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REVIEW ARTICLE



Treatise on Autism Spectrum Disorder

Divesh Pandey, Khushboo Gupta*, Saurabh Sharma, Pranjul Shrivastava

Faculty of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh Corresponding author: khushboo.gupta@kalingauniversity.ac.in

ABSTRACT

Autism Spectrum Disorder is a neurological and developmental disorder that appears at early-childhood and lasts for the entire life. It has an impact on how a person acts, interacts with people, communicates, and learns. ASD refers to a group of illnesses that encompasses Asperger's syndrome and pervasive developmental disabilities. Any person with ASD may have difficulty communicating with you or suffer from eye contact anxiety. They may appear to be in their "own world" on a regular basis. ASD is diagnosed at the age of three and can last for the rest of one's life; however, signs and symptoms could gradually improve. Within the first year of life, some children exhibit ASD features. In other people, symptoms may not develop for another 1 year or longer. Some children with ASD learn new abilities and achieve developmental milestones until they reach the age of 18 to 24 months, at which point they cease learning new skills or lose the ones they already have. The cause of autism and other ASDs is yet unknown. Early diagnosis can be extremely beneficial to children with autism spectrum disorder (ASD) and their families. However, diagnosing ASD isn't always straightforward. Because there is no test for it, clinicians must rely on monitoring the behaviour of very young children and listening to their parents' worries. ASD manifests itself in a variety of ways. Some "on the spectrum" people have serious mental health problems. The first-line treatment is usually behavioural therapy, with pharmaceutical medications added to help patients function in their everyday activities. **KEYWORDS:-** Asperger's syndrome, pervasive developmental disabilities

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INTRODUCTION

ASD is a neurological and developmental disorder that appears at childhood and lasts for the entire life. It has an impact on how a person acts, interacts with people, communicates, and learns. ASD refers to a group of illnesses that encompasses Asperger's syndrome and pervasive developmental disabilities. Dr. LEO KANNER (psychiatrists) and Dr. HANS ASPERGER (paediatrician) invented the term "autism" in 1940. This is a word for a condition characterised by socialising, communication, and limiting and repeated interests in infants. Because people with ASD have a set of signs and symptoms that appear simultaneously and identify a specific anomaly or condition or set of concurrent things (such emotions/actions), autism is referred to as a "SPECTRUM".

Any person with ASD may have difficulty communicating with you or suffer from eye contact anxiety. They may also have a limited range of interests and engage in repeated actions. They may spend a long time putting things back in order, or they may repeat the same sentence. They may appear to be in their "own world" on a regular basis. ASD is a complex developmental disease marked by chronic difficulties with social communication, a lack of or limited interests, and a predictable pattern of behaviour. While autism is a lifelong illness, the degree to which these issues limit one's ability to operate differs from person to person with autism.

Disorders that fall under the autism spectrum:

Autistic disorder: When an infant exhibits all of the signs and symptoms of autism, he or she is diagnosed with autism.

Asperger's Syndrome: It is known as high-functioning Autism, is marked by considerable social/emotional difficulties as well as intense interest on specific things. There are no linguistic or cognitive developmental deficits. Hans Asperger, a Viennese doctor, first discovered Asperger's syndrome (also known as Asperger's Disorder) in the 1940s, when he noticed autism-like mannerisms and social and communication impairments in boys with normal IQ and language development. Many doctors thought Asperger's syndrome was just a milder type of autism, so they labelled these people "high-functioning autism."

PDD NOS (Pervasive Developmental Disorder Not Otherwise Specified): PDD is also referred as Atypical Autism though it is diagnosed when a child exhibits most but not all the autism symptoms. For example, if a youngster has delayed speech and exhibits certain repetitive habits, he is likely to be diagnosed with PDD (NOS).(2)

Rett Syndrome: Rett Syndrome is a condition that affects a person's ability Rett Syndrome is a rare and severe condition caused by a chromosomal X deficiency that primarily affects females. Rett Syndrome is defined by a normal period of development followed by a gradual loss of skills, most commonly communication skills and deliberate hand movements.

