PEDIANEWS

The Official Newsletter of RxPups-Student Society of PediatricAdvocates

UNIVERSITY OF GEORGIA College of Pharmacy

Our Mission

The Student Society of Pediatric Advocates is a student organization affiliated with the University of Georgia College of Pharmacy. We are a student group associated with the Pediatric Pharmacy Advocacy Group. The Mission of the SSPA is to bring awareness to the proper use of medication therapy in pediatric populations through various service and education- based initiatives. Service activities center around lending our medication-based knowledge to pediatric patients and their parents in our community. Educational activities are directed toward student members in an effort to safely and effectively extend pharmacy practice to pediatric populations by building relationships with mentors and professionals in the health care community, as well as supplementing didactic coursework with lectures by specialists and our peers. Overall, SSPA advocates for the safety and happiness of young patients while learning and having fun along the way. The purpose of our newsletter is to educate pharmacy students about pediatric pharmacy and advocate for pediatric patients within the University of Georgia College of Pharmacy.

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The Ketogenic Diet and Epilepsy

By: Chloe Baskowitz, Pharm. D. Candidate 2022

Epilepsy affects over 400,000 children in the United States, representing the most common childhood neurologic condition. It is characterized by 2 or more unprovoked seizures separated by at least 24 hours, or one seizure with a high risk for more. A seizure consists of excessive neuronal firing, representing abnormal electrical activity in the brain. While there is no cure for epilepsy, there are a multitude of anti-seizure medications on the market, each with their own various mechanisms and side effects. Unfortunately, epilepsy fails to be controlled with medications in roughly 25% of children. These are classified as drug-resistant cases. Thus, parents often look for alternative ways of managing their child's seizures. Epilepsy may be especially concerning in children, as there is a higher risk for developmental, intellectual, and mental health comorbidities.

The ketogenic diet has been a feasible option for assisting in the management of epilepsy dating back to the 1920s. It has an extensive role in history; it even was an option before anticonvulsant medications became the mainstay therapy. So how does it work? Although the exact mechanism for suppressing seizures is unknown, the diet essentially mimics starvation, including the biochemical changes associated with starvation. This creates a state of ketosis, in which ketone bodies are created by the liver as the body breaks down fat for energy. In normal circumstances, the body uses glucose, from carbohydrates, as the energy source. If this is depleted, the body switches to using ketones as a source of energy. These ketones are also structurally similar to GABA, which may have a direct anticonvulsant effect. Other potential hypotheses include reduced inflammation in the brain, reduced glutamate levels, and enhanced GABA synthesis.

This diet is often recommended in children after 2 anti-seizure drugs have failed. For certain severe epilepsy syndromes, it may be recommended even earlier. Those younger than 2 years old may be an ideal age population as it is easier to control their diet compared to older children.

What foods are included in a ketogenic diet? There are many variations, but in essence it consists of a high-fat, adequate protein, and low carbohydrate diet, where caloric intake is still maintained for daily needs. The classic keto diet, also known as the long-chain triglyceride (LCT) diet, allows for 3-4 grams of fat for every 1 gram of carbohydrates and protein. This results in 90% of the calories coming from fat. It is often initiated in the hospital and may or may not include a 24-hour fasting period for faster onset of ketosis. During this time, the patient will be monitored, and the family will be educated on maintaining this diet. Additionally, the patient may continue taking their seizure medication but can eventually start to wean off of them.

https://www.delish.com/food/a21729395/keto-diet-food-list/

A less restrictive form of the keto diet is the modified Atkins diet. This has no fluid or calorie restriction, foods are not weighed and measured, there is no restriction on protein, and carbohydrates are still monitored. It is often started outside of the hospital setting, and carbohydrates are limited to a generous 15-20 grams per day. It is still found to be effective but may be better suited for adult patients who have a harder time following strict diets or those with milder epilepsies. Another alternative is the low glycemic index treatment.

