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Review Article

Autism Spectrum Disorder: Comprehensive Understanding, Pharmacological Management and the Pharmacist Role: a literature review

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Abstract

Autism Spectrum Disorder (ASD). This is a condition known as "Different Abilities." is a neurodevelopmental disorder characterized by deficits in social communication, sensory processing alterations, and repetitive behaviors. Its global prevalence is estimated at 1 in 160 children, with a reported prevalence of 0.8% in Mexico. ASD is more commonly diagnosed in males, and prevalence data in Latin America are frequently underestimated due to socioeconomic barriers. As a multifactorial and highly heritable condition with a profound psychosocial impact that often triggers a grieving process within families, ASD requires an interdisciplinary approach in which behavioral interventions constitute the cornerstone of treatment, while pharmacological therapy serves as an off-label adjunct aimed exclusively at managing specific symptoms or comorbidities, such as Attention-Deficit/Hyperactivity Disorder (ADHD), epilepsy, and sleep disorders. Currently, only risperidone and aripiprazole have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of irritability associated with ASD. Nevertheless, the clinical profile observed in the region indicates that more than 50% of pediatric patients are exposed to polypharmacy, increasing the risk of drug interactions and adverse effects, primarily metabolic and neurological and compromising treatment adherence due to resistance to change and sensory barriers commonly experienced by children. In this context, the pharmacist emerges as an essential member of the multidisciplinary team, playing a crucial role in ensuring pharmacotherapeutic follow-up, identifying and resolving medication-related problems, and providing health education to caregivers.

Keywords: Autism Spectrum Disorder; pharmacotherapy; treatment adherence; pharmaceutical care; pediatrics; pharmacotherapeutic follow-up.

Introduction

Autism Spectrum Disorder (ASD) is a group of neurodevelopmental disorders in which symptoms result from deficits in neurobiological network connections. It is primarily characterized by impairments in communication and social interaction, sensory and cognitive development issues, and the presence of restricted and repetitive behaviors, interests, or activities. In addition, there is evidence of a predisposition to other types of mental health issues and comorbidities in patients diagnosed with ASD. These manifestations begin in early childhood, however, symptoms may not become apparent until years later [1] [2] [3].

Over the past 20 years, diagnoses of ASD have risen dramatically, to the point where it is now considered the most common developmental disorder [2]. Following the publication of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) in 2013, ASD now encompasses in a single diagnosis what was previously classified as Kanner's autism, Asperger's syndrome, childhood disintegrative disorder, and unspecified pervasive developmental disorder. This restructuring of the diagnosis has complicated epidemiological records and the clinical perception of the condition [1].

Epidemiologically, the World Health Organization (WHO) estimates that 1 in 160 children worldwide has some form of ASD, with a higher prevalence among boys. Epidemiological data show that the prevalence of ASD ranges from 1% to 1.5%, and specifically in Mexico, the prevalence is 0.8%. It is believed that the increase in ASD in recent years may be attributed to improvements in detection systems and changes in diagnostic criteria; however, in Latin America, the data are heterogeneous and frequently underestimated due to limitations in epidemiological surveillance systems and socioeconomic barriers that can delay diagnosis [4].

ASD, being a neurodevelopmental disorder with a multifactorial etiology (genetic, neurological, and social), requires a mandatory interdisciplinary approach, which includes behavioral, educational, psychological, and, if necessary, pharmacological interventions. It is important to note regarding this last point that pharmacological treatment is complementary, and this is where the pharmacist plays an extremely important role as part of the multidisciplinary team. Their involvement ranges from medication dispensing and pharmaceutical care to health education, as well as promoting treatment adherence and pharmacotherapeutic monitoring aspects that are particularly critical in a highly vulnerable population such as pediatric patients, given the high burden of polypharmacy associated with the condition [5].

The purpose of this narrative review is to compile, analyze, and synthesize the available evidence on four key areas: a comprehensive understanding of ASD, available pharmacological treatments, the circumstances in which they are necessary, and their implications, factors that influence treatment adherence; and the importance of the pharmacist's role in managing this disorder. This research is primarily focused on the context of the Latin American pediatric population and an audience of healthcare professionals, with a special emphasis on the pharmacy team.

Development

The methodology involved compiling a narrative based on a selection of articles containing the keywords "autism," "therapeutic adherence," "ASD treatment," and "pharmacist" from platforms such as Elsevier, SciELO, PubMed, and Google Scholar to discuss findings related to autism, its treatment, and the role of the pharmacist in this context.

