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RESEARCH ARTICLE

Clinical Efficacy and Safety of *Sarasvata Ghrita* in the Management of Cognitive Deficit–A Prospective Open Label Study

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ABSTRACT

Introduction: Cognitive deficit describes deficit in global intellectual performances. It is a condition which usually begins in childhood, and the patient shows significant limitations in their ability to learn and function. Its cause may be congenital or may occur due to environmental factors such as brain injuries, neurological disorders, or mental illness, etc. The cognitive deficit can be correlated with *Budhimandyata* in *Ayurveda.*

Objective: To evaluate the efficacy and safety of *Sarasvata Ghrita* in the patients suffering from cognitive deficit.

Materials and methods: A prospective, open-label study was carried out at Advanced Center for *Ayurveda* in Mental Health and Neurosciences, Bengaluru (ACAMH and NS). Fortyfive cognitive deficit children satisfying the selection criteria were selected from the out patient department (OPD) of ACAMH and NS, NIMHANS, Bangalore, were administered *Sarasvata Ghrita* (6 gms) twice daily before food with lukewarm water for three months. Assessment parameters Intelligent Quotient (IQ) by Binet Kamat test (BKT), mini mental state examination (MMSE), abnormal behavior check (ABC) and parental perception evaluation were assessed at the baseline, on the 60th day and on the 90th day. Paired sample t-test was used to compare mean change from baseline to the 84th day. A p-value of <0.05 was considered significant.

Results: At the end of the 90th Day, compared with baseline statistically, significant improvement was observed in BKT IQ score, MMMSE score, ABC list score and the parental perception score ($p < 0.001$). Hematological and biochemical laboratory parameters were also assessed before and after the trial (there was not any significant change in them).

Conclusion: *Sarasvata Ghrita* taken internally by cognitive deficit children is helpful in improving their IQ, MMSE and ABC scores. It was also found safe as it does not produce any adverse event.

Keywords: *Budhimandyta*, Cognitive deficit, *Sarasvata Ghrita*

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INTRODUCTION

Cognitive deficit or cognitive impairment is an inclusive term to describe any characteristic that acts as a barrier to the cognition process.[1] The term may describe deficits in global intellectual performance, such as mental retardation. Learning disorders, dyslexia are some specific types of the cognitive deficits, the other may be drug induced cognitive/memory impairment such as cognitive impairment caused by glucocorticoids, and benzodiazepines.[2]

It is an intellectual impairment which begins in childhood due to which child shows significant limitations in their ability to learn and function. It may range from vast intellectual impairment with minimal functioning to mild impairment in specific tasks. The areas which may get affected in cognitive deficit may be attention, decision making, perception, judgment, reasoning, memory, language, general knowledge and many more. In children, the impairment leads to poor orientation in academic tasks, school work will be disorganized, and frequently incomplete and are prone to behavioral disturbances. The cause of Cognitive deficits may be congenital or may be caused by environmental factors such as brain injuries, neurological disorders or mental illness.[3,4]

Buddhimandyata (mental retardation) is a condition explained under certain *Balgrahas* described in various Ayurvedic classics including *Kashyap samhita,*[5] *Madhava Nidana,*[6] *Susruta samhita,*[7] etc. *Buddhimandyata* (mental retardation) is a disease condition where the manah or psyche and '*Manovahastrotas*' get affected. There are three functional categories of *Manas*, i.e., *Satva*, *Raja* and *Tama*.

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In *Balbuddhimandyata tamoguna* is found to be profoundly vitiated as compared to *Rajah and Satvaguna*. It is also believed that there is a significant deficit of *Sattva Guna* in both qualitative and quantitative form in these children. Due to this reason, the children suffering from *Buddhimandya* are unable to perform the intellectual functions in comparison to their normal counterpart.

