



A study of evaluation of safety and efficacy of memomet, a multi herbal formulation (memomet) in the treatment of behavioural disorder in children

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ABSTRACT

This study shows the efficacy of Memomet in the treatment of ADHD in children. Total 86 patients were recruited in the study. There were 56 children in the treated group and 30 in placebo treated group. The children were subjected to various test parameters like Yale's behavioural scale for children with ADHD, Conner's test and Malin's test. Both Memomet and Placebo was given at the dose of 1 tsf twice daily for 4 months. At the end of the study period both the groups were evaluated for response to treatment. It was observed that group treated with Memomet responded significantly compared to placebo.

Keywords: Memomet; ADHD; Bacopa; Centella; Hyperactivity; Behavioural problem; Children

INTRODUCTION

Behavioural disorders which present a very important problem in paediatric practice, may be associated with normal physical development and intelligence or with disturbance of the cerebral function. Learning and behavioural disabilities may be of various degrees and associated with deviation in the functioning of the central nervous system. Hyperactivity: Moves around constantly, stands where one should sit, may often leave one's seat, and talk excessively. Hyperactivity symptoms are usually oblivious by 5 years of age and peak severity at the age of 7 to 8 year (Cutler, 2003). Inattention symptoms are most likely to manifest at about 8 to 9 years of age and commonly remains lifelong (Donovan, 2000). Impulsiveness in children are acts without thinking gives wrong statements at wrong time, impatient most of the times. Impulsive behavior is commonly linked to hyperactivity and get peak at the

age of 7 to 8 years.

Genes that control the relative levels of chemicals in the brain known as neurotransmitters seem to be different in ADHD children and levels of these neurotransmitters are out of the normal balance. Children suffering from ADHD are not seen to be bad, lazy or stupid, but it is difficult for their teachers, parents and classmates to manage them. Children suffering from ADHD find difficulty in following instructions. ADHD affects the academic performance of children. This disorder was at first described by Dr. Heinrich-Hoffman in 1845. The story of fidgety Philip was an accurate description of a little boy who had ADHD. After this several scientific papers have been published. Probable cause of ADHD is unknown. It is observed that ADHD is passed down from one generation to another. So it may be an inherited genetic tendency. Some researchers stated that in the key area of the brain of the children with ADHD, chemicals which are necessary for controlling hyperactivity and impulsiveness are not produced properly. Some researchers stated that food and environmental allergies as well as immune response to nutrients such as vitamins and amino acids affect the functioning of nervous system and deficiency of neurotransmitters (Loo, 1998).

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Received on: 01-03-2012

Revised on: 09-03-2012

Accepted on: 28-03-2012

Some studies suggest that children with ADHD may have low levels of zinc in their body. Some scientists reported an ADHD treatment of children with traditional treatment along with zinc. Again, foods rich with zinc include oysters, other seafood, beans etc. Omega 3 fatty acid has a beneficial effect on children with ADHD. Omega 3 fatty acids have shown good results in learning problems and other neurological problems. Docosahexaenoic acid is an omega 3 fatty acid, which plays an important role in optimal synaptic functioning. Fish oil contains Omega 3 fatty acids. There are some studies that have shown, ADHD children of 8 to 12 years of age improved their mental skills after taking fish oil. Caffeine, as found in coffee, and other herbal stimulants are proposed as an alternative to stimulant drugs in the treatment of ADHD in children. Studies in context with ADHD have demonstrated significant benefits with the administration of caffeine. However, Caffeine also has its side effects (Schechter, 1985). ADHD is a complex disorder and most commonly encountered in the population today. This is a disorder for which no physiological, biochemical or psychological origin has been identified. There are many drugs available but parents are concerned about giving their child a psychoactive mid altering medicine for a long period of time.

