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Homoeopathic management of attention deficit hyperactivity disorder: A randomised placebo-controlled pilot trial

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ABSTRACT

Objective: To evaluate the usefulness of individualised homoeopathic medicines in treatment of Attention Deficit Hyperactivity Disorder (ADHD).
Design: Randomised placebo-controlled single-blind pilot trial.
Setting: Central Research Institute (Homoeopathy), Kottayam, Kerala, India from June 2009 to November 2011.
Participants: Children aged 6-15 years meeting the Diagnostic Statistical Manual of mental disorders (DSM-IV) criteria for ADHD.
Interventions: A total of 61 patients (Homoeopathy = 30, placebo = 31) were randomised to receive either individualised homoeopathic medicine in fifty millesimal (LM) potency or placebo for a period of one year.
Outcome measures: Conner's Parent Rating Scale-Revised: Short (CPRS-R (S)), Clinical Global Impression-Severity Scale (CGI-SS), Clinical Global Impression-Improvement Scale (CGI-IS) and Academic performance.
Results: A total of 54 patients (homoeopathy = 27, placebo = 27) were analysed under modified intention to treat (ITT). All patients in homoeopathy group showed better outcome in baseline adjusted General Linear Model (GLM) repeated measures ANCOVA for oppositional, cognition problems, hyperactivity and ADHD Index (domains of CPRS-R (S)) and CGI-IS at T3, T6, T9 and T12 (P = 0.0001). The mean baseline-adjusted treatment difference between groups at month 12 from baseline for all individual outcome measures favoured homoeopathy group; Oppositional (−16.4, 95% CI – 20.5 to − 12.2, P = 0.0001), Cognition problems (−15.5, 95% CI − 19.2 to − 11.8, P = 0.0001), Hyperactivity (−20.6, 95% CI − 25.6 to − 15.4, P = 0.0001), ADHD I (−15.6, 95% CI − 19.5 to − 11.6, P = 0.0001), Academic performance 14.4%, 95% CI 8.3 to 20.5, P = 0.0001), CGISS (−1.6, 95% CI − 1.9 to − 1.2, P = 0.0001), CGIIS (−1.6, 95% CI − 2.3 to -0.9, P = 0.0001).
Conclusion: This pilot study provides evidence to support the therapeutic effects of individualised homoeopathic medicines in ADHD children. However, the results need to be validated in multi-center randomised double-blind placebo-controlled clinical trial.

Keywords: Attention deficit hyperactivity disorder, Fifty millesimal, Homoeopathy, Placebo, Randomised clinical trial

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a common childhood hyperkinetic disorder that impairs social, acadaemic and occupational functioning in children, adolescents in the age group of 3-17 years; estimated prevalence in United States is found to be 5 million children (9% of this age group). Boys (12%) continued to be more affected than girls (5%) from ADHD. When compared with children who have excellent or very good health, children who have fair or poor health status are more likely to have ADHD (8% vs. 21%).[1,2] Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[3] categorises ADHD into inattention without hyperactivity, hyperactive and impulsive types. There is no overall prevalence documented in India for ADHD, however, in study conducted in Primary School Children of Navi Mumbai, India,[4] the prevalence was found to be 12.3% with boy-to-girl ratio of 3:2, while in a study conducted at Delhi, it was found to be 17.7%.[5] It was more prevalent in nuclear type of families and in families where a single parent was working, especially where the father was the sole bread earner and doing semi-skilled or un-skilled type of work.[4] Complementary and alternative medical (CAM) therapies are commonly used by parents for their children who have ADHD or autism spectrum disorders and parents usually seek homoeopathic treatment for ADHD.[6-9]

Lamont[10] conducted a double-blind placebo-controlled partial cross-over trial in which homoeopathic medicines in centesimal potency were superior to placebo and acted well in 200C potency. Frei and colleagues[11-14] used individualised homoeopathic medicines in LM (50 millesimal) potencies and the results appear to be similar to the effects of methylphenidate particularly in pre-school children. In these studies, amelioration of symptoms by 50% as shown on the Conner's Parent Rating Scale (CPRS) was achieved after average treatment duration of 5.1 months. However, they are of the view that randomisation at the start of treatment in a randomised clinical trial (RCT) of homoeopathy has a high risk of failure in demonstrating a specific treatment effect, if the observation time is shorter than 12 months. Further, the use of polarity analysis[14] in one of the studies, lead to an increase in the success rate of the first prescription from 21% to 54% and 68% to 84% of the fifth prescription. But a randomised double-blind placebo-controlled pilot study on ADHD children, conducted by Jacobs *et al.*,[15] had shown negative results.

On critical analysis, four pitfalls were presumed by Frei and colleagues[16] for negative results in the Jacobs study. They are: (a) restriction to three prescriptions caused pressure to physicians in prescription, (b) short period of observation (18 weeks), (c) effects of single doses repeated at long intervals are often subject to interference of external factor (such as family conflicts, school-related stress, exciting events leading to unstable amelioration) and (d) inclusion of children having stimulant medication which in turn reacted slowly to homoeopathy.

