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A Case Study Approach: Psychopharmacology for Atypical Antidepressants

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Abstract

Major depression is one of most common mental illnesses affecting 6.7% of American adults each year. Depression leads to disruption in daily lives and life's pleasures accompanied by serious medical problems which may lead to suicide (MHA, 2018). The advance practice psychiatric nurse practitioner must conduct an assessment and workup to rule out disorders such as hypothyroidism, anemia, kidney or renal impairment, cancers, or cardiac illness (Weber & Estes, 2016). Children with a traumatic childhood, particularly those that constitute major setbacks in life are at greater risk for depression later in life. The aim of this paper is to review diagnostic criteria and considerations of psychopharmacology, present a case study to review general indications for prescribing atypical antidepressants. Conclusions and implications for best practices using a case study approach will be addressed.

Key words: antidepressants, psych mental health nurse practitioners,

Introduction

Major depression is one of most common mental illnesses affecting 6.7% of American adults each year. Depression incidence has cost the U.S over $67 billion in direct cost to Medicare resulting in occupational injury and morbidity (Asfaw & Souza, 2012). Depression leads to disruption in daily life and life's pleasures accompanied by serious medical problems which may lead to suicide (MHA, 2018). According to the latest DSM-V, depression does not discriminate. It affects persons from every walk of life including children and the elderly (APA, 2013). Major Depressive Disorder (MDD), also known as Clinical Depression, is characterized by an inescapable and ongoing low mood often accompanied by low self-esteem, loss of interest or pleasure in activities than a person used to find enjoyable (MHA, 2018). The advance practice psychiatric nurse practitioner must conduct an assessment and workup to rule out disorders such as hypothyroidism, anemia, renal impairment, cancers, or cardiac illness (Weber & Estes, 2016). Risk and prognostic factors include temperamental, environmental, genetic and physiological, and course modifiers. Neuroticism, a negative affectivity is a well-established risk factor for the onset of major depressive disorder, and high levels appear to render individuals more likely to develop depressive episodes in response to stressful life events. Children with a traumatic childhood, particularly those that constitute major setbacks in life are at greater risk for depression later in life. First-degree family members of individuals with major depressive disorder have a two to fourfold higher risk than the general population to develop depression. Any major non-mood disorders can increase the risk of developing depression later in

life (APA, 2013). The Food and Drug Administration (FDA) has approved five atypical antidepressants for use in treating depression. These five drugs are Bupropion (Wellbutrin, Forfivo XL, Aplenzin), Mirtazapine (Remeron), Nefazodone (Serzone, Dutonin), Trazodone (Desyrel, Oleptro), and Vortioxetine (Trintellix). The aim of this paper is to discuss and review diagnostic criteria and considerations of psychopharmacology, present a case study, and to review general indications for prescribing atypical antidepressants. Conclusions and implications for best practices using a case study approach will be addressed.

Review of Diagnostic Criteria and Considerations: MDD is an episodic, frequently recurring syndrome requiring five or more criteria to be present for at least two weeks. One of the presenting criteria must be either persistent depressed mood or pervasive anhedonia. Other symptoms can include sleep disturbance, appetite loss or gain, weight loss or gain, fatigue, psychomotor retardation, or agitation including feelings of worthlessness or thoughts of suicide (DSM-5). The DSM-5 includes a note indicating to not include symptoms that are clearly attributable to another medical condition. Coding and recording procedures according to the DSM-5 indicates that for recurrent moderate episode (incomplete sentence/thought) 296.32 (F33.1) (APA, 2013).

Neurobiology: The understanding of the neurobiology of depression has been evolving and changing over the last decade. In the classic monoamine theory of depression, the emphasis was on a decadency of norepinephrine (NE, serotonin (5HT), and dopamine (DA). Although this theory corresponds to the use of current antidepressant, there is little data to support it and some research results give conflicting evidence (Stahl, 2013; Cogburn, 2018). This theory has been supplemented with a more complicated view that involves how the neurotransmitter symptom regulates information processes in key areas of the neurological system related to symptoms of depression (Stahl, 2013).

