Review Article

Major Depression Disorder in Adults: A Review of Antidepressants

Danita R. Potter, PhD, RN
Professor, Program Director, College of Nursing, Northwestern State University, Shreveport, LA.

Correspondence: Danita R. Potter, PhD, Professor, Program Director, College of Nursing, Northwestern State University, Shreveport, LA. E-mail: potterd@nsula.edu drpotter41@yahoo.com

Abstract

Depression is one of the most commonly diagnosed and debilitating illness in the United States (US) (AADD, 2018; NIH, 2018) and it afflicts over 300 million people around the world (WHO, 2018). Though genetics, biological make-up, environment, and psychological factors play a role in the predisposition of depression, it crosses all ages, racial/ethnic groups, and socioeconomical status (NIH, 2018). Depression incidence has cost the U.S over 67 billion in direct cost of Medicare resulting in occupational injury and morbidity (Asfaw & Souza, 2012). Although patients experience many recurrent episodes, Major Depressive Disorder (MDD) is the "most common mood disorder having at least one single major depressive episode" (Stahl, p. 239). the purpose of this paper is to discuss and review current drugs and treatment for MDD.

Key words: major depression, depression in adults, antidepressants, psych mental health nurse practitioners

Introduction

Depression is one of the most commonly diagnosed and debilitating illness in the United States (US) (AADD, 2018; NIH, 2018) and it afflicts over 300 million people around the world (WHO, 2018). Though genetics, biological make-up, environment, and psychological factors play a role in the predisposition of depression, it crosses all ages, racial/ethnic groups, and socioeconomical status (NIH, 2018). Depression incidence has cost the U.S over 67 billion in direct cost of Medicare resulting in occupational injury and morbidity (Asfaw & Souza, 2012). Persons with depression have significant functional impairment including cognitive, emotional, and physical resulting from "dysregulation of interacting neural networks involving prefrontal cortex, amygdala, hippocampus, anterior cingulate cortex, and basal ganglia" (Richardson & Adams, 2018, p. 439). Depression leads to a lack of enjoyment of life which including mood disorders in emotional cognitive behavioral, or somatic regulation (Stahl, 2017). Although patients experience many recurrent episodes, Major Depressive Disorder (MDD) is the "most common mood disorder having at least one single major depressive episode" (Stahl, p. 239). For the purpose of this assignment, MDD and drugs for its treatment are discussed below.

Review of Diagnostic Criteria and Considerations

According to DSM-5 (2017) diagnostic criteria, MDD requires five or more of the following symptoms during the same two-week period and represent a change from previous functioning; at least one symptoms is either 1) depressed mood or 2) loss of interest or pleasure. The symptoms consist of depression mood most of the day, nearly every day, as indicated by either subject report such as felling sad, empty, hopeless or observation made by others such as appears tearful or irritable mood in children or adolescents. Markedly diminished interest or pleasure in all, or almost tall, activities most of the day. Significant weight loss

when not dieting or weigh gain or decrease or increase in appetite early every day. Insomnia or hypersomnia nearly every day. Psychomotor agitation or retardation nearly every day. Fatigue or loss of energy nearly every day. Feelings of worthlessness or excessive or inappropriate guilt nearly every day. Diminished ability to think or concentrate, or indecisiveness, nearly every day. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide (DSM-5, 2017). Early optimal and rapid pharmacological treatment without delay is recommended with MDD. This type of approach would not only consider the start low and go slow approach to pharmacology, but also include screening as an essential first step in optimizing treatment (Oluboka et al., 2017).

Review of General Indications

General drug indications for depression includes antidepressants namely tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), dopaminergic norepinephrine reuptake inhibitors (DNRIs), and atypical antidepressants. Depression, a complex illness involving more than "simple replacement of insufficient neurotransmitters", thus there is common conceptualization regarding serotonin and/or norepinephrine (NE) (Higgins & George, 2013, p. 252).

The five drugs chosen for this paper includes Celexa (Citalopram), Lexapro (Escitalopram), Prozac (Fluoxetine), Paxil (Paroxetine), and Zoloft (Sertraline). SSRIs are potent antidepressants used to treat both anxiety and depression symptoms. General principles of antidepressants include improvement of symptoms by 50% and the inhibition of serotonin reuptake, whereby when an SSRI is given 5HT rises due to blockade of serotonin transporter (SERT). SSRIs specifically block the presynaptic serotonin reuptake and allowing for serotonin in the synapses (Stahl, 2013).

