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COGNITIVE REHABILITATION FOR MILD ALZHEIMER'S DEMENTIA: WITH AND WITHOUT CHOLINESTERASE INHIBITORS

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INTRODUCTION:

Cognitive deficits are perhaps the most devastating residual problems following brain pathology. They have been significantly related to the eventual affectation of independence in self care[1].

Memory is one of the basic components of cognition. A defective memory affects all the other higher cognitive functions, which include: orientation, judgement, problem solving, etc [5]. We as individuals, have the ability to draw on our past experiences and learn new information through the process of memory. This provides us with the sense of continuity in the environment and frees us from dependency in the here-and-now situations[1].

Memory normally deteriorates as age advances, a condition called as 'Senile Dementia'. It also deteriorates due to various pathological changes in the brain. One of the most severe pathological changes occurs in the condition termed as 'Alzheimer's disease'.

Alzheimer's disease is a neuro-degenerative disease and a common cause of dementia. It is characterized clinically by progressive cognitive deterioration together with declining activities of daily living skills and neuropsychiatric symptoms or behavioral changes. The most striking early symptom is memory loss which usually manifests as minor forgetfulness that becomes steadily so pronounced that the patient is not able remember his own name. Alzheimer's disease is a particularly disabling condition as the intellectual impairment extends to the domains of

language (aphasia), skilled movements (apraxia), recognition (agnosia), decision-making and planning.

There is currently no cure for Alzheimer's disease, although there are drugs which offer symptomatic benefit, specifically with respect to short term memory impairment. But these drugs are not without harmful side-effects, which sometimes out weigh the benefits. There are several alternative treatment techniques available, like: Ayurveda, herbal medicines (Gingko Biloba), and cognitive training.

Researchers have started to describe the application of cognitive rehabilitation for people with Alzheimer's disease, especially in the in the early stages where the changes in memory and cognitive functioning have started having a prominent impact on the person's well-being. This is based on the understanding that despite difficulties with memory and other cognitive functions, people with Alzheimer's disease still have the ability to learn new associations and information and to adjust their behavior and responses.

Cognitive rehabilitation for people with Alzheimer's disease does not aim to cure or reduce impairment at the neurological level. Rather, the aim is to work together to find ways of dealing with the problems that arise as a result of cognitive changes, so as to be able to participate within their own personal and social context.

It is stated that the occupational therapist specifically identifies how cognitive impairments affect the performance of daily living tasks. Occupational therapists therefore need to focus attention on the evaluation and restoration of

cognitive skills as a pre-requisite to the overall goal of promoting achievement of optimal functional independence[33].

Therefore, this study was undertaken to evaluate the efficacy of a Cognitive rehabilitation protocol on the cognitive and functional abilities and their impact on the quality of life in patients with mild Alzheimer's disease.

AIMS AND OBJECTIVES

- TO EVALUATE THE EFFECTIVENESS OF A SYSTEMATIC COGNITIVE REHABILITATION FOR PATIENTS WITH MILD ALZHEIMER'S DISEASE.

- TO COMPARE THE RESULTS OF THE INTERVENTION IN PATIENTS WITH MILD ALZHEIMER'S DEMENTIA WHO ARE ON CHOLINESTERASE INHIBITORS AND THOSE WHO ARE NOT.

HYPOTHESIS:

- **H_1:** COGNITIVE REHABILITATION HELPS TO IMPROVE THE COGNITION, FUNCTIONAL STATUS, AND THE QUALITY OF LIFE OF PEOPLE WITH MILD ALZHEIMER'S DEMENTIA.

- **H_2:** THERE IS NO SIGNIFICANT DIFFERENCE IN THE IMPROVEMENTS SEEN BETWEEN THE PATIENTS RECEIVING CHOLINESTERASE INHIBITORS AND THOSE NOT RECEIVING THEM.

RELATED LITERATURE:

The symptoms of Alzheimer's disease as a distinct entity were first identified by Emil Kraepelin. The characteristic neuro pathology was first identified by Alois Alzheimer, a German psychiatrist after whom the disease is named, in 1906. In this sense the disease was co-discovered by Kraepelin and Alzheimer[1].