Systematic review[17] of homoeopathic therapy on ADHD in children, however, concluded that there is little evidence to prove the efficacy of homoeopathy for the treatment of ADHD. Furthermore, development of optimal treatment protocol before undertaking further RCTs was recommended.

Keeping in view the above pitfalls, the present study was designed to evaluate the effectiveness of individualised homoeopathic medicines in LM potencies in the treatment of ADHD children, to gather data from Indian subcontinent for definitive study and to derive optimal homoeopathic treatment protocol for ADHD by considering all points for individualisation. Homoeopathic individualisation means that every aspect of patient's individuality was considered.

Objectives

Primary objective

To evaluate the usefulness of individualised homoeopathic medicines in treatment of ADHD.

Secondary objectives

To deduce feasibility of study design and to gather data for sample size calculation of definitive study.

MATERIAL AND METHODS

Trial Design

A randomised controlled single-blind (parallel arm) study was conducted on ADHD children at Central Research Institute (Homoeopathy), Kottayam, to evaluate the efficacy of individualised homoeopathic medicines in LM potencies. The Council's Ethical Committee approved the study protocol. Investigator experienced in dealing with this disorder was trained in the protocol. Written informed consent was received from the guardians

of all the children enrolled. The study had also been registered retrospectively in Clinical Trial Registry India, CTRI/2011/12/002305. Consultant psychiatrist was also engaged for the study.

Patients and Setting

The total study period was for a period 2 years and 6 months (June 2009-November 2011) including one year of interventional treatment, which was conducted at Central Research Institute, Kottayam, Kerala, a premiere institute under Central Council for Research in Homoeopathy for psychiatric disorders. Children in the age group of 6-15 years and meeting the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) criteria for ADHD[3] were included.

Children with any chronic physical or neurological disorder, history of drug abuse, seizure, Tic disorder, Tourette syndrome, severely ill patient requiring hospitalisation and patients who were on anti-ADHD or psychoactive medications in the previous two weeks were excluded.

Intervention

Investigators were instructed to make an in-depth interview with the patient, as per the guidelines laid down by Dr. Samuel Hahnemann in 6th edition of Organon of Medicine.[18] The children enrolled in the study were not on any other non-pharmacological intervention like operational therapy, play therapy and behavioural modification. Kentian method[19] of evaluation and repertorisation using Hompath software[20] was used to reach the similimum. However, final decision was made after consultation with materia medica.The homoeopathic medicines in LM potencies were procured from a company certified for Good Manufacturing Practices (GMP).

Homoeopathic intervention group

Patients randomised to the homoeopathic group received individualised homoeopathic medicine for one year customised to each patient, which started with 0/1 potency, followed by next higher potency, serially, as per need of the case. The Investigator had trained the pharmacist regarding the preparation and dispensing of LM potencies with precision as follows: One globule (poppy-seed size) of the desired potency was dissolved in 120 ml of distilled water, containing 2.4 ml (2% v/v) of dispensing alcohol, pre-mixed in it, followed by ten uniformly forceful downward strokes given against the bottom of the phial. The medicine was given once daily in the morning, on empty stomach as long as improvement continued.[18]

The parents/guardians of the the children enrolled in the study were advised to give ten uniformly forceful downward strokes to the bottle with the hand on a hard surface and to take three tea-spoonfuls (15 ml) of this solution and mix it in eight tea-spoonfuls (40 ml) of water in a clean glass after stirring the solution before each dose of medicine taken. One tea spoonful (5 ml) of this solution constituted one dose.

Placebo group

Patients randomised to the placebo group received placebo, which was similar in all the manners to that of homoeopathic group including the process of administration. However, it constituted un-medicated poppy size sugar globule impregnated with dispensing alcohol. Any change triggered after administration (improvement/deterioration) was followed by placebo only.

Due to ethical reasons, patients with acute complaints were given individualised homoeopathic medicines.

Outcome Measures

The primary outcome measures were changes in Conner's Parents Rating Scale-revised: Short (CPRS-R (s)),[21] Clinical Global impression severity scale (CGI-SS),[22] Clinical Global Impression–improvement scale (CGI-IS);[22] CGI-SS is based on a seven point scale ranging from 1 to 7 where 1 indicates normal, not at all ill, and 7 indicates most extremely ill. Similarly in CGI-IS, 1 indicates patient very much improved and 7 indicates very much worse. CPRS-R was completed by parents/guardians. The investigator and consultant psychiatrist guided in translating into local language for better understanding if required. CGI-SS, CGI-IS were assessed by the investigator and consultant psychiatrist. Data related to these questionnaires were collected at baseline and at monthly intervals for 12 months. In addition, the record of academic performance in school was also collected before and after the treatment. However, the parents were advised to consult the investigator prior to scheduled visit, if they found it required for any other complaint apart the prime disease, i.e., ADHD.

