Efficacy of A *Brahmi* Based Unani Formulation In The Management of Autism: A Randomized Double Blind Placebo Controlled Study

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Abstract :
Autism is a heterogeneous syndrome caused by significant impairment in three core domains: social interaction, language and range of interests. Despite the general consensus revolving around a developmental onset, little agreement exists around primary causes. At present, the intervention for Autism mainly comprises of rehabilitation therapies and behavior modification techniques. *Brahmi* (*Centella asiatica* Linn.), which is an imperative medicinal drug possesses significant medicinal properties, especially those involving cognition. It is one of the prominent herbs for revitalizing the nerves and brain cells. A randomized double blind placebo controlled clinical trial was carried out at UDAAN for the Disabled, Lajpat Nagar, New Delhi, India. This study particularly focuses on the role of *Brahmi* in managing the symptoms of Autism in children aged 2-10 years.

Keywords: Autism, *Centella asiatica*, *Brahmi*,

Introduction:
Autism being a 'spectrum disorder' points that a child's symptoms can present in a wide variety of combinations, from mild to severe. As per DSM IV-TR, Autism is a neuro developmental disorder which has its onset prior to 3 years and the presence of deficits or unusual behaviors within three domains: reciprocal social interaction, communication, and restricted, repetitive interests and behaviors. Autism typically affects a child's ability to communicate, form relationships with others and respond appropriately to the environment. Some children with Autism are relatively high functioning, with speech and intelligence intact. Others are mentally retarded or have serious speech & language delays . A meta-analysis of ASD prevalence rates suggests that approximately 37 in 10,000 individuals are affected[1]. Behavioral descriptions and observations primarily aid in warranting a diagnosis of ASD. Although there is much evidence that autism is a neuro-developmental disorder with a very strong genetic component, there is not yet a valid biomarker or biological test [1]. Autism occurs about 4 times more often in boys than girls. Intellectual disability frequently co-occurs with ASD, although the percentage of co-occurrences has reduced from 75% to 50% over recent decades (Centers for Disease Control and Prevention, 2000).
The clinical features of Autism include marked impairment in use of multiple non-verbal behaviors such as eye to eye gaze, facial expression, body postures, and gestures to regulate social interaction, failure to develop peer relationships, does not enjoy seeking enjoyment, interest and achievement with others and lack of social or emotional reciprocity. There is delay or total lack of development of spoken language, in individuals with adequate speech, there is marked impairment in the ability to initiate or sustain a conversation with others, presence of stereotyped herd repetitive use of language or idiosyncratic phrases, lack of spontaneous make-believe play or social imitative play. Restricted, repetitive and stereotyped patterns of behavior, interests and activities include preoccupation with one or more stereotyped pattern of

interests, inflexible adherence to routines/rituals, stereotypic and repetitive motor mannerisms (hand flapping, finger flapping, spinning, rocking back and forth etc), and persistent preoccupation with specific objects / parts of objects. [2]

What causes autism has been a subject of wide research and controversy over a long period of time. Literature points to factors such as specific genetic abnormalities, differences in brain development, autoimmune conditions, neurological impairments and biochemical imbalance. However, yet there exists no such experimental work or findings that may help be all means to claim that autism is only caused by either or all of the above mentioned factors. No two children with autism have exactly the same profile, making it a heterogeneous condition.

At present, no medications are prescribed as such to treat the core symptoms of Autism. Perhaps, Risperidone and Aripiprazole are the only FDA approved medications for managing irritability in children who are between 5-16 years. *Centella asiatica* Linn. (locally known as *Brahmi*) is an imperative medicinal drug which possesses significant medicinal properties, especially those required in improving cognition[3]. In Unani system of medicine, it has been extensively used as Muqawwi-e-Dimagh (brain tonic), Muqawwi-e-Asab (nervine tonic) and Musakkin-e-Asab (tranquiliser) drug in various neuro-psychiatric disorders e.g. Zof-e-Dimagh (cerebral asthenia), Zof-e-Asab (neuroasthenia), Zof-e-Hafiza (poor memory), Nisyan (amnesia), Junoon (insanity) , Akhtanaqur Rahem (Hysteria)[4]. It aids in brain repair by having a particular activity on cerebrum and has a prominent role in revitalizing the nerves and brain cells [5]

Brahmi is most commonly used as a nervine tonic that enhances learning and academic performance, improves mental alertness, sharpens short-term and long-term memory and rectifies speech disorders, increase concentration and intellectual ability in children. Considering such benefits of the drug, a *Brahmi* based Unani formulation was used in the present study to manage the symptoms of Autism in children of both genders in the age range of 2-10 years.