Childhood Disintegrative Disorder (CDD): It is a very unusual disorder in which children grow normally in all areas at first, with skill regression occurring considerably later than in other disorders on the spectrum. Children with Childhood Disintegrative Disorder lose skills in all areas of development (language, social, behavioural, and motor). (6)

CLINICAL FEATURES

ASD is diagnosed at the age of three and can last for the rest of one's life; however, signs and symptoms could gradually improve. Within the first year of life, some children exhibit ASD features. In other people, symptoms may not develop for another 1 year or longer. Some children with ASD learn new abilities and achieve developmental milestones until they reach the age of 18 to 24 months, at which point they cease learning new skills or lose the ones they already have.

Previously diagnosed independently, Asperger's syndrome, Autistic disorder, and PDD-NOS (pervasive developmental disorder not otherwise defined) were all included in an ASD diagnosis. All of these illnesses are now considered to be part of the autism spectrum disorder. (5)

Here's a rough timeline of what this could entail:

- From Birth: Difficulty keeping eye contact
- By 9 months: they haven't responded to their name.
- By 9 months: They don't have facial expressions that convey their feelings (like surprise or anger)
- By 12months: He is not engaging in simple interactive games such as Tickling Game or Build with blocks.
- By 12 months: No (or just a few) hand motions, such as hand-waving, are used.
- By 15 months: They are not sharing their interests with others (by showing someone a favourite toy, for example)
- By 18 months: He or she isn't pointing or seeing where others are pointing any longer.
- By 24 months: He or she has stopped noticing when others are sad or upset.
- By 30 months: No "pretend play" such as caring for a baby doll or playing with figurines is allowed.
- By 60 months: He or she is no longer playing turn-taking games like duck-duck-goose.

Starting at the age of 36 months, autistic children may have difficulty expressing their thoughts or comprehending those of others. (7)

SIGN & SYMPTOMS

> Social interaction And communication Skills:-

Social communication and relational skills may be onerous for those with ASD. Such as:

- Avoids or does not maintain eye contact
- Does not reply to his or her name by the age of nine months
- By 9 months of age, does not exhibit facial expressions like cheerfulness, unhappiness, temper or shock.
- Does not play simple interactive games like Tickling Game or Build with blocks at the age of 12 months
- By the age of 1 year, child makes little or no gestures (e.g., does not wave goodbye)
- By the age of 18 months, does not point or glance at what you point to.
- By the age of 24 months, does not notice when others are distressed or sad. Is unconcerned about his peers.
- At 36 months or older, has difficulty comprehending or communicating about other people's feelings.
- Does not play turn-taking games by the age of 60 months.
- Shows little interest in peers.

Restricted or Repetitive Behaviours or Interests:-

ASD patients may have unusual habits or hobbies. These hobbies or interests distinguish ASD from conditions characterised solely by difficulties in social communication and interaction.

- Arranges toys or other items in a line and becomes irritated if the order is disrupted.
- Repeats phrases and words over and over (i.e., echolalia)

- Always plays with toys in the same way
- Is fixated on pieces of objects (e.g., wheels)
- Gets upset by slight changes
- Has obsessive hobbies
- Flaps hands, moves the body, or spins in circles
- Follows a certain routines
- Have unusual reactions to sound, smell, taste, sight, and touch.

> Additional Characteristics

Many people with ASD have other symptoms.

- · Language skills that have been delayed
- · Movement skills with a lag
- Impaired cognition or learning abilities
- Excessively active, impulsive, or inattentive behaviour
- Epilepsy (seizures) or a seizure disorder
- Unusual sleeping and eating patterns
- Problems with the gastrointestinal tract (e.g., constipation)
- Out-of-the-ordinary mood swings or emotional reactions
- Anxiety, tension, or over-worrying
- A lack of fear or a higher fear level than expected (5)