Sample Size

Being a pilot study, 30 patients in each group are sufficient to gather data for sample size calculation, for larger definitive study. Keeping in view 20%

dropouts, 72 patients were to be initially enrolled (36 in each group) but only 61 patients were enrolled.

Randomisation and Blinding

Patients were randomised in two groups, Group I ($n = 30$): Homoeopathic group and Group II ($n = 31$): Placebo group. Both homoeopathic medicines and placebo were made in identical form so that they were indistinguishable. Patients were blinded about the prescription, whereas due to individualised nature of homoeopathic prescription it was open to the investigator. Block randomisation with block size of 2 was considered for randomisation to divide the patients equally either to homoeopathic or placebo group. Random numbers were generated with the help of computer-based software available at www.randomizer.org.[23]

Statistical Analysis

Statistical analysis was done using SPSS version 20. Comparisons between homoeopathy and placebo groups were performed at baseline (T0) to assess randomisation effect using independent *t*-test for continuous variable and Chi-square test for categorical variables. Seven patients who were observed to be wrongly randomised at baseline, during site visit, were not considered for analysis. Missing data were replaced by last assessed value as per the last observation carry forward method (LOCF) under modified Intention to treat (mITT) analysis. An analysis of covariance with follow up at different times as the dependent variable; baseline and treatment group as covariate and independent variable was undertaken to account for potential baseline differences. The questionnaires: Four domains of CPRS-R, CGI-SS and CGI-IS was obtained at time periods T3, T6, T9 and T12 were compared using a General Linear Model Analysis of covariance (GLM-ANCOVA) for repeated measures with time period T0 as covariate in respect to time and time vs group.

Further comparison of all outcome measures at T0, T12 was tested simultaneously using multivariate repeated measures analysis of variance (ANOVA). Another multivariate repeated measure ANOVA was carried out to examine whether change was the same between the two interventions. In the former repeated measures ANOVA, time (2 levels: Pre and post) was treated as a within subject factor, but there was no between subject factor, that is between two groups. In the latter repeated measures ANOVA, groups (2 levels: Homoeopathy vs. Placebo) was fitted into the model as a between subject factor.

Paired *t*-test was also carried out for assessing the difference (T12-T0) in individual variable in each group. The treatment differences were compared between groups using univariate GLM with baseline as covariate. Resulting baseline adjusted treatment effects are given together with 95% Confidence Interval (CI) and corresponding *P* values. In all the analyses, $P < 0.05$ was considered significant.

RESULTS

A total of 61 children diagnosed with ADHD were enrolled. Seven children were excluded from analysis after enrolment for not following randomisation. Out of 54 patients (homoeopathy = 27, placebo = 27) analysed under mITT [Figure 1], 43 (79.6%) were male and 11 (20.4%) were female. The mean (SD) age was 9.3 years (2.8 years), CGI-SS was 3.8 (0.5). As per ADHD Index,[15,24] 13 children were markedly atypical with significant problem H:5; P:8; 24 were moderately atypical with significant problem H:12; P:12 and 17 were mildly atypical with possible significant problem (H: 10; *P*: 07). The baseline characteristics of the patients are given in Table 1. Both the groups were comparable at baseline ($p \geq 0.05$).

There were nine different remedies prescribed during the course of the study, taking into account the remedy changes that occurred at 3 and 6 months of follow up. The most frequently used and effective medicines were *Calcarea carbonicum* ($n = 8$), *Lycopodium* ($n = 6$), *Phosphorus* ($n = 5$), *Hyoscyamus* ($n = 2$), *Sulphur* ($n = 2$), *Belladonna* ($n = 1$), *Argentum nitricum* ($n = 1$), *Natrum muriaticum* ($n = 1$) and *Pulsatilla* ($n = 1$). Seven patients belonging to the homoeopathy group required a change of prescription during the follow up; two patients who were prescribed *Belladonna* at baseline required a change to *Pulsatilla* at third month and *Calcarea carbonicum* at sixth month, respectively, two other patients who were prescribed *Phosphorus* at baseline required *Calcarea carbonicum* at sixth month, two patients who were prescribed *Lycopodium* at baseline required *Phosphorus* and *Calcarea carbonicum* at sixth month, respectively, while one patient who was prescribed *Belladonna* at baseline required change to *Phosphorus* after sixth month. These patients required change of medicine at various time points because either they remained status quo of their symptoms or