1. Understanding Autism Spectrum Disorder (ASD)

1.1 Definition and diagnostic criteria

Over the years, the concept of autism has evolved; for many years, it was used interchangeably with schizophrenia and psychosis. In 1940, Dr. Leo Kanner developed the first modern descriptions of what we now consider Autism Spectrum Disorder. Starting in 1980, it was classified as Pervasive Developmental Disorder (PDD), a classification that was revised in 2013 with the publication of the fifth edition of the DSM-5. In this edition, autism was redefined as Autism Spectrum Disorder and placed within the category of neurodevelopmental disorders, a term that remains in use today [5].

According to the World Health Organization's International Classification of Diseases and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), it is defined by the presence of persistent deficits in communication and social interaction across multiple contexts, along with restricted and repetitive patterns of behavior, interests, or activities; these deficits can lead to complications in personal, family, educational, occupational, and other important areas of functioning. It is also noted that the manifestations of these disorders typically begin in early childhood, in most cases starting at 18 months; among these manifestations are sensory dysfunctions (perception of visual, auditory, tactile, or gustatory stimuli), motor and behavioral disturbances, sleep disorders (prolonged or fragmented), or feeding disorders. Thirty to forty percent may have

intellectual disabilities, and 33% may have early or late-onset epilepsy, however, these manifestations may or may not be evident until years later, when social demands exceed the individual's limited capacity [1] [3] [4].

The DSM-5, published by the American Psychiatric Association, identifies the following severity levels for ASD:

Level 3: Requires substantial support. The patient exhibits severe deficits in social communication skills, has difficulty interacting with others, rarely initiates a conversation, struggles to cope with change, and exhibits repetitive behaviors.

Level 2: Requires substantial support. The patient exhibits deficits in verbal or nonverbal communication skills, however, is capable of initiating social interactions on certain occasions, responds in a restricted and atypical manner to attempts at socialization, exhibits repetitive behavior, and has difficulty coping with changes.

Level 1: Requires support. They show minimal interest in interacting with others, require support in social situations, have difficulty planning and organizing, which interferes with their independence, and their restricted behaviors interfere with their functioning in various contexts [4].

The diagnosis is clinical and consists of direct observation of behavior, structured interviews with caregivers, and the use of standardized tools such as the ADOS (Autism Diagnostic Observation Schedule) and the ADI-R (Autism Diagnostic Interview-Revised). The evaluation must be conducted by a multidisciplinary team that includes neurologists, psychiatrists, psychologists, and speech therapists [3].

1.2 Epidemiology

The lack of studies on ASD means that individuals with this disorder and their families do not receive a timely and accurate diagnosis to establish a treatment plan that improves their quality of life. This is because, in Latin America, the shortage of professionals specializing in this disorder and the lack of adequate equipment result in high diagnostic costs, thereby hindering both diagnosis and research on ASD.

This issue results in insufficient data for epidemiological databases; however, it is known that the incidence of this condition is high worldwide and has been increasing over the years. The World Health Organization (WHO) indicates that 1 in every 160 children worldwide has some degree of autism, with a higher prevalence among males.

Epidemiological data show that the prevalence of ASD is between 1% and 1.5%. In Latin America, Mexico has a prevalence of 0.87%; however, studies in this region are scarce, making it difficult to determine the epidemiological profile of the area [4].

ASD affects men approximately four times more often than women, although recent research suggests that symptoms are more often masked in women, which can lead to a delayed or incorrect diagnosis. Comorbidity is high: between 70% and 90% of people with ASD have at least one associated disorder, the most common being attention-deficit/hyperactivity disorder (ADHD), intellectual disability, epilepsy, sleep disorders, and anxiety disorders [1].

1.3 Etiology and neurobiology

Autism is a neurodevelopmental disorder with a multifactorial etiology, in which various genetic variations interact with environmental factors. Approximately 100 genes that could influence the development of ASD have been studied, including NLGN, PTEN, MECP2, ANK, SHANK, TBR1, SYNGAP1, BOLA 2, and CDLK5. This pathogenic genetic burden is more common in women than in men [4].

The etiology of autism involves a significant and highly diverse genetic influence; a mutation in a single gene may be sufficient to cause it, or more than 1,000 genes may be required, and different genetic mechanisms may be at play.