Celexa (Citalopram) is an SSRI approved by Food and Drug Administration (FDA) for depression and it is also used off label for premenstrual dysphoric disorder (PDD), obsessive-compulsive disorder (OCD), panic disorder, generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), and social anxiety disorder (Stahl, 2017). Onset of therapeutic actions is usually not immediate but are often delayed 2-4 weeks. Celexa works by boosting the neurotransmitter serotonin, blocking serotonin reuptake pump, desensitizes serotonin receptors, and increases serotonergic neurotransmission. Dose and use includes 20-40 mg per day and dosage forms include tablets, orally disintegrating tablet, and capsule. Tablets can be prescribed as 10 mg, 20 mg, and 40 mg scored. Capsule form can be prescribed as 10mg, 20 mg, 40 mg.

Notable side effects include sexual dysfunction such as delayed ejaculation, erectile dysfunction, and decrease sexual desire in both men and women. Other side effects include activation, gastrointestinal problems, insomnia, sedation, agitation, tremors, headache, dizziness, sweating, bruising, rare hyponatremia, and syndrome of inappropriate antidiuretic hormone secretion (SIADH). Weight gain has been reported but is not likely. Sedation occurs in significant minority. Best augmenting agents for its side effects consists of trying anther SSRI r another antidepressant monotherapy prior to resorting to augmentation approaches. Overdose is rare and it is safe for long-term use. Tape no usually necessary, but it is prudent to avoid withdrawal reactions. Drug interactions include tramadol which increases the risk of seizures in patients taking an antidepressant. It may increase TCA levels so use with caution with TCAs. Celexa is comprised of two enantiomers, R and S, mirror images of each other. Some of the pros, according to Cogburn's (2018) lecture and Stahl (2013), Celexa has a low inhibition of p450 enzymes meaning that it has few drug to drug interactions resulting in being safer for the liver. It has intermediate half life and it is similar to Lexapro (Escitalopram) by it is half as potent. Some of the Cons include dose-dependent OT interval prolongation with does of 10-30 mg daily due to risk of doses of greater than 40 mg per day not recommended. Celexa can be sedating due to its mild antagonism at H1 Histamine receptor. Additionally, it has side effects including gastrointestinal effects such as nausea and vomiting, but less than Zoloft (Sertraline). Some special population considerations include renal, hepatic, cardiac, elderly, children and adolescent

groups. Those with renal impairment do not require dose adjustment for mild to moderate impairment but use caution for those with severe impairment.

Hepatic impairment should be used at doses higher than 20 mg per day. Patients with hear problems may cause abnormal heart changes in electrical activity with dose higher than 40 mg/day, thus treating patients with SSRIs with acute mania or recent heart attack may improve survival rates and mood. Some of the drug can be found in breast mild (trace amounts). Patients and healthcare providers must weigh the benefits of breast feeding with risks and benefits of antidepressant treatment versus the nontreatment to both infant and mother (Stahl, 2017).

Lexapro (Escitalopram) is an SSRI that is more effective than Celexa (Citalopram). Lexapro is FDA approved for MDD (ages 12 and up) and generalized anxiety disorder (GAD). It is also used off label for OCD, PTSD, social phobias, premenstrual dysphoric disorder. It works by boosts neurotransmitter serotonin blocks serotonin reuptake pump, desensitizes serotonin receptors, and presumably increase serotonergic neurotransmission. When it doesn't work, Stahl (2017) suggests considering increasing the doses, switch to another agent or adding an appropriate augmenting agent, consider psychotherapy, consider evaluation for another diagnosis for possible comorbid condition. For dosage using 10-20 mg per day. Dosage forms include tablets (5mg, 10mg, 20 mg), capsule (5mg, 10 mg, 20 mg), and oral solution (5mg/5 ml). Does initially with 10 mg/day, increase to 20 mg/day if necessary; single dose administration morning or evening.

According to Stahl (2017) there are no test for healthy individuals. Best augmentation if often with another SSRI or another antidepressant monotherapy prior to resorting to augmentation. Notable side effects include sexual dysfunction, gastrointestinal disturbances, insomnia, sedation, agitation, tremor, eating, bruising, SIADH. For overdose, though few are reported, symptoms associated are vomiting, sedation, heart rhythm disturbances, dizziness, tremor, amnesia, confusion, coma, convulsions. Pros consist of low overall inhibition of P450 enzymes leading to fewer drug to drug interactions, intermediate half-life, and more effective in acute response and remission than Celexa (Citalopram). Other pros include that it is not habit forming and safe for long-term use (Stahl, 2017 p.253).