For most of the twentieth century, the diagnosis of Alzheimer's disease was reserved for individuals between the ages of 45-65 who developed symptoms of pre-senile dementia, which was considered to be a more or less normal outcome of the aging process. In the 1970s and early 1980s, because the symptoms and brain pathology were identical, the name 'Alzheimer's disease' began to be used, within and outside the medical profession, equally for individuals with age over 65 years and older with senile dementia, and was eventually adopted for all individuals with the common symptom pattern and disease course in the psychiatric and neurologic nomenclature.

❖ **CLASSIFICATION OF ALZHEIMER'S DISEASE:**

- **DSM-IV-TR** Coding of Dementia due to Alzheimer's Disease**:**

  Dementia due to Alzheimer's disease:

  a) **294.10:** without behavioral disturbance

  b) **294.11:** with behavioral disturbance

  Code Alzheimer's disease (331.0) on Axis III

- **Proposed ICD-10-CM** Coding of Dementia due to Alzheimer's Disease:

  a) Dementia due to AD, with early onset (G30.0x)

  1) **G30.00:** without behavioral disturbance
  2) **G30.01:** with behavioral disturbance
  3) **G30.00:** unspecified

b) Dementia due to AD, with late onset (G30.1x)
1) **G30.10:** without behavioral disturbance
2) **G30.11:** with behavioral disturbance
3) **G30.10:** unspecified

Alzheimer's disease generally presents in three stages:

- **Stage 1:** (Duration of disease 1 to 3 years). Memory-new learning defects, remote recall impaired. Visuo-spatial skills topographic disorientation, poor concentration.
- **Stage 2:** (Duration of disease 2 to 10 years).Language - Fluent aphasia. They also have acalculia and ideomotor apraxias. Personality changes Indifference and apathy.
- **Stage 3:** (Duration of disease 8 to 12 years). Intellectual functions severely disoriented. Sphincter disturbances like; urinary and faecal incontinence.

EPIDEMIOLOGY

Although AD has been described at every period of adult life, the majority of patients are in their sixties or older. A relatively smaller number have been in their late fifties or younger. Average duration of the disease is approximately 7-10 yrs, although cases are known where reaching the final stage occurs within 4-5 yrs or up to 15 yrs.

DIAGNOSIS

The diagnosis is made primarily on the basis of history, clinical observation and tests of memory and intellectual functioning over a series of weeks or months, with various physical tests (blood tests and neuroimaging) being performed to rule out alternative diagnoses. Functional neuroimaging studies such as PET or SPECT scans can provide additional supportive evidence for the diagnosis. No medical tests other than brain biopsy are available to diagnose Alzheimer's disease conclusively, post mortem.

Thus Alzheimer's disease is primarily a clinical diagnosis based on the presence of characteristic neurological features and the absence of alternative diagnosis.

Initial suspicion of dementia may be strengthened by performing the MMSE, after excluding clinical depression. Psychological testing generally focuses on memory, attention, abstract thinking, the ability to name objects, visuo-spatial abilities, and other cognitive functions. Results of psychological tests may not readily distinguish Alzheimer's disease from other types of dementia, but can be helpful in establishing the presence of and severity of dementia. They can also be useful in distinguishing true dementia from temporary (and more treatable) cognitive impairment due to depression or psychosis, which has sometimes been termed as 'pseudo-dementia'.

