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The most common treatment methods through comparing the studies results of children with autism spectrum syndrome

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ABSTRACT

Autism (ASM) is a group of neurodevelopmental condition capable of being diagnosed very early in childhood with variety of symptoms such as inability to communicate effectively, aggressive behaviour, and abnormal repetitive routines. The review compares the treatment of ASM with alternative modalities and pharmaceutical medications with evidence that parents prefer to use alternative medicine than pharmaceutical medications in treatment of ASM due to side effects and safety concerns associated with pharmaceutical medications. However, the review also highlights that pharmaceutical medications has no straightforward cure but have specialised drugs that can help manage specific associated symptoms with the syndrome, the (FDA) has only verified 2 drugs for ASM treatment (aripiprazole and risperidone) which help autistic children manage irritability problems associated with ASM syndromes, other drugs have not been adequately studied and not yet approved, therefore there are no evidence to support their use.

Keywords: Autism, pharmaceutical, Alternative modalities, Medications, Risperidone, Treatment.

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1. Introduction

ASM spectrum syndrome is a combination of various defects that are neurodevelopmentally linked; generally the symptoms of this syndrome are more apparent between the ages of 2-3 years [1] . Some of the symptoms experienced by individuals with this syndrome include deficiency in ability to communicate effectively, poor behavioural skills such as signs of aggression and abnormal routine behaviour.

Although, behavioural treatment is usually carried out first before any other form of treatment such as pharmacological or medical therapies, this is done so that the individual with the syndrome can be able to function or carry out daily activities while undergoing treatment. The type of treatment a child who has ASM syndrome receives is dependent on the needs of the patients, in some cases the patient might have mild symptoms while in some other cases the symptoms might be more complicated and serious, therefore the range of treatment varies from patient to patient.

They may include various forms of medications and therapies which would help improve areas where there are deficiencies such as improved speech and behaviour and some other medications to help manage any condition related to ASM [2]. Various treatment methods have been utilized to treat ASM, the pharmaceutical medications use besides the complementary utilize of alternative modalities (CAM) which has been widely utilized by parents. They have both recorded various levels of success in terms of treatment of ASM spectrum syndrome; the major purpose for the current work is to review the treatment of ASM spectrum syndrome using pharmaceutical medications versus complementary alternative modalities (CAM).

1.1. ASM children treatment

Reports and research have reported or revealed that the best form of treatment for the syndrome is through a combination of training that involves communication such as language therapy, educational therapy and behavioural therapy [3]. There are other forms of treatment such as physical therapy and occupational therapy which would help to correct difficulties in movement and locomotion.

1.2. Prevalence of cam and pharmaceutical medications for symptoms of ASM

The use of usage of complementary alternative modality is increasing continually for both adults and ASM children spectrum syndrome, it is reported by the for complementary and alternative modalities national centre (NCCAM) that more than three-quarter (3/4) of adults in America use CAM as a method of treating ASM. The usage of this method on children depends on the parents, however it is expected that children of 2-50% residing in the USA are given therapy of CAM as a form of treatment for ASM.

A lot of children with various type of severe illness or health complications such as asthma, cancer and even neurological syndromes such as ASM syndrome are being treated using CAM therapy, there are different kinds of CAM therapy that were being utilized to treats ASM children but the most commonly utilized one was biologically-based therapy which about 30-35% of families utilized in treating ASM [4]. Pharmaceutical therapy can be helpful in managing and reducing the effect of the symptoms relating to ASM i.e. the behavioural and mental health symptoms [5]. However, there are no major or standard medication utilized in treating ASM, there have prescription or usage of psychotic drugs and anti-depressants, there is also a certain level of uncertainty to the pharmacological cure appropriateness. Although, not enough proof is there to show the psychotropic medication utilize in ASM, there are two major drugs that have shown high level effectiveness in relieving behavioural symptoms in patients with ASM: risperidone [6]and aripiprazole [7].

