EFFECT OF POLY HERBAL FORMULATION ON COGNITIVE DEFICITS IN ALUMINIUM-TREATED RATS

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Summary

The aim of the present study is to determine the nootropic effect of Manasamitra Vatakam. The effect of Manasamitra vatakam (MMV) on aluminium-induced cognitive deficits was studied in a one-trial step-through passive avoidance task.
Aluminium chloride (1000 mg/kg/day) was administered to Wistar rats for 40 days to produce significant cognitive deficits ($p<0.05$). Aluminium-treated rats received Manasa Mitra vatakam (50 mg/kg/day) for 20 days starting day 21.
Manasa Mitra vatakam significantly prolonged the shortened latency of step-through induced by aluminium administration [300 (214.17-300) vs 60.5 (16-213); $p<0.05$].
The result suggests that Manasa Mitra vatakam improves learning and memory in aluminium-treated rats.

Keywords: Manasa Mitra vatakam (MMV), aluminium, cognitive deficits, passive avoidance task.

Introduction

Aluminium, a non essential element, is ubiquitous in industrial societies. Usually human exposure is primarily through the diet. The typical adult intake of aluminium estimated to be 3- 12 mg/day according to dietary aluminium studies conducted in various countries [1]. Because of the supposed biological inert properties and its low oral absorption, the aluminium absorption from food stuffs, beverage cans, and drugs and cosmetics cannot be ignored. However, it is well established that aluminium is neurotoxic, and when ingested it can access into the brain.

Some epidemiological studies have suggested possible relationship between the water aluminium content and Alzheimer's disease [2-6]. Whereas in contrast, exposed workers to aluminium showed impairment of cognitive function [7-9]**.** Most recent investigations have demonstrated that aluminium linked to β –amyloid deposition in *in-vivo* and *in-vitro*, induces oxidative stress in the brain [10, 11]**,** increased β amyloid deposit in transgenic mice models [10] induces neuropathological changes in brains [12, 13]**.**

Manasa Mitra vatakam is a herbo mineral drug formulation used in the ayurvedic system of medicines for cognitive deficits. It has claimed to enhance cognition and to ameliorate various forms of brain deficits. MMV contains over 15 different ingredients of which the following are suggested to improve memory functions: Jal-brahmi (*Bacopa monnieri*), Mandookaparni (*Centella asiatica*), Ashwagandha (*Withania somnifera*), Shankapushpi (*Evolvulus alsinoides*), Jatamansi (*Nardostachys jatamansi*), Vacha (*Acorus calamus*), Malkangni (*Celastrus paniculatus*) and Sonth (*Zingiber officinale*).

Aluminium has for long been implicated in clinical conditions like senile and presenile dementia of the Alzheimer type, Guam Parkinsonism - dementia complex, Guam amyotrophic lateral sclerosis and dialysis encephalopathy [14]. It has been shown to produce cognitive deficits in rodents, which can be utilized as models for the above conditions [15, 16]**.** The present study was undertaken to confirm the nootropic effects of Manasa Mitra vatakam in aluminium-induced cognitive deficits in rats.

Materials and methods

Animals: Adult wistar rats of either sex (120 - 170 gms; 6 months) and aged wistar rats of either sex (>220 gms; 12 months) were utilized. The animals were housed two per cage under standard light/dark cycle with food and water provided ad libitum. The experiments were performed between 900 and 1400 hrs.

Drugs: Manasa Mitra vatakam obtained from Ariya vidya sala, Kotakkal Kerala, in a freshly prepared aqueous suspension (50 mg/ml/kg) was administered using an intragastric tube. Aluminium chloride ($AlCl_3.6H_2O$; Sarabhai Chemicals Ltd.) dissolved in distilled water (1000 mg/10ml/kg) was administered orally once daily. The animals consumed 4.14 mmol aluminium/kg/day for 40 days.

Procedure: The rats were weighed before and at the end of the period of drug administration. The spontaneous motor activity (SMA) of the animal was recorded for 30 minutes using the Columbus activity meter. The rota-rod performance of animals was assessed in 5 trials on an Ugo-Basile rota-rod treadmill as described by Dunham and Miya [17].

Passive avoidance paradigm: A one-trial step-through passive avoidance task was carried out as previously described [18]. Rats were administered aluminium chloride (1000 mg/kg/day) once daily using an intragastric tube for a period of 40 days. From day 21 of aluminium treatment, MMV (50 mg/kg/day) was also administered once daily. Control groups received equal volume of vehicle (distilled water). At the end of the treatment schedule, the rats were subjected to passive avoidance paradigm.

