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ABSTRACT

Autism Spectrum Disorder (ASD) is a neuro-developmental disorder commonly seen in children. Autism is a disorder that affects behavior and communication. Autism may be diagnosed at any age, it is said to be a 'developmental disorder' because symptoms generally appear in the first two years of life. ASD may be a lifelong disorder, treatments and services can improve a person's symptoms and ability to function. All children should be screened for autism as per the American Academy of Pediatrics recommendations. This review article is written to summarize the medications used to manage ASD which will be helpful to physicians.

INTRODUCTION

Autism spectrum disorder (ASD) develops in early childhood and is characterized by restricted repetitive behaviors, interests, and activities qualitative abnormalities in social interactions, markedly aberrant communication skills. Behavioral and developmental features that suggest autism include the absence of smiling when greeted by parents and other familiar people; Developmental regression; Absence of protodeclarative pointing; Abnormal reactions to environmental stimuli; Absence of typical responses to pain and physical injury; Language delays and deviations; Susceptibility to infections and febrile illnesses; Absence of symbolic play; Repetitive and stereotyped behavior; Abnormal social interactions. Signs and Symptoms screening of autistic disorder is crucial because it allows for early referral of patients for further evaluation and treatment. Children's siblings with autism are at risk for developing traits of autism and even a full-blown diagnosis of autism. Therefore, siblings also undergo screening not only for autism-related symptoms but also for social problems, language delays, learning difficulties, and anxiety or depressive symptoms.¹⁻⁴

DIAGNOSIS

Examination for patients with suspected autism spectrum disorder may include the findings: Abnormal motor movements (eg, clumsiness, awkward walk, hand flapping, tics); Dermatologic anomalies (eg, aberrant palmar creases); Abnormal head circumference (eg, small at birth, increased from age 6 months to 2 years, normal in adolescence); Orofacial, extremity, and head/trunk stereotypies (eg, purposeless, repetitive, patterned motions, postures, and sounds); Self-injurious behaviors (eg, picking at the skin, self-biting, head punching/slapping); Physical abuse inflicted by others (eg, parents, teachers); Sexual abuse: External examination of genitalia is appropriate; if bruises and other evidence of trauma are present, pelvic and rectal examinations may be indicated.⁵⁻⁷

MANAGEMENT

The established therapies for autistic disorder are nonpharmacologic and may include individual intensive interventions. Individuals with autism spectrum disorder and unspecified pervasive developmental disorder typically benefit from behaviorally oriented therapeutic programs developed specifically for this population. Autistic

children should be placed in these specialized programs as soon as the diagnosis is suspected.

Nonpharmacologic therapy

Intensive individual special education;

Speech, behavioral, occupational, and physical therapies (eg, assisted communication, auditory integration training, sensory integration therapy, exercise/physical therapy);

Social skills training in some children with an autism spectrum disorder, including those with comorbid anxiety disorders; children with autism spectrum disorder and comorbid ADHD may benefit less from social skills training

Pharmacotherapy

No pharmacologic agent is effective in the treatment of the core behavioral manifestations of autistic disorder, but drugs may be effective in treating associated behavioral problems and comorbid disorders (eg, self-injurious behaviors, movement disorders). The possible benefits from pharmacotherapy must be balanced against the likely adverse effects on a case-by-case basis (eg, venlafaxine may increase high-intensity aggression in some adolescents with autism.

Medications used in managing related behavioral problems and comorbid conditions in children with autism include the following:

Second-generation antipsychotics (eg, risperidone, aripiprazole, ziprasidone);

SSRI antidepressants (eg, fluoxetine, citalopram, escitalopram);

Stimulants (eg, methylphenidate).⁸⁻¹¹

MEDICATIONS

The established therapies for autistic disorder are nonpharmacologic. These therapies may include behavioral, educational, and psychological treatment. No pharmacologic agent is effective in the treatment of the core behavioral manifestations of autistic disorder. However, medication may be effective in the treatment of comorbid disorders, including self-injurious behaviors and movement disorders.¹²

Second-Generation Antipsychotics

The atypical antipsychotic agents risperidone and aripiprazole have been approved by the FDA for irritability associated with autistic disorders.¹³

Risperidone:

Risperidone is an atypical antipsychotic agent that is indicated for irritability associated with autistic disorder in children and adolescents aged 5-16 years. Risperidone is a mixed serotonin-dopamine antagonist that binds to 5-HT₂ with very high affinity and binds to the dopamine D₂ receptor with less affinity. Affinity for the dopamine D₂ receptor is 20 times lower than that for the 5-HT₂ receptor. Risperidone is FDA approved for irritability and aggression in children with ASD, 5 years and older.

The combination of serotonin antagonism and dopamine antagonism is thought to improve negative symptoms of psychoses and reduce the incidence of extrapyramidal side effects in comparison with conventional antipsychotics.¹⁴

Aripiprazole:

Aripiprazole is indicated for irritability associated with autistic disorder in children and adolescents aged 6-17 years. Aripiprazole is thought to be a partial dopamine (D₂) and serotonin (5-HT_{1A}) agonist, and to antagonize serotonin (5-HT_{2A}). Aripiprazole is available as a tablet, an orally disintegrating tablet, or an oral solution.

Risperidone and Aripiprazole have shown benefit for challenging and repetitive behaviors, but associated adverse effects limit their use to patients with severe impairment or risk of injury.^{15, 16}

Ziprasidone:

Ziprasidone appears to have the potential for improving symptoms of aggression, agitation, and irritability in children, adolescents, and young adults with autism. It is a second-generation antipsychotic drug, is used off-label to treat serious behavior disorders associated with autism, such as self-injurious behavior. It elicits its effects through antagonism of D₂, D₃, 5-HT_{2A}, 5-HT_{2C}, 5-HT_{1A}, 5-HT_{1D}, and alpha₁-adrenergic receptors.

In addition, it has a moderate antagonistic effect for histamine H1. It moderately inhibits the reuptake of serotonin and norepinephrine.¹⁷

SSRI Antidepressants

SSRIs are widely prescribed for children with autism or a related condition. These agents are used off-label to help with intractable repetitive behaviors, such as compulsion.

Fluoxetine:

It selectively inhibits presynaptic serotonin reuptake, with minimal or no effect on the reuptake of norepinephrine and dopamine.¹⁸

Citalopram:

It enhances serotonin activity by selective reuptake inhibition of serotonin at the neuronal membrane. Dose-dependent QT prolongation has been reported with citalopram. This agent is contraindicated in patients with congenital long QT syndrome.¹⁹⁻²¹

Escitalopram:

It is an S-enantiomer of citalopram. The mechanism of action is thought to be potentiation of serotonergic activity in the central nervous system (CNS), resulting from the inhibition of CNS neuronal reuptake of serotonin.²²

Stimulants

Stimulants may be effective for treating hyperactivity associated with autism. The magnitude of response, however, is less than that seen in developmentally normal children with attention deficit hyperactivity disorder.

Methylphenidate:

It is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space. Methylphenidate is a racemic mixture composed of the d- and l-enantiomers. The d-enantiomer is more pharmacologically active than the l-enantiomer.²³

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