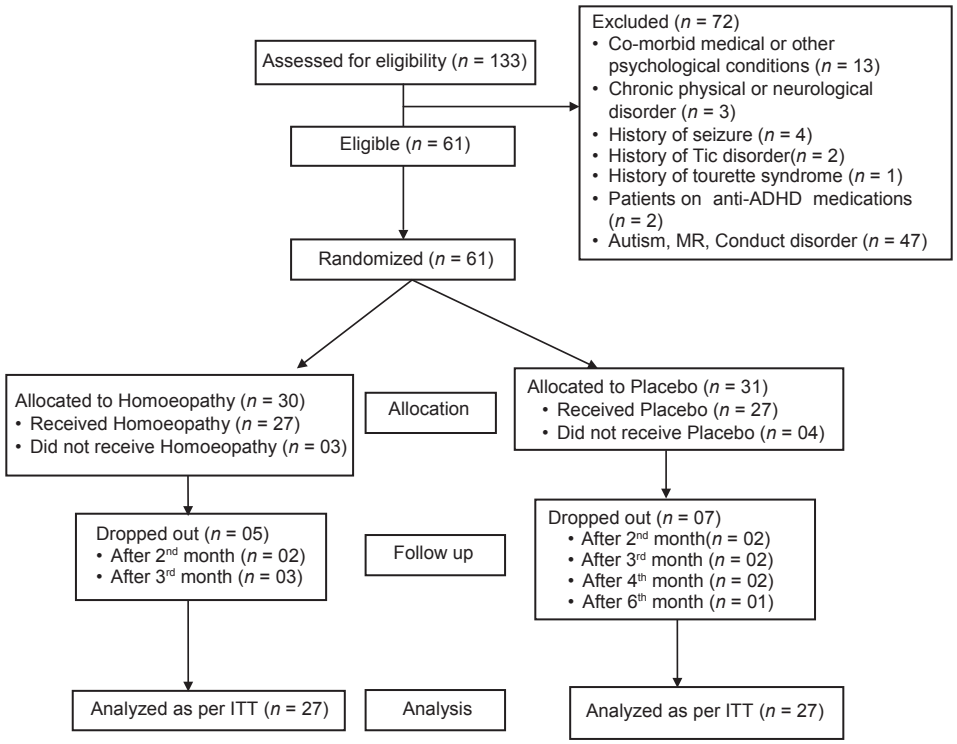

Figure 1: Consort flow of patients in the trial

presented with different symptom picture. The same remedy was continued for the entire course of the study in 20 patients in the homoeopathy group. The statistical analysis of medicines, which were prescribed in the study period without any change in prescription with respect to CPRS-R scale, is given in Table 2. The prescribing indications of the medicines are given in Table 3.

Table 4 shows the scores of four domains of CPRS-R and CGI-SS, questionnaires at 3 (T3), 6 (T6), 9 (T9) and 12 months (T12) of treatment in homoeopathy group only [oppositional (P = 0.0001), cognitive problems (P = 0.0001), hyperactivity (P = 0.0001), and ADHD Index (P = 0.0001) of CPRS-R, CGI-SS (P = 0.0001) and CGI-IS (P = 0.0001)]. Independent of treatment group, there was no significant difference at different time points for oppositional (P = 0.21), Cognition problems (P = 0.20), Hyperactivity (P = 0.51), CGI-SS (P = 0.46) except for ADHD-Index (P = 0.04).

Analysis was also performed to test whether the changes within and between the groups in ADHD children for overall CPRS-R and all variables, that is, academic performance, CGI-SS and CGI-IS values were significantly different at T0 and T12. Table 5 shows significant improvement in ADHD children treated with homoeopathic medicines (P = 0.0001), while no significant improvements detected in the placebo group (P = 0.17). Similarly, there was significant change (P = 0.0001) in overall scores (CPRS-R, CGI-SS, CGI-IS, academic performance) in homoeopathic group (P = 0.0001) and insignificant difference in placebo group (P = 0.33). However, there was significant difference between the groups for CPRS-R (P = 0.005) and overall scores (P = 0.0001). Homoeopathic medicines were more effective than placebo for decreasing ADHD-Index score with an effect size of 0.7 and CGI-SS and CGI-IS with an effect size of 0.59 and 0.54, respectively [Table 5].

Post hoc analysis of the results for ADHD-Index with effect size 0.7 as per two-tailed independent *t*-test [Table 5], sample size of 27 per group, α = 0.05, gives power of 71%, non-centrality parameter of 25%. The acute complaints presented in all the children irrespective of intervention group were treated with individualised homoeopathic medicine apart from the main complaint of ADHD. The data of the same is given in Table 6. After wanning of acute complaints within 2-3 days, the children in placebo group continued placebo and the children in medicinal group were reassessed