Some of the causative factors for *Buddhimandyata*, mentioned in various Ayurvedic classics includes *Dauhridd Avamanana* (non-fulfillment of desires of pregnant women), *Beejadosa* (genetic factor), *Apathya Ahara-Vihara* (incompatible diet and lifestyle), *Vegadharana* (suppression of natural urges), *Yonidosa* (gynecological disorders) and *Nastikata* (non-belief on God) leads to vitiation of vatadosha thus gives rise to various fetal abnormalities like *Kubja, Kuni, Pangu, Jada/Mandabudhi,* etc. [8,9]

Coming to the management part, no adequate treatment for *Buddhimandyata* (cognitive deficit) is available in conventional system of medicine, in present scenario. However, Ayurveda has emphasized the role of medhya rasayanas indifferent psychiatric disorders including *Buddhimandyata* (mental retardation). In light of above, the present clinical study has been conducted to evaluate the role of *Sarasvata Ghrita* for its efficacy as well as safety in the children who were presented with mild to moderate cognitive deficit.

OBJECTIVES

To evaluate the efficacy and safety of *Sarasvata Ghrita* in the management of cognitive deficit.

MATERIALS AND METHODS

Study Design

The study was an interventional, open-label executed at ACAMH and NS, NIMHANS, Bangalore, and a peripheral unit of CCRAS, Ministry of AYUSH. The study was approved by Institutional Ethics Committee and was done in accordance with WHO–Good Clinical Practices Guidelines. The Clinical trial has also been registered in Clinical Trial Registry of India (CTRI/2014/03/006656)

Study Participants

A total of 45 participants were enrolled in the trial, from ACAMH and NS. Patients were screened in accordance with the inclusion and exclusion criteria mentioned in the protocol. All the 45 patients following the screening criteria were recruited in the study after obtaining the written informed consent.

Inclusion Criteria

Children of either sex aged between 8–13 years with IQ 63–80 as per Binet Kamat test (BKT), willing and able to participate for three months (consent was obtained from parents/guardians.

Exclusion Criteria

Children with severe infection and/or clinically significant hepatic, respiratory, renal, cardiac, or hematological disorders were excluded from the study. Also those children with abnormal laboratory values at admission like serum creatinine >0.2 mg/dl, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) >3 times of their upper limit; serum bilirubin or alkaline phosphatase >1.5 times the upper limit were also excluded. Patient's guardian who cannot be relied upon to comply with the test procedures or who were unwilling to give informed consent were also not included for the study. Those children were also removed from the study those were having any intramuscular, intravenous corticosteroids within four weeks prior to study entry. Likewise, children having a history of recent and clinically significant drug abuse, preexisting blood dyscrasias, poorly controlled epilepsy, history of head injury, those to whom BKT cant not be administered were also excluded, in whom another investigational drug was used within three months were also excluded. Children who were unlikely to comply with the protocol, e.g., bone marrow hypoplasia, leucopenia, thrombocytopenia were also not included in the study.