1.3. Pharmaceutical therapies and why?

Medical practitioners and healthcare providers usually prefer to use pharmaceutical medications because it is helpful in treating specific type of behaviour exhibited by the ASM patient i.e. aggression, self-injury. By minimizing these symptoms that are very apparent in the ASM patient, it enables the patient to focus on other aspects such as effective communication. Studies have shown that medication is more effective when combined with therapies that relate to behavioral symptoms [8].

Drugs such as aripiprazole and risperidone was accepted through FDA, to be able to cure children irritability accompanying ASM, however there are other drugs that have been utilized and shown improvement in symptoms for ASM children , but they are nit yet approved by FDA. It is very important that parent should work very closely with health providers and medical experts to ensure proper usage of these drugs as all drugs carry some level of risks and some of the risk are quite severe [9].

1.4. CAM therapies and why?

These therapies are usually considered as a more natural approach with little or no side effect, pharmaceutical medication was reported to have adverse effect as against CAM therapies which was a big factor in their disparity [10] . Although adults who us CAM therapies prefer to combine with pharmaceutical medication as it is likely to be more successful when utilized in that form. A study carried out by [11], showed that about 75% of families chose therapies based on their personal perception of the safety concerns attributed to the particular form of therapy utilized as well as absence of side effects.

Other reasons attributed to usage of CAM therapy are the longer visits offered in the CAM settings, there is a perception that there is more attention given to patients who use CAN therapy as opposed to other form of treatment.

1.5. Cam therapy in ASM

Complementary alternative medicine involves and encompasses all forms of practices and methods that is needed in preventing, treating a particular syndrome. It also involves promoting health and wellbeing of individuals. CAM therapy has become very popular and well known among parents with autistic children [12], the major aim or reason for using CAM therapy is to prevent stress in family, reduce symptoms of ASM, health deficiency and at the same time improve quality of life [13].

However, the usage of CAM treatment seems to be very common in Caucasian families that have a high net income, it was also reported that even before the diagnosis that nearly half of the children have received CAM therapies and 9% of the population utilized a harmful CAM procedure called chelation [14]. Previously a high usage of CAM therapy has been reportedly utilized in ASM children spectrum syndrome 52 to 74% compared to other studies [15].

1.6. Applied behavioral analysis (ABA)

This type of CAM therapy is mostly utilized in schools and clinic, its major aim is to help ASM children spectrum syndrome learn and exhibit positive behavioural characteristics. There are different forms of behavioural analysis depending on the condition of the patient, the training involves simple verbal lessons on behavioural intervention [16]. There have also been positive reports that this particular form of Cam therapy is better than pharmaceutical medications, as children who have undergone this form of treatment ended up having and possessing effective communication skills as well as capability of socially interacting with other individuals appropriately [17].

Table 1-A. Chelation in ASD

Comparators	Dose	Outcome Measure	Finding	Comments
Placebo completers n=15	Sic round of DMSA in three days	ATEC, PDD-BI, SAS, ADOS, PGI	No significant difference between active treatment and control	Very high attrition rate, no power calculation, not real placebo
None	10 mg/kg twice daily.	ATEC	Significant Improvement	Open label small sample size, Multi component intervention

1.7. Chelation therapy

This type of CAM treatment involves the removal of certain metals from a person's body by administering various chemical substances [18]. The relationship or link between chelation and ASM began in the 90s, claims that certain vaccines with very high levels of mercury can lead to ASM spectrum syndrome have not been proven so as the fact that chelation therapy can also be utilized or helpful in treating ASM is yet to be proven. There are however certain reports of patients dying after undergoing this form of treatment, the treatment basically removes metal out of the body to reduce or prevent damage to the internal organs.