Looking at the extent of behavioral problem faced by children and the side effects encountered alternative therapy has always been preferred by both physicians and parents, however, most of the herbal products available in the market either contain too many ingredients and heavy metals or have no authentic placebo controlled trials conducted, therefore it was decided to conduct a double blind randomized clinical trial with Memomet syrup in children with various behavioral problems in children. Memomet is a well standardized herbal product which contains only three ingredients Bacopa monniera 125 mg, Convulvulus pleuricaulis 100 mg and Centella asiatica 100 mg. Since ancient time Bacopa Monnieri has been used to improve concentration. It can be used for ADHD. Brahmi (Bacopa) carries properties that improve mental functions by a modulation of the cholinergic and GABAergic neurotransmission (Mathew, 2011). Brahmi works scientifically as it restores the frontal cortical muscarinic and cholinergic receptor activities and hence it will improve the mental quotient, memory span, concentration ability and stress threshold. Brahmi (Bacopa) will also help reduce the level of tribulin, an endogenous Mono Amine Oxidase inhibitor, which is elevated in certain degrees of anxiety. Brahmi can also ameliorate some of the attention fluctuations and other behavioral problems. It possesses exhibiting anti-parkinsonian activity significantly by enhancing the dopamine post-synaptic receptor activity. In proper dosage (Shukla, 1987), Brahmi also works as safe and natural sedative and tranquilizing agent and hence it offers protection against convulsions and is also bene-

ficial in insomnia. The product helps to improve articulation and helps in correcting speech defects if used over the times.

Centella asiatica is traditionally used as a tonic to support a healthy brain and nervous system. Centella asiatica is recommended to facilitate mental clarity, attention span, concentration, healthy brain function, and a generally balanced mood. Centella asiatica is also a favorite food of elephants and, as we all know, elephants never forget! Recent studies have suggested that Centella asiatica improves cerebral blood flow (CBF) and circulation in general, thereby allowing oxygen-rich blood to penetrate deep into the brain. Studies have also suggested that this herb may be beneficial as a mood tonic (Ragavendra 2009).

Shankhpushpi has been extensively used in behavioural problems in children and also in learning and memory (Indurwade 2000). This plant has also been found to be acting on CNS (Sharma 2009).

MATERIALS AND METHODS

A total of 86 children aged 6-12 years participated in the study. All the participants were recruited in our hospital. None of them had a H/O treatment for ADHD. Patients were diagnosed with ADHD based on DSM IV criteria and assessment intervention with participants and their parents. The clinical trial was performed using a 2:1 assignment ratio for the treatment group (n=56) and a control group (n=30). Participants were given either Memomet syrup or Placebo at the dose of 1 tsf twice daily for 3months. The assignment ratio was designed to minimize the numbers of untreated control, yet still to provide adequate statistical power.

During the course of the treatment the participants were only given Memomet or Placebo. Parents were given full explanation and signed the consent form. Verbal agreement to participate in the study was obtained from the children.

The raw materials for the trial were obtained from authentic suppliers and were examined and certified as free of bacteria, fungus and heavy metals. Standardization was done by using TLC. Memomet syrup was prepared at a cGMP approved facility and the placebo was prepared by a pharmaceutical company and was designed to taste, smell and look similar to Memomet syrup. Both Memomet and the placebo were filled in identical looking PET bottles.

None of the participants had received any form of treatment for ADHD prior to clinical trial. Children between 6-12 years of age who met DSM IV criteria for ADHD were included in this study.

The study was conducted over 4 months period and the participants were assigned using a table of random numbers, to one of the two groups: the treatment group (n=56) and the placebo group (n=30). Randomization was done by a research assistant, who

was distant from the interaction; had no involvement with the participants, was the only member of the team responsible for dispensing the appropriate formula for each participant in identical PET bottles, labeled by the name. Dispensing was then carried out by the blinded team member according to the name on the label. Participants were to receive either Memomet or the Placebo according to the randomization chart. The parents of the participants were supposed to meet the investigator at the interval of 3-4 weeks. Additionally, parents were asked to look for any side effects like insomnia, abdominal pain, nightmares, anxiety, and rashes and so on.