Assessment and Screening: According to Weber and Estes (2016), screening and assessment for persons suspected of depressive mood or probable diagnosis of depression must go through a workup to exclude other disorders and possible illnesses. In addition to a work-up, the clinician can use the Mood Disorder Questionnaire (MDQ), an important screen tool which can help the clinical rule out depressive disorder or bipolar disorder. The MDQ can help the provider form a differentiation as to whether the patient has had prior hypomania or manic episodes which may indicate bipolar disorder. Another screening tool is the Patient Health Questionnaire (PHQ-9) and the Center for Epidemiological Studies Depression Scale (CEDS). Both have been used in primary care to screen for depression and other mood disorders and can be used in the waiting room. Both are useful as screening tools but should not be used for diagnostic purposes. When the clinician chooses tools for diagnostic purposes, the tools should be reliable and valid such as the Beck Depression Inventory and the Inventory Depressive Symptomatology (IDS) and Self Report. These have been used to assist he clinician to diagnose and manage progress of treatment (Weber & Estes, 2016).

Another major responsibility of the clinician is screening for the presence of suicidality and level or severity of risk of suicide. The Substance Abuse and Mental Health Services Administration (SAMHSA, 2018) has developed a five-step suicide assessment, evaluation, and triage method to identify both risk and protective factors. The Suicide assessment Five-Step Evaluation and Triage, SAFE-T Assessment of Suicide risk includes: 1) identify risk factors; 2) identify protective factors; 3) conduct suicide inquiry; 4) determine risk or level of intervention, and 5) documentation (Weber & Estes, 2016, p.899).

Children and the elderly are the most vulnerable when it comes to depression with increased risks of suicide. Cautions exist for the use of SSRI's in children or teenagers with suicidal depression. As these patient begin to improve with treatment, there is an increased risk of the act of suicide due to an increase in physical energy (as cited in Weber & Estes, p. 909).

Case Study

Ms. T. is a 69-year-old African American woman who is recently divorced with five children and over 30 grandchildren. She was employed by a

*telecommunication company for over 20 years and now enjoyed retirement. Her hobbies include going to nearby casinos to gamble four times a week with friends. She takes her retirement check and exhausts it all on gambling, leaving no money for personal items or to pay her bills. She lives with her mother in a rural community. In the last 6 weeks, her oldest daughter noticed that Ms. T does not want to go gambling anymore and she is often very sad and uninterested in hanging out with friends. The daughter decided to bring her to a therapist. The waiting room assessment tool was used to screen for any possible behaviors that would warrant further evaluation. A suicide screen tool was used to assess risk of suicidal level and safety. Denies any recent losses or deaths in family. Patient denied suicidal thoughts. Daughter reports dry and irritated skin to lower legs, vital signs: BP 120/82, HR 80, RR 12, Temp. 98.2*F, weight 265 lbs. Allergies: NKDA.*

Upon interviewing Ms. T. and her daughter indicated that for the last month her mother has been very tired, staying in her room on most days, disinterested in her normal routines or hobbies, neglecting hygiene, and exhibiting an increased appetite. The patient responds to yes or no answers and her head is face down to the floor most of the session. Patient denies pain or SOB. Her past medical history is without significant falls, head injury, heart/respiratory conditions. Patient has no known drug allergies. Upon mini-mental (Mini-Cog): Appearance: Hair unkept, clean today (daughter stated that earlier she gave her a bath) and dressed in pants and t-shirt. She described her mood as being down and out. Her affect was flat. Memory, language, attention and executive functioning were intact. Her old records revealed that she had a prior diagnosis of MDD and upon asking the daughter regarding her mother's past history she indicated that her momma was overweight, irritable, and low libido.

Old records indicated she had been previously treated for depression with bupropion. Ruled out disorders such as hypothyroidism, anemia, renal impairment, cancers, or cardiac illness. Patient reported a rash with use of bupropion. Today's visit labs reveal chemistry levels within normal limits, Complete blood count (CBC) within normal limits, cholesterol within normal limits, and glucose within normal limits. Body mass index greater than 24 with a fasting blood sugar of 112 mg/dl. Liver function studies within normal limits, Bilirubin Urea Nitrates (BUN) and creatinine within normal limits. Denies suicidal attempts or thinking in past or currently. Labs: TSH, T4, T3 all within normal ranges. Other labs: patient screen for cancer was negative.

