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Research Article

Impacts of Early Interventions in the Treatment of Autism Spectrum Disorder from a Medical Perspective

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Abstract

Introduction: The autistic spectrum disorder (ASD) manifests itself from the earliest age, often before the age of 3 until adulthood. The early diagnosis of the disorder is essential both for families and for people with ASD, as it allows guiding treatments and interventions.

Objective: To map and analyze the scientific literature regarding the impact of early intervention in the treatment of the autistic spectrum from the medical perspective.

Method: This is research of the integrative review type and supported by the adapted PRISMA protocol, in which the online search occurred through the SciELO, Medline/Pubmed, LILACS and Epistemonikos databases, and the temporal cut-off established for the search of the studies was from 2012 to March 2022.

Results: The results showed that of the total of 22 of the selected studies, 81.8% were published between 2020 to 2022, showing that the database with the largest scientific collection regarding TEA was sciELO(50%). As most of the studies were Brazilian, the dominant language was Portuguese; however, the studies with more robust designs were published in the United States of America.

Conclusion: It was concluded from the scientific literature that there is no early pharmacological intervention that can treat ASD; these alternatives are only to minimize the clinical picture related to hyperactivity, aggressiveness, and other more severe alterations. What do exist are early behavioral interventions, which are considered the gold standard for symptom control as well as for optimizing the treatment of the person with ASD.

Keywords: Autism Spectrum Disorder; Early Diagnosis; Early Medical Intervention; Autism; Autistic Disorder

Introduction

Current studies reveal that autism has been studied for several years, since the concepts about this disorder are still based on the Diagnostic and Statistical Manual of Mental Disorders, DSM-5 (2014) [1,2].

Autism spectrum disorder (ASD) manifests early, i.e., often before the age of 3 until adulthood. Depending on the degrees of autism, it is characterized by a dyad of qualitative deficits, namely around social communication and in restricted and repetitive patterns of behavior, interests, or activities [1].

As published by the CDC (Center of Diseases Control and Prevention) in December 2021, ASD affects one in 44 individuals and can be a costly lifetime disorder [2]. Due to the prevalence, costs, and variety of behavioral needs, early intervention is vital to teach skills across multiple domains and prevent the development or exacerbation of behavioral deficits and excesses [3]. It is worth adding that about 75% of autistic people show mental deficits and 1% of the world's population is diagnosed with ASD [2].

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder, defined as a complex developmental disorder, from the behavioral point of view, with different etiologies that manifests itself in varying degrees of severity[4]. Thus, autism is understood as a state or a condition, which seems to be reclusive in itself [4].

The pattern of development may change according to the degree of cognitive impairment, being worse in children. Those with severe cognitive impairment are more likely to show disruptive behaviors, such as aggressive behavior, more intense stereotyping, and consequently, less likely to develop language and socialization, requiring more intense and long-lasting treatments [5,6].

Often, people with ASD lack the skills to establish varied and spontaneous games of imagination or imitation, appropriate to individual levels of human development, as well as a tendency to establish rigid and repetitive behaviors and an interest in non-functional routines or rituals [7].

Early diagnosis of the disorder is essential both for families and for individuals with ASD, as it will enable the guidance of treatments and interventions, thus contributing to a deeper understanding of the disorder's characteristics. Currently, it has been observed that, although the diagnostic characteristics have been studied for decades, there are still numerous divergences and questions to be answered in this field of investigation [2,7].

The justification and relevance of this research was based on the problem that ASD is diagnosed late, in other words, only after the average age of five. However, at this stage, children with autism already face severe problems in social interaction and language, with the establishment of repetitive and often disruptive behaviors and non-functional routines, as they accumulate cascades of delays and losses that will negatively impact their development and, consequently, the prognosis of the disorder.

In this sense, this study sought subsidies from scientific evidence allusive to medical actions regarding the understanding of ASD and its strategies for early diagnosis. In view of the above, the guiding question emerged: what are the impacts of early intervention in the treatment of autism spectrum from the medical perspective?