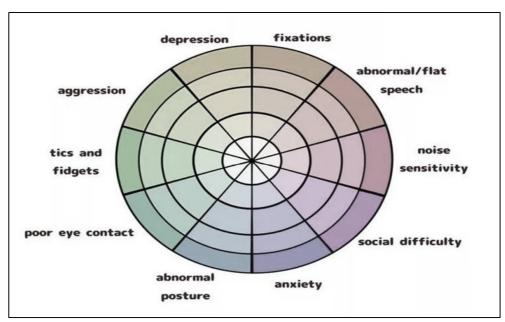


Fig no. 01 Traits of disease

ETIOLOGY-

The cause of autism and other ASDs is yet unknown. The conceptions of aetiology have evolved over time. It was long assumed to be the product of a child's poor upbringing. This historical psychosocial idea has been disproved, as research shows that the aetiology is multifactorial and includes a major genetic component. Although the cause is unknown, there is a small percentage of cases (less than 10%) in whom autism is associated with another illness known as "secondary" autism. Tuberous sclerosis, fragile X syndrome, phenylketonuria, and congenital problems caused by rubella and CMV are all forms of "secondary" autism. (2)

The following are some suspected ASD risk factors:

- Having an autistic relative in the close family
- Specific genetic variants
- Genetic illnesses such as fragile X syndrome and others
- Being the child of older parents
- · Birth weight that is too low
- Metabolic inconsistencies
- Environmental sensitivity to heavy metals and contaminants
- A history of viral infections in the mother
- Valproic acid or thalidomide (Thalomid) exposure during pregnancy (7)

➢ Genetic Factors-

According to family research, autism has been demonstrated to be both familial and heritable. Siblings of kids with autism have a greater recurrence risk than the regular populace, ranging from 2% to 8%. Monozygotic twins had a greater concordance rate than dizygotic twins, according to twin studies—90 percentage versus 10%, respectively. Other genetic investigations, such as linkage studies, show genetic loci on numerous chromosomes, including chromosome 7 and chromosome X, implying a complicated pattern of inheritance. (2)

- Monozygotic twins have a higher incidence than dizygotic twins.
- Autistic toddler's siblings have a 2% chance of developing the disorder.

Environmental factors-

Several factors in the environment have been looked into as possible causes of autism. According to epidemiological studies, several environmental variables, such as prenatal rubella and cytomegalovirus infections, are responsible for a small number of occurrences of autism. The relevance of heavy metals in the aetiology of autism is debatable, and additional research is needed.

Vaccines have raised concerns among the public as suspected autism triggers. The potential negative effects of the measles, mumps, and rubella (MMR) vaccine, as well as thimerosal, a mercury-based preservative used in some vaccines, have both been linked to autism. These two concepts are unrelated; because thimerosal would inactivate a live vaccine, it has never been used in MMR immunizations. (2)

Air pollution –

According to studies, early life exposure to air pollution has been identified as a risk factor for autism.

- → During the third trimester of pregnancy, children of mothers who lived near a motorway and were exposed to traffic-related pollution were twice as likely to have ASD. Near a motorway was defined as a distance of 1,014 feet, or about 3.5 football fields.
- → Children with a mutation in the MET gene, as well as high levels of air pollution exposure, may be at an elevated risk. (8)

o The ASD hypothesis and the measles, mumps, and rubella vaccine-

In a 1998 study, a link between both the MMR vaccine and autism spectrum disorder was established. Since then, the number of children who have received the MMR vaccine has decreased. Measles outbreaks have resulted as a result of this. As a result of these considerations, large-scale global research to investigate this potential association has been conducted. There's really no connection between both the MMR vaccine and ASDs, according to these research. The measles vaccine has been proven to be both safe and efficient in preventing the spread of this potentially lethal disease. As a result, despite the absence of scientific evidence linking MMR vaccine to autism, MMR vaccine administration should be pushed to avoid measles outbreaks. (2)

DIAGNOSTIC CRITERIA -

Early diagnosis can be extremely beneficial to children with autism spectrum disorder (ASD) and their families. However, diagnosing ASD isn't always straightforward. Because there is no test for it, clinicians must rely on monitoring the behaviour of very young children and listening to their parents' worries. ASD manifests itself in a variety of ways. Some "on the spectrum" people have serious mental health problems. Others are quite bright and capable of living on their own.

