Updates in Management of Autism Spectrum Disorder, A Review

Abstract:

Autism is a neurodevelopmental disorder characterized by poor social interaction, verbal and nonverbal communication difficulties, and restricted repetitive behavior. Despite advancements in early detection and intervention, no therapy has yet been proven to completely reverse the core symptoms of autism. Because ASD affects each individual differently, people with ASD have distinct strengths and challenges, as well as distinct treatment requirements. The majority of behavioural therapies used in conjunction with medication therapy are currently used to treat autism. Anxiety and aggression can be reduced and language, cognitive, adaptive, and social skills can all be improved with behavioural intervention; however, the effect is not stable and requires extensive cooperation between families, communities, and schools. Antidepressants, stimulants, antipsychotics, alpha agonists, and anticonvulsants are some of the drugs that are frequently used to treat anxiety, ADHD symptoms, compulsions, and other repetitive behaviours, as well as mood instability, irritability, aggression, and sleep disturbances. The importance of pharmacological therapy for co-morbid diseases related to ASD is gradually increasing with age. These drugs, which include stimulants and anti-psychotics, are crucial in the clinical care of patients with ASD. However, the development of targeted medicines for subgroups of ASD when the genes causing the ASD are known and the neurobiology and prospective targeted treatments were investigated to restore the neurobiological defects at least in the animal models has led to numerous recent successes in patients as reported here.

Keywords: autism, ASD, behavioral therapy, educational therapy, pharmacology treatment of autism

Introduction:

Autism is a neurodevelopmental disorder characterized by poor social interaction, verbal and nonverbal communication difficulties, and restricted repetitive behavior. The prevalence of this diagnosis has risen in recent decades, but it is unclear whether this is due solely to increased awareness of milder forms of the disorder among medical providers [1].

ASDs represent a broad spectrum of associated cognitive and neurobehavioral deficits, including socialization and communication deficits, as well as restricted and repetitive patterns of behavior. Autism Spectrum Disorders (ASDs) are organic neurodevelopmental disorders caused by genetic or neurobiological factors rather than psychological or environmental factors [2].

Despite advancements in early detection and intervention, no therapy has yet been proven to completely reverse the core symptoms of autism. Because ASD affects each individual differently, people with ASD have distinct strengths and challenges, as well as distinct treatment requirements [3]. As a result, treatment plans are typically collaborative and tailored to the individual. Treatment aims to target core behaviours, improve social interactions and communication, and decrease disruptive behaviour [4].

Treatments can be given in a variety of settings, including education, health, community, and home settings, or a combination of these. It is critical that providers communicate with one another, as well as with the person with ASD and their family, to ensure that treatment goals and progress are met [5].

The majority of behavioural therapies used in conjunction with medication therapy are currently used to treat autism. Anxiety and aggression can be reduced and language, cognitive, adaptive, and social skills can all be improved with behavioural intervention; however, the effect is not stable and requires extensive cooperation between families, communities, and schools. Antidepressants, stimulants, antipsychotics, alpha agonists, and anticonvulsants are some of the drugs that are frequently used to treat anxiety, ADHD symptoms, compulsions, and other repetitive behaviours, as well as mood instability, irritability, aggression, and sleep disturbances. However, these medications have numerous adverse effects including drowsiness, increased appetite and weight gain, disrupted sleep, elevated prolactin, and extrapyramidal symptoms. They also are unable to treat the primary symptoms of communication skills and stereotyped behaviours [4, 5].

Even as behavioural interventions remain the mainstay of autism spectrum disorder (ASD) treatment, several potential targeted treatments addressing ASD's underlying neurophysiology have emerged in recent years. These appear to have the potential to become a mainstay treatment in the future for addressing the core symptoms of ASD [6].

After early (beginning before the age of four) intensive behavioural and educational therapy in autistic children, there is an improvement in cognitive, communication, adaptive, and social functioning, as well as a reduction in inappropriate behaviours such as aggression, hyperactivity, and temper tantrums [7]. It was hypothesised that early, intensive applied behaviour analysis (ABA) intervention would result in remarkable outcomes, such as nearly half of the children receiving this treatment gaining significant IQ points and being mainstreamed into regular classes [8].

