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Review Article

Effectiveness and Safety of Ayurveda Intervention in Children and Adolescent with ADHD: A Systematic Review with Meta-Analysis.

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ABSTRACT

Introduction: Ayurveda-based interventions are being given to children and adolescents for their benefits in the treatment of attention deficit hyperactivity disorder (**ADHD**), but no systematic review of the overall evidence of Ayurveda intervention in ADHD has been conducted. This study aims to determine the effectiveness of Ayurveda intervention in children and adolescents with ADHD.

Methods: Electronic databases like PubMed, The Cochrane Library (CENTRAL), AYUSH research portal, Digital Helpline for Ayurveda Research Articles, and Researches in Ayurveda—online directory of PG and PhD thesis—were searched in addition to hand searching of Ayurveda journals and clinical trial registries to identify ongoing or completed trials. Randomised controlled trials or quasi-randomised trials or randomised comparative clinical trials comparing Ayurvedic interventions were included.

Results: A total of 39 studies were identified; 10 met the inclusion and exclusion criteria and were systematically reviewed. Due to different forms of Ayurvedic intervention used and variable quality of data, only three studies were included in the meta-analysis. The meta-analysis shows that Ayurveda interventions have their benefits in reducing symptoms of ADHD.

Conclusions: In this present review, some concerns, like small sample size and low methodological qualities of included studies, limit our ability to draw reliable conclusions regarding the effectiveness of Ayurveda intervention for children and adolescents with ADHD. Well-designed clinical trials reported in adherence to standard reporting guidelines are warranted.

Introduction

Attention deficit hyperactivity disorder (**ADHD**) is one of the most common neurobiological disorders in children and adolescents, characterised by a persistent pattern of inattention and/or hyperactivity-impulsivity that is frequently displayed and more severe than typically observed in individuals at a comparable level of development (Polanczyk et al., 2007; Vahia, 2013). Worldwide, the estimated prevalence ranges between 6% and 8% among school-aged children, with boys being more likely than girls to develop ADHD (Gentile et al., 2006). In India, the prevalence is not officially reported but is expected to be similar to other countries. The symptoms of ADHD usually become evident in preschool or early years; however, the median age of onset is 7 years (Choudhary et al., 2019a). For many individuals, ADHD symptoms improve during adolescence as age increases, but the disorder can persist into adulthood.

ADHD has a negative impact on children and their parents' lives and also inflicts a financial cost burden on families. It also causes social problems for children such as weak peer relationships, low self-esteem, poor academic performance, and low quality of life (Harpin, 2005). Several treatment approaches are available either in isolation or in combination, but pharmacotherapy remains the mainstay choice by using psychostimulants. Drugs such as methylphenidate and dextroamphetamine, which inhibit the reuptake of noradrenaline and dopamine, and the non-stimulating prefrontal cortex noradrenaline reuptake inhibitor atomoxetine are the standard western treatment of

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ADHD (Biederman, 2005; Spencer et al., 1996). A third of ADHD patients who take stimulants report significant adverse effects like anorexia, weight loss, abdominal pain, sleep disturbances, irritability, depressed mood, and loss of appetite (Schachter et al., 2001; Sonuga-Barke, 2009).

Increasing concerns about side effects and questions regarding the long-term safety of pharmacological treatment have led to the investigation and acknowledgement of alternative therapeutic medicines. More than 50% of parents of children diagnosed with ADHD treat their children's symptoms by using one or more complementary or alternative medicines (Sarris et al., 2011).

Ayurveda, one of the ancient traditional systems of medicine is widely practiced in the Indian subcontinent, primarily aims at holistic management of health and disease and has a sound philosophical, experiential, and experimental bases. The holistic concepts of Ayurveda emphasise health promotion, disease prevention, early diagnosis, and personalised treatment (Patwardhan, 2012, 2014). Ayurvedic treatment aims to restore the deranged equilibrium of doshas (regulatory functional factors of the body*)* through various techniques, procedures, regimens, diet, and medicines to provide an effect (Sridharan et al., 2011).

There is no direct reference to ADHD in Ayurvedic texts. Based on symptomatology, ADHD can be correlated to various abnormal behavioural traits described in texts under the feature of Vata Prakriti (Vata constitution; VA-1), the definition of Unmada (insanity; SAT-D.1647) such as Anavastitha Chittatva (unstable state of mind due only to Vata Dosha; AAB-2), Manovibhrama (confusion of mind; SAT-D.5679), Smritivibhrama (agitated memory; SAT-D.9075), Sheelavibhrama (impaired character; SAT-D.7715), Chestavibrma (abnormal movements; SAT-D.3244), and Acharavibhrama (impaired behaviour; SAT-D.1268) (Mohita et al., 2015; Singhal and Kumar, 2010). On the basis of understanding of Ayurveda pathophysiology, it may be said that ADHD occurs due to vitiation of Dhee (understanding; SAT-A.196), Dhriti (retaining power of the mind; SAT-A.197), and Smriti (memory/reminiscence/recollection; SAT-A.198), which causes abnormal conduct resulting in improper contact of the senses with their objectives and giving rise to inattention, hyperactivity, and impulsivity (Singhal and Kumar, 2010). Ayurveda treatment for ADHD usually comprises of a multipronged strategy by using a combination of different types of medicines (herbal, herbo-mineral, or metallic formulations) as for internal or external application and/or Panchakarma procedures (five internal bio-cleansing therapies; SAT-I.77) depending upon the predominance of doshas (Choudhary et al., 2019a; Mohita, 2015; Singhal and Kumar, 2010).

In recent years, various published clinical researches in Ayurveda have shown its efficacy in reducing symptoms of ADHD. However, to date, no comprehensive systematic review has been conducted to assess the quality of studies published, the strength of their clinical effects, and to summarise the overall evidence for the efficacy and safety of Ayurveda intervention in ADHD. Understanding this is the main aim and objective of this paper.

Methodology

The review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (Moher et al., 2009) and recommendations from the Cochrane collaboration (Higgins et al., 2020). The review was registered in Prospero with registration number—PROSPERO 2019 CRD42019129676, and the protocol for this review has been published (Choudhary et al., 2019b).

The literature review was done to locate all published papers and research studies investigating Ayurveda intervention in children and adolescents with ADHD between January 2000 and August 2020. Electronic databases like PubMed, The Cochrane Central Register of Controlled Trials (CENTRAL)/The Cochrane Library, AYUSH Research Portal, Digital Helpline for Ayurveda Research Articles, and Researches in Ayurveda—online directory of PG and PhD thesis—were searched. Clinical trial registries like Clinicaltrials.gov and the Clinical Trials Registry of India were also searched to identify ongoing or completed trials. The search strategy was constructed around search terms relating to or describing the intervention 'Ayurveda' and search terms for 'ADHD.' The search strategy was adapted for each database as necessary, and the list of search terms is provided in Appendix 1 for search terms.

The term coined 'Ayurveda interventions' includes treatment or practices based on fundamental principles of Ayurveda through the usage of internal or external medications, Panchakarma therapy, lifestyle advocacy, diet therapy, and others; intake of herbs or medicinal plants described in Ayurvedic literature or found in the Indian subcontinent; as a single herb or polyherbal or herbo-mineral or metallic formulation or extract form in any form (such as powdered, decoction, tablet, butter oil, etc.) for any dosage, vehicle, and duration of treatment. In addition to hand searching of journals, the bibliographic references of the included papers were also used to identify other relevant studies.

Inclusion

1. Study type—Randomised controlled trials or quasi-randomised trials or randomised comparative clinical trials.
2. Participants—Children and adolescents (age 5–18 years) diagnosed with ADHD irrespective of its subtypes.
3. Intervention—Ayurveda intervention alone or in combination with conventional therapy.
4. Controls/comparator—Conventional treatment; or placebo/sham treatment; or combination of Ayurveda and non-Ayurveda intervention; or Ayurveda intervention as a comparator in comparative clinical trials.
5. Outcome measures—Improvement noted in ADHD symptoms from baseline to the last follow-up by using Conner's rating scale, ADHD rating scale, or any other validated scale.
6. Full papers available in English or Indian language.
7. Studies were excluded if interventions other than Ayurveda like homoeopathy, yoga, Chinese traditional medicine, Siddha, Unani system of medicine, and other systems of medicines practiced worldwide but not based on fundamental principles of Ayurveda.

Selection of Studies

Three review authors (KC, PD, and SG) independently assessed the titles and/or abstracts of studies retrieved using the search strategy and those from additional sources. After the exclusion of duplicates from eligible articles, full-text articles were retrieved and reviewed in full to determine whether they meet inclusion and exclusion criteria as outlined. Any disagreement about the eligibility of particular studies was resolved through discussion with a fourth reviewer (MG). Any essential information found missing or unclear or to be sought from a particular study, authors were contacted via email or telephone for getting details. If records could not be obtained from the trial author, the study was excluded. The excluded studies were documented with reasons.

Data Extraction and Management

Three review authors (KC, PD, and SG) independently extracted data from the included studies for assessment of study quality and evidence synthesis by using *a-priori* developed data extraction form. Extracted data included details like authors name, year of publication, study setting, study population, participant demographics, details of intervention and control/comparator, study methodology, outcomes, any adverse event or adverse drug reaction reported, number of dropouts or withdrawals with reason and results of the study, etc. by following standard guidelines prescribed as Preferred Reporting Items for Systematic Reviews and Meta-analyses and the recommendation of the

Cochrane collaboration. Discrepancies were discussed with a fourth review author (MG) until a consensus was reached.