Special populations considerations include renal impairment, hepatic impairment, and cardiac impairment. Those with renal impairment caution with severe renal impairment. The recommended dose for those persons with hepatic impairment is 10 mg/day. Persons with cardiac problems consider evaluate systematically for cardiac problems, its safe with heart problems, and treatment with this drug helps reduce risk and improve survival following heart attack. For children and adolescents, Celexa is approved for depression ages 12-17 and caution to weigh the risks and benefits against risks and benefits of non-treatment. Also, monitor children/adolescents face to face regularly particularly during first several weeks of treatment (Stahl, 2017, 254). Effective June 2015, the US FDA required changes to content and formal pregnancy and lactation information (some drug is found in breast milk) on drug labels including elimination of pregnancy categories. Cons include dose-dependent QT interval prolongation with doses of 10-30 mg daily and nausea and headache. According to Stahl (2013) the solution to improving the properties of racemic drug is to the removal of the unwanted R enantiomer, resulting in Lexapro (Escitalopram). This maneuver appears to remove the antihistaminic properties. Lexapro is the SSRI for which pure SERT inhibition is mot likely to explain almost all of its pharmacological actions and is considered the best tolerated.

Prozac (Fluoxetine) has 5HT2c antagonist actions which may explain many of its unique clinical properties. In addition to the blocking of serotonin action at receptors, Prozac (Fluoxetine) disinhibits the release of both norepinephrine (NE) and dopamine (DA) contributing to its tolerable profile (Stahl, 2013). Cons of this SSRI include a long half-life so decreased incidence of discontinuation syndrome and its good for patient with compliance issues. Prozac brad names include Prozac, Prozac weekly, and Sarafem. It is available in generic form. Dosing and use include 20-40 mg for depression and anxiety disorders; and 60-80 mg for bulimia. Dose forms are capsules (10mg, 20 mg, 40 mg, 60 mg), tablet 10 mg, liquid 20 mg/5ml-

120 ml bottles, and weekly capsule of 90 mg. It is FDA approved for MDD (ages 8 and older), OCD, premenstrual dysphoric disorder, bulimia, bipolar depression, and treatment -resistant depression. It is also used off label for social anxiety disorder, and PTSD. Side effects include sexual dysfunction such as delayed ejaculation, erectile dysfunction, decreased sexual desire in men and women, gastrointestinal disturbances insomnia, sedation, tremors, headaches, dizziness, sweating, bruising, and SIADH. Weight gain and sedation have been reported, but not expected. Special population considerations include renal, hepatic, cardiac impairment, elderly and children/adolescents. There are no dose adjustments for renal impairment, but for hepatic impairment use lower dose or administer less frequently, and for cardiac impairment Prozac is safe. Elderly patient may tolerate lower doses better and reduction in the risk of suicide with antidepressants compared to placebo in those 65 or older (Stahl, 2017). Prozac (Fluoxetine) has pros and cons due to its unique antagonist actions and clinical properties. According to Cogburn (2018), Prozac (Fluoxetine) initially increases energy levels as a pro, thus Stahl (2013) suggested that for patients who already have agitation problems, the 5HT2c antagonism can be activating contributing to more agitation, insomnia, and anxiety. Other cons include long half-life and active metabolite may build up which may warrant precautions in persons with hepatic illnesses, significant P450 interactions so this would be caution with person on multiple medications, initial activation which may increase anxiety and insomnia, and more like to induce mania than some of the other SSRIs.

Paxil (Paroxetine) is an SSRI with muscarinic anticholinergic and norepinephrine transporter (NET) inhibitory actions. This drug with its calming and sedating effects is preferred by clinicians for patient with anxiety symptoms. Paxil (Paroxetine) inhibits the enzyme nitric oxide synthetase, which theoretically is responsible for male sexual dysfunction's. Paxil is known for causing "withdrawal reaction upon sudden discontinuation symptoms" these can include akathisia, restlessness, gastrointestinal problems, dizziness, and tingling. (Stahl, 2013, 299). Healthcare provider (HCP) may consider the controlled release formulation to off-set its side effects. Paxil (Paroxetine) is available in Paxil and Paxil CR, which FDA approved and are commonly prescribed for MDD, OCD, Panic disorder, social anxiety disorder, posttraumatic stress disorder (PTD), generalized anxiety disorder (GAD), premenstrual dysphoric disorder (PMDD) and vasomotor symptoms (Stahl, 2017). Paxil (Paroxetine) works by boosting the neurotransmitter serotonin blocks serotonin reuptake pump, desensitizes serotine receptors, increase serotonergic neurotransmission has mild anticholinergic cations, and mid norepinephrine actions. Dose for depression 20-50 mg and 7.5 mg at bedtime for vasomotor symptoms.