Study Interventions

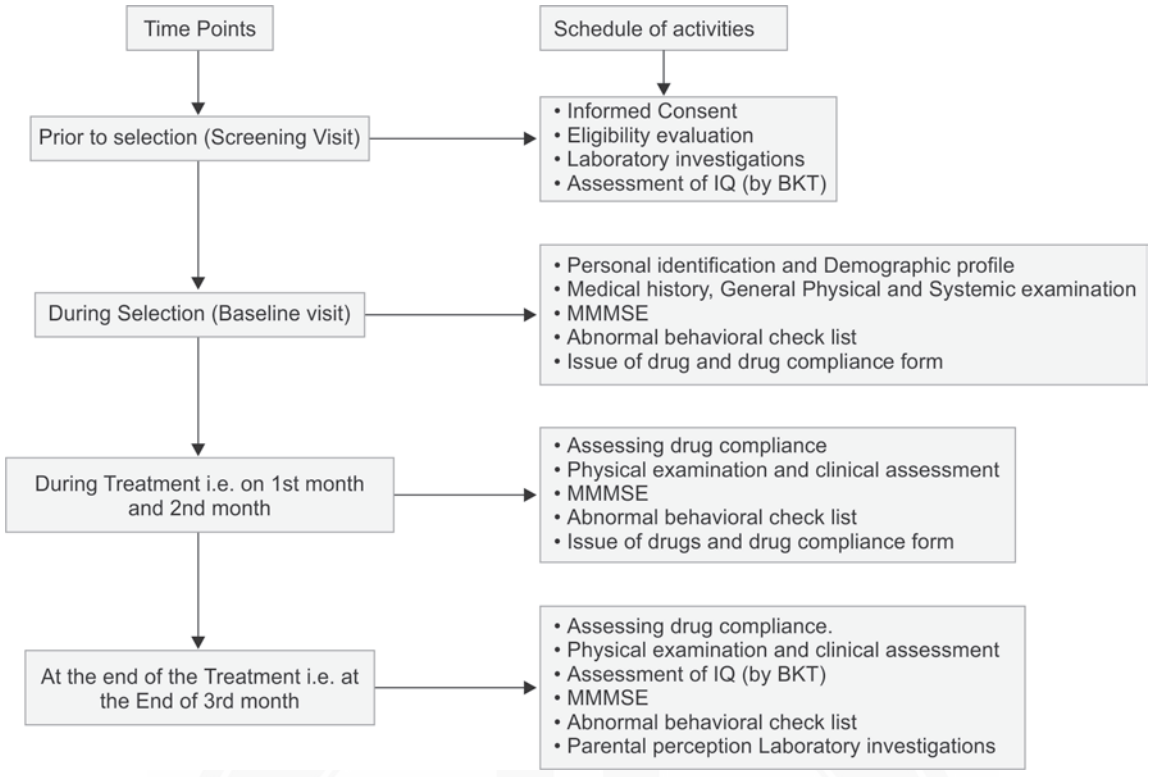
The study medications included *Sarasvata Ghrita*[10] in the dose of 6 gms twice a day before food with warm water (ushnodaka) for a period of three months. It was procured from GMP certified *Ayurvedic* pharmaceutical industries and standardized following the standard laid in Ayurvedic Pharmacopoeia of India.

Study Procedure

On the enrolment day at baseline (Visit 1), the patient's demographic profile, medical history, general physical and systemic examination were recorded. Subsequent visits were planned at an interval of one month, 2nd month, and 3rd month. Patients were assessed and given study medications at each subsequent visit. Details of clinical assessment and study schedule are given in Flow Chart 1.

At the study site data of all the patients were recorded in pre-designed case report forms (CRFs) and was also

Flow Chart 1: Study schedule



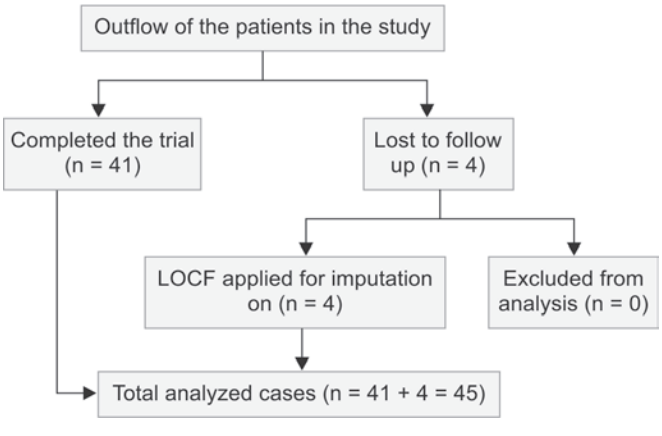
entered in electronic formats (e-formats) designed in ms-excel with many data validation checks to ensure correct data entry. The e-formats and xerox of the CRFs along with the laboratory investigations reports of the patients were sent by the participating centers to the council's headquarters on weekly basis for the purpose of clinical trial monitoring.

