



# An Open Label Single Arm Clinical Trial to Evaluate the Effectiveness of Individualized Homoeopathic Intervention in Inattention Symptoms of ADHD Patients – Study Protocol

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## Abstract: Objective:

Attention deficit hyperactivity disorder (ADHD) is one of the most common childhood neuropsychiatric condition that affects preschoolers, children, adolescents, and adults around the world. It is characterized by a pattern of diminished sustained attention, and increased impulsivity or hyperactivity. This study aims to know the impact of Homoeopathic Individualized medicines in the management of attention problems of children diagnosed with ADHD. It also helps to understand the reduction of inattentive symptoms of ADHD after using homoeopathic medicines.

## Materials and Methods:

The study design is Interventional Study-Before & After treatment without a control group. Child with behavioral problems reporting at OPD and peripheral units of NHRIMH will be screened using verbal screening form and DBD Rating Scale. The cases fulfilling inclusion and exclusion criteria's will be enrolled in the study after approval of Psychiatrist and patients consent. The trial sample size is calculated as 40. The DSM V Level I Scale will be used to identify the inattentive domain at baseline. DSM V Level II Scale will be used at Baseline and every month for assessing the inattentive symptoms. Letter cancellation test will be performed at Baseline, 3, 6, 9, 12<sup>th</sup> month to assess the attention span. Strength and Difficulty Questionnaire will be used at Baseline, 3, 6 and 12<sup>th</sup> month to identify the Quality of life of child and parents. Clinical Global Impression – Improvement Scale is used at 3, 6, 9, and 12<sup>th</sup> month to know the global improvement of the case.

## Discussion and Conclusion:

Among ADHD, Inattentive type is most commonly presented and it affects the scholastic performance and the overall quality of life of the child. This trial provides a novel impression in the assessment and improvement of inattentive symptoms and attention span of the child diagnosed with ADHD. It also helps in preventing the further decline in child's quality of life.

**KEY WORDS:** ADHD, Inattention, Interventional study, Homoeopathy

**INTRODUCTION:****BACKGROUND AND RATIONALE:**

Attention deficit hyperactivity disorder (ADHD) is one of the most common childhood neuropsychiatric condition that affects preschoolers, children, adolescents, and adults around the world. It is characterized by a pattern of diminished sustained attention, and increased impulsivity or hyperactivity.<sup>1,2</sup>

According to the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-V),<sup>3</sup> ADHD is characterized by: Inattention, Hyperactivity and Impulsivity. In ICD – 10, ADHD is used as the term “Hyperkinetic disorder” in which the cardinal features are impaired attention and hyper activity.<sup>4</sup>

According to a recent systematic review conducted from 175 studies across the world, the overall pooled estimate of ADHD prevalence in children was 7.2% and it is higher in the Middle East and North America regions and lower in African and Asian countries.<sup>5,6</sup> Meta-analysis done in China reveals a pooled prevalence of 6.26% among children as ADHD.<sup>7</sup>

The prevalence of ADHD among children in India is consistent with the worldwide prevalence. And the pooled prevalence among children and adolescents is 7.1% (95% CI: 5.1% to 9.8%). Overall mean value of worldwide prevalence of ADHD in children were 2.2% and prevalence among adolescents (aged < 18 years) and individual below 18 years of age were 5.29%. The worldwide prevalence among males is of 9.40% and among females is of 5.20%. Estimated prevalence of ADHD in India was 1.3 per count of 1000 children.<sup>8,9,10,11</sup>

The younger siblings of children who have been diagnosed with ADHD have 13 times higher risk of getting ADHD than those who do not have the disorder and inheritance among adolescents from 70% to 80%.<sup>12,13</sup>

The role that the prenatal environment might play in the development of ADHD despite demonstration of associations between prenatal risk factors (e.g. prematurity, maternal smoking during pregnancy) and ADHD children, there remains insufficient evidence in this context to support a definite causal relationship.<sup>14</sup>