Table 1-B. Chelation in ASD

Authors	Year	Type and duration of study	Sample size	Type of intervention
Adams et.al [19]	2009	Randomized double blind, placebo controlled, parallel group Duration: 3days	N= 77 (m=69, F= 8) Age: 3-8yrs	Dimercaptosuccnic acid

D.A Gaier and M.R Gaier	2006	Open label Duration:2-7 months	n = 11 (m = 10, f =1) Age: 6- 14 years	1) Leuprolide acetate. 2) Meso 2,3 dimercaptosuccinic acid

ADOS: ASM Diagnostic Observation Schedule; ATE: ASM Treatment Evaluation Checklist; ASD: ASM Spectrum Syndrome
PGI: Parent Global Impressions; SAS: Severity of ASM Scale

2. Material and methods

2.1. Therapy of music

This is a technique that involves no risk, it helps individuals that have emotional challenges or problems as well as cognitive deficiencies to improve their overall ability to perform and function. It also helps in improving various skills such as effective communication, motor skills, and sensory skills.

Individuals with ASM spectrum syndrome are usually very responsive to music due to its capability to involve and inspire at the same time, it involves unstructured sessions of playing and listening to music [20].

Table 2. Therapy of music in ASD

Authors	Year	Study duration and type	Size of sample	Intervention type	Comparators	Dose	Outcome Measure	Finding	Comments
Arezina	2011	Randomized, crossover. Duration: 3days	n= 6 (m=5, F= 1) Age: 36-64 months	Interactive MT (musical instrument play, music, songs, books)	Non-music interactive play. Independent play	18 sessions of 10 minutes each.	Behaviour observation of videotaped sessions.	Significant more interactions during interactive music therapy than the 2 groups or comparat	Blinding not reported. No much data regarding the process of diagnosis.

2.2. Occupational therapy

This therapy helps with various activities that are needed to be carried out daily such as learning to button a shirt, to hold or make use of spoon or fork etc. It can also involve or relate to activities that pertains to school and work. It all depends on what the patient or child suffering from ASM syndrome needs at that point in time, there are two major forms of this therapy: evaluation and therapy.

Evaluation would determine the kind of care the child requires at that moment such as stamina, transition to new activities, level of aggression, posture and other related motor skills, interaction level with caregivers [16]. After evaluation has been carried out a proper well-structured program is organised for the child, although there is no certain or complete treatment program, but a well-structured program has been known for improving the whole child wellbeing. The major aim of occupational treatment is to aid individuals with ASM mend the life quality both in school and at home.

2.3. Naturopathic medicine

This form of medical treatment allows the freedom to explore herbal supplements as well as nutritional supplements in order to help manage symptoms relating to ASM, various tests are also carried out to determine if there is any imbalance in hormonal levels, allergies, or deficiency in vitamins. After all this evaluations and tests have been carried out, it is now easy to determine or know the major supplement required for effective treatment of the individual.

Study has revealed that ASM children tend to have insufficient level of certain nutrients required by the body for proper functioning of the body and improvement tend to occur when the children take the supplement required to boost the nutrient that they are deficient [20].

2.4. Speech therapy

Speech therapy addresses the problems associated with the inability to properly communicate and also problems as regards language; it also helps individuals with ASM to improve social communication as well as verbal and non-verbal communication. The major goal of speech therapy is to bring about effective communication and more functional ways in which an individual or child with ASM can communicate [21].

The level of communication is different from person to person, some autistic patients have problems with speaking generally, while others can speak but can't hold a conversation or understand basic body language or expressions. One of the first step to speech therapy is evaluation by a speech pathologist to access the major problems or issues concerning the speech. After evaluation goals for the speech therapy is created, some of the skills and areas worked on during speech therapy include responding to questions, proper understanding body language, making correct facial expressions, and making correct and clearer sounds when speaking.

2.5. Sensory integration therapy

Such therapy is a program for ASM children to let them use all their senses together i.e. sight, touch, smell, hearing and taste. Study reports that sensory integration therapy helps in improving ASM related symptoms such as abnormal routine behaviour and behaviours that are related to processing of sensory information.

This type of therapy was first proposed by an occupational therapist in 1950s by A. jean Ayres, it makes use pf playful activities to ascertain or determine how the brain react to movement, touch or any of the major senses [22].

