant use as the approach may differ based on clinical scenario. Consider consulting pharmacist or psychiatry for additional support in complex patient cases.**

References:

1. Basic Clin Pharmacol Toxicol. 2005 Jun; 96(6):399-409.
2. J Affect Disord. 2015 Jul 15; 180:179-184.

CLINICAL PEARL:

When switching from one antidepressant to another, one must consider patient-specific factors and customize the approach based on clinical scenario