The management of children with ADHD is firstly focused with behavioral therapies including parent training, classroom management, and peer interventions.<sup>15</sup> Medications are considered if ADHD symptoms are moderate to severe and not responsive to behavioral therapy. The common medications used are psychostimulants (e.g. methylphenidate [Ritalin], dextro-amphetamine, and mixed amphetamine salts such as dextro-amphetamine / amphetamine [Adderall])<sup>16,17</sup>

Adverse effects of stimulant medication are generally dose dependent and include reduced appetite, abdominal discomfort, headache, irritability, anxiousness, sleep problems, and a small reduction in height velocity that may aggregate with time and/or reverse after discontinuation of the treatment.<sup>18,19</sup>

As in the management of ADHD, conventional medicine has limited scope after prolonged medications with notable drug effects and it mainly depends on parent behaviour therapy. Few stimulant medications were also prescribed having adverse side effects. The alternative medical treatment showed the effectiveness of homoeopathic management with favourable improvement without any drug effects.<sup>20</sup>

ADHD can have a significant social impact on affected individual's lives, causing disruption at school, work and in relationships. It may reduce the quality of life of children, adolescents and adults. Severity of ADHD symptoms and a high load of child hyperactive and impulsive symptoms in childhood were associated with dropout from school as there is an increased risk for unfavorable educational outcomes in childhood and adolescence. Symptoms in adulthood with more inattentive features were associated with greater occupational impairment. Additional adult comorbidity was major predictor of long-term work disability among children.<sup>21</sup>

Children with untreated ADHD may develop significant conduct problems and antisocial behaviors in the long course (such as fighting, early substance experimentation and rash driving) and may affect a child's emotional well-being in several ways, including anxiety, lower self-esteem, poor psychosocial health and poor quality of life.<sup>22,23</sup>

A study conducted in National Homoeopathy Research Institute In Mental Health (NHRIMH), Kottayam to evaluate the usefulness of individualized homoeopathic medicines in treatment of ADHD showed evidence to support the therapeutic effects of individualized homoeopathic medicines in children with ADHD.<sup>24</sup>

Attention is an important and complex cognitive function, depending on mutually interacting neural systems of the brain. In ADHD, Inattentive type of ADHD is most commonly presented. Two studies conducted by Berger and Posner (2005) and Fan et al. (2002) showed that the attention network model is considered as a fundamental interest in the studies of attentional disorders, including the Attention Deficit Hyperactivity Disorder (ADHD).<sup>25</sup>

There were no studies found using homoeopathic interventions in assessing the attention problems in ADHD children.

#### **MATERIALS AND METHODS:**

It is an Interventional Study-Before & After treatment without a control group. The sample size has been calculated as 40. The patients will be enrolled from Out Patient Department and other peripheral centers of National Homoeopathy Research Institute in Mental Health, Kottayam, Kerala, India. The latest revision of the Helsinki declaration on human experimentation and Good clinical practices of India has been adopted in this clinical trial<sup>26</sup>. The protocol has been designed following the guidance provided by Institutional Review Board. The finalized protocol has been subjected to Institutional Ethical Committee approval. Further review of the protocol and final approval from the university has been obtained. The CTRI registration number is CTRI/2022/03/040872.

