RESEARCH ARTICLE

Study on effectivity of black tea as adjuvant therapy in improving neurocognitive performance of patients with early onset of Alzheimer by Montreal Cognitive Assessment

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ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disorder leading to significant deterioration in neurocognitive performance of the patients. The disease puts great financial as well as physical and emotional implications on caregivers cum family. Apart from western classical medicine the disease can also be treated non-pharmacologically viz. adjuvant therapy with Black tea, a very popular beverage in Indian context. This research aims to study the effectivity of black tea as an adjuvant therapy with standard drug Donepezil in improving the cognitive performance of patients with early onset of Alzheimer evaluated by psychometric assessment using Montreal Cognitive Assessment (MoCA) Scale which is a simple, rapid and reliable screening tool to identify cognitive problems. The average MoCA score of normal controls at baseline was 28.4 ± 1.11 and a score of 28.6 ± 0.98 was observed after a follow up of 6 months. Initially, patient volunteers with early onset of Alzheimer who were given the drug Donepezil had an average score of 19.9 ± 1.32 at baseline that was improved to 21.5 ± 1.16 after 6 months. However patient volunteers who were provided with 6 cups of black tea along with the drug Donepezil showed an improvement of score from 19.8 ± 1.31 to 22.1 ± 1.21 after 6 months follow up.

Key words: Alzheimer's disease; neurocognitive; western classical medicine; adjuvant therapy; Black tea; Donepezil; psychometric; Montreal Cognitive Assessment

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and with time patients suffer from gradual but worrisome decline in cognitive performance with inability to perform daily basic functioning's viz. regular feeding, washing or toilet. Mood alterations, depression, agitation, etc. are likely to develop with the progression of the disease and the patient requires assistance for management of work related activities in early stages to care giving for basic activities like bathing, dressing, feeding etc. in later deteriorated conditions.[1-5] The disease puts enormous financial burden along with severe physical and emotional stress on the care givers and other family members of the patient. AD patients require formal medical and social services as well as informal care from the family members. Despite the availability of several therapeutic options with western classical medicine, AD can also be treated via adjuvant therapy.[1-5] Adjuvant therapy is the treatment that is given in addition to the primary treatment. Most adjuvant therapy comes in the form of food, beverage, spice or condiments which has the advantages of patient compliance without altering the normal life style. Black Tea (*Camellia sinensis*) is one of the most widely consumed beverages of the world in general and India in particular.[6] Health benefits of tea are directly correlated with its poly phenol contents and can satisfy the purposes of an adjuvant therapy from the points of cost effectiveness, patient compliance, ease of availability and preparation. Research evidences have shown the multiple health benefits of black tea.[7-14] CTC Black tea, TV 25 variety grown in the non-traditional tea belt of IIT Kharagpur has shown significant poly phenol content and antioxidant potentials.[6] Patho physiologically in AD, apart from accumulations of beta amyloid plaques, tau proteins, and neuro fibrillary tangles, there are alterations in neurotransmitter levels, increased sensitivity to oxidative stress (OS), decrease in cholinergic transmission etc.[1]

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Hippocampus, associated with critical learning and memory is extremely vulnerable to damages in AD. The limbic system and cortex are also affected in this disease.[15] Intake of dietary antioxidants has shown to reduce potentially somatic cell and neuronal damage by free radicals.[16] Neuro imaging in medical research plays a vital role in Alzheimer research. Apart from Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), advanced imaging modalities including structural and functional MRI and positron emission tomography (PET) studies with biomarkers and amyloid tracers help in understanding the AD patho physiological process. [17- 18]

In addition to imaging techniques and lab pathological estimations, psychometric studies have a significant role in evaluating the cognitive performance of Alzheimer patients. Psychometric tests offer the advantages of cost effectiveness, ease of administration, being reliable with quick and easy scoring, being helpful for clinical research purpose as it offers the flexibility of group testing thus simultaneously saving time and cost.[19, 20]