Like the modified Atkins diet, this diet is less restrictive with a goal carbohydrate intake of 40-60 grams per day. It is more flexible, based on portion sizes, and fats make up about 60% of the calories. Finally, there is the medium chain triglyceride (MCT) diet, in which fats are only coming from MCT fats, which can produce ketones more easily than LCT fats. This enables a lower total fat intake. MCT can be taken as oil capsules, such as coconut oil, and is usually given with meals. The exact amount varies but typically starts at 40% of calories and can range up to 60%.

While there are several variations of this diet, there are also important factors to consider. Due to the severe restrictions, a child's diet has to be monitored very carefully, making it potentially difficult to eat outside of the house, at school, or even at restaurants. Potential complaints seen in those on ketogenic diets include bloating, constipation, potentially growth inhibition, and hyperlipidemia, with the latter two being neither significant nor common. Hypoglycemia may be seen within the first week but usually resolves quickly. This is weighed against the benefits that include having an alternative to anticonvulsant medications, which have many drugs interactions and side effects themselves. A ketogenic diet may have fewer side-effects, be more affordable, and even be more efficacious. Additional considerations include the need for vitamin and mineral supplements to ensure a balanced diet, and the patient needs to be monitored every 1-3 months for routine labs and growth progress.

There have been a multitude of studies comparing the efficacy of the ketogenic diet versus that of standard medication use. In general, the keto diet has been found to reduce seizures by up to 50%, and about 10-15% of patients even become seizure-free. Observational studies suggest a seizure reduction can be seen within 2-3 months on the keto diet, thus you would not discontinue for failure unless the patient was on the diet for at least 3 months. However, there are no clear maximum or minimum duration timelines for therapy. 80% of those who discontinued a keto diet after 2 years of seizure freedom remained seizure-free long term. Over time, there is the chance to discontinue the keto diet. Typically, children are kept on the diet as long as it helps them, usually averaging about 1 to 2 years. The diet is then tapered over several months to avoid shocking the body.

While the keto diet has many positive aspects and a long-standing place in epilepsy management history, it is extremely important to not initiate this type of restrictive life-style without first consulting both a doctor and a nutrition specialist.

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What is Multisystem Inflammatory Syndrome in Children (MIS-C)?

By: Sara Niazi, Pharm. D. Candidate 2022

Multisystem inflammatory syndrome in children (MIS-C) is a condition in which different organs become inflamed, including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs. MIS-C is considered a syndrome — a group of signs and symptoms, not a disease — because much of it is unknown, including its cause and risk factors. MIS-C is a new pediatric syndrome associated with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that is dangerous and potentially lethal; therefore, prompt recognition and medical attention is extremely important. MIS-C is rare, and most children eventually get better with medical care. However, some kids with MIS-C rapidly get worse, to the point where their lives may be at risk.

In the U.S., more African American and Latino children have been diagnosed with MIS-C compared to children of other races and ethnic groups. Studies are needed to help determine why MIS-C affects these children more often than others, but factors may include: differences in access to health information and services as well as genetics. Most children with MIS-C are between the ages of 3 and 12 years old, with an average age of 8 years old. Some cases have also occurred in older children as well as in babies.

The causes of MIS-C are also unknown. However, many children with MIS-C had the virus that causes COVID-19, or had been around someone with COVID-19. This rare syndrome attacking children shares common features with other pediatric inflammatory conditions including: Kawasaki disease, staphylococcal and streptococcal toxic shock syndromes, and bacterial sepsis and macrophage activation syndromes. It can also present with unusual abdominal symptoms with excessive inflammatory markers. Most cases of MIS-C have features of shock, with cardiac involvement, gastrointestinal symptoms, and significantly elevated markers of inflammation, with positive laboratory test results for SARS-CoV-2. Children with MIS-C may have a fever and symptoms such as abdominal pain, vomiting, diarrhea, neck pain, rash, bloodshot eyes, or fatigue. Parents should contact their child's doctor, nurse, or clinic right away if their child is showing symptoms of MIS-C. Parents should be aware that not all children will have all the same symptoms. It is important to seek emergency care right away if the child is showing any of these emergency warning signs of MIS-C or other concerning signs of the following:

- trouble breathing
- pain or pressure in the chest
- new confusion
- inability to wake or stay awake
- pale, gray, or blue-colored skin, lips, or nail beds, depending on skin tone
- severe abdominal pain

Note that this list is not all possible symptoms. Parents should be instructed to call their child's medical provider for any other symptoms that are severe or concerning to them. They could also call 911 or call ahead to their local emergency facility and notify the operator that they are seeking care for someone who has or may have COVID-19. Doctors may perform tests to look for inflammation or other signs of disease which may include blood tests, chest x-ray, heart ultrasound (echocardiogram), and abdominal ultrasound. Most children who become ill with MIS-C will need to be treated in the hospital. Some will need to be treated in the pediatric intensive care unit (ICU).

Since many children with MIS-C had the virus that causes COVID-19, or had been around someone with COVID-19, it is important to know the symptoms and emergency warning signs of COVID-19 as well.

People with COVID-19 have had a wide range of symptoms reported – ranging from mild symptoms to severe illness. Symptoms may appear 2-14 days after exposure to the virus. People with these symptoms may have COVID-19:

- fever or chills
- cough
- shortness of breath or difficulty breathing
- fatigue, muscle or body aches, headache
- new loss of taste or smell, sore throat, congestion or runny nose
- nausea or vomiting, and diarrhea

This list does not include all possible symptoms. CDC will continue to update this list as they learn more about COVID-19.

The CDC issued a Health Advisory on May 14, 2020 that outlines the following case definition of MIS-C as an individual aged <21 years presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological); AND no alternative plausible diagnoses; AND positive for current or recent SARS-CoV-2 (COVID-19) infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms.

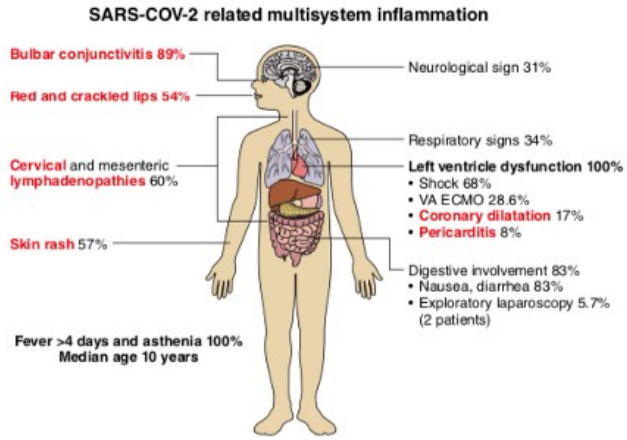
Since MIS-C is a rare complication temporally associated with COVID-19, any child with suspected MIS-C should also be evaluated for infectious and noninfectious etiologies. Persistent fever without a clear clinical source is the first clue. Any fever that is accompanied by symptoms concerning in their severity or coincident with recent exposure to a person with COVID-19 should raise suspicions. Some children clinically progress rapidly and may develop hemodynamic compromise. These children should be followed and cared for in a hospital with tertiary pediatric/cardiac intensive care units whenever possible. A child with persistent fever (≥3 days) who is moderately to severely ill with clinical signs of organ dysfunction (e.g., gastrointestinal, respiratory, cardiac, skin, or neurologic) should be evaluated for MIS-C. Initial evaluation should include measurement of vital signs, assessment of perfusion and oxygen saturation. Early consultation and coordination with the nearest pediatric infectious disease and rheumatology specialist and pediatric referral center for optimal testing and management should be considered. Laboratory screening for systemic inflammation may be considered and initial lab screenings may include complete blood cell count (CBC) with differential, urine analysis, ESR, and CRP, with the addition of ferritin, LDH, comprehensive metabolic panel, pro-BNP, troponin, and fibrinogen depending on initial clinical suspicion and/or evidence of inflammation on initial lab screening. Note that none of these laboratory studies are specific to the diagnosis of MIS-C, so even if there is evidence of significant systemic inflammation, alternative diagnoses must still be considered (e.g., pyelonephritis, appendicitis). Severely ill-appearing patients and those in compensated shock or shock should be evaluated and treated in the emergency department/critical care setting. Transfer to a referral center should be arranged. Laboratory tests, as described above, should be performed for initial evaluation regardless of duration of fever. Consultation with pediatric subspecialists (infectious diseases, cardiology, rheumatology) at a local or regional pediatric referral center should be initiated but should not delay transfer to a referral center.