ASD is associated with alterations in functional brain connectivity, particularly in networks involving the prefrontal cortex, the limbic system, and the cerebellum. Imbalances have been described in the glutamatergic, GABAergic, dopaminergic, and serotonergic neurotransmission systems, which currently constitute the main pharmacological targets [6].

Various studies indicate that there may be a history of perinatal neurological risk and a prevalence of symptoms in preterm infants (PTIs) or those with low birth weight (LBW). Since autism has a highly heritable genetic basis, it is estimated that it may occur more frequently if there are family members with ASD or another neurodevelopmental disorder [1].

1.4 Psychosocial impact in families

ASD has a profound impact on families, especially on primary caregivers, who may go through a series of stages similar to those of grief. Initially, they may experience a state of shock caused by unexpected news, in this case, the ASD diagnosis. This is followed by a stage of denial, during which they may seek second opinions in the hope that the diagnosis will be different. This is quickly followed by the phase of irritation and guilt,

during which parents try to uncover the underlying cause of the child's condition. Subsequently, the stage of despair sets in, which can develop into a depressive state, and finally, the stage of acceptance. This may occur after receiving relevant scientific information about the condition, thereby facilitating an appropriate intervention model. Receiving an ASD diagnosis triggers a crisis within the family. Qualitative studies of Latin American families indicate negative repercussions on the family environment, stemming from mental health issues such as stress, depression, and/or anxiety. Additionally, families experience social overload and difficulties in accessing reliable information and support services [7].

The social stigma associated with ASD also represents a significant barrier; it has been reported that families often face negative judgments, experience poor or non-existent emotional support, as well as rejection and/or discrimination in educational and community settings, which can negatively impact both the support families receive and parental stress levels, as well as their quality of life and their ability to seek specialized care [8].

Lack of awareness and sociocultural beliefs about ASD can lead to delayed diagnoses, thereby hindering early intervention for its treatment. In a multidisciplinary model, this can impede pharmacological treatment when necessary; in the Latin American context, medication adherence may be compromised due to social, economic, family, and individual factors [9].

2. Pharmacological Treatment of ASD

2.1 General Principles of Pharmacological Management

It is essential to understand that, to date, there is no medication that cures ASD or alters the course or cause of the condition. Pharmacological treatment is aimed solely at managing specific symptoms that may arise in patients with ASD and that can affect their functioning and quality of life, such as irritability, impulsivity, and hyperactivity; it may also be aimed at managing associated comorbidities such as epilepsy, anxiety, depression, hyperactivity, obsessive-compulsive disorder, ADHD, tics, eating disorders, sleep disorders, and seizures, among others [10] [11].

It is important to note that the treatment of ASD takes a multidisciplinary approach; therefore, a comprehensive treatment plan is necessary, with behavioral and psychoeducational interventions as its core components, while the use of medication serves as a supplement to the core treatment. The decision to initiate pharmacological treatment must be made with caution, weighing the expected benefits against the risks that may arise during treatment, such as potential adverse effects; this is where parents play a fundamental role in the therapeutic partnership [10].

The prescription of medications in pediatric patients must be approached with care, as many of the drugs used lack validated clinical trials in children with ASD; consequently, there is limited information on safety and efficacy, and their use is primarily based on off-label evidence. This lack of information can be attributed to the difficulties in developing and approving pharmacological treatments for ASD due to clinical, genetic, and pathophysiological heterogeneity, a lack of follow-up studies, and the difficulty in obtaining parental consent [11] [12].

The choice of pharmacological treatment should be based on the target symptom, that is, those behaviors or symptoms that most significantly impact the quality of life of both the patient and their family [13]. This is why treatment must be specific and tailored to each patient, taking into account age, symptoms, and diagnosis; the goal of treatment is to improve the course of ASD and prevent additional difficulties in learning and cognitive decline [14].

Currently, there are no approved medications for core symptoms and/or comorbidities; most of the drugs used are psychotropic and affect the central nervous system, and only risperidone and aripiprazole are authorized by the FDA for comorbidities. Which is why behavioral treatments, supportive therapies, educational support, and parent training remain the foundation of ASD interventions, with pharmacological interventions being limited; for these, regular monitoring of clinical response and adverse effects is essential [11] [12].