2.6. Herbs

Lately, the need or use of plant-based medications has been on the increase. Plant-based medicines preferred therapy choice by parents or as an addition to pharmaceutical therapies (Gonzales *et al*., 2016). Environmental pro-oxidant factors may trigger oxidation stress in some ASM patients. Green tea (*Camellia sinensis* extract) therapy may be utilized to minimize oxidative stress. *Camellia sinensis* extract contains chlorogenic aid, gallic acid, caffeic acid, flavonol derivatives together with catechins. Based on the available literature, the most frequently utilized plant-based medications include Acorus gramineus, Poriacocos Schisandra hinensis, Glycyrrhiza uralensis and Acorus gramineus [22].

2.7. Camel milk

Another type of alternative treatment with regenerative properties and capable of treating and managing various health issues and complications such as heart disease, cancer, ASM and some auto immune diseases [23]. There have been reports due to studies carried out by researchers that camel milk contains a high amount of immunoglobins, which gives camel milk the ability to help stabilise the immune system, the presence of antioxidants as well in the milk prevents accumulation of (ROS) which prevents OS and damage to the body [24].

2.8. Gluten & Casein free diet

Gluten/Casein free diet is one of the various alternative methods utilized in treating ASM children spectrum syndrome, it involves carrying out a well-structured and organized food regime of avoiding food containing gluten i.e. food found in rye, wheat and barley and also casein i.e. food found in products as dairy [25]. Research has shown that the reason for emphasizing and carrying out such strict diet is due to the datum that ASM children have a very high sensitivity to food that contain gluten/casein and also the processing time of this proteins in the brain is significantly slower in ASM children than in normal children [11].

2.9. Acupuncture

Acupuncture is a traditional form of treatment very common in china, the procedure is carried out by inserting needles in specific part of the body, although there have been complications and infections because of wrong placement of the needles. According to the university of Hong Kong researchers acupuncture is an operative treatment mode for persons with ASM spectrum syndrome, it was revealed that electroacupuncture improves the core functions in ASM children especially in the aspect of comprehension of language skills, there have also been investigations as to the safety and level of effectiveness of acupuncture where some trials have focutilized on tongue and manual scalp acupuncture [21].

Table 3. Acupuncture in ASD

Author	Year	Study duration and type	Size of sample	Intervention type	Comparators	Dose	Outcome Measure	Finding	Comments
Allam et.al	2008	Randomized single blind parallel group Duration: 9 months	n= 20 (m=12, F= 8) Age: 4-7yrs	Acupuncture (Scalp) plus language therapy	Language therapy n=10	Twice weekly	Arabic language test	Significant improvement in acupuncture group.	No placebo conditions. No detailed baseline characteristics
Chan et al	2009	Randomized parallel group Duration: 6 weeks	n =32 (m =26, f =6) Age: 4-6yrs	Seven-needle star stimulation plus convention education therapy n= 16	Conventional educational therapy n =16	One 5-10 min session per day, 5 days per week.	Parents rating questionnaire, Quantitative EEG	Significant improvement in acupuncture group.	No blinding No placebo condition, no detailed baseline characteristics.

3. Results

3.1. Pharmaceutical medications in ASM

It is to be noted that pharmaceutical therapies cannot completely cure or treat ASM, however some of the medications are capable of improving ASM related symptoms, therefore specific medications are utilized based on the particular symptom exhibited by the patient that needs to be addressed [26].

However, the FDA has given its approval to two major drugs (Aripiprazole and risperidone) for treatment and management of ASM symptoms, psychotropic drugs have been noted to be very useful in treating behavioural symptoms in ASM i.e., aggression, anxiety and self-injury [27]. There has also been successful usage of serotonin uptake inhibitors such as sertraline to help manage repetitive behaviours as well as anxiety; antipsychotic drugs such as risperidone have been useful in managing and treating self-injury [8].