Metformin, arbaclofen, cannabidiol, oxytocin, bumetanide, lovastatin, trofinetide, and dietary supplements such as sulforophane and N-acetylcysteine are among the medications discussed. Atypical antipsychotics, serotoninergic agents, alpha-2 agonists, and stimulant medications are among the medications commonly used to treat the comorbidities associated with ASD. Targeted treatments for Fragile X syndrome (FXS), the most common genetic disorder leading to ASD, serve as a model for new treatments that may be beneficial for other types of ASD [2, 9].

Objective:

In this article we summarize current evidences regarding updates in management of autism spectrum disorder.

Participants and Methods:

Study Design: Review article.

Study duration Data will be collected between 1 December, 2021 and 30 February 2022.

Data collection Medline and PubMed public database searches have been carried out for papers written all over the world on management of autism spectrum disorder. The keyword search headings included “autism, ASD, behavioral therapy, educational therapy, pharmacology, pschology", and a combination of these were used. For additional supporting data, the sources list of each research was searched.

Criteria of inclusion: the papers will be chosen based on the project importance, English language, and 20 years’ time limit. Criteria for exclusion: all other publications that do not have their main purpose in any of these areas or multiple studies and reviews will be excluded.

Statistical Analysis:

No predictive analytics technology has been used. To evaluate the initial results and the methods of conducting the surgical procedure, the group members reviewed the data. The validity and minimization of error were double revised for each member's results.

Diagnosis:

The diagnosis of ASD is made solely on the completion of descriptive criteria because there are currently no specific biomarkers or diagnostic tests available. Clinical genetic testing is advised because it has a relatively high yield in people with ASD, can educate about potential medical therapies or workup, and can assist with family planning [10- 12].

Doctors in pediatrics, psychiatry, or psychology clinics can diagnose ASD; ideally, a team of experts from different fields should be involved. Clinicians shouldn't depend exclusively on parent reports or tools like the ADOS since diagnoses based on a combination of clinician observation and caregiver accounts are consistently more trustworthy than those based on either observation or reports alone. Children who do not have language difficulties, as well as those who are female, from ethnic minorities, or poor socioeconomic position are frequently diagnosed later [7, 13].

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders, several sub-diagnostic categories were eliminated, such as Asperger syndrome, pervasive developmental disorder not otherwise specified, and disintegrative disorder. Instead, autism spectrum disorder was used to describe both the lower and higher functioning forms of autism (ASD). Additionally, the criteria for this diagnosis were reduced from three (social reciprocity, communicative intent, and restricted and repetitive behaviours in DSM IV-TR) to two (restricted and repetitive behaviours in DSM 5) in DSM 5 [14, 15].

Each of the social communication/interaction criteria must be met by a person, including the inability to reciprocate social or emotional engagement, significant relationship maintenance issues, and issues with nonverbal communication. Additionally, they must satisfy two of the four requirements for restricted and repetitive behaviour, which are: stereotyped or repetitive speech, motor movements, or object use; excessive adherence to routines, ritualised conduct, or excessive resistance to change; extremely confined interests, abnormal in intensity or focus; and hyper or hypo responsiveness to sensory input or unusual interest in sensory components of environment. For a diagnosis to be made, the symptoms must result in functional impairment. Irritability, hyperactivity, aggressive behaviour, anxiety, mood problems, and insomnia are just a few of the accompanying symptoms that can be found with autism spectrum disorder [14, 16].

Management Approaches:

1- Psychosocial and Behavioral Therapies:

In order to address communication, social skills, play, daily living abilities, academic skills, and inappropriate behaviour, educational and behavioural interventions are crucial. Individualized therapy is necessary for autistic people due to their wide range of symptoms and functional abilities. There is general agreement that it is crucial to start therapy as soon as possible, whether that be right away after a diagnosis or even in cases of suspected diagnosis. Parents, siblings, and classmates' participation and education are also crucial [1, 7].