Out of the total 45 patients enrolled in the study, four dropped out during the course of the study. Imputation was applied on those four patients. Hence, data of a total 45 patients was used for statistical analysis (Flow Chart 2).

Outcomes

The primary outcome measure was mean change in IQ (by BKT). The secondary outcome measures were a change in modified child mini-mental scale examination (MMMSE), abnormal behavioral test and parental perception evaluation.

Flow Chart 2: Outflow of the patients in the study



Statistical Analysis

Primary outcome and secondary outcome measures were analyzed as mean change in the response from baseline to 3rd month by using paired t-test. A p-value of < 0.05 was considered significant. Relief was assessed as a percentage change in terms of presence of any symptom at baseline and at 3rd month. All statistical analysis was performed using SPPS version 15.0

RESULTS

Data of 45 patients (26 male and 19 female) was used for statistical analysis. Out of which maximum patients 30 (67.7%) were in the age group of 11–13 years. Table 1 shows the demographic profile of the patients.

Among the total patients 29 (64.4%) patients were of *Vata-pittaja Sharirik Prakriti*. Socio-economic condition was good (above poverty line) in 22 (48.9%) patients. Maximum number of patients was residing in urban area 31 (68.9%). Physical parameters of the patients recorded at baseline of the patients are shown in Table 2.

Effect of the study medications was assessed by paired t-test on IQ (by BKT) (Graph 1), MMMSE (Graph 2) and abnormal behavioral test (Graph 3) compared at baseline and at 90th day. Table 3 shows the results of the analysis on those parameters. Parental perception evaluation

Table 1: Demographic profile of the patients

Demographic profile (n = 45)	
Age group	
08–10	15 (33.3)
11–13	30 (66.7)
Sex	
Male	26 (57.7)
Female	19 (42.3)
Religion	
Hindu	37 (82.2)
Muslim	7 (15.6)
Christian	1 (2.2)
Socio-economic status	
Above poverty line	22 (48.9)
Below poverty line	23 (51.1)
Habitat	
Urban	31 (68.9)
Semi-urban	8 (17.8)
Rural	6 (13.3)
Sharirik prakriti	
Vata-Pittaja	29 (64.4)
Vata-Kaphaja	10 (22.2)
Pitta-Kaphaja	06 (13.3)

Values are expressed as n (%)

Table 2: Distribution of patients according to physical parameters

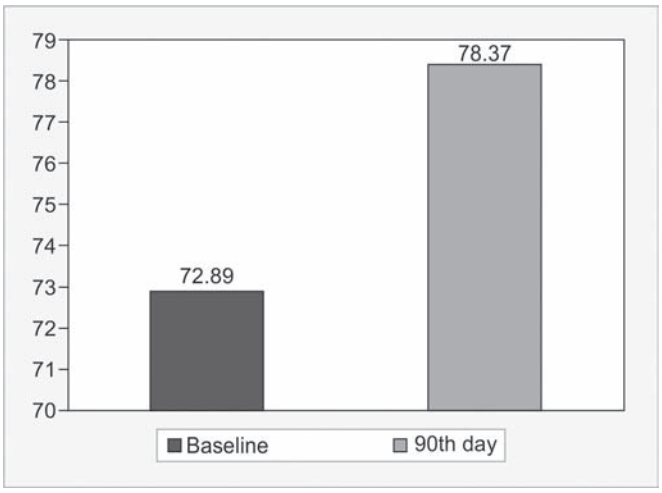
Physical parameters (n = 45)	
Height (m)	1.381 (0.1230)
Weight (kg)	30.62 (8.814)
Respiratory rate (per minute)	19.47 (3.108)
Pulse rate (per minute)	93.16 (5.584)
Blood pressure (mm Hg)	
Systolic	96.04 (5.584)
Diastolic	61.62 (2.972)

Values are expressed as mean (sd)