Exams & tests -

✓ Language milestones & Speech evaluation-

One of the most crucial diagnostic criteria for ASD diagnosis is the existence of a verbal delay or impairment. Children with ASD who are diagnosed early have a wide range of language abilities, which are a significant predictor of future results. Several speech and language diagnostic screening tests are available to help identify certain components of expressive and receptive language ability. It's crucial to identify language and speech difficulties caused by ASD from those caused by other reasons. The ability to characterise the strengths and limitations of language abilities in children with ASD is critical for determining the most effective treatment technique as well as the child's risk of developing ASD. Several tests are used to characterise different areas of speech and language acquisition and skills, assisting in the diagnosis of the issue area for each patient.

✓ Peabody Picture Vocabulary Test-V (PPVT-V)-

This is a non-timed receptive vocabulary test for Standard American English that is designed to measure the examinee's receptive vocabulary ability quickly. It's one of the most used tests for evaluating linguistic skills. It can be used by anyone between the ages of two and ninety. The exam can be used for a variety of purposes, including measuring academic aptitude, revealing high and low linguistic talents, and identifying potential learning issues. It can be used to identify language difficulties in children who have experienced delays in their emotional and mental development, as well as to assess their verbal IQ, which is useful in ASD. It's a quick test that should take no more than 20–30 minutes to complete.

✓ Clinical Evaluation of Language Fundamentals (CELF-5)-

This exam is used to evaluate a student's language and communication skills in a range of situations, to diagnose a language problem, as well as to clarify the disorder's nature and treatment choices. Physicians can assess a student's general language competency and obtain information that will help them determine if the child has a language problem by administering four to six tests. Once a language issue has been identified, the testing process can move on to detecting substantial disparities in understanding and expression.

The test is adaptable, allowing you to conduct only the tests that are required to meet the assessment and evaluation objectives. This data is an important aspect of the overall evaluation process since it may be utilised to gather evidence about a student's communication ability in a variety of situations. The CLEF-5 features a better balance of items across receptive and expressive modalities, as well as linguistic content and organisation. It keeps track of standardised exam and composite scores, as well as growth scale values, in order to track a student's progress over time.

✓ Expressive Vocabulary Test-third edition

It is a norm-referenced, independently administered test that assesses children's and adults' expressive vocabulary and word recollection. The exam can help build theories about an individual's test performance and vocabulary ability by supplementing quantitative information offered by standard scores.

✓ Autism screening test (such as the Checklist for Autism in Toddlers [CHAT] or the Autism Screening Questionnaire)-

Developmental screening/assessment necessitates a more in-depth examination of the infant's development. Your child will get a brief examination, and you may be asked to fill out a questionnaire for him or her. Structured questionnaire surveys or checklists centred on studies that provide questions regarding an infant's growth, including vocabulary, movement, thought, behaviour, and emotion, are used for cognitive and behavioural screening. A medical practitioner, as well as other health, neighbourhood, or education providers, can do developmental screening. Developmental screening is less common than most other types of developmental monitoring since it is more formal than developmental testing. Even if there is no known concern, developmental screening is a common aspect of certain well-child examinations with all infants. (9) The American Academy of Paediatrics (AAP) recommends behavioural and developmental screening for all newborns during routine visits to children of all ages:

- 9 months
- 18 months
- 30 months

In fact, AAP suggests that all children should be strictly tested for ASD through routine visits by a well-child doctor to:

- 18 months
- 24 months

If the infant is at high risk of Autism (e.g., has a sibling, brother, or other ASD family member), or if behaviours commonly associated with ASD are present, more screening may be required. Extra testing can be considered with your health care provider if the kid is at a higher risk of developing difficulties due to preterm birth, low birth weight, environmental risks such as lead poisoning, or other factors. If a kid has a long-term health problem or is diagnosed with an illness, he or she may be subjected to developmental testing and screening in many parts of life, just like children without special needs. (9)

Genetic testing-

Genetic testing can look for certain DNA alterations that have been associated to ASD and may lead to additional health problems. The results of genetic testing may be relevant for family planning in rare cases. A chromosomal microarray (CMA) test and testing for fragile X syndrome are currently available at Boston Children's Hospital for ASD (in boys). For children with certain symptoms, other genetic tests may be useful. Some genes may be added to standard testing as new ones are discovered to be essential in ASD. (10)