Assessment of Risk of Bias in Individual Studies

Two reviewers (KC and PD) independently assessed the risk of bias (**RoB**) for each included randomised controlled trial with the help of a revised tool—RoB2 as proposed by the Cochrane collaboration (Higgins et al., 2020), assessed with the help of an automated excel tool available online (Higgins, 2020). The RoB was classified as low, with some concerns, or high RoB by evaluating domains like randomisation process, deviation from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. Any differences in opinion were resolved by discussion or arbitration involving a third reviewer (MG). The findings in the RoB were summarised as 'risk of bias summary' and 'risk of bias graph.'

Measures of Treatment Effect

Dichotomous outcomes were not present in any of the included studies; however, if they are included in future updates, the treatment effects will be presented as relative risk. For continuous outcomes, the mean change from baseline for each group was recorded with corresponding SDs, with a 95% CI wherever available. Review Manager software (RevMan V.5.3) was used for analysis (The Cochrane Collaboration, 2020) to get a pooled estimate of treatment effect as mean difference with a 95% CI or standardised mean difference (**SMD**) with a 95% CI in cases of outcomes with different scales.

Assessment of Heterogeneity

Where pooling was appropriate, heterogeneity was assessed using the chi-square test and I^2 which describes the variation of effects that may be due to heterogeneity rather than sampling error (Higgins and Thompson, 2002). Random and fixed-effect models were examined, and where possible, the fixed-effect model was used. The I^2 statistic value greater than 75% was considered a significant heterogeneity, and when found, an attempt was made to determine potential reasons for it by examining individual study and subgroup characteristics.

Data Synthesis

We initially planned for combining the data from individual trials for the meta-analysis when the interventions will be sufficiently similar, that is, individual trials comparing the same ayurvedic formulation versus the same control intervention. If not available, we will combine the data of ayurvedic intervention from individual trials having the same outcome measures, irrespective of procedural or non-procedural intervention, type of preparation, route of administration, or dose used for comparison with controlled intervention.

The following comparisons were tabulated: Ayurveda versus placebo and Ayurveda versus conventional medicine. Where sufficient data were available, a meta-analysis was undertaken by using RevMan5.3 software. As the limited number of randomised trials were identified and due to the unavailability of data from most of the trials, the subgroup analyses were not performed according to the gender of participants, types of Ayurvedic intervention (procedural or non-procedural, internal or external medicine, and others), type of formulation (herbal, herbo-mineral, metallic, etc.), and treatment duration.

Results

Results of the Search

A total of 39 potential records were initially identified through electronic databases and other additional searches. After the removal of duplicates, 28 records were left for further screening. After screening 28 records for titles and abstracts, 14 full-text articles were retrieved and assessed for eligibility, while 14 others were excluded due to reasons like non-related (n = 4), CTRI (n = 2, ongoing not completed), not published as a full article (n = 1), and seven number of the thesis that could not be retrieved even after communications were made to institutions. Of the 14 full-text articles assessed for eligibility, four were further excluded as all were non-randomised trials. Overall, 10 studies were included for qualitative analysis, and only three studies were included for the meta-analysis. The flow diagram for the selection of studies is depicted in Figure 1.

Included Studies

We retrieved 10 eligible studies, including six published trials and four unpublished PG trials. Among them, two studies were a double-blind placebo-controlled two-arm trial (Kalra et al., 2002; Mahapatra and Mahapatra, 2015), one double-blind placebo-controlled four-arm trial (Ojha et al., 2007), two double-blind placebo-controlled three-arm trial (R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010; Singhal and Kumar, 2010), one single-blind placebo-controlled trial (S.S. Nirmalkar and C.Joshi, unpublished data,2012), one open-label placebo-controlled trial (C.R. Bhat et al., unpublished data, 2006), and three two-arm randomised comparative clinical trials (Bhalerao et al., 2013; A.M. Deokar and M. Auropremi, unpublished data, 2017; Gupta and Mamidi, 2013). Together, these studies enroled 385 participants. All the trials were published in the English language and were conducted in the Indian continent. The characteristics of the included studies are provided in Table 1.

Excluded Studies

Among potentially relevant studies, we excluded four studies and the details of which are provided in Table 2. Three of the studies were single-arm trials (C. Antony and M.S. Muraleedhar, unpublished data, 2015; Ragamala and Dash, 2017; J. Sudhakaran and C.V. Jayadevan, unpublished data, 2014) while one was a non-randomised three-arm comparative clinical trial (Thushara and Mangalasseri, 2016).

Types of Intervention Used

Of the 10 included trials, 12 types of different Ayurvedic formulations were tested. Among them, eight types of Ayurvedic formulations were tested against controlled intervention in eight trials and four types of Ayurvedic formulations were compared against each other in two trials. The control intervention included a placebo in seven trials and conventional medicine in one trial. According to the category of Ayurvedic formulations used, three formulations were composed of a single herb and nine formulations were compounds of herbs. Three trials included complex Ayurvedic intervention in form of both procedural and non-procedural intervention. It included intake of Ayurvedic formulation as non-procedural intervention and *Shirodhara* as procedural intervention. The duration of treatment ranged from 30 days to 6 months. The composition, dose, and duration of Ayurvedic formulation varied and its details are provided in Table 3. There were no two trials in this review comparing the same Ayurvedic formulation with the same control group.

Types of Outcomes Measured

All the trials reported the outcome as improvement in ADHD-related symptoms with the help of assessment tools. Six trials used a Likert type of four-point rating scale (0–3) for measurement of each symptom based on the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV)criteria for ADHD to obtain total ADHD score and subtotal score for two domains of ADHD, that is, hyperactive-impulsivity type and

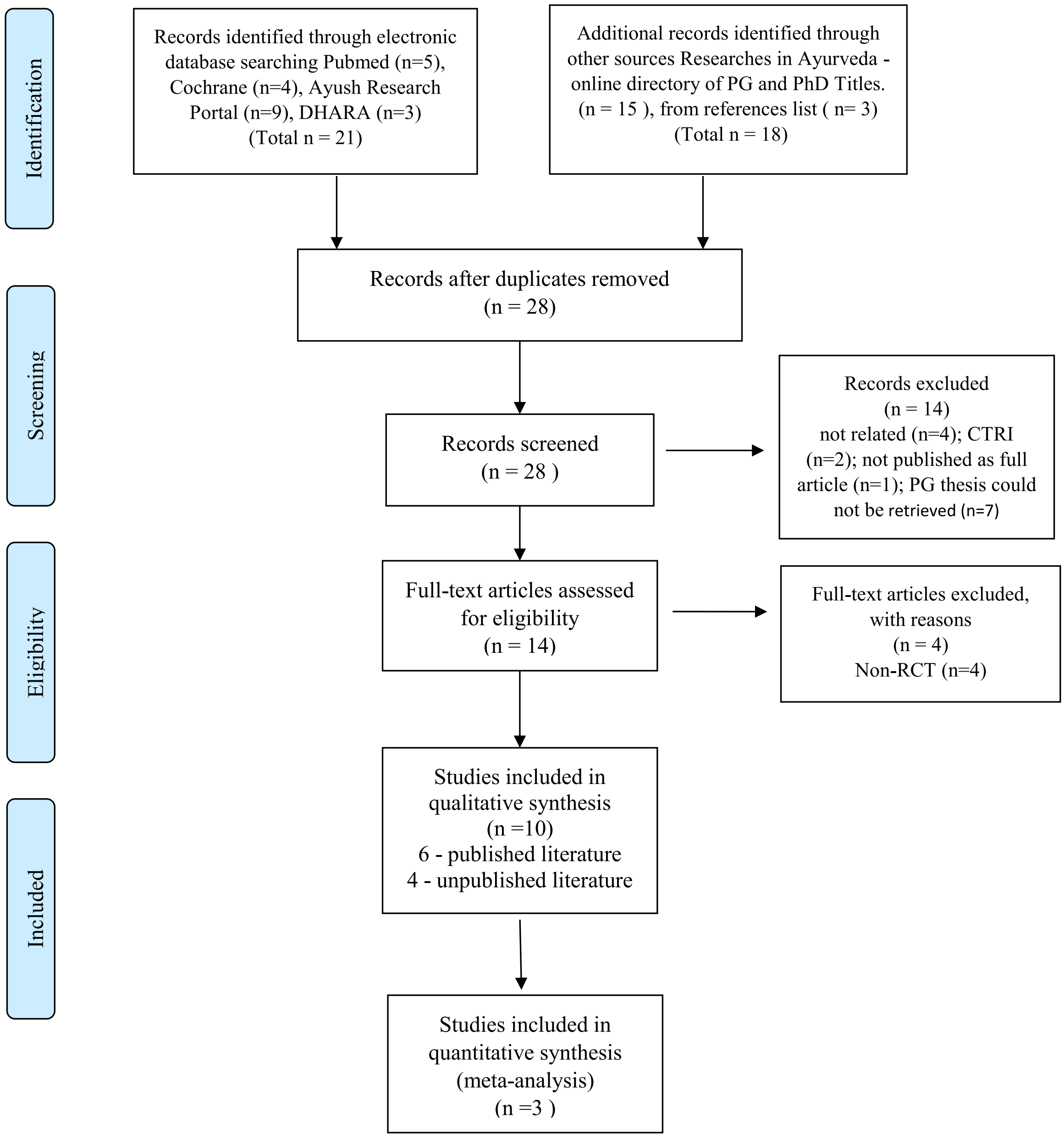


Fig. 1. Flowchart of study selection. DHARA, Digital Helpline for Ayurveda Research Articles; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses; RCT, randomised controlled trial; CTRI, Clinical Trials Registry - India; Non-RCT, non-randomised controlled trial.

inattentive type of ADHD. The other four trials used validated scales like Conner's 10-point rating scale, Dupaul ADHD rating scale, and National Institute for Children's Health Quality (NICHQ) Vanderbilt assessment scale—parent and teacher informant. In addition to that, reaction time by Vernier chronoscope, Finger Dexterity test, change in the coefficient of the division of attention span, Kaufman Assessment Battery for Children, Mindomatics software to test cognitive functions by using finger tapping test, choice reaction time, choice discrimination test, etc. were also used as other outcome measures. All the trials specified a timeline for the measurement of outcomes.