PATHOLOGY:

- Microscopy: There are several neuropathological changes found in the brain in AD:

a) The deposition of an abnormal protein (amyloid beta) outside nerve cells in the form of amyloid. These are called diffuse plaques and also forms the core of more organized plaques called senile or neuritic plaques. Recently, evidence has

begun to accumulate implicating simpler, soluble forms of amyloid (oligomers) in the pathological process, and the presence of plaques; amyloid does not correlate well with the degree of dementia. Amyloid also accumulates in the walls of the small blood vessels in the brain. This is termed as amyloid angiopathy (congophilic angiopathy). Accumulation of abnormal protein filaments inside nerve cells in the brain, formed from aggregation of tau proteins, which normally stabilize microtubules. In AD, an abnormally phosphorylated form of tau protein accumulates as paired helical filaments. Tau protein accumulates in several forms:

1) As masses of filaments inside nerve cell body termed as neurofibrillary tangles.
2) Inside nerve cell processes in the brain termed as neurophil threads.
3) Inside nerve cell processes that surround amyloid plaques, termed as dystrophic neuritis or plaque neuritis.

There is diffuse atrophy and loss of neurons, neuronal processes and synapses in the cerebral cortex and certain sub cortical regions. This results in gross atrophy of the affected regions and enlargement of the lateral ventricles.

- Neurochemistry: The neurotransmitters, serotonin, acetylcholine, norepinephrine, and somatosonin are at decreased levels. Glutamate levels are usually elevated.
- Disease mechanism: Three major competing hypotheses exist to explain the cause of the disease:

1) The oldest hypothesis is the ‘cholinergic hypotheses’. It states that AD begins as a deficiency in the production of acetylcholine, a vital neurotransmitter. Much early therapeutic research was based on this hypothesis, including, the restoration of the ‘cholinergic nuclei’. All of the first-generation anti-Alzheimer’s medications are based on this hypothesis and work to preserve acetylcholine by inhibiting acetyl cholinesterases (enzymes that break down acetylcholine). These medications though beneficial, have not led to a cure. In all cases, they have served to only treat symptoms of the disease and have neither halted nor reversed it. These results and other researches have led to the conclusion that

acetylcholine deficiencies may not be directly causal, but are a result of widespread brain tissue damage, damage so widespread that cell-replacement therapies are likely to be impartial.

2) The other two hypotheses, each have their advocates, and have often been described as the ‘tau-ist’ and the ‘Ba-ptists’ viewpoints in scientific publications by the researchers. ‘Tau-ists’ believe that the tau protein abnormalities come first and lead to a full disease cascade.

‘Ba-ptists’ believe that beta amyloid deposits are the causative factor in the disease, e.g., the presence of the APP gene on the chromosome 21 is believed to explain the high incidence of early onset AD pathology in patients with Down’s syndrome, who carry three copies of chromosome 21 and thus APP itself. The ‘ba-ptist’ theory is finding new supporters due to recent discoveries of impaired vascular and cerebrospinal fluid transport of the beta amyloid out of the brain tissues, resulting in a greater risk for plaque formation. A third protein, α-synuclein, which has already been shown to be important in Parkinson’s disease, has also been demonstrated to be associated with amyloid plaques in AD. This hypothesis has been given the name ‘syn-ners’ among AD researchers. There is also a ‘triple-lesion’ hypothesis that proposes a pathological interaction among these three candidate proteins. The extent of each protein’s contribution may determine whether or not the ‘lesion disorder’ manifests as AD, Parkinsonism or other degenerative diseases.

The presence of plaques and tangles, however, does not always correlate well with clinical Alzheimer’s, in other words, not all people who have plaques and/or tangles manifest symptoms of the disease. Loss of synapses correlates much better with the decline of cognition than the presence of plaques and tangles, as well as loss of dendritic spines. Some recent research is focusing on the possibility that plaques and tangles arise as a defense against another, as yet undiscovered, process or substance that itself causes the disease. Researchers are intrigued by the idea that the plaques and tangles might not be the problem, but rather a symptom of the

problem. The plaques and neurofibrillary tangles may be the result of the brain's efforts to contain the abnormal proteins produced by the disease.