Specific screening tool-

> Autism Diagnostic Interview-Revised (ADI-R)-

The Autism Diagnostic Interview-Revised is a type of assessment in which the assessor conducts an interview with the individual's parents. The interview includes questions regarding social relationships, communication, language, and behaviour patterns. The questions inquire about a person's historical and current habits, as well as the quality of interactions over the course of their lives. Over a hundred questions will be asked about repetitive and restricted behaviour, responding to

others, smiling, greetings, emotions, comforting, and a range of other topics will be asked by the assessor. (10)

> Autism Diagnostic Observation Schedule (ADOS)-

The ADOS is a diagnostic tool for autism. The ADOS is made up of a series of structured and semistructured subtests that cover a wide variety of social interaction and communication issues. There are five segments in the assessment.

The module is chosen based on the individual's developmental stage. The first module is for toddlers who speak in a limited or non-verbal manner. The second module is for clients who employ phrases in their speech but do not talk smoothly. Module three is for children and adolescents who can talk fluently, whereas module four is for teenagers and adults who can converse fluently. The fifth module focuses on toddlers. (9)

> Childhood Autism rating scale-

Clinicians use the CARS to tell the difference between children who satisfy ASD criteria and those who meet developmental delay criteria. Relationships, imitative behaviour, emotional responses, ability to adjust to change, use of the senses and sensitivity to foods, sounds, and things, intellectual response, verbal communication, and activity level are 15-item questionnaire on the scale.

> Gilliam Autism rating scale-

The GARS is a technique that aids doctors in determining the severity of autism in children aged three to twenty-two years. The questionnaire asks about stereotypical and characteristic behaviour, as well as social interactions and communication competence, in people with autism. (10)

Universal Test of Nonverbal Intelligence (UNIT)-

The UNIT is an intelligence test that can be used instead of more typical intelligence exams. It is used to make a nonverbal cognitive assessment. Six key subtests are included in the evaluation. Some of the skills that can be mastered include symbolic memory, spatial memory, object memory, cube design, analogical reasoning, and mazes.

The Symbolic Memory subtest measures short-term visual memory and complex sequential memory. The Visual Short-Term Memory subtest assesses spatial memory. The Object Memory subtest evaluates a person's ability to recognise and retain significant symbolic content in the short term. The Cube Design subtest assesses visual-spatial reasoning. The UNIT is made up of four scales: memories, symbolic, reasoning, and non-symbolic. These scores are added together to create the Full-Scale Intelligence Quotient. The Memory Quotient is an assessment of advanced memory skills such as quick recall, recognition, and conceptualization. The Symbolic Quotient is a metric for problem-solving aptitude. Your capacity to think critically and solve problems in both known and novel situations is measured by your Reasoning Quotient. When faced with conceptually confusing and meaningless material, the Non-symbolic Quotient tests problem-solving ability. (10)

Mullen scales of early learning-

The Mullen is a test that assesses cognitive growth throughout time. The five major measures employed in the assessment are visual reception, gross and fine motor, verbal ability, and vocabulary development. The Mullen generates a score at the end of the process that is used to assess overall intellect. (10)

▶ Wechsler Adult Intelligence Scale-IV (WAIS-IV)-

The WAIS-IV is a test that assesses adults' and older teenagers' intellect and cognitive abilities. The evaluation has been revised multiple times and is now undergoing changes, with a release date set for 2021. The most widely used intellectual evaluation system in the world is the World Intellectual Evaluation System (WAIS). There are ten core subtests and five supplemental subtests in the current version. The full-scale IQ is calculated using the results of the ten core subtests. (15) The test is broken down into four primary index scores, each representing one of the intelligence components. The Verbal Comprehension Index, Perceptual Reasoning Index, Working Memory Index, and Processing Speed Index are among the index scores. The Verbal Comprehension Index assesses abstract verbal thinking, semantic comprehension, verbal comprehension and expression, the amount of general cultural material gained, and the ability to communicate abstract social practises, rules, and phrases. Visual spatial processing, problem solving, visual motor construction, nonverbal abstract problem solving, inductive reasoning, visual spatial reasoning, and quantitative reasoning are all assessed using the Perceptual Reasoning Index. The Working Memory Index assesses attention, encoding, auditory processing, numeric reasoning, focus, and mental number manipulation. The Processing Speed Index includes tests to assess a person's ability to code and target symbols, associative memory, and graphomotor speed. (10)