The apparatus consisted of two compartments, an illuminated compartment (27 x 30 x 21 cm) and a dark compartment (10 x 30 x 21 cm) having a grid floor through which shock could be delivered. These compartments were separated by a guillotine door. On completion of the treatment schedule each rat was placed in the illuminated compartment and 10 sec. later the door was raised and the latency to enter (LTE) the dark compartment was noted and upon entry, the door was closed and a foot shock administered (100 V for 2 sec.). Twenty-four hours after the acquisition trial the rat was again placed in the illuminated chamber and the response LTE was again noted up to a maximum of 300 sec. (Retention trial). The difference between LTE in the acquisition and retention trial was noted. For those animals that did not enter the dark compartment for 300 sec., score was taken as 300.

Statistical analysis: The results are expressed as Mean ± SEM and Median ± interquartile range. $p<0.05$ was taken as significant. Data was analysed using Student's t-test (unpaired) for weight and SMA, Chi-square test for rota-rod-test and Wilcoxon rank sum test for latencies.

Results

The locomotor activity, rota-rod performance and latencies of various groups are presented in Table 1. There were no significant differences between test and control groups with regard to weight, SMA and rota-rod performance. Administration of $AlCl_3$, MMV or both did not significantly alter these parameters. There was no significant difference in the initial latencies to enter (LTE) between the test and control groups. However, the initial latencies in the aged groups were more, than in the young adult rats. On testing for the retention latency, $AlCl_3$-treated rats showed significantly reduced latency compared to vehicle treated group [61(34 - 217.7) vs 291.5 (190 - 300); $p<0.05$]. On treating $AlCl_3$-treated rats with Manasa Mitra vatakam (MMV) there was a significant improvement in their latencies to enter [300(214.17 - 300) vs 60.5 (16 - 213); $p<0.05$]. This shows that Manasa Mitra vatakam (MMV) was able to reverse the cognitive deficit produced by aluminium.

Table 1: Effect of Manasa Mitra vatakam (MMV) on locomotor activity, rota-rod performance and passive avoidance paradigm in $AlCl_3$-treated rats

Groups	Weight (gms)	Locomotor activity (score)	Rota-rod (%)	Initial latency (sec)	Retention latency (sec)
Vehicle	149.67+10.64	187.83+43.22	83.33	28(23-36.5)	291.5(190-300)
$AlCl_3$	148.22+7.5	214.33+52.33	77.78	25(12-34)	61.0 [a](34-217.7)
$AlCl_3$+Vehicle	141.16+10.06	186.33+28.03	88.88	26(20.5-34.5)	60.5(16-213)
$AlCl_3$+MMV	133.71+10.60	178.50+60.69	85.71	26(12.5-32)	300.0 [b](214-300)

Latencies are expressed as Median ± 25th to 75th percentiles (interquartile range) Weight and activity score are expressed as Mean ± SEM [a]$p<0.05$; [b]$p<0.05$ and compared to respective vehicle groups. (n=6-9 per group)

Discussion

In the present study, Manasa Mitra vatakam (MMV), a compound herbal preparation was found to improve cognition in two rat models of cognitive deficits. Manasa Mitra vatakam (MMV) prevented the cognitive deficits produced by subchronic aluminium administration. The animal models utilized in the present study are in pathophysiological terms more akin to human conditions of intended use of nootropic agents. The passive avoidance paradigm is widely utilised for testing learning and memory in rats and mice [19]. In this study the test and control groups were balanced for weight, spontaneous motor activity, motor endurance and motivational factors which could confound the results. Aluminium is linked to a number of human conditions with cognitive deficits including SDAT and produces cognitive deficits in rodents [14-16]. It produces lipid peroxidation [20], neurofibrillary degeneration [21] and alteration in brain cyclic nucleotide [15], choline levels [14] leading to cognitive deficits. The results of this study show that Manasa Mitra vatakam (MMV) prevents the cognitive deficits produced by aluminium.

Conclusion

In conclusion, the cognitive enhancing properties of Manasa Mitra vatakam (MMV) showed in this study warrant the study of its mechanism of action and also controlled clinical trials to establish its place in therapy of cognitive disorders.

Acknowledgement

This project is funded by Indian Council of Medical Research (ICMR).

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