Risk of Bias in Included Studies

The RoB assessment is summarised in Figure 2.1 (RoB graph: review authors' judgements about each RoB item presented as percentages across all included studies) and Figure 2.2 (RoB summary: review authors' judgements about each RoB item for each included studies).

Randomisation Process

In most of the included trials, it is only mentioned that "participants were randomly allocated into the groups" and no further details about the randomisation process were provided. Only two studies (Bhalerao et al., 2013; A.M. Deokar and M. Auropremi, unpublished data, 2017) have reported the randomisation method of using a computer-generated randomisation list. In most of the studies, no information was found on allocation concealment except Kalra et al. (2002) used coding of drugs, and Ojha et al. (2007) described the use of coded medicine and sealed envelopes. Only two studies (Bhalerao et al., 2013; Kalra et al., 2002) have described the baseline data in terms of descriptive statistics (mean or median with standard deviation) and found to have no apparent imbalance at the baseline between intervention groups. While most of the studies did not describe baseline data, the overall RoB in this domain is low with Kalra et al. (2002) and Ojha et al. (2007), high with Gupta and Mamidi (2013), and the rest of the studies with some concerns.

Table 1
Characteristic of included studies.

Author, year, country	Type of study design and study setting	Sample characteristic	Intervention	Control	Measurement	Outcomes/ assessment parameters	No. of dropouts/ withdrawal	Results/ significant findings	Safety/ Adverse events
A. Randomised clinical trial									
(i) Published literature									
Kalra et al. (2002), India	Randomised, double-blind, placebo-controlled, hospital-based study	Screening = 195; enroled N = 60; aged 6–12 y; exp. grp.: n = 27, 9.1 ± 2.5, 26/1 (M/F); cont. grp.: n = 27, 8.7 ± 2.4, 21/6 (M/F)	Tab. Mentat (515 mg) two tablets per day for 6 mo	Placebo in the same dosage	Baseline, 2, 4, and 6 mo	Coding subtest of MISIC, four subtests of KABC, Conner's 10-point rating scale, Bender Gestalt test for young children Brain SPECT scan (pre and post)	Dropouts = 6 (three from each group) and four participants showed consistently variable results. So, statistical analysis was carried out on 50 participants.	Significant improvement in Conner's rating scale scores for Mentat group compared to the placebo group at 4 and 6 mo of evaluation.	Not reported
Ojha et al. (2007), India	Randomised, double-blind, four-arm group trial, hospital-based OPD study	N = 48; aged 6–15 y; group A: n = 10; group B: n = 10; group C: n = 10; group D: n = 10	Group A—MN1 granules (200 mg/kg/d in 2 divided doses with milk) for 3 mo Group B—MN1 granules + Shirodhara (with milk, 30–45 min daily for 2 wk) Group C—Placebo Group D—Placebo (MN2 granules; same dosage) + Shirodhara	-	Baseline and 3 mo	Improvement in symptoms based on DSM-IV criteria, coefficient of division of attention span (CD), reaction time (RT), and finger dexterity tests (FDT). Draw A man test—IQ	Dropouts = 8	Statistically significant improvement was noted in combination group compared to placebo group at 3 mo of treatment.	Not reported
Singhal et al. (2010) and Singhal and Kumar (2010), India	Randomised, double-blind, three-arm group trial, hospital-based OPD study	N = 55: aged 6–16 y; group 1: n = 17; group 2: n = 14; group 3: n = 12	Group 1—Syp. Ayurvedic compound (1 ml/kg/d in three divided doses daily for 3 mo) Group 2—Syp. Ayurvedic compound (1 ml/kg/d in three divided doses daily for 3 mo) and Shirodhara (with milk) for 45 min for 2 wk Group 3—Placebo (sugar-based Syp.) 1 ml/kg/d in three divided doses daily for 3 mo		Baseline and 3 mo	Improvement in symptoms based on DSM-IV criteria, change in CD, RT, and FDT. Draw A man test—IQ, Audio and visual RT by vernier chronoscope (electrical)	Dropouts = 12	Statistically significant improvement was noted in the combination group compared to placebo group at 3 mo of treatment.	Reported no events
Gupta and Mamidi (2013), India	Randomised, two-arm comparative clinical trial,	N = 20; aged 5–12 y; Naladadi group: n = 10; Kushmanda group: n = 10	Naladadi Ghrita 5 ml twice a day before meal for 1 mo	Kushmanda Ghrita 5 ml twice a day before meal for 1 mo	Baseline and 30 d	ADHD rating scale-parent	Dropouts = 0	Statistically significant improvement was noted on ADHD rating	Not reported

(continued on next page)

Table 1 (*continued*)

Author, year, country	Type of study design and study setting	Sample characteristic	Intervention	Control	Measurement	Outcomes/ assessment parameters	No. of dropouts/ withdrawal	Results/ significant findings	Safety/ Adverse events
	hospital-based OPD study							scale at 1 mo of treatment compared to baseline in both groups. Difference in both treatment groups was statistically insignificant.	
Bhalerao et al. (2013), India	Phase 2—(therapeutic confirmatory) randomised, open-label, comparative clinical trial	N = 40; aged 6–12 y; group 1: n = 14; age = 9.86 ± 1.46 y; M/F ratio: 12:2; group 2: n = 13; age = 9.23 ± 1.59 y; M/F ratio: 11:2	Group 1—Brahmi Ghritam 2tsf (approximately 10 ml) with lukewarm water or milk around 7–8 AM on empty stomach for 2 mo	Group 2—Methylphenidate 0.25–1 mg/kg/d as per the judgement of the clinician, average dose being 5–10 mg/d	Baseline and at regular 15 d interval for 2 mo	Dupaul ADHD rating scale/ ADHD rating scale-IV, other psychometric evaluation tests by using Mindomatics software (FT, SRT, CRT, CDT, DPST/DLST/ DSST and CST; DVTT, NWM, and IPRT)	Dropouts = 13, 6 from Brahmi group and 7 from methylphenidate group.	Non-significant difference was noted between two treatment groups at 2 mo of treatment.	Reported no events
Mahapatra and Mahapatra (2015), India	Randomised, double-blind, placebo-controlled, hospital-based OPD study	N = 35; aged 7–13 y; exp. grp: n = 15; cont. grp: n = 15	Saraswatarista (without gold) 0.1 ml/kg/d in two divided doses with equal amount of water after meal for 12 wk	Placebo in same dosage form	Baseline, 6 wk, and 12 wk.	NICHQ Vanderbilt assessment scale—parents and teachers' informant, overall clinical assessment of results	Dropouts = 5	Statistically significant improvement was noted in Saraswatarista group compared to placebo at 12 wk of treatment.	Reported no events
(i) Unpublished literature									
C.R. Bhat et al., unpublished data (2006), India	Randomised, open-label, placebo-controlled clinical trial, hospital-based OPD study	N = 20; aged 7–12 y; group A: n = 10; group B: n = 9	Group A—Mandukparni syrup 40 ml/d in four divided doses daily for 6 wk	Group B—Placebo syrup 40 ml/d in four divided doses daily for 6 wk	Baseline and 6 wk	Four-point rating scale based on DSM-IV criteria for ADHD symptoms, and IQ by adopting Gujarati adaptation of Wechsler Intelligence scale for children	Dropouts = 1	Statistically significant results in the inattentive and impulsivity type of ADHD was noted in Mandukparni group at 6 wk of treatment compared to placebo group.	Not reported
R. Raut and A. Kumar, unpublished data (2011) India	Randomised, double-blind, three-arm group trial, hospital-based OPD study	N = 53; aged 6–16 y; group A: n = 15; group B: n = 15; group C: n = 15	Group A—Syp. Shishukalyan Yoga 1 (1 ml/kg/d in three divided doses daily for 3 mo)	-	Baseline and 3 mo	Improvement on core symptoms based on DSM-IV criteria, CD, RT, and	Dropouts = 8	Statistically significant improvement was noted in combination group compared	Reported no events

(*continued on next page*)

Table 1 (*continued*)

Author, year, country	Type of study design and study setting	Sample characteristic	Intervention	Control	Measurement	Outcomes/ assessment parameters	No. of dropouts/ withdrawal	Results/ significant findings	Safety/ Adverse events
			Group B—Syp. Shishukalyan Yoga I (1 ml/kg/d in three divided doses daily for 3 mo) with Tila Taila Shirodhara Group C—Syp. Shishukalyan Yoga II (placebo) (1 ml/kg/d in three divided doses daily for 3 mo)			FDT. Draw A man test—IQ		to placebo group at 3 mo of treatment.	
S.S. Nirmalkar and C. Joshi, unpublished data (2012), India	Randomised, single-blind, placebo-controlled, hospital-based OPD study	N = 34: aged = 7–12 y; group A: n = 15; group B: n = 15	Group A—Vrudhadaruka Rasayana (churna form) 10–12 g/d in two divided doses with ghrita after meal for a period of 1 mo	Group B—Placebo (churna form, fired wheat powder) 10–12 g/d in two divided doses with ghrita after meal for a period of 1 mo	Baseline, 30 d of treatment, and two follow-ups at 15 and 30 d after treatment	Four-point rating scale based on DSM-IV criteria for ADHD symptoms	Dropouts = 4	Trial drug showed significant improvement compared to placebo at 30 d of the treatment, and the effect was noticed to be still significant at follow-up.	Not reported
A.M. Deokar and M. Auropremi, unpublished data (2017), India	Randomised, open-labelled, hospital-based OPD study	N = 20, aged 5–12 y; group A: n = 10; group B: n = 10	Group A—Brahmi churna 3 g/d in three divided doses orally with honey before meal for 45 d	Group B—Mandukparni churna 3 g/d in three divided doses orally with honey before meal for 45 d	Baseline and 45 d	Four-point rating scale based on DSM-IV criteria for ADHD symptoms	Dropouts = 0	Within-group analysis, both the groups reported significant improvement in hyperactive-impulsivity and inattentive type of ADHD symptoms at 45 d of treatment whereas the intergroup comparison reveals a significant difference between two groups. Brahmi churna is more efficacious.	Not reported

ADHD, attention deficit hyperactivity disorder; KABC, Kaufman Assessment Battery for Children; MISIC, Malin's Intelligence scale for Indian Children; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders Fourth Edition; NICHQ, National Institute for Children's Health Quality; IQ, Intelligence Quotient.