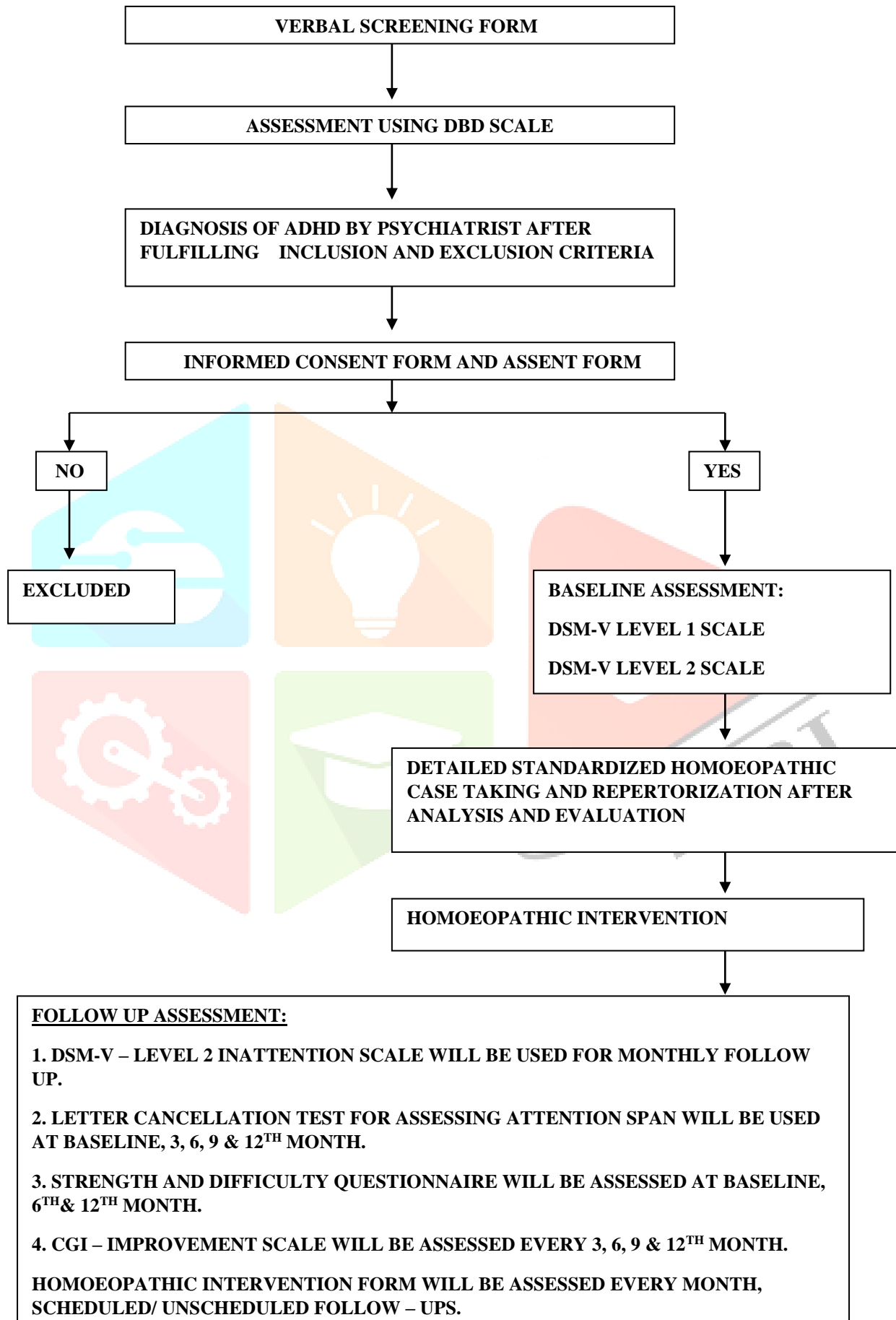
#### **SCREENING AND ENROLLMENT:**

Children presenting with behavioral changes from Out Patient Department and peripheral OPD of NHRIMH will be screened with questions developed using verbal screening form. The cases will be verified using DBD Rating Scale and diagnosed by Psychiatrist of the Institute. The cases will be enrolled in the study after consent and conditions fulfilling inclusion and exclusion criteria's. A copy of patient Information sheet will be given to the parent /caretaker after explaining the details of the study. The Informed consent form will be obtained from parents or caretaker based on the availability. An assent form also will be obtained from the patient aged more than 12 years. Detailed case taking will be done in the standard Homoeopathic case record format prepared for the study

#### **INCLUSION CRITERIA:**

Children from 6 years to 18 years of age, both genders satisfying ADHD diagnostic criteria of DSM 5 without any other major psychiatric and systemic illness will be included in the study after getting the consent.