One of the popular evidence-based strategies is applied behaviour analysis (ABA). The foundation of ABA interventions is reconditioning the desired behavior. The fundamental idea is to break down particular abilities or activities into smaller components and teach these in a systematic and gradual way through reinforcement. It has demonstrated notable advancements in IQ, academic ability, and language. Different ABA interventions include discrete trial training (DTT), early intensive behavioural interventions (EIBI), pivotal response training (PRT), and verbal behavioural intervention (VBI). DTT is offered to children in preschool (ages 3-5) and is taught in a classroom setting [5, 16].

The repetition of learning trials is a crucial element, and it includes precise intervention aims along with positive reinforcement (verbal praise, tokens, or culinary treats). Theoretically, early, intense ABA intervention might provide astonishing results, such as over half of the

kids getting the therapy increasing their IQ significantly and mainstreaming into regular schools [17, 18].

Pivotal Response Treatment (PRT), a treatment that employs a more naturalistic behavioural approach and focuses on both specific abilities and motives, is another intervention that has shown some promise in addressing the main symptoms of ASD [19]. According to the notion, PRT produces more significant/generalizable improvements in areas that the therapy does not expressly target, such joint attention. Additionally, it requires less time than ABA therapy [20]. PRT was found to be beneficial for functional and adaptive communication abilities in 53 children with autism and substantial language delay in a randomized, controlled experiment [21]. In another randomized clinical research comparing PRT and ABA therapies, it was discovered that PRT was more effective than ABA after three months of treatment for enhancing verbal expressive communication [22]. Additionally, it was discovered that kids were less disruptive during PRT than they had been in the past [23].

Interventions for social skills have also been researched, although typically as parts of other kinds of therapy. They are frequently offered in a group setting and have been investigated more thoroughly in people with medium to higher cognitive functioning levels. Interventions for social skills include video modelling, social narratives, and peer-related mediation [24]. Emotional control, fundamental conversational skills, nonverbal communication, perspective-taking, and initiating, responding to, and maintaining social contacts are only a few examples of the objectives of social skills training. Children and adolescents with autism spectrum disorder who also suffer from co-occurring anxiety problems may benefit from cognitive behaviour therapy (CBT). CBT has been found to be a successful treatment for anxiety in randomised controlled trials, but it may work better for higher functioning people [25].

There are also several strategies with unknown advantages. These include animal-based treatment, music therapy, auditory integration therapy, and sensory integration therapy. The focus of sensory integration treatment is on the sensory information's neurophysiological processing, which is known to differ in autistic people. Allowing the child to interact with an environment in an adaptive fashion can help them create a coping strategy to address the underlying sensory-motor dysfunctions, rather than teaching them a skill or proper behaviour.

Full body motions are engaged during treatment in settings that provide tactile, proprioceptive, gravitational, auditory, visual, and vestibular stimulation [17, 21]. Language impairments and sensory abnormalities, which are frequently linked to auditory problems, are the foundation of auditory integration treatment. Children are exposed to filtered and modified music as part of the treatment (in terms of volume and pitch). It is predicated on the idea that continual exposure to altered sounds may change how the central auditory processing system functions and affect language and behaviour [10].

Another strategy that has gained popularity is animal-based therapy. Dogs, horses, and dolphins are just a few of the animals used in various animal-based interventions. For

instance, dolphin therapy involves engaging with captive dolphins. It is thought that these animals can aid in improving human communication. Another animal-based intervention is horse-riding therapy, which is predicated on the notion that it integrates social, cognitive, and gross motor functioning. Additionally, it is thought that the motions of riding aid in self-regulation in kids and enhance their attention spans, distractibility, and social drive [26].

Along with jogging, martial arts, swimming, or yoga/dance, horseback riding is referred to as an exercise intervention because it can improve a variety of behavioural outcomes, including stereotyped behaviour, social-emotional functioning, cognition, and attention. The foundation of music therapy is the idea that certain aspects of musical improvisation and teamwork with other musicians may aid in the social interaction and communication skills development of autistic people. Despite the absence of definitive evidence, music therapy may aid in the participants' emotional and motivational reactions [24, 27].