Thus, the purpose of this study was to map and analyze the scientific literature regarding the impact of early intervention in the treatment of autism spectrum disorder from a medical perspective.

Methods

This is an integrative literature review, which covers primary research and studies by different authors, discussing the methods used and the results found among them. Regarding the literature review method, this is the one proposed by Mendes (2008) [8]. This type of research approach broadly and thoroughly analyzes the scientific literature available in each period for the full understanding of an event through previous research [8].

The first stage of the study was conducted based on a guiding question: what are the impacts of early intervention in the treatment of autism spectrum disorder from the medical perspective? Subsequently, in the second stage, the authors defined the inclusion criteria: articles from national and international primary sources, published between 2012 and May 2022 in the SciELO, Pubmed, LILACS and Epistemonikos databases in English, Portuguese, and Spanish. Articles outside the predetermined period for the study were excluded, as well as those that were not related to ASD and medical interventions, reviews, meta-analyses, gray literature, state of the art, and articles in other languages.

The third step consisted of implementing the search descriptors in Portuguese; "Transtorno de Espectro Autista", "Diagnóstico Precoce", "Intervenção Médica Precoce", "Autismo" and "Transtorno Autístico" in English; Autism Spectrum Disorder, Early Diagnosis, Early Medical Intervention, Autism and Autistic Disorder and in Spanish; Trastorno del Espectro Autista, Diagnóstico Precoz, Intervención Médica Temprana, autismo e Transtorno Autístico. To combine the descriptors, "AND" and "OR" were used within the following categories: Health Sciences and primary studies. The online search for the execution of the main research was carried out between the months of August and September 2022.

Potentially eligible studies were previously selected by title and abstract reviewed by two investigators independently. After this refinement step, those that did not meet the inclusion criteria were excluded. All primary studies selected in this step were read in their entirety.

The authors used Mendeley (Copyright©2009-2013Mendeley Ltd. https://www.mendeley.com/download-desktop-new/) and Excel®2016 spreadsheets for reference management and duplicate removal, and to ensure confidence of data selection and organization, the independent reviewers met once again to resolve conflicts and discuss uncertainties related to study selection.

The selection criteria for the articles followed the requirements of the adapted Prisma strategy, according to Moher (2009) [9], represented according to (flowchart 1) regarding the different steps applied to the selection process of the included and excluded articles in the integrative literature review.

Considering the ethical aspects, the authorship of the researched articles was assured in this integrative review, so that all studies used were cited. The consent of the Research Ethics Committee for this type of research is not necessary since there was no involvement of human beings in the study and no institutions as a source of research.

Results

The integrative review sample was composed of 22 primary studies in the period from 2012 to May 2022. The period in which there were more publications concerning early interventions for ASD was from 2020 to 2022 (81.8%), which draws attention to the period of greatest global pandemic peak in which social isolation made people stay at home, which contributed to professionals and researchers to start producing even more. Regarding language, English was the dominant language in the studies. The database with the greatest hegemony involving ASD was SciELO (50%), followed by Pubmed/Medline (41%), and lastly LILACS (9%). All studies selected in Epistemonikos were excluded, as they were not related to the year and guiding question.

The country that produced the most research involving ASD was Brazil (50%), followed by the United States of America (32%), and the remaining (4.5%) analogues were distributed among the United Kingdom, China, New Zealand, and Ecuador. Of the (50%) of Brazilian studies published, most (73%) were published in the Portuguese language, evidencing the great vulnerability of Brazilian researchers to master the English language in the scientific scenario.

As for the method adopted in the studies, 40.9% were randomized clinical trials (RCT) (level of evidence 2 and 3); only one (4.5%) RCT was published in Brazil, the others (54.6%) were distributed in cross-sectional, longitudinal, case series and case report studies (level of evidence 5, 6 and 7). It is notorious the scarcity of scientific productions in Brazil involving ASD with a more robust design.

Figure 1 presents the selection of studies in a more didactic and understandable way.