The following table lists the medications most commonly used in Mexico for the adjunctive pharmacological treatment of ASD:

Table 1. Medications most commonly used in Mexico for adjunctive pharmacological treatment of ASD

Type of medication	Drug
Antipsychotics	-Risperidone -Aripiprazole
Antidepressants	-Fluoxetine
Stimulants and non stimulants	-Atomoxetine
Antiepileptics	-Valproic acid
Sleep aid	-Melatonin

2.2 Antipsychotics

Given the heterogeneity of ASD, there are medications used to manage symptoms or comorbid conditions that may arise. These include antipsychotics, which are typically prescribed to treat conditions characterized by psychotic episodes and are primarily used for

schizophrenia. “Autism is not a disease” is a condition that varies in terms of abilities; each case is different, which complicates the choice of pharmacological treatment. There are options for speech therapy, occupational therapy, and psychological therapy that help improve their abilities and behavior.

Antipsychotics are classified into two groups: first-generation antipsychotics, which, within their mechanism of action, show a greater affinity for dopamine D2 receptors, which can lead to a higher incidence of extrapyramidal effects; on the other hand, there are second-generation antipsychotics, better known as atypical antipsychotics, so named for their low affinity for dopamine receptors, with less evidence of extrapyramidal crises.

In Autism Spectrum Disorder, the use of atypical antipsychotics is prevalent due to their lower incidence of adverse effects; among these, the Food and Drug Administration (FDA) has approved only risperidone and aripiprazole for its treatment, with risperidone being the first-line medication for the management of children with ASD [6].

2.2.1 Risperidone.

Risperidone was the first antipsychotic to be approved by the FDA in 2006 for children aged 5 to 16 years for the treatment of irritability, disruptive behaviors, self-harm or aggression toward others, and sudden mood swings; it is the drug with the most studies regarding its outcomes in this disorder and the efficacy achieved [6] [15] [16]. It is an antidopaminergic neuroleptic belonging to the benzisoxazole class, with high affinity for serotonergic and dopaminergic receptors and lower affinity for adrenergic and histaminergic receptors. It is an antagonist of dopamine D2 receptors located in the mesolimbic pathway and, to a greater extent, acts as an antagonist on serotonin type 2 (5-HT2) in the frontal cortex; it also exerts moderate blockade on alpha-1 adrenergic receptors and mild blockade on alpha-2 adrenergic and histamine H1 receptors; these receptors modulate the release of neurotransmitters such as dopamine, norepinephrine, glutamate, GABA, and acetylcholine, among others; by decreasing the activity of dopaminergic pathways, mood disorders can be improved [12] [15] [17].

The dosage of risperidone may vary depending on the clinical presentation. In the pediatric population, for children weighing more than 50 kg, it is recommended to start treatment with a dose of 0.5 mg once daily, which can be adjusted based on the patient’s response; with an optimal dose of 1 mg/day. For pediatric patients weighing less than 50 kg, an initial dose of 0.25 mg is recommended, with an optimal dose of 0.5 mg/-day for this group [17] [18].

It is absorbed orally without being affected by food, with a bioavailability of 75–90%. It reaches peak plasma concentrations within 1–2 hours, has high affinity for plasma proteins (88% protein binding), and is highly fat-soluble. Its half-life is 3 hours, and it is metabolized in the liver; one week after administration, it is excreted in the urine and, to a lesser extent, in the feces [14] [18].

Side effects and adverse reactions can vary depending on the dose and the patient; among the most common are sedation, drowsiness, insomnia, headache, sleep disturbances, agitation, depression, anxiety, dizziness, tremor, mania, and undoubtedly one of the most common is metabolic changes, including an increase in body mass index. The patient’s progress and metabolic parameters (weight, blood glucose, and lipid profile) must be closely monitored [6] [17] [18].

2.2.2 Aripiprazole.

Aripiprazole, like risperidone, is an atypical antipsychotic that was approved by the FDA in 2009 for the treatment of irritability associated with ASD in patients aged 6 to 17 years, although it has also been used in patients as young as 4 years old [6] [11]. It is a partial agonist of dopamine D2 and serotonin 5HT1a receptors and an antagonist of serotonin 5HT2a receptors. Studies have demonstrated its efficacy at doses ranging from 5 mg to 15 mg/day, improvements can be observed 8 weeks after treatment begins and show cognitive and behavioral improvements similar to those of risperidone, reducing hyperactivity, irritability, and stereotypies, and leading to an improvement in overall functioning [6] [11].