2- Pharmacological Therapy:

Since the efficacy of using medications to treat the primary symptoms of autism has not been demonstrated, they are mostly used to treat the related symptoms of autism spectrum disorder. The following are only a few examples of the targeted linked symptoms: irritability, aggression, self-harming behaviours, anxiety, hyperactivity, impulsivity, inattention, and insomnia [28].

Sometimes it is necessary to use pharmaceutical interventions to help patients participate in therapy and improve their day-to-day functioning. For children with ASD and those who have typical development, the same psychopharmacological management strategies apply. Prescribers should be aware that children with ASD are more susceptible to the negative effects of medication and more likely to experience them than children without ASD [9]. In contrast to children who are neurotypical, pharmaceutical treatment should therefore be initiated at lower doses and increased gradually. To objectively assess the effectiveness of treatment in various settings, it is essential to collect objective symptom measures from various sources before and after the intervention [13].

Drugs should be cautiously introduced at modest doses because autism (and more so in ID) appears to be a sign of unpredictable adverse reactions to psychiatric medications. Additionally, there is a noticeable difference in the type of treatment given to males and females: girls are more likely to receive sedatives, whereas males are more likely to receive a prescription for a cocktail of drugs. Additionally, due to the possibility of adverse effects that are specific to women, extra consideration should be given to sex when administering pharmaceutical treatment. For instance, aripiprazole is one of the few atypical antipsychotic drugs that does not result in hyperprolactinemia, gynecomastia, or galactorrhea and is generally used to treat irritability in autistic children [25, 28].

Furthermore, some drugs used to treat co-morbid ASD, like modafinil for ADHD and the anticonvulsant carbamazepine, can lessen the effectiveness of contraceptive pills. Always keep these dangers in mind and let patients know about them [29].

Overall, most children (but not all) who take these two drugs have less irritability and agitation, which includes aggression, self-injury, and other disruptive behaviours. Both medications belong to a class of medications known as atypical antipsychotics and are partial agonists or mixed dopamine- and serotonin-receptor antagonists. Not all comparable drugs are effective in treating ASD [3, 17]. Both medications have the potential to have negative side effects, such as drowsiness and weight gain, which raises the risk of future health issues as illustrated in (Table1).

Table (1): Evidence for use of medication in autism spectrum disorder [28].

	Age (years) for use as indicated by US FDA	Target symptoms	Common adverse effects
Risperidone	5–16	Agitation or irritability in ASD	Increased appetite, sedation, weight gain
Aripiprazole	6–17	Agitation or irritability in ASD	Nausea, weight gain
Atomoxetine	6–15	Typically for ADHD symptoms	Decreased appetite nausea, irritability
Methylphenidate	≥6	ADHD	Sleep disruption, decreased appetite
Guanfacine	6–12	ADHD	Fatigue, sedation, decrease in pulse and blood pressure

ASD=autism spectrum disorder. ADHD=attention-deficit hyperactivity disorder. FDA=US Food & Drug Administration.

3- Dietary Interventions:

There is still a lot of interest in nutritional therapies among patients' families and physicians due to the fact that many people with ASD experience GI issues and that these microbiota changes are thought to contribute to the manifestation of GI and non-GI symptoms. As a result, no single nutritional therapy can be recommended as a conventional treatment for ASD despite the fact that various dietary treatments have been researched. This is because there is a lack of solid scientific data about the impact of therapeutic diets on autism (Table 2) [31].

Table 2: A summary of nutritional interventions for autism spectrum disorders [31].

