Background

Major Depressive Disorder (MDD) is considered one of the most common mental health conditions in the youth population. Death by suicide remains one of the leading causes of mortality in children and incidence increases with age\(^1\). Since the COVID-19 pandemic, the incidence of depressive symptoms in children has increased significantly. The estimated prevalence of depressive symptoms in the youth population across the world was 25.2% in 2022\(^2,3\).  

MDD is defined by the Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) as a depressed mood or loss of interest for most of the day that persists for 2 weeks or more. In addition to depressed mood the patient must experience four or more additional symptoms that lead to significant impairment or distress. The other symptoms are defined as: significant unintentional weight loss or gain, decrease in appetite, sleep disturbances, psychomotor changes visible to others, fatigue or low energy, sense of worthlessness or inappropriate guilt, inability to think or concentrate and recurrent thoughts of death or suicidal ideation. These symptoms must be present in the absence of bereavement\(^4\).  

Treatment of MDD in children and adolescents is a multimodal approach. The treatment consists of supportive therapy, cognitive behavioral therapy (CBT) or pharmacologic treatment with selective serotonin reuptake inhibitors (SSRI), selective norepinephrine reuptake inhibitors (SNRI) or other antidepressant medications\(^5\).  

Management

In 2017, the Guidelines for Adolescent Depression in Primary Care (GLAD-PC) published recommendations regarding treatment. They state that when indicated to initiate pharmacological treatment, the choice of medication should be a SSRI\(^5\). Examples of SSRIs include citalopram, sertraline, fluoxetine, escitalopram, and paroxetine\(^6\). Fluoxetine and escitalopram are currently the only 2 SSRIs FDA approved for treatment of MDD in children and adolescents.  

When initiating a patient on an SSRI it is important to understand the risk associated with the medication. All of the SSRIs carry a black box warning (BBW) for increased risk of suicide in children and young adults. There have been studies done to evaluate the correlation related to use of SSRIs and suicide risk, but none have been able to prove a statistically significant outcome. A meta-analysis published in 2016 proposed that suicidal ideations or suicidal attempts may be more likely to occur in patients who are treated medically rather than with placebo. Adverse effects, such as hypomania or mania, may be linked to increasing the suicidal thoughts rather than being caused directly by the medication\(^7\). It is important to understand that this risk exists, so patients and parents are equipped with tools to keep themselves safe. When children and adolescents are diagnosed with depression, the
most important aspect to treatment is that patients have a safety plan established to help deescalate a situation that may become dangerous to themselves.

Selective serotonin reuptake inhibitors have a wide array of side effects that can influence the choice of antidepressant that is used for a patient. The most common side effects experienced in everyday life include, nausea, diarrhea, insomnia, dizziness, and fatigue. Some of the more severe adverse effects that could occur are serotonin syndrome, withdrawal syndrome, which may occur when abruptly stopping one of these medications, and activation of hypomania or mania. If these adverse effects are not tolerable by a patient, they can try switching to another agent. The onset of therapeutic effect for these medications may also take 4 to 6 weeks to occur, so it is extremely important that patients are monitored closely for approximately 2 months following the initiation of an SSRI or any antidepressant.

While these side effects are seen at therapeutic doses, overdose of SSRIs may be another route that patients could utilize if they are having suicidal ideations. If the SSRI is taken in excess, there are also serious risks associated with this. Some of the potential toxicities that could be seen are seizures, QTc prolongation, decreased consciousness and serotonin syndrome. If a patient does attempt to overdose on an SSRI, the expected duration of the toxicity would last for approximately 24 hours. Overdose is a risk that exists and is something to be aware of in patients who are on SSRIs.

**Conclusion**

Based upon available data and experience, it is the position of the Pediatric Pharmacist Association (PPA) that pharmacologic therapy plays an important role in treatment of MDD in children and adolescents. When initiating treatment, the recommended first choice of therapy should be a selective serotonin reuptake inhibitor. When initiated on pharmacologic therapy, a patient should be closely monitored throughout the initial phase of treatment and be equipped with a support system as well as an action plan to reduce self-harm. If the patient experiences negative side effects and is unable to tolerate the medicine, the recommendation stands that the patient can try another SSRI or may try other agents such as SNRI or other antidepressants.

With the increasing prevalence of childhood depression, it is important to treat each patient on an individual basis and understand that this is not “one drug fits all” situation. Pharmacologic therapy is important in treating depression, but cognitive behavioral therapy and emotional supportive therapy are also key pieces to managing these patients.

**References**