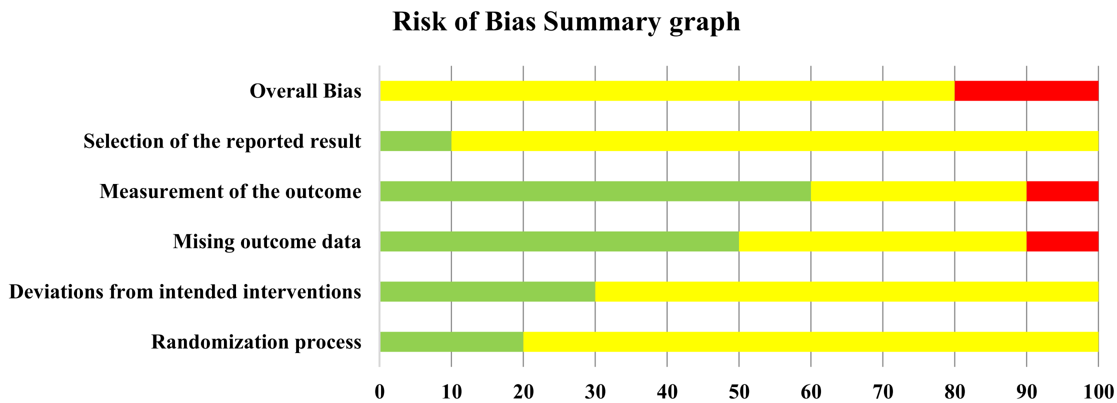
Table 2
Characteristic of included studies (excluded).

First author, year, country	Type of study design and study setting	Sample characteristic	Intervention	Control	Measurement	Outcomes/ Assessment parameters	No. of dropouts/ Withdrawal	Results/ Significant findings	Safety/ Adverse events	Reason for exclusion
J. Sudhakaran and C.V. Jayadevan, unpublished data, (2014),India	Single-arm, open-labelled, hospital-based OPD study	N = 15; aged 5–12 y	Shodhana and Shamana therapy Duration of intervention = 2 mo	-	Baseline, 2 mo of treatment, and 1 mo after treatment	Conner's rating scale	Dropouts = 0	Significant improvement in reducing the total score on Conner's rating scale for ADHD	Not reported	Single-arm trial
C. Antony and M.S. Muraleedhar, unpublished data (2015), India	Single-arm, open-labelled, hospital-based OPD study	N = 20; aged 5–12 y	Brahmi and Vacha (Brahmi swarasa bhavita Vacha churna) in a minimum dosage of 30 mg and maximum dosage of 60 mg twice daily before food with *navaneeta* (butter)	-	Baseline, 90 d of treatment, and 1 mo after treatment.	Conner's parent rating scale—revised	Dropouts = 2	Significant difference noted at the end of treatment and its effect was sustained during follow-up period	Not reported	Single-arm trial
Thushara and Mangalasseri (2016), India	Three-arm, comparative clinical trial, hospital-based study	N = 30; aged 5–12 y	Group 1—Ayurvedic treatment modality (Naladadi Ghrita 5 ml twice daily after meals; talam with Panchagandha churnam and Kshirbalataila in evening around 3.30 pm for 45 min Group 2—Combined approach (Ayurvedic treatment modality and behavioural therapy) Group 3—Behavioural therapy Duration of therapy = 1 mo	-	Baseline, 1 mo of treatment, and 1 mo after treatment	Conner's rating scale	Dropouts = 0	The percentage of improvement noted in combined approach was more than compared to individual groups	Not reported	Non-randomised comparative clinical trial
Ragamala and Dash (2017), India	Single-arm, open-labelled, hospital-based OPD/IPD study	N = 40; aged 7–12 y	Takradhara (Takra processed with few medhya drugs like Brahmi, Jatamamsi, Vacha, Aswagandha churnas) for about 30–45 min for 14 d and then again repeated after every 2 mo for three consecutive sittings. Duration of intervention = 6 mo	-	Baseline and 6 mo	Self-prepared scale based on DSM-IV criteria for ADHD symptoms by obtaining a four-point rating scale	Drop outs = 0	Mild improvement in overall result of therapy	Not reported	Single-arm trial

ADHD, attention deficit hyperactivity disorder; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders Fourth Edition.

Table 3
Composition, dose, and duration of Ayurvedic formulation in included studies.

Study ID	Medicine name	Textual reference	Contents	Dosage and duration
Kalra et al. (2002)	Tablet Mentat	Patent formulation	Extracts: *Bacopa monnieri* (136 mg), *Centella asiatica* (70 mg), *Withania somnifera* (52 mg), *Evolvulus alsinoides* (52 mg), *Nardostachys jatamansi* (52 mg), *Valeriana wallichii* (50 mg), *Embelia ribes* (50 mg), *Prunus amygdalus* (50 mg), *Tinospora cordifolia* (36 mg), *Terminalia chebula* (36 mg), *Emblica officinalis* (36 mg), *Oroxylum indicum* (32 mg), and *Celastrus paniculatus* (32 mg). Powders: *B. monnieri* (80 mg), *Orchis mascula* (18 mg), *Mucuna pruriens* (18 mg), *Elettaria cardamomum* (18 mg), *T. arjuna* (18 mg), *Foeniculum vulgare* (18 mg), *Ipomoea digitata* (18 mg), *Zingiber officinale* (14 mg), *T. belerica* (14 mg), *Myristica fragrans* (14 mg), *Syzygium aromaticum* (10 mg), and Muktapishti (3 mg)	Two tablets per day for 6 mo
C.R. Bhat et al. unpublished data (2006)	Mandukparni syrup	-	Mandukparni (*Centella asiatica* Linn.)	40 ml/d in four divided doses daily for 6 wk
Ojha et al. (2007)	Manas Niyamak Yoga granules	-	Brahmi (*B. monnieri*), Mandukparni (*C. asiatica*), Shankhpushpi (*Convolvulous pluricaulis*), Jatamansi (*N. jatamansi*), Vacha (*Acorus calamus*), Ashwagandha (*W. somnifera*), Vidanga (*Em ribes*), Madhuyasti (*Glycyrrhiza glabra*), Chitraka (*Plumbago zeylanica*), and Pippali (*Piper longum*)	200 mg/kg/d in two divided doses with milk) for 3 mo
Singhal et al. (2010)	Syrup Ayurvedic compound	-	Brahmi (*B. monnieri*), Ashwagandha (*W. somnifera*), and Tagar (*V. wallichi*)	1 ml/kg/d in three divided doses daily for 3 mo
R. Raut and A. Kumar, unpublished data (2011)	Syrup Shishukalyan Yoga I	-	Brahmi (*B. monnieri*), Vacha (*A. calamus*), Pippali (*P. longum*), Kushtha (*Saussurea lappa*), Sariva (*Hemidesmus indicus*) Siddharthaka (*Brassica campestris*) and Saindhav lavan (sodium chloride)	1 ml/kg/d in three divided doses daily for 3 mo
S.S. Nirmalkar and C. Joshi, unpublished data (2012)	Vrudhadaruka Rasayana	Rasaynaadhyaya of Chakradutta	Vrudhadaruka (*Argyreia speciosa* sweet) and Shatavari (*Asparagus racemosus*)	10–12 g/d in two divided doses with ghrita after meal for a period of 1 mo
Bhalerao et al. (2013)	Brahmi Ghrita	Bhaishjya Ratnavali. Apasmarchikitsa-1	Brahmi (*B. monnieri*), Vaca (*A. calamus*), Kustha (*S. lappa*), and Sankhapushpi (*Convolvulus pluricaulis*) are processed in Go ghritam (ghee prepared from cow's milk).	2tsf (approximately 10 ml) with LW or milk around 7–8 AM on empty stomach for 2 mo
Gupta and Mamidi (2013)	Naladadi Ghrita	A.H. Uttar Sthana Rasayanaadhyaya	Katukarohini (*Picrorhiza scrophularia* flora), Payasya (*Holostemma ada-kodien*), Madhuka (*G. glabra*), Chandana (*Santalam album*), Sariba (*H. indicus*), Vacha (*A. calamus*), etc.; the main content is "Shankhapushpi (*Clitoria ternata*)".	5 ml twice a day before meal for 1 mo
Gupta and Mamidi (2013)	Kushmanda Ghrita	Ashtanga Hridaya in Apasmaar pratishedha adhyaya.	Kushmanda (*Benincasa hispida*) and Yashtimadhu (*G. glabra*)	5 ml twice a day before meal for 1 mo
Mahapatra and Mahapatra (2015)	Saraswatarista (without gold)	Bhaisajya Ratnawali Rasayanadhikara: 178–191	Brahmi (*B monnieri*), Satavari (*A. racemosus*), Vidari (*Pueraria tuberosa*), Abhaya (*T. chebula*), Usira (*Vetiveria zizanoides*) Sunthi (*Z. officinale*), Misreya (*F. vulgare*), Maksika (honey), Sita (sugar), Dhataki (*Woodfordia fruticosa*), Renuka (*Vitex negundo*), Trivrita (*Operculina turpethum*), Pippali (*P. longum*), Devpushpa (*S. aromaticum*), Vacha (*A. calamus*), Kustha (*S. lappa*), Ashwagandha (*W. somnifera*), Vibhitika (*T. bellirica*), Amrita (*T. cordifolia*), Ela (*E. cardamomum*), Vidanga (*E. ribes*), Twaka (*Cinnamomum verum*)	0.1 ml/kg/d in two divided doses with equal amount of water after meal for 12 wk
A.M. Deokar and M. Auropremi, unpublished data (2017)	Brahmi Panchang churna	-	Brahmi (*B. monnieri* Linn.)	3 g/d (adult dose) in three divided doses orally with honey before meal for 45 d. Paediatric dose was calculated by using Young's formula
A.M. Deokar and M. Auropremi, unpublished data (2017)	Mandukparni panchang churna		Mandukparni (*Centella asiatica* Linn.)	3 g/d (adult dose) in three divided doses orally with honey before meal for 45 d. Paediatric dose was calculated by using Young's formula