CLINICAL FEATURES:

- The onset of the mental changes is usually so insidious that neither the family members nor the patient can date the time of its beginning.
- The gradual development of forgetfulness is the major symptom. Once the memory disorder has become pronounced, other failures in cerebral function become increasingly apparent.
- Speech becomes gradually halting, because of failure to recall word needed. The same difficulty interrupts writing.
- Vocabulary becomes restricted and expressive language stereotyped and inflexible.
- Comprehension: The patient may not be able to carry out a complicated request, even then, it is uncertain whether the request was not understood because of inattention or was forgotten. Finally there is an inability to speak in full sentences. There may be dramatic repletion of every spoken phrase – echolalia.
- Skill in arithmetic suffers a similar deterioration. Faults in balancing checkbook, mistakes in figuring the price of items and in making the correct change; all these and others progress to a point where the patient can no longer carry out the simplest calculations.
- There is visuo-spatial disorientation.
- Troublesome alterations gradually appear in social graces. Restlessness, agitation or inertia and placidity may become evident. Dressing, shaving, bathing are neglected. Anxieties phobias, particularly fear of being left alone, may emerge. A disturbance of the normal day and night sleep patterns is prominent in some patients. A poorly organized paranoid delusional state, sometimes with hallucinations may manifest.
- Difficulty with locomotion, a kind of unsteadiness with shortened steps but only slight motor weakness and rigidity, frequently supervenes.

- In the later stages, deterioration of musculature and mobility, leading to bed fastness, inability to feed oneself, and incontinence, will be seen, if death from some cause (e.g., heart attack or pneumonia) does not intervene.

TREATMENT

- Risk reducers:

1) Intellectual stimulation (i.e., playing chess or doing the crossword)
2) Regular physical exercise
3) Regular social interaction
4) A generally healthy diet, low in saturated fat, supplemented particularly with Vit. B complex, Omega-3 fatty acids, especially DHA. High doses of the antioxidant Vit. E (in combination with Vit.C) seems to reduce Alzheimer's risk but is not correctly a recommended preventive measure because of observed increases in overall mortality.
5) Cholesterol- lowering drugs (statins) reduce Alzheimer's risk in observational studies but so far not in randomized control trials.
6) Hormone replacement therapy is no longer thought to prevent dementia based on data from the Women's Health initiative.
7) Regular use of Non-Steroidal Anti Inflammatory Drugs like Ibuprofen and Aspirin reduces the chance of dementia but the risks appear to outweigh the drugs' benefits as a method of primary prevention.

- Acetyl cholinesterase Inhibitors:

AChE inhibition was thought to be important because there is selective loss of forebrain cholinergic neurons as a result of Alzheimer's disease. AChE-Inhibitors reduce the rate at which ACh is broken down and hence increase the concentration of ACh in the brain (combating the loss of ACh caused by the death of the cholinergic neurons). AChE-inhibitors seemed to modestly moderate symptoms but do not prevent disease progression including cell death.

E.g. a) Tacrine: no longer clinically used

b) Donepezil: marketed as Aricept

c) Galantamine: marketed as Razadyne, formerly Reminyl.

d) Rivastigmine: marketed as Exelon.

- NMDA Antagonists :

Recent evidence of the involvement of glutaminergic neuronal exotonicity in the etiology of Alzheimer's disease lead to the development and introduction of Memantine . Memantine is a novel NMDA receptor antagonist , and has been shown to be moderately clinically efficacious .

- Potential treatments :

a) Vaccine: There are ongoing tests of an Alzheimer's disease vaccine. This was based on the idea that if you could train the immune system to recognize and attack beta –amyloid, the immune system might reverse deposition of amyloid and thus stop the disease. In 2006, a new vaccine by researchers in Japan has promising results reducing amyloid deposits between 15.5 and 38.5 % with no adverse side effects .

b) Gingko Biloba : Some studies , summarized in a 2004 conference paper , have suggested that Gingko Biloba shows promise for alleviating the effects of Alzheimer's disease , however , the consumption of Gingko Biloba can have undesirable side effects , especially for those with blood circulation disorders and those taking certain medications . Gingko should not be used by anyone taking anticoagulants , pregnant women , or anyone using the anti depressant drugs – Monoamine oxidase inhibitors[30] .