Regarding side effects, they are similar to those of risperidone and are often less severe in some cases; these may include sedation, drowsiness, weight gain, increased appetite, vomiting, and, in the long term, extrapyramidal symptoms. Studies suggest the need for constant monitoring during aripiprazole treatment, as a significant reduction in high-density lipoproteins, a slight increase in total cholesterol, low-density lipoproteins, triglycerides, and blood glucose were reported in [6] [11].

2.2.3 Other antipsychotics.

Other atypical antipsychotics used for autism spectrum disorder include olanzapine, quetiapine, clozapine, and haloperidol; however, the evidence is very limited, as there are few studies involving small groups, and none of them are approved in their product labels for the indication of controlling inappropriate or dis-

ruptive behaviors. Studies mention that they show a good response in cases such as schizophrenia, ASD, and PDD, but they also mention that they may produce long-term extrapyramidal adverse effects; however, this has not yet been proven [13] [19].

For olanzapine, there are double-blind, placebo-controlled studies involving children aged 6 to 14 years; however, the sample size was very small, consisting of only 11 children. The study lasted 6 weeks and showed improvement on the Pediatric Global Clinical Impression Scale; however, significant weight gain was also reported in patients, which often limits its use [11]. On the other hand, clozapine is not typically used as a first-line treatment because it is impractical, as it requires constant monitoring such as periodic laboratory tests and due to its potential for significant adverse effects, including agranulocytosis and myocarditis, as well as weight gain, constipation, metabolic syndrome, and drowsiness [6] [11].

Haloperidol, a typical antipsychotic, like the previous ones, has very little evidence regarding its use in patients with ASD. One study compared the effect of haloperidol at doses between 1 and 1.5 mg/kg/day in patients aged 10 to 36 years, reporting a greater reduction in irritability, disruptive behaviors, and hyperactivity; it may cause adverse effects such as sedation, constipation, weight gain, and liver function abnormalities, among others. In children, psychomotor retardation and the onset of extrapyramidal symptoms are of greater concern because these patients will require treatment for extended periods [13] [14].

Finally, among first-generation antipsychotics is levomepromazine, which acts by blocking postsynaptic mesolimbic dopaminergic receptors and is capable of exerting central and peripheral effects on adrenergic, muscarinic, and serotonergic receptors, resulting in improved mental symptoms, such as relief from delirium, agitation, restlessness, and mental confusion. It has been used in children aged 4 to 10 years at doses of 0.1 to 0.2 mg/kg/day. The high prevalence of neurological and anticholinergic adverse effects, among others, is noteworthy; therefore, it must be monitored by a specialist such as a pharmacist [20].

2.3 Antidepressants

Studies suggest that dysregulation of serotonin homeostasis in the central nervous system may be linked to the development of ASD, but the exact reason remains unknown. Serotonin is a neurotransmitter that has been shown to be involved in psychiatric conditions such as ASD, as its levels may be elevated or decreased, as may those of dopamine and norepinephrine, this can lead to certain symptoms such as self-injurious behaviors and comorbidities like anxiety, depression, and obsessive-compulsive disorder [12] [14]. Currently, the most commonly used medications are selective serotonin reuptake inhibitors (SSRIs). Their mechanism of action involves inhibiting the presynaptic reuptake of serotonin, thereby increasing serotonin, dopamine, and norepinephrine levels in various parts of the brain. Although they are considered first-line treatments for neurotypical individuals, their use for treating core ASD symptoms is not supported. Studies indicate that autistic patients are more likely to experience adverse events, such as gastrointestinal disturbances, amotivational syndrome, or behavioral disinhibition, which can lead to increased irritability and aggression, therefore, caution must be exercised with dosing, and monitoring by a specialized pharmacist is required [11] [12] [13].

2.3.1 Fluoxetine.

Fluoxetine, a member of the SSRI class, has been widely used in children with Autism Spectrum Disorder. Although it is not approved by the FDA, it has been reported to be effective at doses between 20 and 40 mg/day in reducing anxiety, depression, obsessive-compulsive disorder, and repetitive behaviors; however, multiple significant adverse effects have been noted, such as restlessness, hyperactivity, agitation, insomnia, decreased appetite, and even suicidal thoughts, which were dose-dependent and demonstrated that not all patients tolerate the medication well. Therefore, it is recommended to start with a low dose and gradually increase it to half the maximum safe dose depending on the patient's response [11] [12] [13] [14] [21].