There are also several indications that there is an increased likelihood of a person being prescribed medication for ASM increases as a person gets older, for example a revision reported that the psychotropic drugs use increased from 56% in 6-11years to 73% in 18-21years old [28]. The approval of Risperidone by the FDA was done in 2006, to be utilized to treating irritability issues associated with ASM spectrum syndrome between the ages of 5-16 years old while in 2009 Aripiprazole was also approved for the similar symptoms treatment for children between 6 to 17 years [29].

3.2. Risperidone

Risperidone is a drug as 2nd generation antipsychotic; it was the 1st drug to be permitted by the (FDA) to treat irritability and aggression symptoms relating to ASM between the ages of 5-16years. Several studies were conducted on the level of efficacy of the drug where it was compared to placebo after an 8-week trial as randomized between children of 5-17 years [29], the results presented significant improvements in the

aggressive behaviour number and self-injury episodes exhibited by ASM children spectrum syndrome that were cured with risperidone in comparison to those that were treated with placebo.

However, there have been several side effects experienced by patients after treatment with risperidone such as drowsiness, stooling, and increased appetite [30].

3.3. Aripiprazole

This is another approved FDA psychotropic drug utilized for irritability treatment symptoms among ASM children spectrum syndrome between ages of 6-17 years [31], the drug is also capable of treating several other health complications such as bipolar syndrome and Tourette syndrome. Several studies have also been conducted with major emphasis on the quality of life and the level of improvement of patients regarding irritability, results from study conducted showed that there was a significant enhancement in patients that were subjected to use aripiprazole compared to placebo. Side effects of the drug includes pyrexia, vomiting, respiratory tract infection and also insomnia [32].

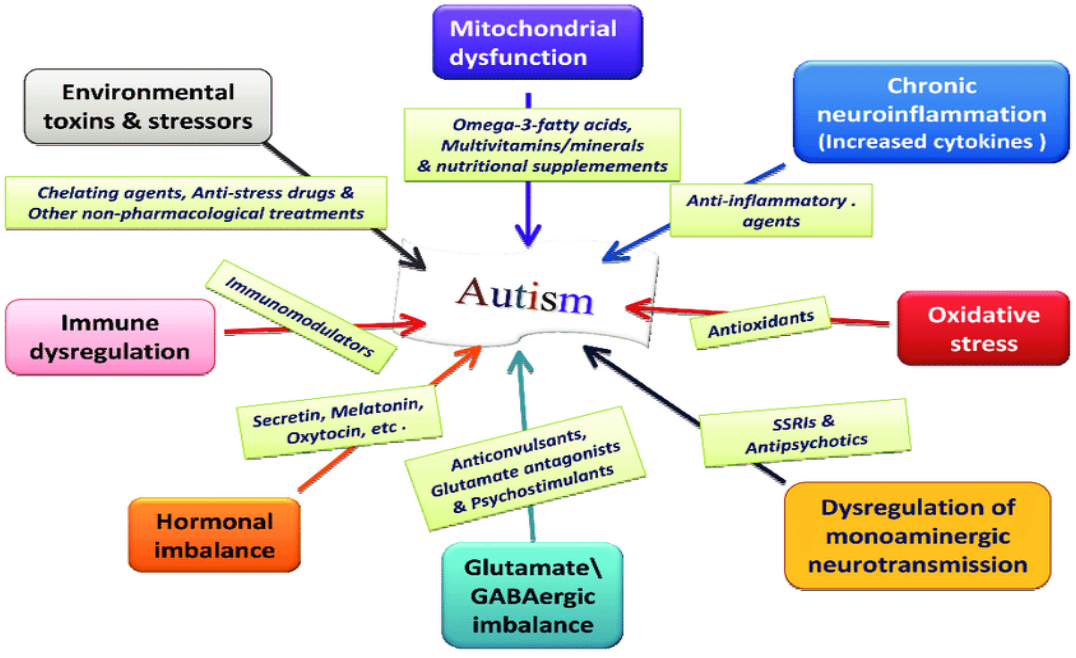
3.4. Clopazine

Before aripiprazole and risperidone was accepted by the (FDA), clopazine an antipsychotic drug was utilized to treat and manage aggressive behaviour in patients with ASM spectrum syndrome. Also, it is utilized to treat patients attempting suicide as well as schizophrenia, the efficacy of clopazine was tested by behrec and his colleagues [33], results of the test showed that after the usage of the drug there was a significant decrease in the aggressive behaviour number or number of days where aggressive behaviour was shown.