Any child ill enough to warrant admission for fever, abdominal pain, diarrhea, and/or organ dysfunction in whom MIS-C is suspected should be cared for in a hospital with tertiary pediatric/cardiac intensive care units. Although decisions about additional testing will be made by the multidisciplinary team managing the patient, pediatricians can prepare families for an expanded laboratory and cardiac workup that may include: Chest radiograph, EKG, and troponin (if any of these or physical examination is abnormal, then consult with pediatric cardiology and consider additional diagnostic testing for myocardial injury (echocardiogram and/or cardiac MRI)), expanded laboratory tests including pro-BNP, triglycerides, creatine kinase, amylase, blood and urine culture, D-dimer, prothrombin time/partial thromboplastin time (PT/PTT), INR, CRP, ferritin, LDH,

should be performed with RT-PCR assay and serologic testing. Later serology may be needed if all negative initially. Serologic tests must be sent prior to administration of intravenous immunoglobulin (IVIG).

Clinicians who suspect MIS-C in a child should use a multidisciplinary approach involving many pediatric specialists, which may include but is not limited to cardiology, infectious disease, immunology, hematology, rheumatology, pediatric hospital medicine, and critical care, to guide individual patient treatment. There are 3-4 sub-types of MIS-C that may require slightly different management based on evolution of symptoms and laboratory values. Optimal treatment for a patient with MIS-C is not known; however, it is best determined by the multidisciplinary clinical team. The following interventions have been used: If patients appear hypotensive and septic during evaluation for MIS-C, treatment with antibiotics, fluid resuscitation, and if necessary, inotropes is appropriate until bacterial infection has been ruled out. Patients with MIS-C are usually treated with IVIG, 2 grams/kg (max of 100 grams); patient cardiac function and fluid status influence the duration of the infusion of IVIG therapy. Patients who do not improve clinically, or whose laboratory values do not improve, have also been treated with steroid therapy (ranging from 2 to 30 mg/kg/day of methylprednisolone depending on severity of illness) and biologics (e.g., anakinra, 2 to 10 mg/kg/day, subcutaneously or intravenously, divided every 6 to 12 hours). A recent large observational study found that initial treatment with both IVIG and steroid therapy led to earlier resolution of fever compared to IVIG alone. Due to rapidly evolving treatment recommendations, consultation with pediatric subspecialists is strongly recommended. If the patient has laboratory or imaging evidence of myocardial injury or findings concerning for coronary artery aneurysms, discussion with pediatric cardiology is suggested prior to use of steroids. Patients treated with steroids and/or biologics often go home with a 3-week taper of steroids and/or biologics. All patients with MIS-C, unless there are contraindications (e.g., platelets <100,000 or active bleeding), should be started on low-dose aspirin for thromboprophylaxis. Consultation with cardiology and hematology should take place to determine whether further intervention is required. Patients diagnosed with MIS-C should have close outpatient pediatric cardiology follow-up starting 1 to 2 weeks after discharge. Timing should be determined in consultation with a pediatric cardiologist. Patients diagnosed with myocardial injury must have cardiology directed restriction and/or release for activities. Patients who receive steroid therapy or treatment with biologics should receive follow-up with the pediatric rheumatologist following discharge. Discharge of patients diagnosed with MIS-C should be coordinated with the patient's medical home. Primary care follow-up is recommended for all patients.