2.3.2 Sertraline

Sertraline is considered a first-line treatment for depression and anxiety; it is the only one approved for use in pediatric patients. It is recommended that treatment begin with a low dose of 25 mg/day during the first week and then be increased to a maximum of 50 mg/day during the second week. It is administered as a single nightly dose, not exceeding 75 mg/day in children, as higher doses may increase the risk of side effects. The medication should be continued for at least 8 weeks to confirm its effectiveness, and discontinuation should be gradual to avoid side effects such as withdrawal syndrome [13] [14] [21].

2.4 Other medications used in the treatment of ASD

2.4.1 Atomoxetine

It is a non-stimulant medication that inhibits the presynaptic norepinephrine transporter in the central cortex. The WHO classifies it as a centrally acting sympathomimetic, it prevents the reuptake of norepinephrine

throughout the brain, leading to increased levels of dopamine and norepinephrine in the prefrontal cortex, and has therefore been reported as effective and identified as a first-line medication for the treatment of attention-deficit/hyperactivity disorder (ADHD), which often presents as a comorbidity of ASD and may be accompanied by irritability. Studies suggest a dose of approximately 1.5 mg/kg/day, not exceeding 100 mg/-day. Regarding its adverse effects, these may include loss of appetite, changes in heart rate and blood pressure, abdominal pain, nausea, vomiting, weight loss, and liver damage, among others [12] [16] [22].

2.4.2 Valproic acid

It is considered a mood-stabilizing medication and can therefore be used in patients with ASD to treat behavioral dysregulation, such as irritability, aggression, hyperactivity, and certain comorbidities such as epilepsy, manic episodes, and bipolar disorder. It works by inhibiting enzymes that reduce GABA metabolism and increasing GABAergic neurotransmission. Recommended doses range from 10 to 15 mg/kg/day. Side effects may include nausea, anorexia, lethargy, tremors, edema, hepatotoxicity, and pancreatitis, particularly in pediatric patients [11] [12] [21].

2.4.3 Methylphenidate

It is a psychostimulant that selectively inhibits the reuptake of norepinephrine and dopamine, increasing the action of both in the prefrontal cortex and other brain areas. Studies have been conducted in children aged 5 to 13 years, using maximum doses of 0.5 mg/kg/day, reporting improvements in impulsivity, hyperactivity, stereotypies, and repetitive behaviors. Adverse effects identified included decreased appetite, insomnia, irritability, hyporexia, headache, and changes in blood pressure, heart rate, and hormonal systems [11] [12] [16] [22].

2.4.4 Melatonin

Various studies conducted over time have shown that sleep disorders occur two to three times more frequently in children with ASD, presenting with impaired sleep quality and reduced sleep efficiency, difficulty falling asleep, frequent awakenings, and anxiety, among other symptoms. This contributes to daytime sleepiness and irritability, which is why it is often prescribed as a treatment for sleep disorders in autistic patients. It is recommended to administer it 30 to 60 minutes before bedtime; for infants, up to 1 mg is recommended; for children, 2.5 to 3 mg; and 5 mg for adolescents. Side effects may include abdominal cramps, decreased alertness, dizziness, drowsiness, and headache [11] [12] [16] [21].

2.5 Pharmacoepidemiological Profile in Latin America

A pharmacoepidemiological study conducted in Mexico analyzed medication use patterns in children with ASD, documenting a predominance of prescriptions for atypical antipsychotics, followed by stimulants and anticonvulsants. A high frequency of polypharmacy was observed, with more than 50% of patients receiving two or more drugs simultaneously. This situation increases the risk of drug interactions and adverse effects, reinforcing the need for specialized pharmacotherapeutic monitoring, as well as specialized pharmacy staff [12].

Pharmacotherapy monitoring in polypharmacy pediatric patients with intellectual disabilities, including those with ASD, has revealed frequent medication-related problems (MRPs), such as unmet needs, inappropriate dosing, and interactions. The detection and resolution of these problems by clinical pharmacists has been shown to improve health outcomes and quality of life for these patients [21].

3. Treatment Adherence in ASD

3.1 Conceptualization of Adherence in ASD

Therapeutic adherence is defined as the extent to which a person's behavior (taking medication, following a diet, or implementing lifestyle changes) aligns with the recommendations agreed upon with the healthcare team. In the context of ASD, adherence is particularly complex due to the disorder's inherent characteristics, such as resistance to change and sensory difficulties, which can interfere with medication administration [23].