Nutritional interventions	Clinical implications or advantages	Limitations or disadvantages
Gluten free casein free diet	RCTs provided evidence of behavioral and GI symptom improvement; no reported adverse effects or nutritional deficiencies	Long treatment time required for response; adherence difficulty; may only be effective in subset of patients
Ketogenic diet	Animal studies and limited cohort studies demonstrate potential for behavioral symptom improvement	Few existing studies, restrictive diet, and potentially unpalatable, limited sampling can cause nutritional deficits
Probiotics	Significant potential for improvement of GI and ASD symptoms	Limited studies and unproven mechanistic theories; mixed reaction by parents and ASD community to current research
Specific carbohydrate diet	Anecdotal reports of symptom improvement	Very few existing studies; no RCTs; very restrictive diet and difficult adherence

Nutritional interventions	Clinical implications or advantages	Limitations or disadvantages
Polyunsaturated fatty acids supplementation	Implicated as a pathophysiologic pathway for ASD; potential for combining with other therapeutic modality	Mixed results regarding supplementation; lack of consistent RCTs
Vitamin A supplementation	Potential mechanism linking vitamin A deficiency to ASD pathophysiology	Correction of vitamin A deficiency via supplementation has proven ineffective and may lead to adverse effects associated with excess vitamin A intake
Vitamin C supplementation	None	ASD nutritional deficiency has been linked to scurvy and other vitamin C–related adverse effects, but there is no apparent link between deficiency and pathophysiology or supplementation and therapy
Vitamin B6 and magnesium supplementation	Proposed mechanism for therapy via supplementation	No conclusive data demonstrating therapy via supplementation; statements against supplementation from scientific bodies (American Psychiatric Association and American Academy of Pediatrics)
Vitamin B12 supplementation	Encouraging early results may demonstrate improvement in ASD symptoms	Paucity of data and studies; ultimately, effects are inconclusive and warrant additional study
Folic acid supplementation	Folic acid supplementation in pregnant mothers may prevent	Results are only gestational, no evidence in therapy for ASD

Nutritional interventions	Clinical implications or advantages	Limitations or disadvantages
	ASD; potential future in screening for ASD related to folate-dependent 1-carbon metabolism and sulfuration pathways	symptoms after birth

Abbreviations: ASD, autism spectrum disorder; GI, gastrointestinal; RCT, randomized controlled trial.

4- Complementary Alternative Medicine:

Melatonin is one of the most well researched complementary and alternative therapies utilised in autism spectrum disorder. Its effectiveness for sleep disruptions in children and adolescents with autism spectrum disorder has been investigated in numerous double-blind, placebo-controlled studies. In 160 children with autism (aged 4 to 10 years old), the greatest of these studies compared controlled-release melatonin alone and in combination with cognitive-behavioral therapy (CBT) to CBT alone and placebo [19].

For the symptom of hyperactivity that is associated with autism spectrum condition, omega-3 fatty acids have been investigated as potential therapies. In children and adolescents with autism spectrum disorder, randomised, placebo-controlled trials have suggested potential reductions in hyperactivity, but the results have not been statistically significant in this population. Supplementing with omega-3 fatty acids has generally been well tolerated and appears to be a secure option to take into consideration for kids with ASD [18, 22].

Results from two randomised controlled trials on vitamin supplementation as a potential treatment for autism spectrum disorder have been conflicting. One study reported no substantial changes in the core symptoms or related behavioural symptoms of ASD, only significant improvements in sleep and gastrointestinal problems when compared to placebo. The results of the other trial revealed a notable overall improvement on parent rating measures, enhanced receptive language, a decline in hyperactivity and tantrums, and increased receptive language [27].

Conclusion:

Instead of trying to cure someone of their autism, the management and treatment of autism focuses more on reducing the functional impact of the autistic characteristics. Behavioral

therapies are the mainstay of the current evidence-based management of ASD in children, which aims to treat the condition's primary symptoms.

The importance of pharmacological therapy for co-morbid diseases related to ASD is gradually increasing with age. These drugs, which include stimulants and anti-psychotics, are crucial in the clinical care of patients with ASD. However, the development of targeted medicines for subgroups of ASD when the genes causing the ASD are known and the neurobiology and prospective targeted treatments were investigated to restore the neurobiological defects at least in the animal models has led to numerous recent successes in patients as reported here. Future therapeutic approaches, including the use of cannabinoids, gut microbiota, and precision medicine, should hopefully improve the lives of autistic people.

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