Chart 1 highlights the main information extracted from the primary studies included in the integrative review, and Table 1 shows the relative and absolute frequencies concerning the years of scientific production related to ASD and interventions.

Figure 1: Flowchart of primary study selection for the integrative review based on the adapted PRISMA model.
Source: Adapted from Moher *et al*., (2009) [9].
Legend: DeCS: Health Sciences Descriptors; MeSH: Medical Subject Headings

Studies Years	f_i	f_{ri}	F_i%	F_{ri}%
2012|-----2014	1	1	4.5	4.5
2014|-----2016	3	4	13.6	18.1
2016|-----2018	1	5	4.5	22.7
2018|-----2020	4	9	18.2	40.9
2020|-----2022	9	18	40.9	81.8
2022-----|	4	22	18.2	100
TOTAL	22	-	100	-

Table 1: Distribution of years of publications related to ASD by frequencies, 2022.

Legend: fi: Simple Frequency; fri: Simple Relative Frequency; Fi: Absolute Simple Frequency; Fri: Cumulative Relative Frequency

Data Base	Authors/Year/ Type of study/ Country	Title	Objective	Main results
Pubmed	Estes., *et al*. (2015) [10]. Randomized clinical trial. USA	Long-Term Outcomes of Early Intervention in 6-Year-Old Children with Autism Spectrum Disorder.	Prospectively examine evidence for the sustained effects of early intensive behavioral intervention initiated between 18 and 30 months of age for children with ASD at age 6.	Early intensive behavioral intervention has been found effective in improving developmental outcomes for young children with ASD. Intellectual, language, and adaptive functioning gains made because of early intervention can be generalized to new domains of functioning such as reduced severity of ASD symptoms after two years.
Pubmed	Adams., *et al*. (2018) [11]. Randomized clinical trial. USA	Comprehensive Nutritional and Dietary Intervention for Autism Spectrum Disorder: A Randomized, Controlled 12-Month Trial	Investigate a comprehensive nutritional and dietary intervention to treat children and adults with ASD.	There were significantly greater improvements in scores for the treatment group compared to the no treatment group (-28% vs. -6%, p = 0.00004). Vitamin/mineral supplementation and essential fatty acids appear to have the greatest clinical benefit, although other treatments appear to have some benefit for some individuals.
Pubmed	Sikich., *et al*. (2021) [12]. Randomized clinical trial. USA	Intranasal Oxytocin in Children and Adolescents with Autism Spectrum Disorder	To evaluate the efficacy of 24 weeks of intranasal oxytocin treatment for improving social function in children and adolescents with autism spectrum disorder.	It showed no significant difference between oxytocin and placebo, each administered daily for 24 weeks.
Pubmed	Wood., *et al*. (2018) [13]. Randomized clinical trial. USA	Cognitive Behavioral Treatments for Anxiety in Children With Autism Spectrum Disorder A Randomized Clinical Trial	To compare the relative efficacy of 2 cognitive-behavioral therapy (CBT) and usual treatment (TAU) programs to assess treatment outcomes on maladaptive and interfering anxiety in children with ASD.	Cognitive-behavioral therapy appears to be a first-line treatment for verbal children with ASD and maladaptive and interfering anxiety, and, when this approach is extended to the medication realm, the result is even more satisfactory.
Pubmed	Singh., *et al*. (2014) [14]. Randomized clinical trial. USA	Sulforaphane treatment of autism spectrum disorder (ASD)	To evaluate whether daily interventions with Sulforaphane at dietary achieved levels can reduce the severity of socially impaired behavior in ASD.	Substantial improvements in the individual trajectories of patients with ASD were evident and suggest that further investigation of Sulforaphane in ASD is promising.
Pubmed	Mazahery., *et al*. (2019) [15]. Randomized clinical trial. New Zealand	A Randomized Controlled Trial of Vitamin D and Omega-3 Long Chain Polyunsaturated Fatty Acids in the Treatment of Core Symptoms of Autism Spectrum Disorder in Children	Evaluate the effectiveness of vitamin D, long-chain omega-3 polyunsaturated fatty acids, or both on the central symptoms of ASD.	This work suggests the possible efficacy of omega-3 LCPUFA alone or in combination with vitamin D in managing some core symptoms of ASD, including social-communicative functioning and some domains of sensory issues.