Table 1: Baseline characteristics of mITT population

Variable	Homoeopathy (*n*=27)	Placebo (*n*=27)	*P* value
Age (in years)	8.6 (2.2)	9.9 (2.8)	0.05
Gender			0.50
Male	23 (85.2%)	20 (74.1%)	
Female	4 (14.8%)	7 (25.9%)	
Weight (in kg)	28.5 (6.8)	31.8 (7.9)	0.10
Height (in cm)	129.1 (10.8)	133.9 (6.5)	0.50
Duration of complaints (in years)	4.3 (2)	5.7 (3.1)	
Academic performance			
UT marks in percentage	58.7 (13.9)	51.9 (16.4)	0.10
CPRS-R			
Oppositional	63.3 (8)	63.7 (8.3)	0.84
Cognition problems	66.7 (4.8)	67.4 (5.9)	0.63
Hyperactivity	75.8 (6.3)	79.3 (7.4)	0.06
ADHD index[a]	67.4 (3.8)	69.3 (4.9)	0.10
Markedly atypical with significant problem	5 (19%)	8 (30%)	0.54
Moderately atypical with significant problem	12 (44%)	12 (44%)	
Mildly atypical with significant problem	10 (37%)	7 (26%)	
CGI-SS	3.8 (0.4)	3.7 (0.6)	0.20
Mildly ill	4 (14.8%)	10 (37%)	0.12
Moderately ill	22 (81.5%)	15 (55.6%)	
Markedly ill	1 (3.7%)	2 (7.4%)	

Data are presented in mean (sd), *n* (%). CPRS-R: Connors' parent rating Scale-revised: Short; CGISS: Clinical global impression severity scale; UT: Unit test. [a]Ref. ADHD: Attention deficit hyperactivity disorder; mITT: Modified intention to treat

and the medicine was prescribed accordingly i.e., either initial prescription was continued or changed medicine if required was administered as per the discretion of homoeopathic investigator.

DISCUSSION

The main results emerged from this study are: (1) there was significant changes in the outcome measures of CPRS-R, CGI-SS and CGI-IS scores compared with baseline in homoeopathy group, (2) the improvement was found to be stable over time of 12 months period and (3) there was significant academic improvement in ADHD children treated with homoeopathy. A significant improvement has been observed in homoeopathy group in all parameters. There was clinically significant decrease from moderately atypical to average typical, which should not raise concern in ADHD-Index. The absolute mean reduction in CGI symptom severity was 1.7 favouring homoeopathy.

Patients participating in the study were selected by a rigorous diagnostic evaluation following DSM-IV for ADHD and ruling out any other diagnosis that may imitate ADHD. The main strength of this study is the involvement of consultant psychiatrist in rating the changes. More assessment questionnaires like continuous performance test,[15] questionnaires related to cognitive behavior[16] and double-blind

Table 2: Outcome assessment of medicines prescribed with statistical analysis of various domains of CPRS-R scale

Name of the medicine prescribed (*n*)*	Mean diff. (baseline-12 months) (SE)	95% CI	*t* value	*P* value	Outcome assessment (*n*)		
					Improved	Static	Worse
Calcarea carbonicum (4)							
Oppositional	26.7 (3.0)	16.9 to 36.5	8.6	0.003	4	0	0
Cognitive problems	23.5 (3.5)	12.2 to 34.7	6.6	0.007	4	0	0
Hyperactivity	28.0 (2.0)	21.6 to 34.3	14.0	0.001	4	0	0
ADHD	23.5 (3.7)	11.6 to 35.3	6.3	0.008	4	0	0
Hyoscyamus (2)							
Oppositional	20.0 (6)	–56.2 to 96.2	3.3	0.18	2	0	0
Cognitive problems	18.0 (1)	5.2 to 30.7	18.0	0.03	2	0	0
Hyperactivity	25.5 (2.5)	–6.2 to 57.2	10.2	0.06	2	0	0
ADHD					2	0	0
Lycopodium (5)							
Oppositional	9.4 (2.8)	1.3 to 17.4	3.2	0.03	4	1	0
Cognitive problems	17.6 (4.5)	4.9 to 30.2	3.8	0.01	4	1	0
Hyperactivity	21.4 (5.6)	5.6 to 37.1	3.7	0.02	4	1	0
ADHD	17.4 (4.8)	3.8 to 30.9	3.5	0.02	4	1	0

Contd...

Table 2: Contd

Name of the medicine prescribed (*n*)*	Mean diff. (baseline-12 months) (SE)	95% CI	*t* value	*P* value	Outcome assessment (*n*)		
					Improved	Static	Worse
Phosphorus (4)							
Oppositional	6.2 (3.6)	–5.3 to 17.8	1.7	0.18	2	2	0
Cognitive problems	9 (5.1)	–7.5 to 25.5	1.7	0.18	2	2	0
Hyperactivity	10.7 (12.5)	–9.2 to 30.7	1.7	0.18	2	2	0
ADHD	9.2 (10.7)	–7.8 to 26.3	1.7	0.18	2	2	0
Sulphur (2)							
Oppositional	8 (7.0)	–55.5 to 71.5	1.6	0.35	2	0	0
Cognitive problems	3 (8)	–98.6 to 104.6	0.3	0.77	1	0	1
Hyperactivity	5 (18)	–223.7 to 233.7	0.2	0.82	1	0	1
ADHD	0 (9)	–114.3 to 114.3	0.0	01.0	1	0	1