Adherence should be understood as a multidimensional phenomenon that encompasses not only taking medication correctly but also attending follow-up appointments, undergoing monitoring tests, and implementing recommended behavioral changes. In the case of children with ASD, the responsibility for adherence falls primarily on the caregiver, which adds an additional layer of complexity to the process [7].

3.2 Factors Influencing Adherence

The factors influencing adherence in children with ASD are numerous and are intricately interrelated. Among the patient related factors, the following stand out: sensory difficulties with swallowing medication, behavioral resistance to new routines, and the presence of comorbidities that complicate management. Drug related factors include taste, dosage form, dosing frequency, and the presence of adverse effects [23].

Caregiver related factors are particularly relevant. Educational level, beliefs about medication, the burden of care, and available social support directly influence

adherence. Caregivers with limited knowledge of ASD or with misconceptions about psychiatric medications tend to show lower adherence, sometimes discontinuing treatment without consulting the physician [7].

Systemic factors such as access to health services, medication availability, treatment cost, and the quality of the doctor-patient-family relationship also significantly influence adherence. In Latin American contexts, economic and geographic barriers are frequent determinants of treatment discontinuation [4].

3.3 Cultural and mistaken beliefs held by caregivers

Cultural beliefs surrounding ASD and psychotropic medication are one of the main barriers to adherence in Latin America. A study conducted in Lima, Peru, identified common misconceptions among parents of children with ASD, including the association of antipsychotics with addiction, the fear that medications will "change the child's personality," or the perception that ASD can be cured through diet or alternative therapies [7]. Although in the case of homeopathic medicine which is a different type of medicine the results speak for themselves, it does not cause lethargy, and it is urgent to conduct research to distinguish therapeutic effects that cause lethargy and are nonspecific, this is why research plays a crucial role in the treatment of ASD.

A recent study published on Zenodo documented the influence of cultural beliefs on the medication management of parents of children with ASD, showing that mistrust of conventional treatment and a preference for traditional remedies are prevalent factors that pharmacists must actively address through culturally sensitive communication strategies [9].

Health education aimed at caregivers should consider these beliefs as a starting point, adopting an approach of intercultural respect that does not invalidate the caregiver's perspectives but provides scientifically grounded information in an accessible and empathetic manner. Pharmacists, due to their role in the healthcare system and their frequent contact with families, are in a unique position to carry out this educational work [24].

3.4 Strategies to improve adherence

Strategies to improve adherence in [ASD] should be individualized and multifaceted. From a pharmacological perspective, simplifying the treatment regimen, selecting appropriate dosage forms (oral solutions, extended-release formulations), and taking the child's sensory preferences into account can make it easier for the child to take the medication. The use of pill organizers, alarms, and medication logs can help caregivers track the regimen [23]. However, in the case of medication for [ASD] combined with psychiatric treatment, it cannot be individualized or tailored to each specific case, as every case of [ASD] is unique; therefore, research is urgently needed to provide substantial and effective interventions for these types of cases.

Educating the caregiver about treatment goals, the mechanisms of action of the medications, expected side effects, and warning signs is essential. Structured psychoeducational interventions have been shown to significantly improve adherence and caregiver satisfaction. Regular follow-up by the healthcare team, including the pharmacist, helps to detect adherence barriers early and implement timely solutions [5].

4. The Role of the Pharmacist in Addressing ASD

4.1 The pharmacist as part of the multidisciplinary team

Pharmacists are healthcare professionals with specialized training in pharmacology, pharmacokinetics, pharmacotherapy, and pharmaceutical care skills that uniquely position them to contribute to the comprehensive management of patients with ASD. Their effective integration into the multidisciplinary team, alongside neurologists, psychiatrists, therapists, psychologists, and social workers is essential to ensuring the safety and effectiveness of pharmacological treatment [25].

Despite this potential, in many Latin American contexts, the pharmacist remains a peripheral figure in ASD management, limited to dispensing duties without active participation in therapeutic decisions. The meaningful integration of pharmacists into specialized ASD care teams remains an unmet need in the Latin American healthcare system [5].

4.2 Pharmacotherapeutic monitoring

Pharmacotherapy monitoring (PTM) is the service through which the pharmacist takes responsibility for the patient's medication-related needs, and identifies, prevents, and resolves medication-related problems (MRPs) in a continuous, systematic, and documented manner. In children with ASD, PTM is particularly important given the complexity of the medication regimen and the vulnerability of this population [21].