For assessment of degree of cognitive impairment in neurodegenerative diseases, generally tests like Mini-Mental State Examination (MMS), the Alzheimer's Disease Assessment Scale (ADAS) and others are used. Montreal Cognitive Assessment (MoCA), test is a 10-minute, 30-point cognitive screening test recommended by National Institute of Health and the Canadian Stroke Network for detection of vascular cognitive Impairment and Canadian Consensus Guidelines for Diagnosis and Treatment of Dementia for detection of Mild Cognitive Impairment and Alzheimer's disease. MoCA has been found to be advantageous as a simple, rapid and reliable screening tool to identify cognitive problems, serving as a cognitive screening tool for several neurological diseases that affect younger populations and is suitable to test illiterate or subjects with lower education.[19, 20] This work aims to study the effectivity of CTC black tea in patients with early onset of Alzheimer by psychometric studies using Montreal Cognitive Assessment (MoCA) scale.

MATERIALS AND METHODS

Ethical permission and Patient selection:
After obtaining the permission from the Institutional Ethical Committee (IEC number: SSSICOP/IEC/2016/01), a total of 150 volunteers (both normal and patients) were selected for a study period of 6 months. After explaining the total study matter in vernacular, proper written consent of the patients were taken. Patient volunteers with early onset of Alzheimer were recruited for the study based on proper inclusion-exclusion criteria. All efforts were given to maintain a high compliance between patient and patient's caregiver, as tea and drugs were given to patients by caregiver and the black tea and its preparation protocol were provided by the research item. Patients of both sexes within ages of 55-75 were included in the study. Those having co-morbid disorders like Diabetes, Hypertension, Ischemic diseases/episodes, Parkinsonism and other forms of dementia, Neuropsychiatric disorders etc. or taking drugs for any such co-morbid conditions; as well as heavy smokers, patients in professions likely to get repetitive trauma of different magnitudes in brain like boxing, working in vibrating industries were excluded.

Amongst the selected volunteers, apart from the normal volunteers, there were two treatment groups, of which one group received the standard drug Donepezil (5mg once daily for 6 months) while the other treatment group took 6 cups of black tea per day (tea and preparation procedure was provided by the research team and given to the patients by their respective care givers) along with Donepezil (5mg) at an interval of 2 days for six months. Patients were given black tea without milk and sugar in standard cup (150 ml); 2g of black tea was steeped in hot water for 15 min. The details of the study population flowchart are provided in (**Figure 1**).
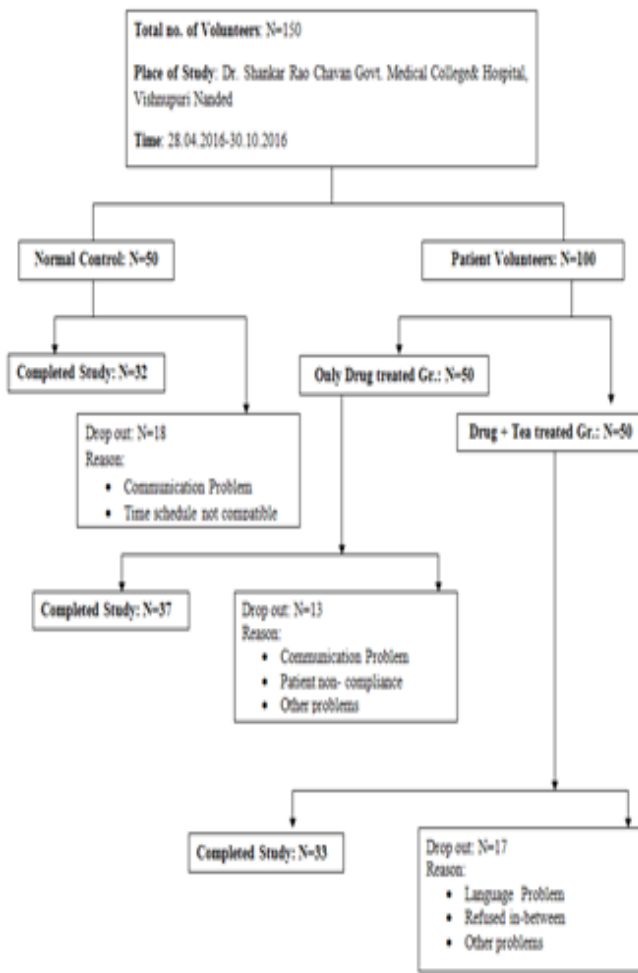
Data collection and test procedure

A baseline interview of the primary care givers of the patients were conducted who informed about the demographic details and other information relating to family history, symptoms of present illness, drugs taken if any, abilities of the patients in performing the routine tasks etc.