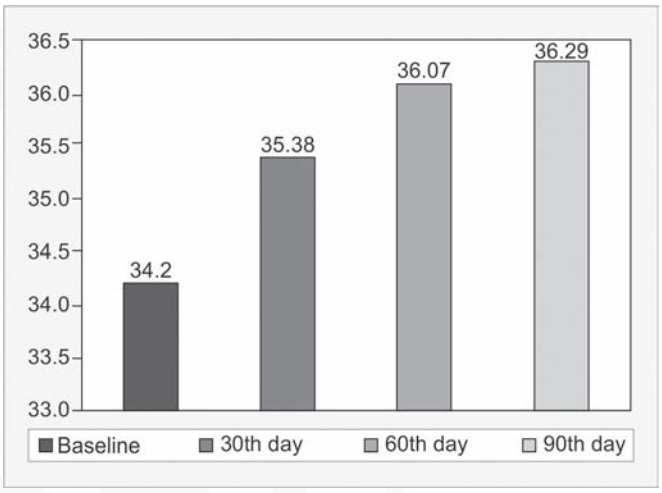
was also assessed after the treatment. Table 4 shows the results of the analysis.

Safety profile

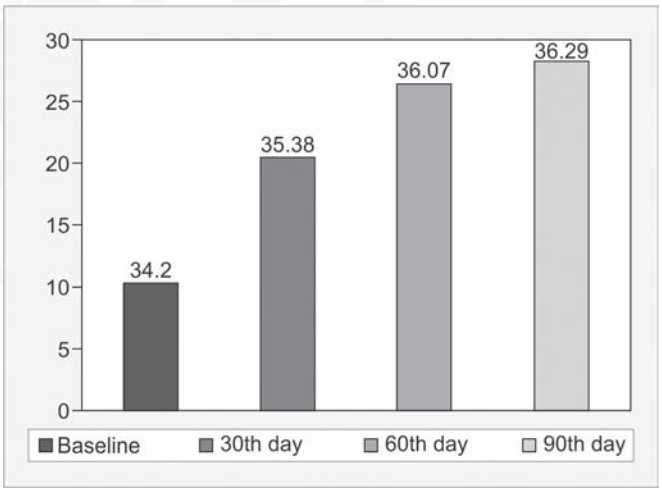
The effect of this treatment on various safety parameters such as liver function tests and renal function tests were assessed on a baseline and on 90th day visit. The values were within limits during the entire trial period (Graphs 4 to 6). Table 5 shows the effect of the drugs on the safety parameters



Graph1: Effect of the treatment on IQ assessed by Binet Kamat Ttest (BKT)



Graph 2: Effect of the treatment on MMMSE score



Graph 3: Effect of the treatment on abnormal behavior checklist score

DISCUSSION

Intelligence, memory and adequate social atmosphere are responsible for the proper development of a child. Many children, particularly those with cognitive deficiency

Table 3: Effect of the treatment on IQ (by BKT), MMMSE and ABT

Parameters (n = 126)	*Baseline*	*30th day*	*60th day*	*90th day*	*$t-value*	*p-value*
IQ (by BKT)	72.89 (5.831)	-	-	78.37 (7.385)	11.215	< 0.001
MMMSE	34.20 (3.027)	35.38 (2.674)	36.07 (1.698))	36.29 (1.471)	6.359	< 0.001
Abnormal behavioral test	27 (22.91)	21.67 (19.42)	17.13 (15.48)	11.22 (9.936)	7.157	< 0.001

Values are expressed as mean (SD), $ compared using paired t-test at baseline and 90th day, *p-value of < 0.05 has been considered as significant