Wechsler Intelligence Scale for Children (WISC)-V-

The WISC is a broad intelligence exam that evaluates a child's abilities. The five key indicators are Oral Comprehension, Visible Spatial, Fluid Reasoning, Working Memory, and Processing Speed. The

examination also assesses whether a toddler has any learning disabilities. In terms of measuring similar indicators, the WISC and the WAIS-IV are comparable. (10)

TREATMENT

The first-line treatment is usually behavioural therapy, with pharmaceutical medications added to help patients function in their everyday activities.

Behaviour therapy:-

Despite the fact that there is no cure for autism, certain approaches can help to drastically reduce the symptoms. Because social and communication difficulties are common in people with autism, behavioural and speech language therapy are frequently used as part of a treatment plan. The fact that no single educational strategy works for all children is a problem for doctors and a source of frustration for parents. The most extensively used and successful therapy for children with autism is behavioural treatment. Many people believe that behavioural intervention is exclusively for children who are too rowdy and act out. That isn't the case at all. The major instruments for building social skills are autism therapies. Behavioural intervention has the advantage of being both effective and safe. The bad news is that it takes a long time and costs a lot of money. Choosing a behavioural therapy type can feel like a guessing game because there are so many. However, when determining where to spend time and energy, whether within or outside of school, behavioural treatment remains the most reliable strategy for children with autism to gain abilities.

Applied Behaviour Analysis (ABA)-

This therapy has been utilised for more than 50 years and is the most well-researched autism intervention. It's a scientifically structured strategy to teaching play, communication, self-care, academic, and social living skills, as well as reducing harmful behaviours. It has been shown in numerous studies to improve results for children with autism.

A therapist uses ABA to break down abilities into component elements and help a kid learn them through repetition, reinforcement, and encouragement. A therapist uses ABA to assess a child's abilities and determine what might be beneficial to him, even if the youngster is not interested in learning specific skills. Even if a child isn't interested, an ABA therapist might focus on welcoming others or toilet training because she recognises their long-term relevance long before a child does.

ABA is frequently the beginning step for children with more severe symptoms. Often in a full-time, classroom-based programme, therapists recommend up to 40 hours of therapy per week. Even as children's skills develop and they begin to make friends and socialise better, ABA can still be beneficial.

Verbal Behaviour Therapy (VBT)

This sort of applied behaviour therapy instructs non-verbal toddlers on how to communicate effectively. Children learn how to utilise words for their intended purpose — to elicit a desired response. It is insufficient for a child to know what a chocolate is called or to point to a chocolate that he desires. VBT aims to help toddlers progress from labelling, which is a first step in learning language, to vocalising their demands - "I want a chocolate."

In a normal session, the therapist will present stimuli based on the child's interests, such as food, activities, or toys. A chocolate in the cabinet or a swing on the playground are examples of stimuli used by the therapist to pique a child's attention. Children are taught via repetition that communication yields positive consequences; They get what they want because they utilise language to beg for it.

Cognitive Behavioural Therapy (CBT)

Children with lesser symptoms of autism are generally prescribed Cognitive Behavioral Therapy, which has been available since the 1960s. Cognitive behavioural therapy seeks to identify the triggers of specific behaviours so that the child can recognise them on his or her own. A therapist introduces practical responses through practise. In other words, children learn to recognise when they are ready to go on a regular behavioural or mental path ("I always stress out on tests") and to replace it with something else ("I'm going to do that relaxation exercise I was taught"). CBT can assist with issues like being too scared or nervous, which are frequent in people with autism.

Developmental and Individual Differences Relationship (DIR) Therapy

DIR therapy (also called Floortime). A therapist — as well as parents — engages children in this therapy by engaging them in activities that they like. It is based on the desire of a youngster to engage with others. When learning new skills, the therapist follows the child's lead.