Pubmed	Wieckowski., *et al*. (2021) [16]. Longitudinal study. USA	Early and Repeated Screening Detects Autism Spectrum Disorder	To evaluate the timing and accuracy of early and repeat screening for autism spectrum disorder (ASD) during childcare visits.	Suggest that screening at the 12-month childcare visit identifies many children at risk. The average age at diagnosis for the entire sample was 23 months, more than 2 years earlier than the national median of 51 months.
Pubmed	Dawson., *et al*. (2012) [17]. Randomized clinical trial. USA	Early behavioral intervention is associated with normalized brain activity in young children with autism	To evaluate the effectiveness of the Early Start Denver Model, a comprehensive developmental behavioral intervention, for improving outcomes for children with ASD.	Suggest that the ESDM intervention is associated with normalized patterns of brain activity related to attention and social engagement, and that these normalized patterns of brain activity are correlated with improvements in social behavior.
Pubmed	Crutel., *et al*. (2021) [18]. RCT-Multicenter. United Kingdom	Bumetanide Oral Liquid Formulation for the Treatment of Children and Adolescents with Autism Spectrum Disorder: Design of Two-Phase III Studies (SIGN Trials)	Demonstrate the superiority of bumetanide over placebo after 6 months of treatment	Suggest that the ESDM intervention is associated with normalized patterns of brain activity related to attention and social engagement, and that these normalized patterns of brain activity are correlated with improvements in social behavior.
SciELO	Jia., *et al.* (2021) [19]. Randomized clinical trial. China	Improvement of the health of people with autism spectrum disorder by exercise	This article conducts exercise intervention on children with ASD to stimulate their exercise ability and improve their self-care ability	The two groups of subjects improved their large muscle motor skills, and the experimental group had a more significant improvement in their large muscle motor skills.
SciELO	Brito., *et al*. (2021) [20]. Randomized clinical trial. Brazil	Effect of prednisolone on language function in children with autistic spectrum disorder: a randomized clinical trial	To describe the effect of prednisolone on language in children with autism spectrum disorder. This study is based upon two hypotheses: autism etiology may be closely related to neuroinflammation; and an effective treatment should restore the individual's language skills.	Prednisolone increased the overall ADL score in children under 5 years of age who had developmental regression ($p = 0.0057$). Total communicative acts of the ABFW also responded favorably in those participants with regression ($p = 0.054$). The ABFW total vocal acts showed the most significant results, especially, in children younger than 5 years ($p = 0.004$, power = 0.913).
SciELO	Oliveira., *et al*. (2022) [21]. Case report. Brazil	Therapy based on sensory integration in a case of autism spectrum disorder with food selectivity	To analyze the relationship between food selectivity and sensory processing dysfunction in a child with Autistic Spectrum Disorder (ASD) and to follow its evolution with a therapeutic approach of sensory intervention.	Analysis of the interaction that the child presented with food was essential in the case studied, because, for the child to be allowed to consume a new food, it is necessary to follow a path that goes through several stages, such as interacting with food, looking, smelling, touching, tasting, and eating. The child needed to give new meaning to the moment of eating to feel safe
SciELO	Montenegro., *et al*. (2022) [22]. Case report. Brazil	Use of a robust alternative communication system in autism spectrum disorder: a case report	To investigate the impact of using a robust communication system, structured in the format of a low-tech communication book, on a child with ASD.	Interventions with augmentative and alternative communication (AAC) present positive results in all targeted behavioral aspects, but communication skills present greater effects than other skills