Table 4: Evaluation of parental perception test

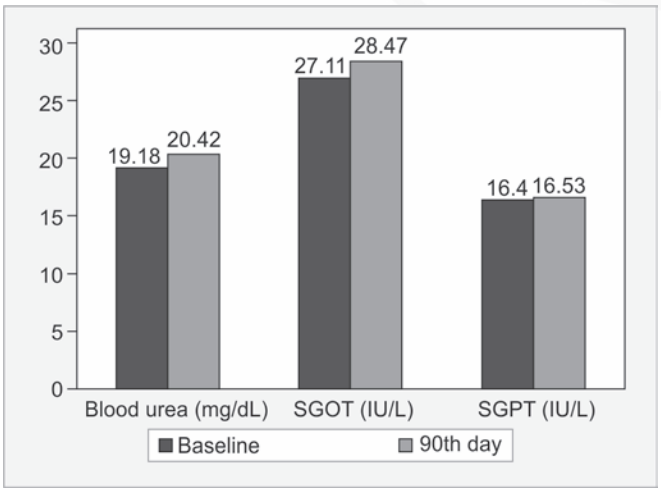
	n	*minimum*	*maximum*	*mean*	*Standard deviation*
Parental perception score	45	10	50	28.41	10.523

Table 5: Effect of the treatment on safety parameters

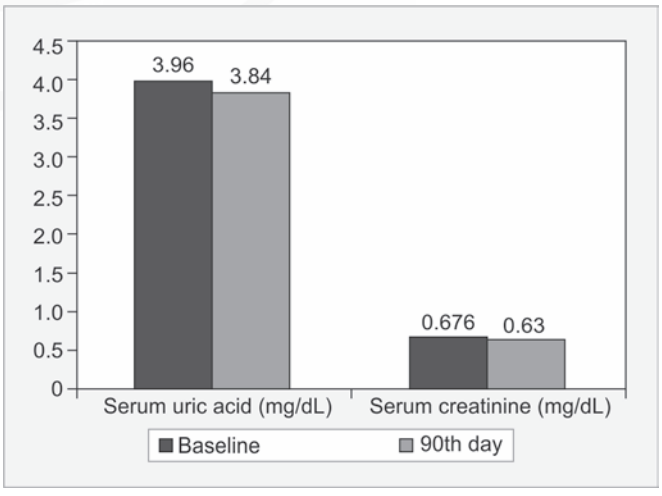
Parameters (n = 45)	*Baseline*	*90th day*	*$t-value*	*p-value*
Blood urea (mg/dL)	19.18 (5.54)	20.42 (6.82)	1.274	0.209
Serum uric acid (mg/dL)	3.96 (1.10)	3.84 (0.93)	0.703	0.486
Serum creatinine (mg/dL)	0.676 (0.45)	0.63 (0.12)	0.643	0.523
SGOT (IU/L)	27.11 (6.02)	28.47 (11.48)	0.851	0.399
SGPT (IU/L)	16.4 (5.53)	16.53 (6.73)	0.140	0.890
Total protein (g/dL)	7.25 (0.42)	7.26 (0.47)	0.029	0.977
S.Albumin (g/dL)	4.46 (0.21)	4.5 (0.25)	0.795	0.431
S.Globulin (g/dL)	2.80 (0.37)	2.76 (0.38)	0.592	0.577
Serum bilirubin (mg/dL)	0.47 (0.19)	0.5 (0.19)	0.838	0.406
Serum alkaline phosphatase (U/L)	279.27 (86.08)	270.82 (86.81)	0.665	0.509

Values are expressed as mean (SD), $ compared using paired t-test at baseline and 90th day, *p-value of < 0.05 has been considered as significant