*The outcome assessment is given for 17 patients (5 medicines). In three patients (one medicine each of *Argentum nitricum*, *Belladonna* and Nat. mur. was prescribed) statistical analysis cannot be done. $p<9.05$ was considered as significant. Improvement: Reduction in symptom score from baseline; Static: No change in symptom score from baseline; Worse: Increase in symptom score from baseline, CPRS: Conner's parent rating scale, ADHD: Attention deficit hyperactivity disorder; SE: Standard error; CI: Confidence interval

Table 3: Indications of medicines prescribed

Name of the medicine	Prescribing indications
Calcarea carbonicum	Mischievous, Desires company, obstinate, timid Lazy to do his works, forgets easily especially what is read chilly pt., perspiration on scalp, craves egg, desires cold drinks, ice cream; aversion to milk and meat
Lycopodium	Desires company, shy, fear to be alone, mistakes in writing, irritable, contradiction intolerance, contradiction disposition to, weeping, mild; fear of dark, ghost, disobedience, timid Makes mistake in writing especially misplacing words and letters as of a mirror image, makes spelling mistakes Difficult to study new lessons or do new assignment Hot patient, pain abdomen<food after Desires warm food, sweets
Phosphorus	Shamelessness, talks during sleep, chilly pt., desires cold food and drinks, fish, salt, ice cream; aversion to milk Fidgety, always do something with hands
Hyoscyamus	Excitement, malicious, fear of insect, snakes, jealous, irritable, aggressive, excessive sexual excitement, handles genitals, irritability, tendency to hurt self when irritated
Sulphur	Hot patient; desires sweets, sugar, meat, aversion egg; itching anus at night Always restless, irritable, very selfish in nature, easily forgets things, careless in handling objects, careless in dress and aversion to take bath
Belladonna	Spits on face, fear of dark, aggressiveness, pulls hair, throws things away; Aversion milk, profuse sweat Irritable and tendency to bite others
Argentum nitricum	Irritable, irritable on contradiction, forgetful, craves sugar Very nervous especially during exam, impulsive child and hurried activities, shows awkward gestures
Natrum muriaticum	Hot patient, aversion to company, sad, irritable on contradiction; craves salt, fish; profuse perspiration Hasty in doing things, sweats with least exertion, child sits alone, does not play with other children, less sociable
Pulsatilla	Hot patient, weeps, desires company, changeable mood, consolation;, desires cold food and drinks Very timid, desires to be cared, desires to hide when others are there at home, warm patient, desires meat and fatty things

methods has not been used, which might have given more strengths to this study.

A clinically significant improvement was found in other trials also[11-14] wherein homoeopathic LM potencies were used. However, findings of Jacobs *et al.*,[15] do not support these observations. It might be due to an observation period of 18 weeks, which was considered very short by other researchers.[16] Use of single dose at long intervals with external interference such as family conflicts, school-related stress exciting events are some of the other factors for negative results.[14] The duration of treatment is a very important factor for assessment of homoeopathic intervention. Frei *et al.*,[14] in their study concluded that observation time shorter than 12 months may lead to high risk failure, which is found in the Jacobs study,[15] whereas in this study a follow up for 12 months was considered, and the improvement is

Table 4: T3, T6, T9, T12 comparisons of CPRS-R and CGI-SS

Variable	Mean (sd)				GLM*	*P*	GLM**	*P*	Effect size
	T3	T6	T9	T12					
Oppositional									
H	60.4 (7)	56.4 (7)	53.6 (8.6)	49.5 (9.5)	0.91	0.21	0.47	0.0001	0.52
P	63.6 (8.4)	63.2 (8.3)	64.4 (8.3)	66.2 (7.6)					
Cognition problems									
H	61.2 (6.1)	56.6 (7.4)	52.9 (8.4)	50.7 (7.7)	0.91	0.20	0.57	0.0001	0.42
P	67.5 (5.1)	67.4 (5.4)	67.4 (5.5)	66.6 (6.2)					
Hyperactivity									
H	68.1 (8.6)	63.7 (9.8)	58.5 (11.1)	55.6 (11.9)	0.95	0.51	0.52	0.0001	0.47
P	78.9 (7.7)	78.3 (7.9)	79.2 (7.1)	78.2 (6.9)					
ADHD index									
H	62.9 (5.1)	58.2 (7.3)	54.9 (8.8)	51.8 (9.1)	0.15	0.04	0.48	0.0001	0.51
P	68.9 (4.6)	68.3 (4.6)	68.9 (4.8)	68.4 (5)					
CGI-SS									
H	3.6 (0.5)	2.9 (0.7)	2.8 (0.7)	2.5 (0.7)	0.95	0.46	0.48	0.0001	0.51
P	3.8 (0.6)	3.8 (0.6)	3.8 (0.6)	4 (0.6)					