Review of General Indications

Mirtazapine (Remeron) is Food and Drug Administration (FDA) approved for Major Depressive Disorder (MDD). Off-label uses may include Panic Disorder, Generalized (GAD) and Posttraumatic Stress Disorder (PTSD). Mirtazapine leads to rapid and sustained improvement in depressive symptoms and is effective in subgroups of depressed patients, particularly anxious patients, those with melancholic depression, treatment-resistant depression, geriatric depression, depression, anxiety associated with alcohol dependence, and agitated elderly patients. Mirtazapine has a range of clinically useful applications including improving sleep, antiemesis, appetite improvement, management of pain, and weight gain (Alam, Voronovich, & Carley, 2013). A snap shot (overview) of atypical antidepressants drugs, developed by Potter (2018) are provided in Table 1. 1. It provides information on drug class, generic name, brand name, mechanism of action, FDA approved indications and off-label indications, dosing, side effects including black box warnings, special populations' precautions, and drug interactions.

According to Stahl (2017), Mirtazapine boosts noradrenergic neurotransmission, blocks alpha 2 adrenergic presynaptic receptors, increases serotonin neurotransmission, and blocks 5HT2C, 5HT3, and histamine 1 receptors. Indications for this drug includes MDD, Seasonal affective disorder, Nicotine addiction, Bipolar Disorder, Attentional Deficit Hyperactivity Disorder (ADHD), and sexual disorders (Stahl, 2017). This medication was chosen to treat Ms. T with because of it side effect profile. Out of all the other atypical antidepressants, Mirtazapine was found to have a unique mechanism and a smaller adverse reaction profile than some of the other atypical antidepressant options.

The advanced practice nurse may also consider and integrative approach to managing major depressive

symptoms. Integrative Medicine (IM) is an intervention that combines conventional medicine with alternative modalities that have been shown to be safe and effective (www.cancer.gov). An integrative approach to treat MDD may be better tolerated by the older adult. For example, an older adult is more likely to present with other underlying comorbidities, a long history of adverse effects from previously prescribed conventional medicines, and chronic psychosocial factors (Lill, 2015). Due to these potential complications that may not respond to medication alone, it would be prudent for the nurse practitioner to at least consider an integrative treatment approach, including pharmacological and non-pharmacological intervention when assessing.

Lake (2004) addresses the efficacy of IM in treating MDD, and supports the view that combining conventional antidepressants with certain non-conventional therapies improves mood at a more rapid rate than either treatment modality used alone. Non-conventional interventions that have been used in combination with antidepressants include but are not limited to: exercise, nutrition, and mind/body techniques such as general relaxation practices. A study by Thirthalli et al. (2013) explored the role of yoga in treating depression. The design of Thirthalli's study consisted of three groups (yoga alone, yoga along with antidepressant medication and antidepressant medication alone. Findings support that yoga may act at the level of the hypothalamus by its 'anti-stress' effects (reducing cortisol levels), to bring about relief in depression. The nurse practitioner and patient should agree on an integrative approach that best fits the patient's lifestyle. Desired outcomes are to promote health and recovery while reducing the adverse effects of pharmacological treatment alone. The nurse practitioner should educate the patient about potential drug-natural product interactions. For example, Mirtazapine is reported to interact with natural products such as kava-kave, valerian root, chamomile or hops, resulting in an increase CNS depression. There is also the potential for an increase serotonin syndrome if taken with St. John's Wort (Stahl, 2017). Most natural or herbal products are not subject to FDA guidelines for safe and efficacious use.

Conclusions and Implications for Advanced Practiced Registered Nurses (APRNs) : Based on review of the case study presented above, and after ruling out Bipolar and other psychiatric disorders along with anemia, and suicidality, Ms. T. was started on Mirtazapine 15 mg by mouth every night. The rationale for prescribing Mirtazapine is that it's reported safe for long-term use and not habit forming. Mirtazapine is reported to be tolerated better than Bupropion by study participants (Stahl, 2017). In the above case study, the patient presented to the clinic with an existing raised generalized rash to her skin. Bupropion and Mirtazapine has a warning of potential for Steven's Johnston Syndrome (Stahl, 2017) and would therefore not be recommended for this individual. Mirtazapine may cause some notable side effects to include the lowering of white blood cell count, an increase in cholesterol, and photosensitivity. (Weight gain is also a very common side effect of Mirtazapine and of potential relevance given weight gain cited as one of the side effects that led to the discontinuation of bupropion and patient's current high BMI. Bupropion is more commonly associated with weight loss (Stahl, 2017). Patient/family education should include information on these and other potential side effects. The nurse should clearly explain skin protective measures, the importance of checking weekly labs (CBC, LDL & HDL cholesterol, triglycerides, liver function studies, glucose) and monitor body mass index (BMI). During every follow up visit, the nurse will also screen for any suicidal ideation. Assessing for suicidal ideation is the single most important concern in evaluating a person (Lake, 2004). As psychiatric mental health nurse practitioners, it is critical that we understand and know depression as one of the most commonly diagnosed and debilitating illness in the United States (US) (AADD, 2018; NIH, 2018), where it afflicts over 300 million people world-wide (WHO, 2018). It is also essential for the PMHNPs to understand the role of genetics, biological make-up, environment, and psychological factors impacting the predisposition of depression (NIH, 2018).