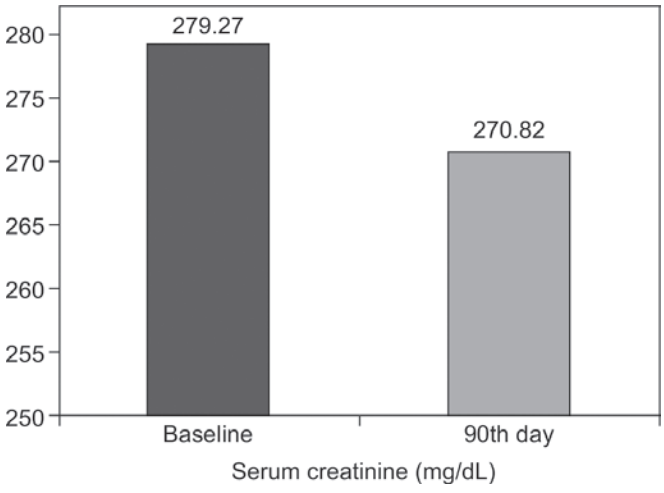
and learning problems are poorly oriented to academic tasks. They lack initiative and perseverance. School work is disorganized and frequently incomplete. There is also evidence that children with learning disabilities pay less attention than normal learners and this cannot be attributed to IQ alone. The IQ alone cannot judge the learning potentiality of a child because, to be a good learner, a child must have less fluctuation of attention, increased power of concentration, spontaneity in word recognition and capacity to memories things quickly and correctly.[11] In this study thus along with BKT IQ scale, modified child MMMSE, Abnormal Behavioral Test, Abnormal Behavior Checklist (ABC) and in the last parental perception evaluation were evaluated. Sarasvataghrita mentioned in *Bhaishajya Ratnavali, swarbheda adhikar*[12] was taken in the study. *Sarasvata Ghrita* a polyherbal medhya compound drug used in traditional medicine for cognition and memory related problems is blended with the drugs



Graph 4: Effect of the treatment on safety parameters (Blood urea, SGOT, SGPT)



Graph 5: Effect of the treatment on safety parameters (Serum uric acid and Serum creatinine)



Graph 6: Effect of the treatment on safety parameters (Serum alkaline phosphatase)

which exerts a variety of pharmacological actions including anti-inflammatory, anti-amyloidogenic, anti-cholinesterase, hypolipidmic and anti-oxidant properties.[13]

In this present study, *Sarasvata Ghrita* was used internally to see the effects on changes of IQ (BKT score), MMSE, ABC and parental perception in the cognitive deficiency children. After a period of 90 days of treatment it was observed that maximum no of children were found to have improved IQ, MMSE, ABC and parental perception. This improvement may be due to breakdown of the pathogenesis of cognitive deficit. *Sarasvata Ghrita* having mostly *Kaphavataghna*[14] properties which assumes that these drugs may clear the pathway of *Manovaha srotas* by which these drugs may help in the improvement of IQ, MMSE and ABC scores. *Vata* is considered as the controller of the mind. So the pacification of the vitiated *Vata* also plays an important role in the action of the drugs. Further, the main content of *Sarasvata Ghrita* is goat's milk, which contains taurine, a type of amino acid which stimulates proliferation and new neuron formation to sustain learning and memory.[15-17]

Sarasvata Ghrita contains drugs which are having *Medhya Prabhava*.[18] It increases the *Satvika* properties of *Mana* which acts as *Samprapti Vighatana*, i.e., breaking of psychopathology to help in the treatment of cognitive deficit.

CONCLUSION

The present study has shown significant result, it can be concluded that *Sarasvata Ghrita* taken internally by cognitive deficit children is helpful in improving their IQ, MMSE and ABC scores. It was also found safe as it does not produce any harmful effect. As *Sarasvata Ghrita* is found effective and safe further studies can also be done where *Sarasvata Ghrita* can be combined with other *Medhya* drugs to get even better results.