Objective of the study

- To examine the Efficacy of *Brahmi* (*Centella asiatica*) based Unani formulation in management of symptoms of Autism assessed with Childhood Autism Rating Scale (CARS).

MATERIAL & METHODS

Total 31 children between ages 2-10 years who were visiting the OPD at UDAAN for the disabled were diagnosed as having Autism as per the DSM IV criteria were recruited and their parents gave voluntarily informed consent to participate in the study. Out of 31, 22 completed the study and the others were drop-outs.

Inclusion Criteria:

- Certified to be in adequate healthy state by panel Pediatrician, ENT Specialist and Therapists.
- Age 2 to 10 years and of either sex.
- Well-educated parents who can understand the experimental nature of the study

Exclusion Criteria:

- Children having other genetic disabilities or cerebral palsy.
- Insufficiency of liver / kidney / marrow functions as per appropriate biochemical tests.
- Chronic uncontrolled illness that may need medical therapy which could interfere with diagnosis, treatment and assessment of the Autistic symptoms.

Drug Used

Both Unani Brahmi (*Centella asiatica*) formulation and Placebo were supplied by Central Research Institute, Hyderabad in coded form.

Dosage and Drug Administration

The recommended adult dosage is 20 gm which is roughly 20 ml per day in two divided dosages.

In the age group of Autism (2 to 10 years) as per our inclusion criteria, the body weight range expected is 10 to 50 kg.

The dosage based on weight was as follows:

10 to 20 Kg: 2.5 ml. twice daily (½ teaspoon twice daily)

20 to 30 Kg: 2.5 ml. (½ teaspoon) in morning and 5 ml (1 teaspoon) at night

30 to 40 Kg: 5 ml. twice daily (1 teaspoon twice daily)

40 to 50 Kg: 5 ml. (1 teaspoon) in morning and 7.5 ml (1 ½ teaspoon) at night

Above   50   to   60   Kg: 7.5   ml.   twice   daily   (1   ½   teaspoon   twice   daily)

Above 60 Kg : Adult dose of 10 ml. twice daily (2 teaspoon twice daily)

Duration of drug administration 3 months

Composition of *Brahmi* based Unani Formulation:

Each 10 gm of Unani formulation contains *Brahmi* (*Centella asiatica* Linn.) - 2 gm, Filfil Siyah (*Piper nigrum* Linn.) -1 gm, Badam Shireen (*Prunus amygdalus* Linn.) - 2 gm, Amla (*Emblica officinalis*) - 2 gm, Khajoor (*Phoenix dactylifera* Linn.) - 2 gm, Jadwar (*Delphinium denudatum* Wall) - 1 gm

Subjects:

Diagnosed cases of Autism spectrum disorders as per the DSM IV or V Autism Criteria, referred by clinical psychologist were selected and followed up for 6 months and assessed 4 times with a range of biochemical and psychological tests. First, at baseline and then thrice in an interval of 2 months. They were randomly divided in two groups – Group A and Group B. One group was given *Unani* formulation (N= 11) and the other was given placebo (N=11) for three months in a double blind manner.

Each child was monitored to improve his/her general health using a balanced non-allergic well tolerated diet along with avoidance of foods that does not suit the child along with administration of mineral supplements. Throughout the 6 months of follow up, each participant was actively encouraged to maintain a high standard of Standard Therapy as a baseline permanent therapeutic intervention, irrespective of group, to see whether the test drug could enhance his/her quality of life, cognitive skills, psycho-social skills, communication ability and general behavior as compared to the placebo.

Psychological Assessment

To assess the efficacy of *Brahmi* Unani formulation in managing the symptoms of Autism, a standardized psychological assessment tool for Autism was used.