Please note that the U.S. Centers for Disease Control (CDC) first issued a health advisory statement on the new COVID-19 (SARS-CoV-2) presentation May 14, 2020. The CDC is calling this new presentation in pediatric patients' multi-system inflammatory syndrome in children (MIS-C). The CDC called for healthcare providers to report any patient who meets the case definition to local, state and territorial health departments in order to collect data to enhance knowledge of risk factors, pathogenesis, clinical course and treatment of this syndrome.



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New Technology Update: MiniMed 770G System

By: Kosha Patel, Pharm. D. Candidate 2022

The most common type of diabetes diagnosed during childhood is type 1 diabetes also known as insulin-dependent or juvenile diabetes. Although it is less common than type 2 diabetes, type 1 occurs in approximately 5-10% of all diabetic patients.[4] The chronic disease state is characterized by an autoimmune reaction in which the body attacks itself and destroys beta cells in the pancreas that make insulin, resulting in little to no insulin production .[4] Insulin is a hormone that controls blood sugar by helping it enter into the cells of the body where it can be used as energy.[4] Without insulin, the cells do not take up the glucose, leading to the accumulation of glucose in the blood which can cause damaging effects to the body.[4] Type 1 diabetes is managed with the use of insulin injections or an insulin pump.[3] The ultimate goal for these patients is to carefully balance their insulin intake with their diet and exercise regimen to keep their blood sugar under control.[3] Due to the constant management and monitoring that this disease state requires, it heavily relies on technology to ensure that patients live healthy and normal lifestyles.

In August 2020, the U.S. Food and Drug Administration (FDA) approved a novel automated insulin delivery and monitoring system, MiniMed 770G, for pediatric patients ages 2 and up with type 1 diabetes.[1] The Bluetooth-enabled system is a hybrid closed loop diabetes management device that automatically monitors glucose levels every 5 minutes and appropriately provides insulin doses based on the glucose measurements.[1] The MiniMed 770G System includes a sensor, an insulin pump, and an infusion patch with each component playing a different role in managing the patient's diabetes.[1] The sensor attaches to the body and works by measuring glucose levels under the skin; it sends the data to the pump automatically.[1,2] The insulin pump regulates the insulin dose adjustments by communicating with the other components of the system.[2] The infusion patch is connected to the pump and allows for continuous insulin delivery through a thin and flexible tube called a catheter.[1,2] Furthermore, a smartphone application tracks glucose values and notifies patients if they are trending outside of the normal range.[2] Caregivers are also able to download a similar application to stay updated on their patient's health status.[2]

As with all new technology that emerges, the risks and benefits of the MiniMed 770G System must be evaluated. Some adverse effects of the device include hypoglycemia, hyperglycemia, and skin irritation or redness around the infusion patch.[1] However, the Smartguard Tech helps prevent the dangerous blood glucose highs and lows that a patient may experience.[2] Additionally, the device has two modes: Manual and Auto Mode.[5] The Manual Mode allows the patient to program basal insulin delivery at a constant rate, while the Auto Mode automatically adjusts basal insulin by constantly increasing, decreasing, or stopping insulin delivery after assessing the measured glucose values.[5] Although the Auto Mode can adjust insulin delivery without the patient's input, the user must manually request insulin doses during meals to counter carbohydrate consumption.[1,5] Moreover, the MiniMed 770G System should not be used in patients who require less than 8 units or more than 250 units of total daily insulin dose per day.[2,5]

Technological advancements have optimized the management and treatment of type 1 diabetes, especially in the pediatric population. The MiniMed 770G System is the first legally marketed device with automatic adjustment of insulin delivery based on continuous glucose monitor values for ages 2 to 6 years.[1] The introduction of this system will inspire pediatric patients to face the challenges of type 1 diabetes with courage and perseverance, so they can focus on achieving their goals while maintaining good health.