	Randomization process	Deviations from intended interventions	Mising outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Low risk	20	30	50	60	10	0
Some concerns	80	70	40	30	90	80
High risk	0	0	10	10	0	20

Low risk Some concerns High risk

Fig. 2.1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Deviation from Intended Interventions

Blinding was reported in six trials; five adopted double-blind methods (Kalra et al., 2002; Mahapatra and Mahapatra, 2015; Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010), and one used single blinding procedure (S.S. Nirmalkar and C. Joshi, unpublished data, 2012). Two studies were open-labelled

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall bias
Kalra et al. (2002)	+	+	!	+	!	!
C.R. Bhat et al. unpublished data (2006)	!	!	+	!	!	!
Ojha et al. (2007)	+	+	!	+	!	!
Singhal et al. (2010)	!	+	!	+	!	!
R. Raut and A. Kumar, unpublished data (2011)	!	+	!	+	!	!
S.S. Nirmalkar and C. Joshi, unpublished data (2012)	!	!	+	!	!	!
Gupta and Mamidi (2013)	-	!	+	+	!	-
Bhalerao et al. (2013)	!	!	!	+	!	!
Mahapatra and Mahapatra (2015)	!	+	!	+	!	!
A.M. Deokar and M. Auropremi, unpublished data (2017)	!	!	+	+	+	!

+ Low risk
! Some Concerns
- High risk

Fig. 2.2. Risk of bias summary: review authors' judgements about each risk of bias item for each included studies.

(Bhalerao et al., 2013; A.M. Deokar and M. Auropremi, unpublished data, 2017) and no information was available on the blinding procedure adopted in two studies (C.R. Bhat et al., unpublished data, 2006; Gupta and Mamidi, 2013). Most studies reported a number of participants analysed with documented reasons for dropped outs and performed modified intention to treat analysis by excluding participants with missing outcome data. However, only one study (Bhalerao et al., 2013) presented a CONSORT flow-like diagram while most of them did not report it. There was no information available for the deviations from the intended intervention that arose because of the trial context in most of the studies. The overall RoB in this domain is low with Kalra et al. (2002); Mahapatra and Mahapatra (2015); Ojha et al. (2007); R. Raut and A. Kumar, unpublished data (2011); and Singhal et al. (2010), while other included studies showed some concerns.

Missing Outcome Data

Three studies (A.M. Deokar and M. Auropremi, unpublished data, 2017; Gupta and Mamidi, 2013; S.S. Nirmalkar and C. Joshi, unpublished data, 2012) reported no dropouts, while the rest of seven studies reported dropouts. Only one study reported a $< 5\%$ dropout rate (C.R. Bhat et al., unpublished data, 2006) while the rest of six studies reported a $> 5\%$ dropout rate (Bhalerao et al., 2013; Kalra et al., 2002; Mahapatra and Mahapatra, 2015; Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010). The reason for dropouts was documented in only two studies (Bhalerao et al., 2013; Kalra et al., 2002). The overall RoB in this domain is low with C.R. Bhat et al., unpublished data (2006); A.M. Deokar and M. Auropremi, unpublished data (2017); Gupta and Mamidi (2013), and S.S. Nirmalkar and C. Joshi, unpublished data (2012), while the rest of them showed some concerns.

Measurement of Outcome

Most of the studies used DSM-IV criteria of ADHD as outcome parameters for assessing improvement in ADHD symptoms by assigning a raw score from 0 to 3 (Likert type of scale) to each symptom and obtaining a total score, or by using Conner's rating scale (Kalra et al., 2002), Dupaul ADHD rating scale (Bhalerao et al., 2013), and NICHQ Vanderbilt assessment scale (Mahapatra and Mahapatra, 2015). Some studies also used other outcome measures for showing improvement in ADHD by conducting tests like total reaction time, finger dexterity test, and coefficient of division for attention span (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010); psychometric tests like finger tapping, simple reaction time, and others (Bhalerao et al., 2013); coding subtest of Malin's Intelligence Scale for Indian Children , four subsets of Kaufman Assessment Battery for Children, and Gestalt test for young children (Kalra et al., 2002). All the included studies reported the same measurement methods and thresholds at comparable time points. Most of the outcomes measured were participant-reported outcome and was found less likely to influence the knowledge of the intervention received. The overall RoB in this domain showed some concerns with C.R. Bhat et al., unpublished data (2006) and S.S. Nirmalkar and C. Joshi, unpublished data (2012), while the rest of the studies were with low risk.

Selection of the Reported Result

An attempt was made to retrieve and compare the original trial protocol with the published article to identify an outcome that was measured and not reported. For most of the studies, we could not retrieve the prespecified analysis plan for each trial by searching trial registries entry, trial protocol, or design paper except for one study (A.M. Deokar and M. Auropremi, unpublished data, 2017), CTRI registration was available.

However, we tried to infer by comparing the outcome measures and analysis listed in the method section of an article or PG/PhD dissertations with those that are reported. Most of the studies conducted were part of postgraduation/PhD curriculum from reputed Ayurveda institutions, and it was assumed that the protocol was submitted to the scrutiny committee in advance, and after obtaining approval, the study was conducted and published in strict compliance to this and lowered RoB to some concern for these studies.

Other Potential Sources of Bias

We did not detect unambiguous sources of bias. We would like to point out, however, that pretrial estimation of sample size was not available in most of the studies.

Effects of Interventions

Multiple types of Ayurvedic interventions were reported in the 10 included studies. Among them, four studies compared Ayurvedic formulations (Mentat, Saraswatarista, Mandukparni, and Vrudhadaruka Rasayana) with placebo, three studies compared multiple combinations of Ayurvedic intervention (procedural and non-procedural) with placebo, two studies compared Ayurveda versus Ayurveda intervention while only one study compared Ayurveda versus conventional medicine. Various outcome measures were used to measure the efficacy of Ayurvedic intervention, which were heterogeneous among the studies. Of the 10 included studies, we could find only five studies (Bhalerao et al., 2013; Mahapatra and Mahapatra, 2015; Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010) with necessary details like the number of participants and mean ± SD for calculating effect size.

Comparison: Ayurveda versus Placebo

DSM-IV Criteria Symptoms. Three studies (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010) assessed the efficacy of Ayurveda treatment over placebo in this domain. Ayurveda treatment reported statistically significant results at the end of 3 months of treatment in reducing core symptoms of ADHD (inattention, hyperactivity/impulsivity) when compared to placebo (Table 4.1).

Reaction Time. Three studies (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010) assessed this domain and showed statistically significant results of Ayurveda treatment over placebo in reducing total reaction time (visual and auditory) at the end of 3 months (Table 4.1).

Attention Span—Change in Coefficient of Division. In this domain, Ojha et al. (2007) reported statistically significant results of Ayurveda treatment over placebo, whereas other two studies Singhal et al. (2010) and R. Raut and A. Kumar, unpublished data (2011) reported statistically insignificant improvement at the end of 3 months of the treatment period (Table 4.1).

Finger Dexterity Test. Three studies (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010) assessed this domain, and a mixture of positive and negative responses to Ayurveda treatment was noted in a subdomain of this test when compared to placebo at the end of 3 months of the treatment (Table 4.1).

NICHQ Vanderbilt Assessment Scale (Parent and Teacher Informant). Only one study (Mahapatra and Mahapatra, 2015) reported this domain and showed the effectiveness of Ayurveda intervention over placebo in both teacher and parent rating scales. The difference noted in the Ayurveda group was statistically significant when compared to placebo at the end of 3 months of treatment (Table 4.1).

Comparison: Ayurveda versus Conventional Medicine

Only one study (Bhalerao et al., 2013) compared the efficacy of Ayurvedic formulation (Brahmi Ghrita) over conventional medicine (methylphenidate) (Table 4.2).

Table 4.1
Comparison—Ayurveda versus placebo.