SciELO	Lin., *et al*. (2020) [23]. Case report. Brazil	Autism associated with 12q	To report the case of a patient with interstitial deletion of the 12q24.31-q24.33 bands and review the current literature, comparing it with previously reported cases, also including a few other cases of deletion involving the 12q24.31 region.	In the neurological evaluation, severe agitation associated with self-aggressive behavior, characterized by blows to the head, resulting in severe self-inflicted injuries, stood out. He presented with spastic hypertonia and vivid tendon reflexes and was unable to walk independently and to speak.
SciELO	Becker., *et al*. (2016) [24]. Experimental study. Brazil	Improvement of autism spectrum disorder symptoms in three children by using gastrin-releasing peptide	To evaluate the safety, tolerability, and possible therapeutic effects of gastrin-releasing peptide in three children with autism spectrum disorder.	This study suggested that GRP may have an effect on the main symptoms of autism in childhood, mainly on compulsions and stereotypes.
SciELO	Mergl., *et al*. (2015) [25]. Clinical Case Series. Brazil	Echolalia´s types in children with autism spectrum disorder	Verification of the type of echolalia and communicative skills in seven boys with ASD, aged four to seven years, who use oral communication	It was indicated that most children in this sample presented echolalia, with the immediate type being more frequent than the delayed type. It was also possible to observe that there was no direct relationship between the type of echolalia and the general performance in the evaluation of language skills. In this study, all children showed performance below expectations in communicative skills and aspects of cognitive development, and less impaired verbal language comprehension.
SciELO	Costa., *et al*. (2022) [26]. Cross-sectional study. Brazil	Parents' perception of auditory hypersensitivity in children with clinical signs of risk for Autism Spectrum Disorder	To ascertain the occurrence and type of auditory hypersensitivity in children with clinical signs of Autism Spectrum Disorder through parental reporting in the context of the COVID-19 pandemic.	Regarding the occurrence of auditory hypersensitivity in children with clinical signs of ASD, it was found that, according to the parents' perception, this was present in (63.6%) of children. The most common manifestation is related to irritability, which suggests a relationship with the limbic system and may, therefore, refer to the type of auditory hypersensitivity called misophonic.
SciELO	Costa., *et al*. (2022) [27] Case report. Brazil	Psychodrama with children within the autistic spectrum disorder: a possible experience?	To discuss a psychodrama tic experience with an eight-year-old child diagnosed within Autistic Spectrum Disorder (ASD).	Thus, we highlight the importance of the bond in psychotherapy as well as the specificities of each case, because children diagnosed with ASD may exhibit a wide range of intellectual and language skills, and it is not possible to standardize expectations and interventions in this area.
SciELO	Gomes., *et al*. (2021) [28]. Cross-sectional study. Brazil	From social interaction to autonomy: ludic experiences in aquatic environment for children with autism spectrum disorder	The present study aimed at assessing ludic experiences in aquatic environment facilitated by a non-governmental organization in Florianópolis, state of Santa Catarina, for the social interaction of children with Autism Spectrum Disorder (ASD).	Aspects intrinsic to the very formatting of the play experiences acted as facilitators of moments of social interaction between the children with ASD and the volunteers, and three of these children showed interest in getting involved and creating play through social interaction.