Childhood Autism Rating Scale (CARS), Second Edition (by Eric Schopler, Mary E. Van Bourgondien, Glenna Janette Wellman, and Steven R. Love,) Is a 15 item behavioral rating scale which helps to identify children 2 years of age and older with Autism and determine symptom severity through quantifiable ratings based on direct observation (Schopler et al.,

The 15 items in the scale are: Social-Emotional Understanding, Emotional Expression and Regulation of emotions, Relating to people, Body Use, Object Use in play, Adaptation to Change, Visual Response, Listening Response, Taste, Smell and Touch Response, Fear or Anxiety, Verbal Communication, Thinking/Cognitive Integration Skills, Level and Consistency of Intellectual Response, General Impressions. The examiner assigned a score of 1 to 4 for each item: 1 indicates behavior appropriate for age level, while 4 indicates severe deviance with respect to normal behavior for age level. The scores for the single items are added together into a total score which leads to the following categories of Severity Group,

15-27.5 – Minimal to No Symptoms of Autism Spectrum Disorder

28-33.5 – Mild to Moderate Symptoms of Autism Spectrum Disorder

34 and higher – Severe symptoms of Autism Spectrum Disorder

Table 1. Monitoring and Follow Ups for 22 subjects who completed the study

Diagnosis of Autism as per DSM IV	Baseline Assessments	Biochemical Testing	Health Management	Complete dosage of *Brahmi*	2nd Follow Up	3rd Follow Up	4th Follow up
√	√	√	√	√	√	√	√

Results

Statistical Analysis was done to analyze if there is any significant difference in the symptoms of Autism in both Group A & B.

Mean of two groups were compared to see which group showed significant difference in the symptoms before and after.

Table 2. Mean Scores on CARS of subjects in Group A (Drug Group, N=11**)**

	CARS Score	
Subject-wise	**Baseline**	**After 6 months**
1	31	39
2	34	31
3	33.5	33
4	36.5	34
5	36	35
6	31.5	18
7	33.5	32
8	34	34
9	32.5	28
10	37.5	32
11	33.5	32
Average	**35**	**29.8**

Table 3. Mean Scores on CARS of subjects in Group B (Placebo Group, N=11**)**

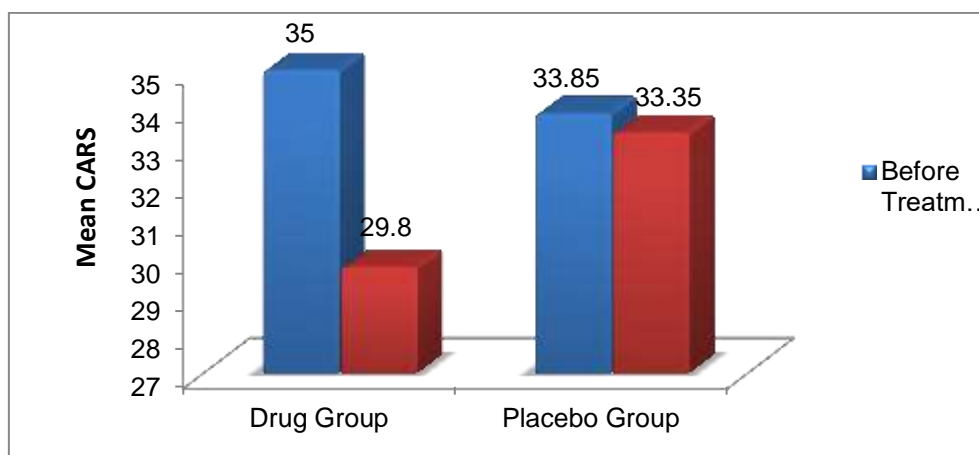|	CARS Score	
Subject-wise	**Baseline**	**After 6 months**
1	32	36
2	33.5	35.5
3	39.5	39.5
4	33	30
5	34.5	36
6	31.5	31.5
7	32	31.5
8	32.5	30
9	34.5	30.5
10	35.5	33
11	32.5	32
Average	**33.85**	**33.35**

Figure 1: Effect of Unani Drug and Placebo on CARS

Discussion

Brahmi based Unani formulation has significant results on learning and memory enhancer. It helps to decrease the level of norepinephrine and dopamine in the brain that results increased cognitive ability[6] It is most commonly used as a nervine tonic that enhances learning and academic performance, improves mental alertness, sharpens short-term and long-term memory and rectifies speech disorders, increase concentration and intellectual ability in children[7]

As we can see from the table, there is a significant difference in the mean scores of subjects in Trial A (Baseline: 35, After 6 months: 29.8) than on Trial B (Baseline: 33.85, After 6 months: 33.35). In Trial A, the subjects showed improvement on parameters like Socio-Emotional Understanding, Body Use, Non Verbal Communication, Visual & Listening Response and Taste, Smell and Touch Response according to CARS. *Brahmi*, being one of the popular herbs for cognitive enhancement has proved to be beneficial in the present study.

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