Domain	Study	No. of participants	Statistical method	Effect size
1. DSM-IV criteria symptoms				
1.1. Inattention	Ojha et al. (2007)	33	Mean difference (IV, fixed, 95%CI)	−0.41 [−0.70, −0.12]
	Singhal et al. (2010)	27	Mean difference (IV, fixed, 95%CI)	−0.87 [−1.11, −0.63]
	R. Raut and A. Kumar, unpublished data (2011)	27	Mean difference (IV, fixed, 95%CI)	−0.72 [−1.42, −0.03]
1.2. Hyperactivity	Ojha et al. (2007)	35	Mean difference (IV, fixed, 95%CI)	−0.72 [−1.10, −0.34]
	Singhal et al. (2010)	18	Mean difference (IV, fixed, 95%CI)	−1.15 [−1.40, −0.90]
	R. Raut and A. Kumar, unpublished data (2011)	18	Mean difference (IV, fixed, 95%CI)	−1.33 [−1.67, −0.99]
1.3. Impulsivity	Ojha et al. (2007)	34	Mean difference (IV, fixed, 95%CI)	−0.62 [−0.96, −0.28]
	Singhal et al. (2010)	9	Mean difference (IV, fixed, 95%CI)	−1.21 [−1.65, −0.77]
	R. Raut and A. Kumar, unpublished data (2011)	9	Mean difference (IV, fixed, 95%CI)	−1.05 [−1.59, −0.52]
2. Attention span—change in coefficient of division				
	Ojha et al. (2007)	40	Mean difference (IV, fixed, 95%CI)	−0.05 [−0.07, −0.04]
	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−0.04 [−0.11, 0.03]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−0.04 [−0.11, 0.03]
3. Reaction time				
3.1. Auditory	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−0.54 [−0.95, −0.12]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−0.55 [−0.93, −0.17]
3.2. Visual	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−0.39 [−0.79, 0.00]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−0.34 [−0.66, −0.01]
3.3. Total	Ojha et al. (2007)	40	Mean difference (IV, fixed, 95%CI)	−0.21 [−0.28, −0.14]
	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−0.44 [−0.84, −0.04]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−0.46 [−0.83, −0.09]
4. Finger dexterity test				
4.1. Time taken for right hand	Ojha et al. (2007)	40	Mean difference (IV, fixed, 95%CI)	−1.01 [−1.18, −0.84]
	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−0.78 [−1.87, 0.31]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−0.83 [−1.28, −0.37]
4.2. No. of errors for right hand	Ojha et al. (2007)	40	Mean difference (IV, fixed, 95%CI)	−4.50 [−6.09, −2.91]
	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−1.39 [−2.95, 0.17]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−1.38 [−3.07, 0.32]
4.3. Time taken for left hand	Ojha et al. (2007)	40	Mean difference (IV, fixed, 95%CI)	−0.73 [−0.98, −0.48]
	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−0.63 [−1.42, 0.17]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−0.66 [−1.54, 0.23]
4.4. No. of errors for left hand	Ojha et al. (2007)	40	Mean difference (IV, fixed, 95%CI)	−4.50 [−5.91, −3.09]
	Singhal et al. (2010)	43	Mean difference (IV, fixed, 95%CI)	−2.17 [−3.40, −0.94]
	R. Raut and A. Kumar, unpublished data (2011)	45	Mean difference (IV, fixed, 95%CI)	−2.17 [−3.33, −1.00]
5. NICHQ Vanderbilt assessment scale—parent informant				
5.1. Overall school performance	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.60 [−3.18, −2.02]
5.2. Reading ability	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.40 [−3.03, −1.77]
5.3. Writing skills	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.54 [−3.16, −1.92]
5.4. Mathematical aptitude	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.73 [−3.22, −2.24]
5.5. Relationship with parents	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.67 [−3.21, −2.13]
5.6. Relationship with siblings	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.47 [−3.03, −1.91]
5.7. Relationship with peers	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.74 [−3.24, −2.24]
5.8. Participation in organised activities	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.60 [−3.18, −2.03]
6. NICHQ Vanderbilt assessment scale—teacher informant				
6.1. Reading ability	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.33 [−2.87, −1.79]
6.2. Mathematical aptitude	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.60 [−3.08, −2.12]
6.3. Written expression	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.54 [−3.07, −2.01]
6.4. Relationship with peers	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.67 [−3.21, −2.13]
6.5. Following directions	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95CI)	−2.33 [−2.87, −1.79]
6.6 Class disruption	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.73 [−3.10, −2.36]
6.7. Assignment completion	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.47 [−3.03, −1.91]
6.8. Organisational skills	Mahapatra and Mahapatra (2015)	30	Mean difference (IV, fixed, 95%CI)	−2.66 [−3.23, −2.10]

Table 4.2
Comparison—Ayurveda versus conventional medicine.

Domain	Studies	No. of participants	Statistical method	Effect size
1. ADHD rating scale				
1.1. Total ADHD score	Bhalerao et al. (2013)	27	Mean difference (IV, fixed, 95% CI)	−4.26 [−9.60, 1.08]
1.2. Inattention subtype score	Bhalerao et al. (2013)	27	Mean difference (IV, fixed, 95% CI)	−3.43 [−7.10, 0.24]
1.3. Impulsivity subtype score	Bhalerao et al. (2013)	27	Mean difference (IV, fixed, 95% CI)	−1.09 [−4.30, 2.12]

ADHD, attention deficit hyperactivity disorder.

Attention Deficit Hyperactivity Disorder Rating Scale. The difference noted between both groups (Brahmi ghrita vs. methylphenidate) was statistically insignificant over the total ADHD score. However, Brahmi ghrita demonstrated its efficacy in treating symptoms of ADHD when compared to baseline at the end of 2 months of treatment.

Comparison: Ayurveda versus Ayurveda

Gupta and Mamidi (2013) compared the efficacy of Naladadi Ghirta and Kushmanda Ghrita by assessing the ADHD rating scale-parent version. The study found no significant difference between both two drugs at the end of 1 month of treatment. (Table 4.3). However, within-group analysis, both drugs reported statistically significant improvement when compared to baseline.

Meta-analysis

Of the included 10 studies, we could identify only three studies (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010) that were homogenous in outcome measures and timelines with sufficient data for meta-analysis. Together, these studies enroled 156 children in the age group 6–16 years, 28 were reported as dropouts, and analysis was performed on 128 participants. The selected studies for meta-analysis had more than two groups and various combinations of Ayurvedic intervention in the form of procedural and non-procedural were used. Hence, considering the complexity of the Ayurveda approach, within each study we decided to combine all the different groups of Ayurvedic intervention as a single unit to compare with placebo to conclude the efficacy of Ayurveda intervention. We acknowledge the substantial differences in treatment approach (as detailed in the description of included studies section). It was felt by the reviewers that pooling was appropriate since, overall, the included studies could be interpreted as addressing the ongoing controversy of whether Ayurvedic intervention has any efficacy over placebo. The evidence generated from the meta-analysis is presented in the forest plot from Figures 3.1.1–3.1.4.

Comparison: Ayurveda versus Placebo
DSM-IV Criteria Symptoms

Inattention. Three studies were included (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010; total n = 87) and the pooled effect estimate shows improvement, which is statistically significant (SMD = −1.31; 95% CI −2.08 to −0.55; $P = 0.0008$, $I^2 = 58\%$).

Hyperactivity. Three studies were included (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010; total n = 71) and the pooled effect estimate shows improvement, which is statistically significant (SMD = −2.22; 95% CI −3.51 to −0.93; $P = 0.0007$, $I^2 = 71\%$).

Impulsivity. Three studies were included (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010; total n = 52) and the pooled effect estimate shows improvement, which is statistically significant (SMD = −2.14; 95% CI −3.76 to −0.52; $P = 0.009$, $I^2 = 59\%$).

Attention Span—Change in Coefficient of Division of Attention. Ojha et al. (2007) assessed statistically significant improvement while Singhal et al. (2010) and R. Raut and A. Kumar, unpublished data (2011) showed changes that were statistically non-significant. The pooled effect estimate of all three studies shows no improvement on attention span (n = 128, SMD = −1.03; 95% CI −2.33 to 0.28; $P = 0.12$, $I^2 = 90\%$).

Reaction Time

Auditory Reaction Time. Two studies were included (R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010; total n = 88) and the pooled effect estimate favours Ayurveda intervention over placebo, which is statistically significant (SMD = −0.94; 95% CI −1.41 to −0.46; $P = 0.0001$, $I^2 = 0\%$).

Visual Reaction Time. Two studies were included (R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010; total n = 88) and the pooled effect estimate favours Ayurveda intervention over placebo, which is statistically significant (SMD = −0.79; 95% CI −1.26 to −0.32; $P = 0.0009$, $I^2 = 0\%$).

Total Reaction Time. Three studies were included (Ojha et al., 2007; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010; total n = 128) and the pooled effect estimate favours Ayurveda intervention over placebo, which is statistically significant (SMD = −1,11; 95% CI −1.66 to −0.57; $P < 0.0001$, $I^2 = 47\%$).

Finger Dexterity Test

Time Taken for Right Hand. Ojha et al. (2007) (n = 40, SMD = −3.55; 95%CI −4.58 to −2.52) and R. Raut and A. Kumar, unpublished data (2011) (n = 45, SMD = −0.92; 95%CI −1.57 to −0.26) assessed statistically significant improvement while Singhal et al. (2010) (n = 43, SMD = −0.60; 95%CI −1.28 to 0.08) showed changes which were statistically non-significant. The pooled effect estimate of all three studies favours Ayurveda intervention over placebo (n = 128, SMD = −1.64; 95% CI −3.16 to −0.11; $P = 0.04$, $I^2 = 92\%$).Number of Errors for Right Hand

Ojha et al. (2007) (n = 40, SMD = −1.71; 95%CI −2.45 to −0.98) assessed statistically significant improvement while Singhal et al. (2010) (n = 43, SMD = −0.50; 95%CI −1.17 to 0.18) and R. Raut and A. Kumar, unpublished data (2011) (n = 45, SMD = −0.48; 95%CI −1.11 to 0.14) showed changes which were statistically non-

Table 4.3
Comparison—Ayurveda versus Ayurveda.

Domain	Studies	No. of participants	Statistical method	Effect size
1. ADHD rating scale				
Total ADHD score	Gupta and Mamidi (2013)	20	Mean Difference (IV, fixed, 95% CI)	1.70 [−2.74, 6.14]

ADHD, attention deficit hyperactivity disorder.