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COVID-19 & Its Impact on Pregnancy

By: Grishma Patel, Pharm. D. Candidate 2022

Currently, about 114 million people worldwide have been affected by coronavirus disease 2019 (COVID-19), and nearly 2.5 million people across the world have died due to the virus.[1] COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is now the fifth pandemic documented since the 1918 flu pandemic.[2] The virus is highly transmissible and can be detrimental in vulnerable populations. Pregnant women are at a greater risk of complications and are disproportionately affected by respiratory illnesses as seen in the past with the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Pregnant women were identified as a vulnerable group for COVID-19 and advised to take additional precautions during the pandemic.[3]

SARS-CoV-2 is a novel, enveloped, single-stranded RNA virus that targets cells, such as nasal and bronchial epithelial cells and pneumonocytes. Infection with SARS-CoV-2 is followed by viral replication and release causing profound lymphopenia through lymphocyte apoptosis and lymphopoiesis impairment. In later stages of the infection, the endothelial barrier integrity is compromised leading to infiltrations of pulmonary capillary endothelial cells causing a reduced inflammatory response and an influx of monocytes and neutrophils.[4] This positive feedback may lead to excessive inflammation and damage to the lungs. The inflammation caused by SARS-CoV-2 can also result in a "cytokine storm" that could lead to a multiorgan failure.

A number of viruses have well-known effects on the mother and fetus during pregnancy and may provide information on the impact of COVID-19 in pregnant women. The effect of influenza A (H1N1) has been found to cause significantly more disease in pregnant women than nonpregnant controls in a recent systematic literature review. This review included approximately 3,000 women and reported an 8% maternal mortality rate along with a 30% preterm birthrate. Similarly, SARS and MERS had significant adverse maternal outcomes with a 25.8% and 28.6% maternal mortality rate, respectively. Both SARS and MERS were associated with preterm birth, fetal growth restriction, and perinatal death in the few cases that were reported. Another study using birth registry data in the United States found that seasonal influenza in early pregnancy was significantly associated with increased preterm birth, as well as increased neonatal and infant mortality.[3]

There is little evidence about the possible impact of COVID-19 in early pregnancy (up to 12-week gestation). Since January 2020, several case series and cohort studies have revealed the presentation and clinical course of COVID-19 in late pregnancy (> 24 weeks gestational age). Thirty-one relevant studies were identified and reported on outcomes of 12,260 pregnant women with confirmed COVID-19. The majority of the women were in their third trimester and had mild to moderate symptoms while a small group of women required critical care admission. There were 146 deaths reported and several preterm births that were due to worsening maternal COVID-19 or obstetric complications unrelated to COVID-19. The largest cohort study from the United States (District of Colombia and New York City) included data from 91,412 women aged 15-44 of which 8,207 were pregnant. Pregnancy was associated with an increased chance of hospitalization, ICU admission, and need for mechanical ventilation. There was no significant reduction in mortality. A study using the same population with data from the first 4 weeks of the pandemic in New York found that pregnant women were less likely to require admission than non-pregnant women with COVID-19. However, this smaller study did not match the age control group. It is difficult to generalize the results of these studies as criteria for hospital/ICU admission and ventilation are not provided, and the results could reflect the health care setting rather than the clinical status of the women.[3]

In the majority of the studies reporting on neonatal outcomes, no serious adverse outcomes were observed in neonates who were born to COVID-19 positive mothers. In studies that compared pregnant women who were positive for COVID-19 to those who were negative, there was no significant difference in rates of adverse outcomes in neonates. Thirteen studies tested neonates for COVID-19, and three studies identified positive cases but were largely asymptomatic or had mild self-limiting symptoms. Several studies reported high rates of preterm birth, but comparison of these studies is limited due to lack of similarity. It has not been established yet whether COVID-19 is an independent risk factor of preterm birth.[3]