However, clopazine was reported to cause increase in weight gain and tachycardia, and could lead to seizures when the drug is being utilized in high doses [31, 34], [35].

Table 4. Clinical trials in ASM spectrum syndrome

Intervention	Study	Sponsors	Description	Start	Estimated Completion



Acamprosate (Campiral, forest pharmaceuticals	Acamprosate in ASM	Children hospital medical center, Cincinnati Ohio	26- week randomized double-blind placebo-controlled phase 2 trial in 36 patients (age 5-17years)	Apr., 2013	Feb., 2016
Atomoxetine (Srattera, lilly)	Effectiveness of Atomoxetine in treating ADHD symptoms in ASM children and adolescents.	Massachusetts general hospital, Boston, Massachusetts	8-week double blind placebo randomized, controlled crossover phase 3 trial in 86 patients (age 5-15 years)	Jul., 2007	Oct., 2015

Figure 1. Drug therapy and different targets in ASM (Baldeep, 2012)

4. Discussion

4.1. Children parents' preference with ASD between CAM and pharmaceutical therapy

One of the major constraints of pharmaceutical treatment of ASD is the limited number of drugs available for treating the condition. For instance, two drugs are there just endorsed for treating ASM via the "Federal Food and Drug Administration" (FDA) – Aripripazole and antipsychotics Risperidone. The target of the two drugs is irritability (behaviour) problem rather than the main problems of associated with ASM [36]. This also poses a limitation to the use of pharmacological therapy for ASM.

As a result of the above constraints to the use of pharmaceutical therapies for the ASD treatment, several parents have resorted to the use of alternative modalities or (CAM) treatments. There is a vast documentation in available literature suggesting wide use CAM among parents of children with chronic illnesses. (Myers, Johnson, & The American Academy of Paediatrics Council on Children with Disabilities [37], particularly parents of autistic children, with documented rate of use as high as 95% (15,11). Majority of families with ASM children has been reported to use CAM for maintenance of general health, however, a number of them have been reported to use CAM for treatment of particular symptoms like sleep problems, hyperactivity, irritability and GI symptoms [15],[38].

Mcpheeters et al., 2011 examined the use of CAM for ASD children, the result of the study indicated that 50%–75% of ASD children use CAM. Another study conducted by reported that one – third of asked for ASD examinations have already utilized CAM, even prior to diagnosis. Body and mind practices were the most often utilized type of CAM for ASD children [39].

Research by Hanson, 2007 reported that 75% of parents of ASD children preferred the use of CAM because they have previously experienced side effects of pharmaceutical therapy or they believe that CAM was thought to be safe and they are mostly without side effects. The aims of using a survey on parental perceptions and use of CAM practices for ASM children spectrum syndromes in private practice by John *et al.*, 2006 indicated that use of CAM treatments was rampant among the population of study (92%) and did not seem to significantly vary with household income, ethnicity, or education. A multicentre study by [40] assessed parents' personal preference of therapies for their children, around eighty-three percent of the parents reported utilizing just pharmaceutical therapies as their predilection, and none of them preferred only CAM therapies. Conversely, 17% of the parents preferred both methods.

5. Conclusion

As medical experts are continually work towards evidence of usage of conventional medical practice due to widespread acceptance of CAM by parents of ASM children spectrum syndrome. While aripiprazole and risperidone remain, the major drugs utilized in managing irritability related ASM symptoms due to the fact that they are the only 2 drugs agreed by the FDA, more trials on other drugs needs to be carried out and approved by the FDA, so as to provide health care providers more options in the treatment of ASM syndrome.

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Conflict of interest

The authors confirm that this article content has no conflict of interest.

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