In the presence of consultant psychiatrist and the research team as well as care givers, a 10 min duration, 30 point MoCA screening test was conducted where the cutoff point was set as 26. MoCA scores were recorded at baseline for both normal control and the treatment groups and after a follow up of 6 months the MoCA score was determined from the performance of the volunteers on the MoCA score sheet.

As per the test format, evaluation was done in eight different domains for evaluating the cognitive performance viz. visuospatial and executive function, naming, language, attention, abstraction, memory, delayed recall and orientation. Visuospatial abilities were assessed by the clock drawing task (3 points) and cube copy (1 point). Executive functions were assessed using an alternate task of drawing a line from a

number to a letter in ascending order. Short-term memory recall task involved two learning trials of five nouns and delayed recall after approximately 5 minutes (5 points). Three different common animals were asked for naming e.g. lion, camel, and rhinoceros (3 points). Attention abilities were evaluated by repeating a list of digits in both forward and backward (1 point each), target detection (1 point) and serial subtraction task (3 points). Volunteers were asked to repeat two syntactically complex sentences (2 points) and the language and fluency task (1 point) were assessed. Abstraction was evaluated by asking to perform similar tasks (2 points) and finally orientation to place and time was tested (6 points).

Statistical analysis

Prism Graph pad version 5.0 was used to carry out data management and analysis of descriptive statistics. Other parameters like sensitivity, specificity, positive likelihood ratio, negative likelihood ratio were also determined (Med Calc version 16.8.4).
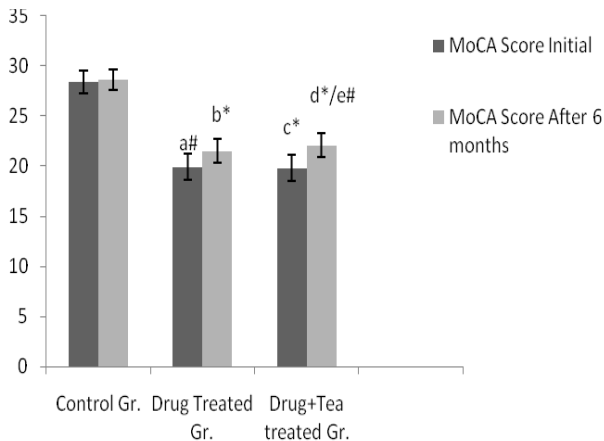
RESULTS

Out of 50 participants grouped under normal control, 32 participants completed the study. Out of 50 participants under the drug treated group, 37 completed the study and 33 out of 50 in drug + tea treated group completed the study. Details of the patient demographics have been provided in Table 1. Considering the subject demographics, average age amongst the control group was determined to be 62.5±5.3, in groups treated with drug donepezil average age was found to be 70.6±2.9 and that in group treated with 6 cups of tea along with donepezil it was 70.2±2.8. The literacy level amongst the controls was found to be 66.6%. In donepezil treated group it was 48.6% and in the group treated with tea and donepezil it was found to be 51.5%.

The initial study data for normal controls showed an average MoCA score of 28.4±1.11 at baseline and a score of 28.6±0.98 after a follow up of 6 months (Fig. 1). Initially, patient volunteers with early onset of Alzheimer who were given the drug donepezil had an average score of 19.9±1.32 at baseline that was improved to 21.5±1.16 (Fig. 1). Another group of patient volunteers who were provided with 6 cups of tea along with the drug donepezil showed the initial MoCA score of 19.8±1.31 that was improved to 22.1±1.21 after 6 months (**Table 1**).