During the trial 3 participants withdrew from the treated group and around 10 from the placebo treated group. The cause of withdrawal from the treated group was mainly personal and also 2 children suffered from normal cold and cough. Withdrawal from the placebo group was mainly due to non-response to treatment.

At the end of the study period of 4 months, each participant was evaluated by DSM IV criteria scale. Diagnostic assessment included a parent and patient interview to identify symptoms of ADHD and other disorders. Corroborative information from adults in other settings including teachers was obtained. Detailed history was taken and physical examination done to identify any systemic illnesses. An assessment of academic functioning was done. The following psychological tests were assessed:

1. Malin's Intelligence Scale for Indian Children (MISIC) (Malin 1971).
2. An Indian Adaptation of the WISC was used to assess the IQ of the children, which gives scores on Verbal IQ, Performance IQ and full scale IQ.
3. Conner's 10-point rating scale. This is an assessment by the parents and is used to identify the hyperactivity of the children. Symptoms are rated on a 3-point scale (0-2: not at all, occasionally, most often). The maximum score received by a subject is 20. The 10-item scale contains overlapping parent and teacher items that are particularly useful for repeated measures in drug trials (Conner 1989/1990).

The Yale Scale is an objective scale with 8 main parameters comprising attention, hyperactivity, impulsivity, tractability, habituation, conduct disorders (socialised and aggressive), negative effects and academics. In each parameter, there were appropriate symptoms and each point was rated as severe (3), moderate (2), mild (1) or nil (0) and the scores were then added up. Statistical evaluation was done to check the significance at 95% confidence limits between the scores of each subgroup, before and after treatment, in both the placebo and active treatment groups and also between the groups. The total scores for each parameter were also checked between the groups and before and after treatment. Paired 't' test was applied to check the level

of significance between pre and post treatment scores in each treatment group and unpaired 't' test to check the significance between the groups.

RESULTS

Results of this clinical trial clearly demonstrates the beneficial effect of Memomet on behavioural response in children. At the time of recruitment the I.Q level of the children were similar. During the course of the treatment all the parents were also interviewed for the response to children and the improvement in symptoms by using Conner's scale. Children were also evaluated by using Yale's behavioural inventory scale for ADHD. The response to treatment with Memomet was significantly more as compared to placebo. There was reduction of symptoms in some parameters in placebo treated group also but it never reached the level of statistical significance.

Therefore, the results of this study demonstrate the safety and efficacy of this product in the treatment of behavioural disorders in children. However, more studies in larger group of children are required to fully evaluate the potential benefit of this product in various behavioural problems in children.

Table 1: Age and sex distribution of children participated

Parameter	Memomet	Placebo
Age	8±1.12	9.1±1.1
Sex	50 boys 6 girls	24 boys 6 girls

Table 2: Psychological tests performed for evaluation of treatment

Parameters	Memomet	Placebo
Misic	92.61±2.17	90.12±3.66
Conner's scale	11.87±3.12	9.12±3.32

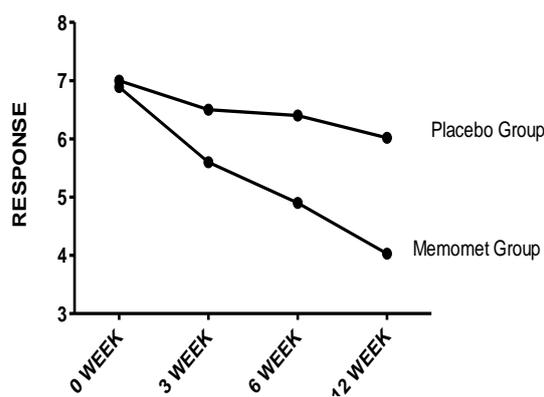


Figure 1: Response of memomet and placebo on attention span

DISCUSSION

Attention deficit hyperactivity disorder (ADHD) has become increasingly prevalent among children. A recent report by the CDC based on phone interviews with parents shows that about 4.4 million children in the