H: Homoeopathy; P: Placebo; *Change within individuals with baseline as covariate; **Difference between treatment groups with baseline as covariate; CPRS-R: Connors' parent rating scale-revised; CGI-SS: Clinical global impression severity scale; SD: Standard deviation

Table 5: Comparison of difference post -to pre- (12 months baseline) in individual groups (Homoeopathy and Placebo) and comparison between groups

Variable	Comparison of individual groups with their baseline (post-pre)						Comparison between groups		
	Homoeopathy (*n*=27)			Placebo (*n*=27)					
	Mean diff. (SE)	95% CI	*P* value	Mean diff. (SE)	95% CI	*P* value	Diff. (95% CI)	*P* value	Effect size
Overall			0.0001‡			0.33‡		0.0001†	0.57
CPRS-R			0.0001‡			0.17‡		0.005†	0.22
Oppositional	−13.7 (1.9)	−17.6 to −9.8	0.0001#	2.5 (1.3)	−0.2 to 5.2	0.07#	−16.4 (−20.5 to −12.2)	0.0001*	0.55
Cognition problems	−15.9 (1.7)	−19.4 to −12.4	0.0001#	−0.7 (1.1)	−2.9 to 1.4	0.49#	−15.5 (−19.2 to −11.8)	0.0001*	0.71
Hyperactivity	−20.1 (2.5)	−25.3 to −15	0.0001#	−1.1 (0.6)	−2.4 to 0.1	0.08#	−20.6 (−25.6 to −15.4)	0.0001*	0.99
ADHD index	−15.6 (1.9)	−19.5 to −11.6	0.0001#	0.9 (0.5)	−2 to 0.1	0.08#	−15.6 (−19.5 to −11.6)	0.0001*	0.70
Acad. perf	13.7 (2)	9.6 to 17.7	0.0001#	0.4 (2)	−4.35 to 5.1	0.87#	14.4 (8.3 to 20.5)	0.0001*	0.51
CGISS	−1.4 (0.2)	−1.8 to −1.1	0.0001#	0.3 (0.1)	0.06 to 0.5	0.02#	−1.6 (–1.9 to –1.2)	0.0001*	0.59
CGIIS (T3-T12)	−1.5 (0.2)	−1.9 to −1.2	0.0001#	0.3 (0.2)	−0.03 to 0.7	0.07#	−1.6 (–2.3 to –0.9)	0.0001*	0.54

#Comparison using paired *t* test within groups. ‡Multivariate analysis comparing post-and pre-measurements within the groups and †comparison of the two groups after one year of treatment. *Baseline adjusted treatment difference between groups; CPRS-R: Connors' parent rating scale-revised; CI: Confidence interval; SE: standard error

clinically significant. Frei and his associates[14] required median of three different medications in a median time of 5 months to bring a change, however, in our study, median of only one medicine was required throughout the treatment period. In seven patients, change of medicine was required in the homoeopathic group. During 12 months treatment period, there was 1.7 and 2 points decrease in CGI-SS and CGI-IS, which is similar to the findings of Frei *et al.*,[12] that is 1.67 points of Conner's Global index. There was also a 13.7% mean improvement in academic performance, which indirectly reflects improvement in cognitive function [Table 5].

Homoeopathic medicines can be prescribed to all ADHD children irrespective of their parent's economic condition due to its cost effectiveness, easy palatability and least side effects, thus it has major advantage over conventional allopathic medicines, which have potential side effects,[11,25] and create concern for parents. At pre-school age, homoeopathy may be the first choice for students and their parents who do not need immediate relief.[11] The treatment was efficacious when medicines were prescribed once daily.

Future studies with definite sample size and double-blind design may be carried out to substantiate the results. Pre-school children may

Table 6: Acute complaints handled in both the groups during the treatment

Acute complaint	Homoeopathy			Placebo		
	No. of patients suffered	Medicine prescribed	Status	No. of patients suffered	Medicine prescribed	Status
Acute sinusitis	0	-	-	1	Bell. 0/1	Improved
Common cold	1	Bry. 0/1	Improved	2	Ars.alb. 0/1	Improved
Otorrhoea	0	-	-	1	Merc.sol. 0/1, 0/2	Improved
Viral fever	0	-	-	1	Bry. 0/1	Improved
Migraine	1	Nux vom. 0/1	Improved	1	Nat.m. 0/1, 0/2	Improved
Common cold	0	-	-	1	Bry. 0/1	Improved
Acute tonsillitis	1	Hep. sulph. 0/1	Improved	1	Rhus. t. 0/1	Improved
Acute suppurative otitis media	0	-	-	1	Hep. sulp. 0/1, 0/2	Improved
Acute bronchitis	0	-	-	2	Ars.alb. 0/1, 0/2	Improved
Acute rhinitis	0	-	-	1	Cina 0/1, 0/2	Improved
Asthma	3	Ars.alb. 0/1, 0/2	02 improved, 01 not improved	2	Ars. Alb. 0/1, 0/2	Improved
Lower RTI	1	Ars.alb. 0/1, 0/2	Improved	1	Ars.alb. 0/1, 0/2	Improved
Acute tonsillitis	2	Ars.alb. 0/1, 0/2	Improved	-	-	-
Acute tonsillitis	1	Rhus tox. 0/1	Improved	-	-	-
Abdominal colic	1	Nux vom. 0/1, 0/2	Improved	-	-	-