The Flowchart of complete study (Figure 1):



**INTERVENTION:**

Detailed case taking will be done in the case record format prepared for the study. Through analysis and evaluation of the complete case, the individual totality is obtained and repertorisation will be done with Synthesis Repertory using RADAROPUS software. Final selection of remedy will be done by consulting with Homoeopathic Materia Medica. After evaluation of each case, selected medicine will be prescribed in 30C potency as initial intervention. On improvement, placebo will be continued. On status que, next higher potency will be prescribed. In case of no improvement or any new symptoms observed on consequent 2-3 months, the case will be retaken and change of remedy is proposed. In case of any acute complaints, the acute totality will be taken and appropriate remedy will be administered and data will be analyzed separately. The Homoeopathic management part will be practiced adhering strict standard operative procedures of Homoeopathic Principles. Homoeopathic assessment will be done on every month using homoeopathic intervention format prepared for the study.

**FOLLOW – UP:**

The enrolled patients will be closely monitored through a follow – up chart every monthly. The follow – up calendar with one year date of visit will be provided to the patient during initial enrollment. The follow up chart contains the details of follow- up dates, time and other measures scheduled for 12 months. A regular telephonic and other available communications will be done via mail, telephonic calls by social worker to have a good compliance.

**DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS FIFTH EDITION (DSM-5) CRITERIA FOR ADHD**

1. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development of the child.

ADHD is mainly characterized by:

A. Inattention

B. Hyperactivity and impulsivity

2. Children below the age of 12 years presents with several inattentive or hyperactive-impulsive symptoms.

3. Child presents with inattentive or hyperactive – impulsive symptoms in two or more places (e.g., at home, school, or work; with friends or relatives; in other activities).

4. On prognostic view, it is found to hinder the achievements in school, social and job activities.

5. The symptoms of inattention or hyperactivity – impulsivity is not associated with other psychiatric disorders (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

It has been mentioned that the children may also present symptoms in a combined manner. So this includes both inattention and hyperactive – impulsive symptoms as Combined presentation (314.01 – ICD F90.2) or Predominantly inattentive presentation (314.00 – ICD F90.0) or Predominantly hyperactive/impulsive presentation (314.01 – ICD F90.1).

Based on severity of symptoms, it has been classified as Mild, Moderate and Severe types of ADHD.

**OUTCOME MEASURES:**

Outcome of treatment will be assessed according to difference in scores of DSM 5 Level 2 Inattention-Parent/Guardian of Child Age 6-17 Swanson, Nolan and Pelham, version IV (SNAP IV), difference in scores of attention span using Letter Cancellation test, differences in scores of assessment of quality of life using SDQ Scale every 6 months and the differences in scores of Clinical Global Impression – Improvement Scale every 3 months.

**Primary outcome:** Level of improvement in the Level 2-Inattention- Parent/Guardian of Child Age 6-17 Swanson, Nolan and Pelham, version IV (SNAP-IV).

**Secondary outcome:**

- Evaluating the group of Homoeopathic medicines that are suitable for ADHD apart from individual medicines.
- Evaluating the improvement in the attention span of ADHD children.
- Evaluating the strength and difficulties faced by ADHD children and their parents through SDQ Assessment.