PTM in pediatric patients with ASD should include periodic review of all prescribed medications, evaluation of each drug's effectiveness in relation to its specific therapeutic goals, monitoring of safety parameters (weight, blood pressure, blood glucose, prolactin in the case of antipsychotics), and detection of drug interactions [12] [18].

A fundamental component of PTM is the assessment of adherence. The pharmacist can use validated tools

such as the Morisky-Green test, counting dispensed medications, or simply conducting a motivational interview with the caregiver to identify patterns of non-adherence and design specific interventions [23].

4.3 Detection and Management of Adverse Reactions and Drug Interactions

Polypharmacy is common in ASD and carries a high risk of drug interactions. Pharmacists, with their specialized knowledge of pharmacology and pharmacotherapy, are the professionals best equipped to detect and evaluate these interactions. Combinations of antipsychotics with stimulants, anticonvulsants, or antidepressants are particularly common and require close monitoring [12].

The early detection of adverse drug reactions (ADRs) is another key role of the pharmacist. In children with ASD, many ADRs may go unnoticed or be mistaken for symptoms of the disorder itself, which can lead to unnecessary escalation of treatment. Effective communication with the caregiver about warning signs and the creation of accessible reporting channels are valuable strategies in this context [18] [24].

4.4 Patient and caregiver education

The pharmacist's educational role is particularly valuable in ASD. Caregivers often have questions about the safety of psychiatric medications, the expected time to respond, and the duration of treatment. The pharmacist can provide clear, accurate information tailored to the caregiver's level of understanding, helping to dispel misconceptions and strengthen the therapeutic alliance [7] [9].

Pediatric pharmaceutical care requires a collaborative process involving the child, parents, physician, and pharmacist. Effective communication, tailored to each family's cultural and educational background, is the cornerstone of this collaboration. The use of visual educational materials, simple language, and individualized counseling sessions has been shown to improve understanding and adherence in this population [25].

4.5 Challenges and areas of improvement

Despite the potential value of pharmacists in the management of ASD, significant challenges limit their effective involvement. The lack of specific training in neurodevelopment and child psychiatry in pharmacy programs, the absence of standardized pharmaceutical care protocols for ASD, and the limited integration of pharmacists into multidisciplinary teams are obstacles recognized in the literature [5] [24].

Research on pharmaceutical care in ASD is still in its early stages, with a limited number of high-quality studies evaluating the impact of pharmacist interventions on clinically relevant outcomes. The development of specific training programs, the creation of clinical practice guidelines that include the pharmacist's role, and investment in applied research are identified needs to strengthen this field [21] [24].

5. Conclusions

Autism Spectrum Disorder [ASD] is a highly complex and heterogeneous neurodevelopmental condition whose management requires a comprehensive, multidisciplinary, and individualized approach. Understanding its multifactorial etiology, neurobiology, and psychosocial impact is essential for any healthcare professional who cares for this population.

Although pharmacological treatment of [ASD] is not curing, it offers effective options for managing specific behavioral symptoms that impact functioning and quality of life. Atypical antipsychotics, particularly risperidone and aripiprazole, have the strongest evidence base; however, their use must be carefully monitored due to the risk of metabolic and neurological adverse effects. This implies that they are not specific to every case, and there is no one-size-fits-all treatment.

Therapeutic adherence is a key challenge in the management of ASD, influenced by factors related to the patient, the caregiver, the medication, and the healthcare system. Cultural and erroneous beliefs held by caregivers are particularly significant determinants in the Latin American context and must be addressed through culturally sensitive educational strategies.

The pharmacist, as a professional with specialized training in pharmacotherapy and pharmaceutical care, plays a strategic role in the management of ASD that goes beyond dispensing. Pharmacotherapeutic monitoring, the detection of ADRs and drug interactions, caregiver education, and the promotion of adherence are functions that the pharmacist can and should perform within the multidisciplinary team. However, it is necessary to invest in specific training, applied research, and integration models that allow this potential to be translated into concrete benefits for patients and their families.

More high-quality studies are needed in the Latin American context to evaluate the effectiveness of pharmaceutical interventions for [ASD], as well as the development of clinical practice guidelines that formally recognize the role of the pharmacist in managing this condition. The search for medications, regardless of their nature, that work effectively and are tailored to the individual case.

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