Notable side effects include sexual dysfunction such as delayed ejaculation, erectile dysfunction in men and women, and decreased sexual desire (Stahl, 2017, p. 562). Other side effects include weight gain, activation, autonomic, bruising/bleeding, and syndrome of inappropriate antidiuretic hormone secretion (SIADH). Some life-threatening side effects include rare seizures, rare induction of mania, and rare activation of suicidality. Special population consideration according to Stahl (2017), consider lower doses, risk of SIADH, and reduction in the risk of suicidality in persons 65 and older. In children and adolescents carefully weight risks and benefits of pharmacological treatment against risk and benefits of non-treatment, monitor face to face regularly, use with caution monitoring for suicidal ideation (Stahl 2017, 565). There are tests for Paxil. Paxil (Paroxetine) has both pros and cons. Pros include short half-life with no active metabolites meaning there is no build-up. Paxil (Paroxetine) has sedating properties which offers initial relief from anxiety and insomnia. Some cons of the drug include significant CYP2D6 inhibition, sedation, weight gain and anticholinergic effects. Paxil (Paroxetine) is likely to cause a discontinuation syndrome (Cogburn, 2018).

Zoloft (Sertraline) is another SSRI used to treat depression. This drug has two candidate mechanisms that distinguishes it: Dopamine transporter (DAT) inhibition and sigma-1 receptor binding. A favorite combination of clinicians is to add bupropion to sertraline sometimes called "Welloft" (Stahl, 2013, p. 298). It works by boosting the neurotransmitter serotonin, blocks the serotonin reuptake pump, desensitizes serotonin

receptors (especially serotonin 1A receptors), increases serotonergic neurotransmission. It also has some ability to block dopamine reuptake pump which could increase dopamine neurotransmission and contribute to its therapeutic actions Zoloft also bind with sigma 1 receptors. Dosing of Zoloft include 50-200 mg per day and its available in 25 mg, 50 mg, and 100 mg scored tablets. It is FDA approved for MDD, PMDD, Panic disorder, PTSD, social anxiety disorder. It is also used off label for generalized anxiety disorder. Indications include obsessive-compulsive disorder (OCD) and depression. Rarely lethal in monotherapy overdose and it is safe for long-term use. To discontinue the medication, taper to avoid withdrawal effects such as dizziness, nausea, stomach cramps.

Drug interactions include tramadol, increase TCA levels when using or switching from other TCAs, caution can cause fatal "serotonin syndrome", don't start an MAOI for at least 5 to 7 days), NSAIDs may impair its effectiveness, possible increase bleeding when combined with NSAIDS or warfarin (Stahl, 2017). There are some notable side effects with Zoloft and these include sexual dysfunction, gastrointestinal constipation, dry mouth, tremors, bruising, bleeding, SIADH, seating, hyponatremia. Some life threating side effects include rare seizures, rare induction of mania, rare activation of suicidal ideation and suicidality, weight gain and sedation are reported, but these not expected. Special population consideration includes low doses, risk of SIADH and reduction in risks of sociality for persons 65 and older. Also consider changes for persons with renal (no dose adjustment) and hepatic impairments use It has both pros and cons. Pros include very week P450 interactions with only sight CYP2D6, short half-life with lower build-up of metabolites, and less sedating when compared to Paxil (Paroxetine). Cons include maximum absorption which requires a full stomach, up to 50% difference and increased number of gastrointestinal adverse drug reactions (Cogburn, 2018).

Medication used to treatment of depression include antidepressants, which are used most common in severe depression. Serotonin Reuptake Inhibitors (SSRIs) are typically the first -line of treatment of moderate to severe depression. SSRIs alter a chemical messenger (serotonin) in the brain. They are proven effective and carry fewer risk of side effects than other medication used to treatment of depression Tricyclic antidepressant are generally referred to as older antidepressants used if other types of medication has failed. Monoamine oxidase inhibitors referred to as older antidepressants that have unique dietary demands (Stahl, 2017).