Study or Subgroup	Ayurveda Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
3.1.1 Inattention									
Ojha et al. (2007)	-0.9918	0.3282	17	-0.58	0.4914	16	37.9%	-0.97 [-1.69, -0.24]	2007
Singhal et al. (2010)	-1.12	0.4348	18	-0.25	0.1965	9	28.2%	-2.25 [-3.28, -1.22]	2010
R. Raut and A. Kumar, unpublished data (2011)	-1.285	0.6531	18	-0.56	0.9639	9	33.9%	-0.92 [-1.76, -0.07]	2011
Subtotal (95% CI)			**53**			**34**	**100.0%**	**-1.31 [-2.08, -0.55]**	
Heterogeneity: Tau² = 0.27; Chi² = 4.78, df = 2 (P = 0.09); I² = 58%									
Test for overall effect: Z = 3.36 (P = 0.0008)									
3.1.2 Hyperactivity									
Ojha et al. (2007)	-1.2935	0.6414	17	-0.575	0.4942	18	41.1%	-1.23 [-1.96, -0.50]	2007
Singhal et al. (2010)	-1.245	0.4005	12	-0.095	0.1364	6	28.2%	-3.21 [-4.75, -1.67]	2010
R. Raut and A. Kumar, unpublished data (2011)	-1.425	0.5744	12	-0.095	0.1364	6	30.7%	-2.63 [-4.01, -1.25]	2011
Subtotal (95% CI)			**41**			**30**	**100.0%**	**-2.22 [-3.51, -0.93]**	
Heterogeneity: Tau² = 0.91; Chi² = 6.95, df = 2 (P = 0.03); I² = 71%									
Test for overall effect: Z = 3.38 (P = 0.0007)									
3.1.3 Impulsivity									
Ojha et al. (2007)	-1.1118	0.6359	17	-0.4935	0.3394	17	50.8%	-1.18 [-1.92, -0.45]	2007
Singhal et al. (2010)	-1.24	0.1706	6	-0.03	0.3675	3	18.8%	-4.41 [-7.47, -1.36]	2010
R. Raut and A. Kumar, unpublished data (2011)	-1.085	0.4133	6	-0.03	0.3675	3	30.4%	-2.34 [-4.34, -0.34]	2011
Subtotal (95% CI)			**29**			**23**	**100.0%**	**-2.14 [-3.76, -0.52]**	
Heterogeneity: Tau² = 1.20; Chi² = 4.88, df = 2 (P = 0.09); I² = 59%									
Test for overall effect: Z = 2.59 (P = 0.009)									

Test for subgroup differences: Chi² = 1.85, df = 2 (P = 0.40), I² = 0%

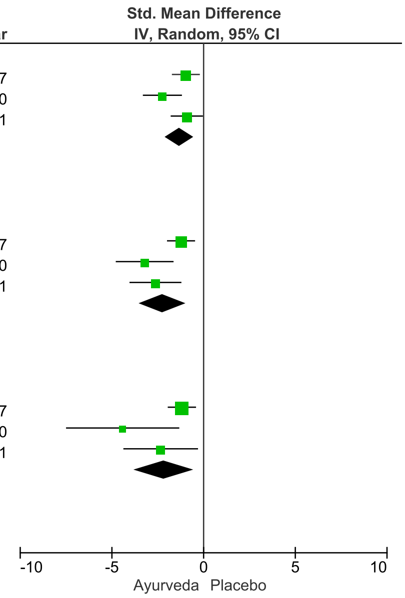


Fig. 3.1.1. Forest plot of comparison: Ayurveda versus placebo, outcome: DSM-IV criteria symptoms.

significant. The pooled effect estimate of all three studies favours Ayurveda intervention over placebo (n = 128, SMD = -0.88; 95% CI -1.65 to -0.11; $P = 0.02$, $I^2 = 74\%$).Time Taken for Left Hand

Ojha et al. (2007) (n = 40, SMD = -1.78; 95%CI -2.52 to -1.04) assessed statistically significant improvement while Singhal et al. (2010) (n = 43, SMD = -0.52; 95%CI -1.20 to 0.16) and R. Raut and A. Kumar, unpublished data (2011) (n = 45, SMD = -0.47; 95%CI -1.10 to 0.16) showed changes, which were statistically non-significant. The pooled effect estimate of all three studies favours Ayurveda intervention over placebo (n = 128, SMD = -0.90; 95% CI -1.71 to -0.10; $P = 0.03$, $I^2 = 76\%$).Number of Errors for Left Hand

All the three included studies Ojha et al. (2007) (n = 40, SMD = -1.94; 95%CI -2.70 to -1.17), Singhal et al. (2010) (n = 43, SMD = -0.85; 95%CI -1.54 to -0.16), and R. Raut and A. Kumar, unpublished data (2011) (n = 45, SMD = -0.90; 95%CI -1.55 to -0.25) showed changes, which were statistically non-significant. The pooled effect estimate of all three studies favours Ayurveda intervention over placebo (n = 128, SMD = -1.20; 95% CI -1.87 to -0.54; $P = 0.0004$, $I^2 = 63\%$).

Adverse Events

Adverse events or effects or toxicity associated with procedural and non-procedural Ayurveda intervention were also evaluated based on the included articles. Only four trials (Bhalerao et al., 2013; Mahapatra and Mahapatra, 2015; R. Raut and A. Kumar, unpublished data, 2011; Singhal et al., 2010) reported 'no adverse events' narratively while in the rest of the six studies it was not evaluated. Out of 10 included studies, seven studies reported drops outs but only two of these documented reasons for dropouts (Bhalerao et al., 2013; Kalra et al., 2002), four of them reported 'discontinued the treatment' and one study as 'drop out' with no further information. Hence, it is difficult to infer whether the dropouts were due to adverse events or lack of drug effect, unpalatability of Ayurveda formulation, or related to Ayurvedic procedures.

Discussion

Summary of Main Results

We found 10 trials, four tested four different types of Ayurvedic formulations against the placebo, three tested multiple combinations of Ayurvedic intervention (procedural and non-procedural) against the placebo, one tested ayurvedic formulation with conventional medicine and two studies were the comparative trials of the Ayurvedic formulation. These studies enroled 385 participants and the duration of treatment ranged from 30 days to 6 months. In addition, the time points for the assessment of the effect of the intervention for the trials were not uniform. All of the included studies took place in India. The participants enroled were of age 5–16 years.

The different type of interventions was tested and made it difficult to combine the data. In addition, the outcome measures were heterogeneous among the studies. We could identify only three studies that were homogeneous in outcome measures and had sufficient data for meta-analysis. Hence, we excluded the rest of the trials due to heterogeneity in outcome measures and lack of presentation of continuous data with means, standard deviation (or standard errors), and the number of participants. Also, in this systematic review, there is a lack of replicable evidence because no single trial compared the same Ayurveda intervention and control.

Thus, the effectiveness of Ayurvedic intervention may not be conclusive but focusing on the evidence obtained from three trials included in the meta-analysis shows that Ayurveda interventions have their

Study or Subgroup	Ayurveda Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Ojha et al. (2007)	-0.065	0.0242	20	-0.0125	0.0158	20	32.0%	-2.52 [-3.37, -1.67]	2007
Singhal et al. (2010)	-0.0735	0.0941	31	-0.03	0.1102	12	33.8%	-0.43 [-1.11, 0.24]	2010
R. Raut and A. Kumar, unpublished data (2011)	-0.045	0.0346	30	-0.03	0.1102	15	34.2%	-0.21 [-0.84, 0.41]	2011
Total (95% CI)			**81**			**47**	**100.0%**	**-1.03 [-2.33, 0.28]**	
Heterogeneity: Tau² = 1.19; Chi² = 20.27, df = 2 (P < 0.0001); I² = 90%									
Test for overall effect: Z = 1.54 (P = 0.12)									

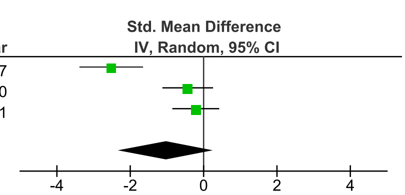


Fig. 3.1.2. Forest plot of comparison: Ayurveda versus placebo, outcome: Attention span—changes in coefficient of division of attention.

Study or Subgroup	Ayurveda Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
3.3.1 Auditory reaction time									
Singhal et al. (2010)	-0.6765	0.5153	31	-0.14	0.6553	12	46.5%	-0.95 [-1.65, -0.25]	2010
R. Raut and A. Kumar, unpublished data (2011)	-0.69	0.5444	30	-0.14	0.6535	15	53.5%	-0.93 [-1.58, -0.28]	2011
Subtotal (95% CI)			**61**			**27**	**100.0%**	**-0.94 [-1.41, -0.46]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%									
Test for overall effect: Z = 3.85 (P = 0.0001)									
3.3.2 Visual reaction time									
Singhal et al. (2010)	-0.5848	0.4886	31	-0.19	0.6312	12	47.1%	-0.73 [-1.42, -0.04]	2010
R. Raut and A. Kumar, unpublished data (2011)	-0.525	0.1744	30	-0.19	0.6312	15	52.9%	-0.85 [-1.50, -0.20]	2011
Subtotal (95% CI)			**61**			**27**	**100.0%**	**-0.79 [-1.26, -0.32]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.80); I² = 0%									
Test for overall effect: Z = 3.31 (P = 0.0009)									
3.3.3 Total reaction time									
Ojha et al. (2007)	-0.655	0.1373	20	-0.445	0.1001	20	31.1%	-1.71 [-2.45, -0.98]	2007
Singhal et al. (2010)	-0.6297	0.4481	31	-0.19	0.6556	12	33.2%	-0.84 [-1.53, -0.15]	2010
R. Raut and A. Kumar, unpublished data (2011)	-0.65	0.4585	30	-0.19	0.6655	15	35.6%	-0.85 [-1.49, -0.20]	2011
Subtotal (95% CI)			**81**			**47**	**100.0%**	**-1.11 [-1.66, -0.57]**	
Heterogeneity: Tau² = 0.11; Chi² = 3.80, df = 2 (P = 0.15); I² = 47%									
Test for overall effect: Z = 3.98 (P < 0.0001)									
Test for subgroup differences: Chi² = 0.76, df = 2 (P = 0.68), I² = 0%									