**CRITERIA FOR BASELINE AND FOLLOW – UP ASSESSMENT:**

Cases will be assessed at baseline with DSM-5 Parent/Guardian- Rated Level 1 Cross-Cutting Symptom Measure – Child Age 6-17 and Level 2-Inattention- Parent/Guardian of Child Age 6-17 Swanson, Nolan and Pelham, version IV (SNAP-IV). Subsequently DSM Level-2- Inattention questionnaire will be used for monthly follow up. The Letter Cancellation Test for assessing Attention Span will be assessed at Baseline, 3, 6, 9 & 12th month. Strength and Difficulties Questionnaire (SDQ) is used for the assessment of quality of life of ADHD children and their parents on baseline, 6th and 12th month. The Clinical Global Impression-Improvement scale will be assessed every 3, 6, 9 & 12th month. Homoeopathic assessment will be done on every month using homoeopathic intervention format prepared for the study.

**DATA COLLECTION:**

Standardized case recording format and predesigned excel sheet shall be used for the data capturing. The diagnostic information are gathered through initial assessment and other basic screening for Disruptive Behavior Disorder will be obtained through DBD scale. The diagnostic and follow – up information related to ADHD will be gathered through Level 2-Inattention- Parent/Guardian of Child Age 6-17 Swanson, Nolan and Pelham, version IV (SNAP-IV). The data regarding improvement status will be obtained through clinical global impression – improvement scale.

**TIMELINE OF THE STUDY:**

Time	Study Period						Close Out
	Enrolment	Post allocation in month					
		3	6	9	12	Every month	
Eligibility screening	+	-	-	-	-	-	-
Informed consent	+	-	-	-	-	-	-
<b>Interventions</b>							
Homoeopathy	+	+	+	+	+	+	-
<b>Assessments</b>							
Verbal Screening Form	+	-	-	-	-	-	-
DSM-V Level 1 Scale	+	-	-	-	-	-	-



DSM-V Level 2 Inattention Scale	+	+	+	+	+	+	+
Letter cancellation test	+	+	+	+	+	+	+
Strength and Difficulties Questionnaire	+	-	+	-	+	-	+
The Clinical Global Impression- Improvement scale	-	+	+	+	+	+	+

#### SAMPLE SIZE:

A study was conducted at NHRIMH, Kottayam from June 2009–November 2011. It was a randomized placebo controlled pilot trial, and sample size of 54 subjects has been included. From this previous study conducted at the institute, 24% improvement was obtained in the cognition problems with Homoeopathic medicine. Considering level of significance  $\alpha= 0.05$ ,  $p= 0.24$  and margin of error as 14%, a minimum sample of 36 cases are required for the study. Considering 10% drop out, the sample size has been calculated as 40.

#### STATISTICAL ANALYSIS:

The data will be statistically analyzed using STATCRAFT version 2.0.3. Descriptive Statistics will be done for demographical variables. The changes in DSM-V Level 2-Inattention- Parent/Guardian of Child Age 6-17 Swanson, Nolan and Pelham, version IV (SNAP-IV) from baseline to end will be assessed using Wilcoxon Signed Rank test based on whether the data satisfies the assumption of the test or not.

#### DISCUSSION AND CONCLUSION:

There are no studies available in the treatment of inattentive symptoms of ADHD. In Homoeopathy, the simillimum will be selected considering all symptoms at physical, mental and emotional level. In the management of child psychiatric cases, it is difficult to arrive at the exact constitutional picture considering the patient as a whole. Yet the most appropriate simillimum can be derived through the Physicians clinical skill which helps in early recovery of illness.

This clinical trial proposes a new area of analysis in improvement and assessment of inattentive symptoms and attention span of the child diagnosed with ADHD. Since there is no confirmatory therapeutic intervention with respect to inattentive symptoms, this trial may provide new openings for randomized controlled trial with large sample size. There are few studies conducted earlier showing positive results in treating ADHD children. This study also emphasizes an overall improvement of the case in ADHD patients.

Comparatively the inattentive type of ADHD cases were found to be frequently diagnosed and children with inattentive symptoms were poor in scholastic achievements.<sup>28</sup>On early identification and with appropriate homoeopathic simillimum, there are increased probability for early recovery without any other drug side effects.

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