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Table 1: Details of patient demographics recruited in the study

Patient Demographics					
Groups	Characteristic				
	Sex		Age	Education	
	Male (n)	Female (n)		Literate (%)	Illiterate (%)
Control	20	12	62.5±5.3	66.6	33.4
Drug Treated	24	13	70.6±2.9	48.6	51.4
Drug + Tea Treated	19	14	70.2±2.12	51.5	48.5

Fig 2: MoCA score at baseline and after 6 months follow-up in the study population

Here volunteers were grouped under normal control (N=32), drug (Donepezil) treated group (N= 37) and donepezil + tea treated group (N= 33). Results are expressed in mean± SD. a# refers to the comparison between the initial MoCA score of the drug treated group with the control group at p<0.005 level of significance; b* shows the comparison with the MoCA score after 6 months at p<0.01between the drug treated group and the initial value of drug treated group; c* shows the comparison between the initial MoCA score of drug+tea treated group with the control group at p< 0.01; d* refers to the comparison with the between the final MoCA score of drug+tea treated group with the initial value of of drug+tea treated group at p< 0.01; e# shows the comparison of MoCA score (after 6 months) between the drug treated and drug+ tea treated group significant at p<0.005

DISCUSSIONS AND CONCLUSION

Considering the effect of the black tea on cognitive performance of patients detected with early onset of Alzheimer evaluated by psychometric studies using MoCA scale. Statistical analysis showed p<0.005 level of significance on comparison between the initial MoCA score of the drug treated group with the control group at baseline and significance at p< 0.01 after 6 months. Significance at p<0.01 level in both cases were obtained in comparing the MoCA score of drug + tea treated group both at initial stage and after a follow up of 6 months. On comparing the level of cognitive performance amongst the drug treated and drug+ tea treated

group, significance at p<0.005 was achieved. Amongst other statistical parameters, sensitivity of the MoCA scale was found to be 98.97% and the specificity was found to be 33.33% with a positive likelihood ratio of 1.48 and negative likelihood ratio of 0.03; the positive predictive value (PPV) being 99.75% and negative predictive value (NPV) being 1.26%.

Literature evidences have already highlighted the multifaceat health benefits of black tea. Here it has been found that improvement in cognitive performance amongst patients provided with both 6 cups of black tea along with drug donepezil was more (basing on the MoCA score) than the patients who received only the drug donepezil. Thus black tea played the role of an adjuvant in promoting the efficacy of donepezil.

Black tea is a rich source of wide range of benzotropolone compounds viz. theaflavins (3-6%), thearubigins (12-18%), small amounts of theaflagallins, the bisflavanols or theasinensins, catechin dimmers without seven membered rings and flavonol glycosides viz. quercetin, myricetin, kaempferol etc. Apart from these it is also rich in phenolic acids, methyl xanthenes like caffeine and amino acids viz. l-theanine.[21] Available research evidences have shown that theaflavins and thearubigins are rapidly absorbed though black tea catechins are not well absorbed. A standard 200 mL cup of black tea was found to contain about 24.2± 5.7 mg of l-theanine.[22] Theanine (γ-glutamylethylamide) is structurally similar to glutamate, a neuro transmitter related to memory and can successfully cross the blood brain barrier thus providing neuroprotection. Moreover it is an established fact that there exists a strong correlation amongst oxidative stress and Alzheimer.[23-27] Black tea theaflavins being catechin dimers possess more number of OH groups for radical scavenging. However the position, orientation and amount of OH groups greatly influence the anti-oxidative potentials of theaflavins. Thus intake of black tea is suggested to provide a dual protective effect by the neuro-boosting effect of L-theanine and antioxidant potentialities of theaflavins; moreover caffeine in black tea along with the L-theanine can also provide a refreshing cum neuro-boosting effect simultaneously. [23-27]

Current therapeutic strategies have undergone a radical change and both pharmacological and non-pharmacological approaches are running parallely

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to combat the chronic and neurodegenerative disorders. Adoption of adjuvant therapy, dietary and lifestyle interventions have come into limelight and are well practiced simultaneously with western classical medicine so as to achieve enhanced therapeutic outcomes. Though many synthetic drugs are available for the treatment of AD, adoption of an adjuvant therapy with black tea has resulted better improvement in cognitive performance. Moreover Black tea is a popular, refreshing, non-alcoholic beverage and widely accepted in the Indian context. However it is reported that bioavailability problem arises with the tea catechins due to poor absorption; still there are potent neuroprotective and antioxidant compounds in black tea that are well absorbed. Development of dosage formulations with such pharmacologically active compounds and their further evaluation can be an important research domain in this regard.

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