RTI: Respiratory tract infection

be enrolled with stratification of age groups during randomisation. This study design was found feasible and the sample size calculation (two-tailed independent *t*-test), with effect size 0.7, would require 38 children in each group with power 85%, $\alpha = 0.05$, for rejecting the null hypothesis in a definite trial.

CONCLUSION

This pilot study provides evidence to support the therapeutic effect of individually selected homoeopathic medicines in children with ADHD. However, the results need to be validated in a larger multi-center prospective randomised double-blind placebo-controlled clinical trial.

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उद्देश्य : ध्यान–न्यून अतिसक्रियता विकार के उपचार में व्यक्तिगत होम्योपैथिक औषधियों के उपयोग का मूल्यांकन करना।

प्रारूप : यादृच्छिक, प्लासिबो नियन्त्रित, एकल ब्लाइण्ड सूचक परीक्षण।

स्थान : केन्द्रीय अनुसंधान संस्थान (होम्यो.), कोट्टायम, केरल, भारत, जून, 2009 से नवम्बर 2011 तक।

प्रतिभागी : 6 से 15 वर्ष तक के बच्चे, जोकि एडीएचडी के लिये मानसिक विकारों के नैदानिक और सांख्यिकी मैन्युल के अनुरूप मापदण्डों को पूरा करते थे।

हस्तक्षेप : कुल 61 मरीजों (होम्योपैथी =30, प्लासिबो = 31) का 50 एलएम पोटेन्सी में एक साल के लिये या तो व्यक्तिगत होम्योपैथी औषधि या प्लासिबो लेने के लिये यादृच्छिकरण किया।

परिणाम साधनः कोनर्स माता–पिता दर पैमान + संशोधित; लघु (सीपीआरएस–आर एस), नैदानिक वैश्विक छाप–तीव्रता पैमाना (सीजीआई–एसएस), नैदानिक वैश्विक छाप–बेहतर पैमाना (सीजीआई–आईएस) और शैक्षणिक प्रदर्शन।

परिणामः कुल 54 रोगियों (होम्योपैथी 27, प्लासिबो 27) का संशोधित गहनता के अन्तर्गत उपचार करने के लिये विश्लेषण किया गया। टी 3, टी 6, टी 9 और टी 12 (पी = 0.0001) पर होम्योपैथी वर्ग के सभी रोगियो ने आधार रेखा पर सामान्य रेखीय प्रारूप, विरोधात्मक समस्याओं के लिये दुहरे लक्षण एनकोवा अनुभूति समस्या अतिसक्रियता और एडीएचडी सूचकांक (सीपीआरएस आर (एस) नैदानिक) और सीजीआई–आईएस क्षेत्र) पर अच्छे परिणाम दिखाये। 12वें महीने पर आधार रेखा पर मध्य आधार रेखा– समायोजित उपचार, वर्गो के बीच में विभिन्नता सभी परिणाम उपाय होम्योपैथी वर्ग का पक्ष लेते हैं विरोधात्मक समस्या (–16.4, 95: सीआई–20.5 से –12.2, पी =0.0001), अनुभूति समस्या (–15.5, 95: सीआई –19.2 से –11.8, पी = 0.0001) अतिसक्रियता (–20.6, 95: सीआई –25.6 से 15.4, पी –0.0001) एडीएचडी (–15.6, 95: सीआई –19.5 से –11.6, पी = 0.0001) शैक्षणिक प्रदर्शन (14.4:, 95: सीआई 8.3 से 20.5, पी =0.0001) सीजीआई एसएस (–1.6, 95: सीआई –1.9 से –1.2, पी=0.0001), सीजीआई जीएस (–1.6, 95: सीआई –2.3 से –0.9, पी=0.0001)

निष्कर्ष : यह पायलट अध्ययन एडीएडी बच्चों में व्यक्तिगत होम्योपैथी औषधियों के उपचारात्मक प्रभाव के समर्थन में प्रमाण उपलब्ध कराता है। लेकिन, परिणाम बहु केन्द्रीय यादृच्छिक डबल–ब्लाईण्ड प्लासिबो नियंत्रित नैदानिक परीक्षण में मान्य होना चाहिए।