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हिंदी सारांश

कॉग्निटिव डेफिसिट के प्रबंधन में 'सारस्वत घृत' की आतुरीय प्रभावकारिता एवं सुरक्षा – ए प्रोस्पेक्टिव ओपन लेबल स्टडी

[1]भोगवल्ली चन्द्रशेखर राव, [2]श्रीनिवास साहू, [3]हेमन्त कुमार गुप्ता, [4]बबीता यादव, [5]श्वेता चौधरी, [6]गुरु चरण भूयान, [7]श्रुति खंडूडी, [8]भगवान सहाय शर्मा, [9]राकेश राणा, [10]रिचा सिंघल

पृष्ठभूमिः कॉग्निटिव डेफिसिट को वैश्विक बौद्धिक निष्पादन की कमी के रूप में परिभाषित किया जाता है। यह वह अवस्था है जो कि बाल्यावस्था में आरंभ होता है एवं रोगी में सीखने एवं कार्य करने की क्षमता में होने वाली कमी को दर्शाता है। यह रोग जन्मजात हो सकता है अथवा पर्यावरणीय कारकों जैसे कि दिमाग पर लगने वाली चोट, तंत्रिका तंत्र संबंधी विकार, या मानसिक बीमारी इत्यादि के कारण भी हो सकता है। आयुर्वेद में कॉग्निटिव डेफिसिट को बुद्धिमंदता के साथ संबंधित किया जा सकता है।

लक्ष्य एवं उद्देश्यः इस अध्ययन का उद्देश्य कॉग्निनिटव डेफिसिट से पीड़ित रोगियों में *सारस्वत घृत* के प्रभावकारिता एवं सुरक्षा का आकलन करना है।

सामग्री एवं विधिः मानसिक स्वास्थ्य एवं स्नायु विज्ञान में आयुर्वेद के उन्नत केन्द्र, बैंगलोर (ए.सी.ए.एम.एच. एवं. एन.एस) में यह अध्ययन किया गया। ए.सी.ए.एम.एच. एवं एन.एस, निम्हांस, बैंगलोर के बहिरंग रोगी विभाग (ओपीडी) से कॉग्निटिव डेफिसिट के निर्धारण की शर्तों को संतुष्ट करने वाले 45 कॉग्निटिव डेफिसिट से पीड़ित बच्चों का चयन किया गया एवं उन्हें तीन महीने तक खाना खाने से पहले दिन में दो बार *सारस्वत घृत* (6 ग्राम) को गुनगुने पानी के साथ दिया गया। मूल्यांकन मापदंडों जैसे कि आईक्यू (बीकेटी), एमएमएसई, एबीसी (असमान्य व्यवहार जांच) एवं अभिभावकों के विचारों का मूल्यांकन 60वें दिन तथा 90वें दिन बेस लाइन के आधार पर किया गया। पेयर्ड सैम्पल टी–टेस्ट का प्रयोग बेसलाइन से 84 वें दिन के मध्य होने वाले परिवर्तन की तुलना हेतु किया गया। पी–वेल्यू <0.05 को महत्वपूर्ण माना गया।

परिणामः 90वें दिन के अंत में बेसलाइन आधारित सांख्यिकी की तुलना करने पर बीकेटी आई क्यू स्कोर, एम.एम.एम.एस.ई (MMMSE) स्कोर, एबीसी सूचीबद्ध स्कोर एवं अभिभावकों के विचार का स्कोर (पी–प्रमाण <0.001) में महत्वपूर्ण सुधार परिलक्षित हुए। हिमेटोलॉजिकल एवं बायो केमिकल लेबोरेट्री मापदंड का आकलन भी परीक्षण के पूर्व एवं पश्चात् (उनमें किसी भी प्रकार का महत्वपूर्ण परिवर्तन नहीं पाया गया) किया गया। उपचार को सुरक्षित पाया गया एवं रोगियों में भी यह प्रभावशाली रहा तथा सभी सुरक्षात्मक मापदंड नियत सीमा के भीतर पाये गये। परीक्षण अवधि के दौरान किसी भी प्रकार का औषध संबंधी दुष्प्रभाव (एडीआर) अथवा प्रतिकूल घटना (एई) परिलक्षित नहीं हुई।

कुंजी शब्दः कॉग्निटिव डेफिसिट, बुद्धिमंदता, सारस्वत घृत।