Most COVID-19 in pregnancy studies recognize s cases by testing women with symptoms. Data from centers in London and New York, where all pregnant women admitted for delivery were tested for COVID-19,

showed that of the women who tested positive, 88% were asymptomatic. This suggests that the cases reported in literature are likely to represent a small portion of cases. With a lack of universal COVID-19 testing, a large number of cases are likely to go undetected. From the current evidence, it is difficult to draw absolute conclusions that pregnant women are at an increased risk of severe consequences from COVID-19. Most pregnant women will experience mild or asymptomatic disease with no significant consequences. However, some centers have seen an increased rate of ICU admissions and need for mechanical ventilation in pregnant women. Although rare, vertical transmission is possible but has minimal impact in the majority of neonates. Vertical transmission is challenging to fully assess without routine neonatal testing. In addition, the lack of population level data makes comparison of pregnant and nonpregnant cohorts difficult.[3] While the overall risk is of severe illness is low, pregnant individuals are at an increased when compared to non-pregnant individuals and should take precautions to protect themselves from COVID-19[5].

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The Prevalence and Risks of Anti-Depressant Prescribing in Pediatrics

By: Madison O'Neal, Pharm. D. Candidate 2024

Prevalence and Background of Antidepressants

In the United States, prescribing anti-depressants across all age groups continues to increase each year. Approximately 3.4% of adolescents from the ages of 12 to 19 are on an antidepressant.[3] Antidepressants are a class of medications that are used to treat a multitude of illnesses, including depression, as well as many other conditions including autism, obsessive compulsive disorder (OCD), migraines, generalized anxiety disorder (GAD), and post-traumatic stress disorder (PTSD).

Within the antidepressant class, there are many types that differ based on their mechanism of action. Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressant in children and adults.[1] SSRIs work by inhibiting reuptake of the neurotransmitter serotonin in the neurons of the central nervous system. This allows for the effects of serotonin to be enhanced, relieving symptoms of anxiety, depression, and many other illnesses that are treated with SSRIs. Commonly prescribed SSRIs include fluvoxamine, paroxetine, citalopram, escitalopram, and fluoxetine. Other classes of anti-depressants include serotonin-norepinephrine reuptake inhibitors (SNRIs), atypical antidepressants, and tricyclic antidepressants.[1]

Antidepressants and Their Efficacy

Antidepressants are used most commonly in pediatric patients to treat anxiety disorders and OCD. The most common type of antidepressant used in pediatrics for the treatment of OCD, and anxiety/depression disorders are SSRIs. There is strong evidence regarding SSRIs and their effectiveness in treating these psychological illnesses in pediatrics. SSRIs have also shown to be effective in treating depression in adolescents with approximately 80% of patients seeing an improvement in their depression. However, when used to treat depression, there is also significant evidence that about 60% of patients who received the placebo also had improvement in their condition. PTSD has also been treated in adolescents using antidepressants, but the data regarding the efficacy of this medication treatment is minimal. In the few randomized controlled trials, there is minimal difference in the placebo and SSRI treatment efficacy with PTSD.[1]

Fluoxetine is the most commonly prescribed SSRI in adolescent clinical trials. In a randomized clinical trial conducted to study the efficacy of fluoxetine on adolescents with OCD and autism, obsessive compulsive behaviors were assessed after 16 weeks of fluoxetine use. Many different methods were used to measure and evaluate OCD behaviors. The primary difference between the placebo and the treatment group was recorded using a scale called the Children's Yale-Brown Obsessive-Compulsive Scale for Pervasive Developmental Disorders (CYBOCS-PDD). When comparing the placebo group to the fluoxetine group, a statistically significant difference was present in the mean values using this scale. Those in the fluoxetine group presented significant improvement in their scores compared to the placebo group.[2] Other methods were also used to measure the outcomes of the clinical trial including the revised Repetitive Behavior Scale, Spence Children's Anxiety Scale, and Aberrant Behavior Checklist-Community Version. All of the methods used to collect results showed a significant difference in the placebo group and the treatment group, indicating that fluoxetine did reduce symptoms of OCD in the treatment population. The placebo group had higher scores on the Repetitive Behavior Scale by 9.11 units and on the Aberrant Behavior Checklist by 4.23 units.