Class Atypical Antidepressants	**Generic Agent**	**Brand Name(s)**	**MOA**	**Indications** *FDA	**Dosing**	**SE/ADR/BBW**	**Drug-Interactions**
Dopamine reuptake inhibitor & releaser, NDRI (NE DA reuptake inhibitor	1.Bupropion	Wellbutrin Forfivo XL, Aplenzin	Boosts neurotransmitters NE & DA, blocks NE reuptake pump increasing NE neurotransmission, blocks DA reuptake increasing DA neurotransmission,	***MDD, *Seasonal affective disorder, *Nicotine addiction,** Bipolar, ADHD, Sexual disorders	225-450 mg in 3 divided doses *SR* 200-445mg in 2 divided doses *XL* 150mg, 300mg, 450mg *hydrobromide ER* 174 mg, 378mg, 522 mg	Dry mouth, constipation, nausea, weight loss, anorexia, tremor, HA, constipation, sweating, Abd. Pain, HTN, rash, rare Seizures, Steven-Johnston Syndrome, Hypomania, rare Suicidal ideation	Tramadol, MAOIs, Fluoxetine, SSRIs, Warfarin CYP450 2D6, CYP450 3A4 inhibition, Haldol, general anesthetics, HTN increases with nicotine TCAs, Lithium, Levodopa Zyban HX Seizures, Thioridazine Proven allergy to Bupropion
serotonin, NE receptor antagonist, Alpha 2 antagonist, NaSSA (noradrenaline & specific serotonergic agent)	2.Mirtazapine	Remeron	boosts neurotransmitters 5HT & NE, blocks alpha 2 adrenergic presynaptic receptor, increases 5HT neurotransmission, blocks 5HT2C, 5HT3, & H1 receptors	***MDD** PD, GAD, PTSD	15-45 mg at HS	Low WBC, photosensitivity, Avoid Alcohol, Risk2Benefits 4Children, Possible activating SEs, Suicidal iieeatin4Children & Adolescents, *Avoid* if known allergy-Remeron	MAOIs, Tramadol, may cause SS
serotonin receptor antagonist, SARI	3.Nefazodone	Dutononin, Serzone	blocks serotonin 2A receptors potently, blocks serotonin reuptake pump and NE reuptake pump	***Depression**, PD, PTSD	300-600mg/d	Hepatotoxicity, HX Seizures, Fetal SS, Risk2Benefits 4Children, Possible activating SEs, Suicide, Cardiac Problems Elderly Hepatic & Renal	Tramadol, MAOIs, Fluoxetine, SSRIs, Warfarin CYP450 2D6, CYP450 3A4 inhibition, Haldol, general anesthetics
serotonin receptor antagonist (S-MM), SARI	4.Trazodone	Oleptro Desyrel	blocks 2A receptors, blobs serotonin reuptake pump	***Depression**, insomnia (primary/secondary), anxiety	150-600mg/d 150-375 mg/d ER	N/V/, edema, blurred vision, dry mouth, constipation, dizziness, sedation, fatigue, HA, incoordination, tremor, syncope, rare rash, sinus bradycardia (long-term)	Tramadol, MAOIs, Fluoxetine, SSRIs, Warfarin
serotonin multimodal (S-MM), Multimodal antidepressant	5.Vortioxetine	Trintellix	increases release of several neurotransmitters: serotonin, NE, DA, Glutamate, Acetylcholine, Histamine	***MDD** GAD, Cognitive S/S of Depression, Geriatric depression	5-20 mg/d	N/V, constipation, sexual dysfunction, rare seizures, rare mania & SI	Tramadol, MAOIs, CYP450 2D6,, Warfarin, NSAIDS

Table 1.1. Psychopharmacology for Atypical Antidepressants

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