United States have been diagnosed with ADHD at one time. Out of these children, about 2.5 million of them were on medication (Bradweijn 2000). Pharmacological treatment of ADHD can have troubling side effects which is why more and more parents are turning towards herbal treatments instead of medication for their children. ADHD is typically treated with the medications methylphenidate or amphetamine, which are stimulant drugs (Nambudripad 1999). While they have been proven to be effective they also have a high risk for abuse and have many side effects such as weight

have shown that caffeine is beneficial to children with ADHD when given in high doses, however the benefits from caffeine have not been shown to reach those seen with pharmacological treatments and there are numerous side effects from caffeine (Wang 1995). Other herbal remedies that have shown promise without side effects are ginkgo biloba, brahmi, Siberian ginseng, gotu kola, and green oats (Zang 1990). All of these herbs enhance alertness without the use of caffeine.

The present double blind placebo controlled study

Table 3: Performance of children after 4 months of treatment with memomet and placebo
a) Mean score in Yale’s behavioural rating scale in children before and after treatment

Symptoms	Memomet (Weeks)				Placebo (Weeks)			
	0	3	6	12	0	3	6	12
Hyperactivity	9.1	8.2	6.3	5.12	10	8.2	8.0	7.2
Tractability	10.1	8.3	7.1	6.2	11.0	10.12	9.5	9.1
Habituation	6	5.1	3.2	3	5.6	5	4.8	4
Conduct disorder socialized	4.12	4.0	3.3	3.0	5.1	4.12	4.0	3.8
Conduct disorder aggressive	5.11	4.2	4.12	2.23	4.7	4	3.12	3.0
Negative effects	4.8	3.12	3.2	2.1	4.22	4.02	4.0	3.13
Academics	10.2	8.18	8.02	7.11	10.2	9.1	9.0	8.12
Impulsivity	9.15	7.1	6.24	5.3	9.2	8.2	8.0	7.6
Language	6.12	5.09	5.0	4.12	6.6	6.09	5.3	5.0
Fine motor	4.17	3.12	3.0	2.12	4.1	4.4	4.2	3.0

b) Mean percentage response of conner’s test report before and after treatment with memomet and placebo

Treatment received	1 st month	2 nd month	4 th month
Memomet	6	31	48
Placebo	2	18	29

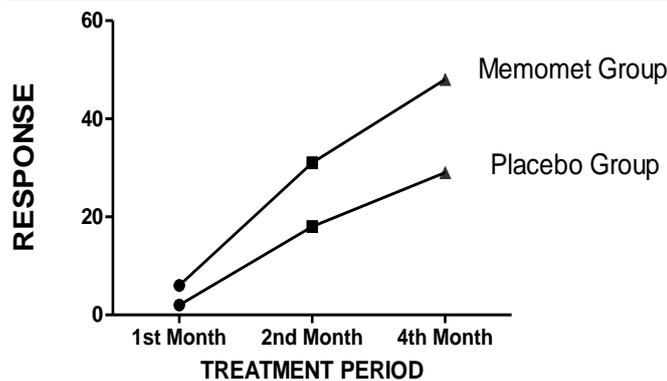


Figure 2: Response of memomet and placebo in children using conner’s behavioural scale

changes, appetite changes, insomnia, and nervous tics. The numbers of children on these drugs is alarming - the production of methylphenidate and amphetamine has increased by 500% and 2000%, respectively, since 1991. More than 50% of prescriptions for these drugs are from pediatricians (Zang 1987). Due to the troubling side effects of these medications many parents are looking into alternative options for dealing with ADHD. Research on herbal treatments have shown promising benefits, most without side-effects (Sun Y 1994). Caffeine has been studied as a potential herbal remedy because of its stimulant properties. Numerous studies

clearly demonstrates the efficacy of Memomet a well research herbal product in the treatment of ADHD in children. This behavioral disorder in children is of great concern for physicians because all the medicines in modern medicine have major side effects and affects growth and development of a child.

ACKNOWLEDGMENT

We are grateful to Matxin Labs Pvt Ltd for supplying the Product Memomet and the Placebo.

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