In regard to other antidepressants such as SNRIs, atypical antidepressants, and tricyclic antidepressants, there is much lower efficacy in treating adolescents when compared to SSRIs. Not only are they generally less effective, but they also tend to have a more severe side effect profile. Because of this, they are typically used as secondary treatment options. For example, SNRIs can cause an increased risk of hypertension.

Although antidepressant prescription in children has been shown to reduce the severity of psychological disorders such as OCD, anxiety disorders, autism, and depression, there are many risks associated with the use of these medications. The typical side effects of SSRIs include but are not limited to sleep issues, gastrointestinal upset, sweating, sexual dysfunction, and dry mouth. These side effects are typically the worst during the initiation of a medication, during a dose increase, or if medication interactions occur. Although medication side effects can occur with SSRIs, the side effect profiles of other antidepressant drugs (SNRIs and tricyclic antidepressants) are typically more severe. In table 1, the average number of side effects endured in a trial studying the effectiveness of fluoxetine prescription in pediatrics is shown. Approximately 21% of patients experienced 3-4 adverse effects in the treatment group compared to 10% in the placebo group.[2]

	No. (%)	
	Fluoxetine (n = 75)	Placebo (n = 71)
Participants with at least 1 AE[a]	34 (45)	30 (42.3)
Total No. of AEs		
Mean (SD)	2.5 (1.6)	2.6 (2.1)
1	14 (41)	13 (43)
2	3 (9)	6 (20)
3	7 (21)	3 (10)
4	7 (21)	3 (10)
5	1 (3)	1 (3)
6	2 (6)	2 (7)
7	0	1 (3)
9	0	1 (3)

Table 1.[2]

In regard to pediatrics, some of the more severe risks that can occur with the use of antidepressants include behavioral activation syndromes, serotonin syndrome, and suicide. Behavioral activation syndromes are characterized by irritability, hyperactivity and mania and are more likely to occur in pediatric patients than adult patients using anti-depressants. This has only been shown to be statistically significant in cases where children have been diagnosed with bipolar disorder and take an antidepressant without taking a mood-stabilizer or antipsychotic as well. Serotonin syndrome is an excess of serotonin that can cause physiological effects such as arrhythmias and seizures. This typically is only an issue in those who take SSRIs/SNRIs alongside other serotonergic agents such as migraine medications (triptans), some pain medications, and dextromethorphan. In order to prevent this from occurring, it is important that parents are educated and aware of the importance of providing a complete medication list to all of a child's doctors of the medications their child is on.

In an effort to further research the suicidality black box warning of antidepressants, the FDA conducted a review of multiple antidepressant trials. Approximately 4,400 pediatric patients were included in this review, and significant evidence was found that spontaneous suicidal thoughts or actions increase upon use of antidepressants. While there were no successfully completed suicides, approximately 1-2 in 100 pediatric patients experienced suicidal thoughts or actions for a short period of time. More current studies have suggested that suicidal thoughts and actions with the use of antidepressants is more likely to occur in adolescents than adults.

While suicidality can be a risk associated with antidepressant use, suicide rates are lowered overall due to

the number of suicide attempts/completions. This is also a trend in the adult population as well, which is why suicidal thoughts is strongly linked to antidepressants in pediatrics. Although why this occurs is unclear, it is likely associated with the methodology used in pediatric trials (parental reporting verses self-reporting) and the behavior activation syndromes that occur upon beginning a medication. The evidence of antidepressant use is also extremely limited due to the lack of trials that have been conducted in pediatric patients. This is also a risk associated with antidepressants in children. It is important to weigh the risks versus benefits before prescribing an antidepressant for an adolescent as well as informing the parents/guardians of the side effects, risks, and methods to avoid some of these dangerous possibilities.[1]

References

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