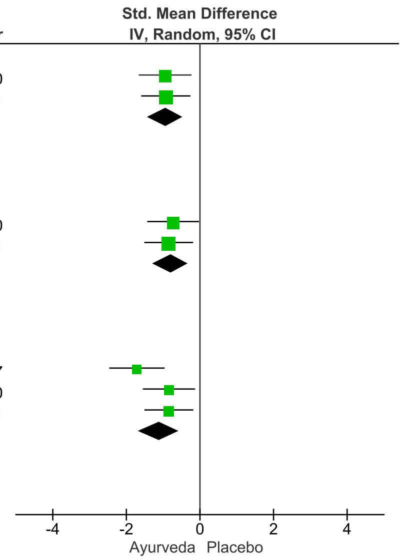


Fig. 3.1.3. Forest plot of comparison: Ayurveda versus placebo, outcome: reaction time.

benefit in reducing symptoms of ADHD. Compared with placebo, Ayurvedic interventions showed statistically significant improvement in reducing inattention, hyperactivity, and impulsivity scores of ADHD symptoms at the end of treatment. The Ayurveda treatment appeared to be effective for improving reaction time and finger dexterity test. The pooled treatment effect of Ayurveda intervention showed no benefit on Attention span. No adverse events were reported in any of these three studies included for meta-analysis. Furthermore, the findings of this review should be interpreted with caution due to the small sample sizes and generally low methodological qualities of the included studies.

Quality of the Evidence

The undertaken systematic review has several methodological limitations. First, most of the included studies provided inadequate information on how the random sequence was generated and concealed. This trail raises some concerns about selection bias. Only two studies have presented the baseline data with a mean (or median), standard deviation (or standard error), confidence interval, and the number of participants for comparison in groups. Secondly, only five of the 10 studies used the double-blinding method which was merely stated as a statement in these studies. There was no information available on outcome assessors whether they were blinded or non-blinded. Hence, detection bias may be a problem. Thirdly, most of the included trials have a small sample size which may lead to diminished power to detect an actual treatment effect. Also, in addition to poor quality of randomisation and blinding, it may be associated with exaggerated effects of the intervention due to systematic error (bias) occurring at different stages of the study such as selection of the patients, administration of treatment, and assessment of outcomes. Fourth, six

Study or Subgroup	Ayurveda Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
3.4.1 Time taken for right hand									
Ojha et al. (2007)	-1.09	0.3789	20	-0.08	0.1086	20	31.4%	-3.55 [-4.58, -2.52]	2007
Singhal et al. (2010)	-0.8681	1.001	31	-0.09	1.8193	12	34.2%	-0.60 [-1.28, 0.08]	2010
R. Raut and A. Kumar, unpublished data (2011)	-0.915	1.0076	30	-0.09	0.5521	15	34.4%	-0.92 [-1.57, -0.26]	2011
Subtotal (95% CI)			**81**			**47**	**100.0%**	**-1.64 [-3.16, -0.11]**	
Heterogeneity: Tau² = 1.65; Chi² = 23.80, df = 2 (P < 0.00001); I² = 92%									
Test for overall effect: Z = 2.10 (P = 0.04)									
3.4.2 No. of errors for right hand									
Ojha et al. (2007)	-5.4	3.3854	20	-0.9	1.3338	20	31.9%	-1.71 [-2.45, -0.98]	2007
Singhal et al. (2010)	-1.621	2.9661	31	-0.23	2.0482	12	33.4%	-0.50 [-1.17, 0.18]	2010
R. Raut and A. Kumar, unpublished data (2011)	-1.605	2.8288	30	-0.23	2.6987	15	34.6%	-0.48 [-1.11, 0.14]	2011
Subtotal (95% CI)			**81**			**47**	**100.0%**	**-0.88 [-1.65, -0.11]**	
Heterogeneity: Tau² = 0.34; Chi² = 7.65, df = 2 (P = 0.02); I² = 74%									
Test for overall effect: Z = 2.25 (P = 0.02)									
3.4.3 Time taken for left hand									
Ojha et al. (2007)	-1.2	0.2875	20	-0.47	0.491	20	31.9%	-1.78 [-2.52, -1.04]	2007
Singhal et al. (2010)	-0.7455	1.1747	31	-0.12	1.1989	12	33.5%	-0.52 [-1.20, 0.16]	2010
R. Raut and A. Kumar, unpublished data (2011)	-0.775	1.3159	30	-0.12	1.4852	15	34.6%	-0.47 [-1.10, 0.16]	2011
Subtotal (95% CI)			**81**			**47**	**100.0%**	**-0.90 [-1.71, -0.10]**	
Heterogeneity: Tau² = 0.38; Chi² = 8.32, df = 2 (P = 0.02); I² = 76%									
Test for overall effect: Z = 2.21 (P = 0.03)									
3.4.4 No. of errors for left hand									
Ojha et al. (2007)	-5.8	2.6675	20	-1.3	1.8093	20	31.2%	-1.94 [-2.70, -1.17]	2007
Singhal et al. (2010)	-2.2584	2.8181	31	-0.09	1.2852	12	33.6%	-0.85 [-1.54, -0.16]	2010
R. Raut and A. Kumar, unpublished data (2011)	-2.255	2.7618	30	-0.09	1.2145	15	35.2%	-0.90 [-1.55, -0.25]	2011
Subtotal (95% CI)			**81**			**47**	**100.0%**	**-1.20 [-1.87, -0.54]**	
Heterogeneity: Tau² = 0.21; Chi² = 5.35, df = 2 (P = 0.07); I² = 63%									
Test for overall effect: Z = 3.57 (P = 0.0004)									
Test for subgroup differences: Chi² = 1.09, df = 3 (P = 0.78), I² = 0%									

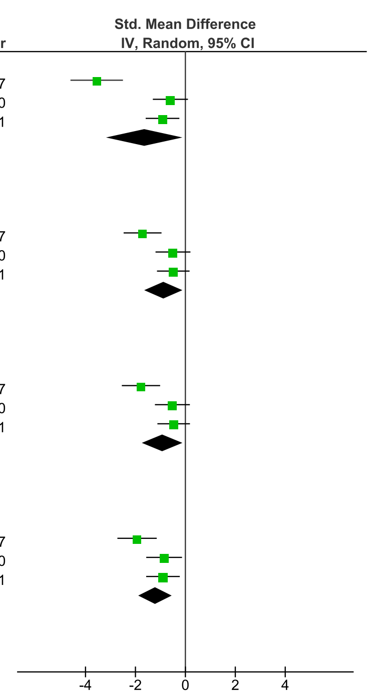


Fig. 3.1.4. Forest plot of comparison: Ayurveda versus placebo, outcome: finger dexterity test.

of 10 included trials reported > 5% dropout rate and detailed information on reasons for dropouts was available in only two studies. Participants with dropouts or lost to follow-up were excluded from analysis in most of the studies. This may be associated with the exaggerated effects of the interventions. Fifth, the assessed outcome parameter was not uniform and only three studies reported the same outcome measures with the same measurable timelines and hence were included in the meta-analyses. So, we were unable to detect the publication bias. The trials identified in this review took place in India, which may compromise the generalisability of the results. The above concerns limits our ability to draw reliable conclusions regarding the effectiveness of the traditional Ayurveda treatment for ADHD. Although it does not mean that the treatment is not safe and effective, it might indicate that the effectiveness and safety have not been investigated adequately.

Conclusions

Implication for Practice

Randomised, double-blind, placebo-controlled trials show the effectiveness of Ayurveda intervention (procedural and non-procedural) over placebo for children and adolescents with ADHD. However, there is a lack of replicable evidence because no trial compared the same Ayurvedic formulation with placebo or conventional treatment.

Implication for Research

There is a need for randomised trials to adhere and comply with standard reporting guidelines as recommended in the CONSORT statement. The studies should enrol an adequate number of participants and use valid methods of random allocation and sequence concealment. Even if the participants or treating physician cannot be blinded considering the complexity of Ayurveda treatment involving both procedural and non-procedural intervention in clinical trials, outcome assessors should be blinded to avoid detection bias. Intention to treat analysis should be performed on all outcomes and all trial data should be made easily accessible. A minimum requirement should be that all data should at least be presented in numeric form. In addition, continuous data should be presented with mean, standard deviations (or standard errors), and the number of participants. Data form graphs, a *P*-value of differences, and statements of significant or non-significant differences are of limited value. Moreover, the trial should use standardised outcome measures which are reliable and validated. Also, there is a need to develop standard treatment duration for interventions to assess the efficacy and need to be followed by long-term follow-up to check whether the effect of the intervention is sustained after the completion of treatment. A good practice of recording and reporting adverse effects should also be used in future trials. Finally, considering the intricacies of Ayush systems, there is a need of developing Reporting Guidelines for Trials in Ayurveda in accordance with CONSORT similar to herbal extension, etc.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: All the authors are working as Research officers for this council—Central Council for Research in Ayurvedic Sciences (CCRAS), New Delhi. This review was funded by CCRAS, Ministry of AYUSH, Government of India.

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Appendix 1

Search terms.

Intervention	Disorder
Ayurved*	ADHD
Ayurvedic medicine	ADHD
Medicine, Ayurveda	Attention deficit hyperactivity disorder
Ayurveda	Attention deficit disorder
Ayurvedic	Attention deficit-hyperactivity disorder
Hindu medicine	Hyperkinetic syndrome
Ayurveda intervention	Attention deficit disorder with hyperactivity
Ayurveda therapy	
Ayurveda herbs	
Ayurvedic drugs	
Ayurvedic formulation	
Ayurveda plants	

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