Relationship Development Intervention (RDI)

RDI is a family-centered approach to treating autism that focuses on specific emotional and social goals in order to foster more meaningful interactions. This involves the ability to build emotional bonds with others and share personal experiences. It is frequently utilised by parents who have been taught by RDI consultants. Goals are made to improve interpersonal engagement abilities such as empathy and overall motivation to interact with others. Adults employ step-by-step approaches to urge development, such as creating eye contact or back-and-forth conversation, as part of RDI's varied aims.

- Pharmacological Therapies:-
- Treatment of irritability and aggression: -

Risperidone -

The first medicine approved by the FDA to manage autism-related irritability was risperidone (Risperdal), a second-generation antipsychotic. Risperidone is a minuscule treatment for aggression, mood outbursts, and self-injurious behaviour in children with autism. Because these behaviours may be long-term, the efficacy and safety of using this medicine over a longer period of time must be determined. (11) Increased hunger, dizziness, drooling, drowsiness, and exhaustion were the most prevalent adverse events (AEs) reported with Risperidone. (6)

Aripiprazole-

The psychotropic medication Aripiprazole (Abilify) was permitted by the FDA in 2009 for the treatment of irritability in children with ASD (ages 6 to 17 years). The drug is prescribed to treat schizophrenia, bipolar I disorder, major depressive disorder, Tourette's syndrome, and other mental illnesses.. Its mechanism of action is unknown, however it could involve partial agonist and antagonist action at dopamine type 2 (D2) and serotonin type 1A (5-HT1A) receptors. (6) The FDA has approved aripiprazole for the treatment of irritability in toddlers and teens with autism aged 6 to 17.

Doses of aripiprazole-

Autistic children - Up to 15 mg/day

Adolescents- Initial dose 2 mg/day; recommended dose 10 mg/day (12)

Clozapine

Clozapine (Clozaril,) was previously used to treat aggressiveness and paroxysm before the approval of risperidone and aripiprazole for the management of ASD indications. Clozapine is a drug that is used to treat schizophrenia and schizoaffective disorder, as well as to prevent people from becoming suicidal. The therapeutic success of this drug in schizophrenia is assumed to be due to antagonism of the D2 and 5-HT2A receptors. The medicine inhibits adrenergic, cholinergic, histaminergic, and other dopaminergic and serotonergic receptors. (6)

Haloperidol-

Haloperidol (Haldol) is a D2 receptor antagonist from the butyrophenone class which is especially potent and selective. It is prescribed for the treatment of schizophrenia as well as the control of Tourette's syndrome tics and vocal outbursts.(6)

Sertraline-

Sertraline (Zoloft), a selective serotonin reuptake inhibitor (SSRI.

o Treatment of aberrant social behaviour:-

Oxytocin-

The endogenous hormone oxytocin (Pitocin) is best known for its function in lactation and parturition. It has also been established that it has a role in the formation of human and animal interactions and social functioning. Researchers looked into the efficacy of intranasal oxytocin to improve these deficiencies because ASD is linked to decreased social interaction and communication, among other symptoms.

Secretin

Exocrine secretions of the stomach, pancreas, and gallbladder are regulated by secretin, another endogenous hormone. It also serves as a neuropeptide from the brain and spinal cord (CNS).

$\circ \quad \ \ \, \textbf{Treatment of hyperactivity and inattention:-}$

Methylphenidate

Narcolepsy and attention deficit hyperactivity disorder are treated with the moderate CNS stimulant methylphenidate (Ritalin). The substance is hypothesised to increase the release of norepinephrine and dopamine into the extraneuronal region by inhibiting their absorption into the presynaptic neuron.

Venlafaxine

Venlafaxine (Effexor) is a Serotonin Norepinephrine Reuptake Inhibitor (SNRI) which is used to treat depression, anxiety, and panic disorder.

o Treatment of repetitive behaviours:-

Fluoxetine

Fluoxetine (Prozac) is an selective serotonin reuptake inhibitor (SSRI) used to treat serious depression, obsessive-compulsive disorder, bulimia nervosa, and panic disorder with or without agoraphobia.