Conclusions and Implications for Advance Practice Registered Nurses (APRNs)

APRNS care for pivotal in caring for persons afflicted with MDD. Patients treated for MDD are seen in a variety of healthcare settings including inpatient, outpatient, and community settings. Knowledge regarding neurobiology, and medications can help patients and families deal with the cognition, physical, and emotional impairments in a comprehensive way such as understanding that a low 5hR has a negative impact on cognition function. In order to improve patients overall functional capacity, APRNs should assesses in all patients presenting with depression (Richardson & Adams, 2018). A recent study analyzed screening tests used for depression include screening for depression and any cognitive symptoms or deficits of depression the Mini-Cog use to assess cognition when screening for dementia takes 2-3 minutes to complete and is often used in primary care settings. Other lengthy screening tools are not practical in primary settings (Richardson & Adams, 2018). In caring of adolescents, one consideration was that essential assessment tools need to be geared toward children (Kwaunpanomporn et al, 2017). O'Conner, Rossom, Henninger et al. (2016) suggested that early screenings are critical steps in successfully treating adults with depression and prevent apathy and further deterioration.

References

Anxiety and Depression Association of America (2018). *Major Depression Disorder*. https://adaa.org/understanding-anxiety/depression

Arnow, B A., (2013). The relationship between the therapeutic alliance and treatment outcome in two distinct psychotherapies for chronic depression. *J Consult Clin Psychol, 81*(4), 627-638.

Asfaw, A., & Souza, K. (2012). Incidence and cost of depression after occupational injury. Journal of Occupational Environment Medical, *54*(9), 1086-1091.

Cogburn, M. (2018). *Antidepressants PowerPoint Lecture*. Northwestern State University College of Nursing.

Healthy Place (2018). Cognitive symptoms (deficits) of depression test. https://www.healthyplace.com/psychological-tests/cognitive-symptoms-deficits-of-depression-test

Higgins, E. S., & George, M. S. (2014). *The neuroscience of clinical psychiatry: The pathophysiology of behavior and mental illness*. (2nd). Philadelphia, PA: Wolters Kluwer Lippincott Williams & Wilkins.

National Institute of Mental Health (NIH, 2018). Depression: Overview. https://www.nimh.nih.gov/health/topics/depression/index.shtml

O'Conner, E., Rossom, R. C., Henninger, M. et al. (2016). *Screening for depression in adults: An updated systematic evidence review for the U.S. Preventive Services Task Force*. Agency for Healthcare Research and Quality https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0085173/?report=printable

Oluboka, O. J., Katzman, M. A., Habet, J., McIntosh, D. , MacQueen, G. M., Milev, R. B. , McIntyre, R. S. , Blier, P. (2018). Functional recovery in major depressive disorder: Providing early optimal treatment for the individual patient. *International Journal of Neuropsychopharmacology 21*(2), 128-144.

Richardson, L., & Adams, S. (2018). Cognitive deficits in patients with depression. *The Journal of Nurse Practitioners—JNP, 14*(6) 437-443

Stahl, S. M. (2-013). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications*. (4th Eds.). UK, Cambridge University Press.

Stahl, S. M. (2017). *Stahl's essential psychopharmacology: Prescriber's guide*. (6th Eds.). UK Cambridge University Press

NURB 5960 Psychopharmacology Extra Point Assignment

Posted: June 25, 2018

Due: _____

Select a DSM 5 disorder and create a brief case study to present it. Identify at least five medications used to treat the disorder. Write an APA formatted paper including at least five references. Make sure you cover the indications, screening tests, prescribing guidelines, lab tests for monitoring, mechanism of action for each drug, on and off label considerations, cultural considerations, side effects, adverse effects, and antidotes for overdose. Include black box warnings and any other FDA relevant information.

Do not copy and paste. Submit to Turnitin, then send your paper to my email address mcogbu@lsuhsc.edu.

I will be grading them. Contact me for the grading rubric.

Each paper is worth up to 5 points added to your Exam #1 grade. **This effects Exam #1 only!** You may write more than one paper, but get my approval for each topic before you begin. A title page is required, spelling/grammar will be graded, and the paper should be long enough to cover the content.

Dr. Cogburn

Rubric

Introduction: Topic is adequately introduced

Body: Revie of diagnostic criteria and considerations, review of general indication for the drug class, any documented off label uses, black box warring or other warmings, lab tests, and frequency of monitoring, discuss neurobiological effects of drug class, evidence of best practices /prescription guidelines, age, gender, or medical co-morbidities that would impact rug metabolism and or efficacy

Conclusion and Implications for APRNs: Identify issues for APR practice, Identify areas, within topic where future development and research are needed, and appropriate summary of findings

Form: Appropriate spelling, grammar, sentence structure, paraph structure, use of references, reference citations, APA format, and lack of errors, paper is well organized and comprehensive.

Total possible points:

Comments