SciELO	Rocha., *et al*. (2019) [29]. Diagnostic study. Brazil	O perfil da população infantil com suspeita de diagnóstico de transtorno do espectro autista atendida por um Centro Especializado em Reabilitação de uma cidade do Sul do Brasil.	To characterize the profile of the population of children with suspected autistic spectrum disorder seen at a CER-II in southern Brazil, to identify sources, reasons for referrals, sociodemographic characteristics, psychometric instruments used in the evaluations, and the levels of diagnosis received.	Sociodemographic characteristics, finding that most users belong to a nuclear family. It was identified that approximately one third of the evaluations carried out denoted autism, and that in 65.63% of these diagnoses there was specification of the level, denoting a majority in mild or moderate, and that the instrument most used by the professionals was the ABC. It is worth noting that there was a significant predominance of males.
Lilacs	Pesántez., *et al*. (2021) [30]. Case report. Ecuador	Utilización de Cannabidiol en un paciente pediátrico con trastorno del espectro autista y epilepsia: informe de un caso.	To evidence the evolution of the treatment after one year of intervention and follow-up, significant advances were evidenced in crisis control and improvement in empathic, adaptive, and relational skills	Cannabidiol may be an interesting therapeutic proposal to treat behavioral symptoms related to autism spectrum disorder. More research is needed to help understand the potential benefit of cannabidiol.
Lilacs	Santos., *et al*. (2020) [31]. Qualitative descriptive research. Brazil	Identificação de alterações genéticas relacionadas à síndrome do X frágil e ao transtorno de espectro do autismo por meio de ferramentas de bioinformática.	Identify gene expression changes that are associated with possible neurobehavioral pathways, present in both FXS and TEA, using bioinformatics tools.	The genes CAPNS1, HNRNPK and HNRPM have been identified as hypo expressed in individuals with Fragile X syndrome. These genes have an important modulating function in long-term potential (LTP) responses, neural plasticity, and in serotonin transporters (SERT) altering responses that encompass mood, cognition, and behavior, as well as interfering with the dopamine receptor (D2R) altering motor functions and reward circuits.

Chart 1: Distribution of studies by database, authors, year, study type, title, objective and results, 2022.

Source: The authors, (2022).

Discussion

The present review identified the interventions immanent to the early diagnosis of ASD in the period from January 2012 to May 2022. Among the studies, an American RCT with 167 children with ASD and maladaptive anxiety showed that cognitive-behavioral therapy (CBT) as an early intervention revealed significantly lower anxiety scores, and that this type of intervention is the standard method in clinical practice [14].

Another RCT evaluated children aged 18 to 30 months allocated into two groups: one group received interventions based on the early onset Denver model (ESDM), considered a naturalistic behavioral intervention that integrates applied behavior analysis (ABA) methods; the second group received traditional community treatment (Community-COM). The ESDM group showed better adaptive behavior and socialization skills and less severe general ASD symptoms compared to the COM group10,17 and further reinforce that interventions with ESDM are associated with improved brain activity by increasing attention, social engagement, and social behavior, concluding that early intervention is the most appropriate approach.

Among the intervention approaches used to promote the development of functional communication skills in individuals with ASD, the use of Augmentative and Alternative Communication (AAC) [22] stands out. The impact was positive in the development of communication after speech therapy intervention using the robust AAC system, as evidenced in the data on the development of receptive, expressive, and behavioral communication skills; and although the results were positive in all targeted behavioral

aspects, communication skills showed greater effects than the other skills.

Researchers suggest that the earliest screening for ASD should be implemented starting at 12 months of age, although this age range of investigation is not currently recommended by the American Academy of Pediatrics [16]. A study conducted by Chinese evaluated the implementation of physical exercise in children with ASD, revealing that exercise involving the large muscles, when learning conventional motor skills, can effectively improve motor movement disorders when compared to learning conventional motor skills [19].

Psychodrama is a therapeutic approach to the study of existential truths through action. Situated at the interface between art and science, based on the essence of this concept, Costa (2022) [27]. published a case report of an eight-year-old child and used psychodrama and concluded that its implementation in the care of children with ASD can generate a decrease in conserved responses and potentiate unprecedented and creative responses based on spontaneity as a catalyst of the creative process, in which the goal is not to "standardize", but to promote health in relation to creativity, sensitivity, and encounter.

Gomes (2021) [28]. emphasizes that playful experiences allow children to cultivate verbal or gestural communication skills and create bonds of trust with volunteers and other children. Research conducted in the city of Quito, capital of Ecuador, states that despite the lack of specific treatment currently available for ASD, early detection and intervention are imperative, as they are the key to a better prognosis [30].

Regarding genetic factors, ASD is a set of neurodevelopmental disorders, characterized by a deficit in social behaviors and non-verbal interactions, such as decreased eye contact, facial expression, and body gestures in the first three years of life, and is generally considered multifactorial, resulting from genetic and non-genetic risk factors [23].