Citalopram

Citalopram (Celexa) is an SSRI that is used as an antidepressant.

Bumetanide

Bumetanide (generics) is a potent loop diuretic used to treat oedema caused by congestive heart failure, liver disease, and kidney illness (including nephrotic syndrome)

Treatment of cognitive disorders:-

Pandey et al

Memantine

Memantine (Namenda) is used to treat moderate-to-severe Alzheimer's disease. It is N-methyl-D-aspartate (NMDA) receptor antagonist. The persistent activation of NMDA in the CNS is assumed to contribute to Alzheimer's disease symptoms.

Rivastigmine

Rivastigmine (Exelon) is an acetylcholinesterase inhibitor used to treat Alzheimer's dementia and dementia caused by Parkinson's disease. Although the exact mechanism of action of the drug is uncertain, it is supposed to work through improving cholinergic function.

o Treatment of insomnia:-

Mirtazapine

Mirtazapine (Remeron) is antidepressant of tetracyclics subclass. It increases central noradrenergic and serotonergic activity.

Melatonin

Melatonin, a sleep-promoting hormone, in a controlled-release formulation of 3 mg per day, paired with cognitive-behavioral therapy.

Recent research:-

Approximately 20 clinical trials are testing present or future ASD treatments in the United States, according to data from the National Institutes of Health. With at least five early- or mid-stage studies underway in the United States, oxytocin nasal spray appears to be the most favoured therapeutic method. The following are some more interesting medications being researched for the treatment of ASD:

Acamprosate (Campral)-

- i. Man-made drug
- ii. Similar chemical structure as amino acid homotaurinate
- iii. Approved for the treatment of alcohol abstinence

Atomoxetine (Strattera)-

- i. Serotonin and norepinephrine reuptake inhibitors (SNRI)
- ii. Used for the treatment of ADHD.

Intrathecal baclofen (Gablofen)-

i. a gamma-amino butyric acid (GABA)nergic ,use in the treatment of severe spasticity of cerebral or spinal origin

DMXB-A-

- i. Derived from nemertine toxin anabasein
- ii. It is analysed for the treatment of critical ASD-related tactile defensiveness.

EPI-743 (Vincerinone)-

- i. Para-benzoquinone class drug
- ii. Originally developed to treat people with hereditary mitochondrial disorders.

RG7314 (Roche)-

- i. Small-molecule antagonist of the vasopressin receptor (V1A)
- ii. It is associated with emotional processing and social problems in ASD patients.(4)

CONCLUSION

Autism is a neurological & developmental malady that lasts a lifetime. The hallmarks of the impairment, such as limited or non-existent speech development, avoidance of social contact or awareness, and behavioural routines, are not experienced in the same way by everyone with autism. PDD NOS (Pervasive Developmental Disorder Not Otherwise Specified), Autistic Disorder, Pervasive Developmental Disorder, Childhood Disintegrative Disorder (CDD), & Rett syndrome are all terms used to describe autism spectrum disorder. Disability begins in children from the age of three and may lasts for a lifetime. Autism is a spectrum disorder having many symptoms like eye contact anxiety, social difficulty, aggression, noise sensitivity, abnormal/flat speech, Abnormal posture, poor sensitivity, depression etc which may improve with time. The main cause of ASD is yet unknown but some suspected factors like having an autistic relative in the close family, Genetic diseases such as fragile X syndrome and others, as well as specific genetic mutations, Being the child of older parents, Birth weight that is too low, Vulnerability to heavy metals and contaminants in the environment, metabolic discrepancies, A history of viral infections in the mother, Valproic acid or thalidomide (Thalomid) exposure during pregnancy may cause the disorder. There are various methods for diagnosis of ASD by examines the suspect, genetic testing etc. As a treatment of ASD, behaviour therapy is considered as first line treatment with pharmacological therapy would be the best to improve the condition. Autism Awareness Day is observed every year on April 2nd. On April 2, the entire planet will become blue in honour of World Autism Awareness Day. It's just all about Autism Speaks' Light it Up Blue campaign, which aims to increase understanding and appreciation of individuals with autism.

Conflict of Interests

The authors report no actual or potential conflict of interests.

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