The number of known genetic disorders associated with ASD has increased with the use of comparative genomic hybridization. This genetic diversity associated with cognitive-behavioral phenotypes similar to autism has created the concept of "syndromic autism" or "complex autism" (autism associated with genetic disorders/ genetic syndromes), which qualifies individuals with at least one dysmorphic/malformation aspect or severe intellectual disability, and the result of his study [23]. with a 2-year-old child showed that in the neurological evaluation he presented severe agitation associated with self-aggressive behavior, characterized by blows to the head, resulting in severe self-inflicted injuries, in addition to spastic hypertonia and vivid tendon reflexes, being unable to walk independently and to speak [23].

As mentioned above, Santos (2020) [31] evidenced that the CAPNS1, HNRNPK, HNRNPM genes have a strong relationship with neurobehavioral genetic markers. In this regard, it is important the modulating function in long-term potential responses, neural plasticity, and in serotonin transporters (SERT), modifying responses that encompass mood, cognition, and behaviors, besides interfering in the dopamine receptor (D2R) and altering motor functions and reward circuits.

With regard to pharmacological interventions, researchers have tested drugs such as Sulforaphane [14], which showed significant improvement among participants who presented with irritabiliety, lethargy, stereotypy, hyperactivity, conscientiousness, communication, motivation, and mannerism, Although consistent improvements in behavior were observed in the majority of those treated with Sulforaphane, this was a study of only 44 male, predominantly Caucasian patients, aged 13 to 27 years, so more robust studies are suggested to generalize the results.

Current studies [18] reveal that there are no approved drug therapies to improve social reciprocity and limit repetitive and rigid behaviors in ASD. Aripiprazole and Risperidone are approved in the US to treat behavioral symptoms; however, consensus guidelines do not recommend their routine use in ASD due to the risk of side effects [18].

Several studies have been conducted involving ASD; however, no treatment capable of curing ASD has been evidenced [24]. The available drug treatment only acts on the secondary symptoms of maladaptation. Most are prescribed off label, as only risperidone and aripiprazole have been approved by the Food and Drug Administration (FDA) for treating the aggression, irritability, and yelling habits seen in patients with autism.

Researchers [20] emphasize that intervention with prednisolone showed more evident language scores in participants younger than five years and with a history of regression of motor development. The side effects observed do not contraindicate its use in autism. It is assumed that a higher dose would achieve more favorable intervention results [20].

It is believed that many children with autistic spectrum disorder have tried intranasal oxytocin therapy based on supposedly promising data [12]. Haloperidol is approved in the European Union (EU) for the management of severe and persistent aggression in children aged 6 to 17 years with ASD, when other treatments fail or are not tolerated [18]. However, reported side effects of haloperidol include persistent dyskinesia and extrapyramidal symptoms [18].

In a RCT conducted in New Zealand in which vitamin supplementation with vitamin D and Omega-3 was used, the findings suggested possible efficacy of omega-3 LCPUFA supplementation alone or in combination with vitamin D in the management of major symptoms of ASD in children [15].

Conclusion

It can be concluded that the period in which there were more scientific publications about TEA was from 2020 to 2022. The database with the largest body of scientific evidence level 2 and 3 and robust design was SciELO. The dominant language in most articles was English. Most of the low-quality studies were developed by Brazilian researchers.

In summary, no studies have shown effective pharmacological interventions for the treatment of ASD, however, the drugs tested in the RCTs were beneficial in controlling behavioral symptoms such as irritability, moodiness, hyperactivity, and neurological spasms.

We conclude that naturalistic early behavioral interventions that integrate applied behavioral analysis (ABA) methods, in addition to Augmentative and Alternative Communication (AAC), insertion of physical activities, multi- and interdisciplinary approach, and activities with playful experiences are still the key to diagnosis, evolution control, and improvement in prognosis, bringing benefits such as: improvements in socio-behavioral interaction and in the discovery of motor and mental abilities in children with ASD.

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