COGNITION:

Cognition can be defined as the person's capacity to acquire and use information to adapt to the environment. The cognitive processes can be classified as:

- Basic processes:

1) Attention
2) Orientation
3) Memory

- Higher cognitive functions:
    1) Initiation
    2) Abstract thinking
    3) Insight / awareness
    4) Executive functions[3,4]

COGNITIVE REHABILITATION:

Cognitive rehabilitation is defined as a systematic functionally oriented service of therapeutic cognitive activities based on an understanding of the patient's brain – behavior deficits.

- American Academy of rehabilitation[3].

TREATMENT APPROACHES IN COGNITIVE REHABILITATION:

- **Functional approach** :

The functional approach begins by identifying the tasks or activities that are of most concern to the client and caregiver . It capitalizes on the individual's assets to improve task performance . The functional approach can be subdivided into 3 different techniques :

1) Adaptation of the task or environment : This involves changing , altering or structuring the task or environment to prevent disruptive behavior or accidents , minimize cognitive or perceptual demands of a task , minimize caregiver burden and support or maintain the client's level of functioning . The caregiver may be trained to alter or structure the task or the environment to support the individual's level of functioning .
2) Functional skill training (task – specific training) : Involves rote repetition of a specific task with gradually fading cues . Emphasis is on the mastery of a specific task , rather than on the mastery of the underlying skills needed to perform the task . Behavioral techniques including positive reinforcement , contingent reinforcement and backward chaining are often incorporated into structured and repetitive training of an action sequence . Treatment involves breaking down a specific task into subcomponents and systematically recording number of prompts required for each subcomponent .
3) Compensation : It teaches the individual to bypass or minimize the effects of the impairments by using a substitute method to perform a task . The client is expected to initiate or implement use of an external aid or strategy to enhance task performance in a variety of different situations . This requires some awareness and acceptance of one's deficits as well as the ability to generalize use of a learning strategy .

Different types of compensation are:

a) Anticipatory
b) Recognition
c) Situational
d) External

- **Cognitive remediation** :

In this approach cognitive skills are conceptualized in terms of higher cortical skills which are divided into discrete sub skills as attention , discrimination , memory , sequencing , categorization , concept formation and problem solving. These skills are hierarchically organized from simple to complex. Lower–level skills provide the foundation for more complex skills behaviors. Treatment emphasizes practice of the specific cognitive skills that have been identified as being deficient. Drills or exercises involving table–top activities are given. Methods and materials used in remedial treatment are often abstract (block designs and shapes) and are closely related to evaluation tasks e.g., digit span test, Random letter test.

There is an assumption that improvement in underlying cognitive skills will have a greater influence on behavior than direct functional skill training because learning will then spontaneously generalize to a wider range of tasks. This also referred to as the ‘ Transfer of training approach’.

Techniques involved in cognitive remediation are:

1) Spaced – retrieval technique : This involves learning trials where specific stimulus (e.g., face) and a specific association (e.g., name) are presented . Learning trials are separated by progressively longer time intervals filled with conversations or mental tracking tasks to prevent rehearsal of the to – be –

remembered information . If an error occurs on retrieval , corrective feedback is provided , and the interval between stimulus presentation and recall is decreased .

2) Dual cognitive support : Involves the provision of cues and the enhancement of the saliency and organization of the to- be – remembered information at both acquisition and retrieval of information .
3) Procedural memory training : Requires the activation of the motor system . In Alzheimer's disease , motor learning has been shown to improve in paradigms that require the self selection of movements .

Other cognitive remedial approaches:

1) Affolter's approach
2) Multi – context treatment approach[4].

REVIEW OF LITERATURE

- **Reichenbach and Kirchman[23] (1991)** conducted a study comparing a multi-strategy program with a traditional nursing home care for residents with dementia. The results show that the multi-strategy program lead to significant improvement in morale, activities of daily living and mental functioning compared to the traditional nursing care group who showed decreases on the same areas.

- **Sixsmith et al[25] (1993)** did an evaluation of 3 experimental homes for older people with dementia, which showed regaining of lost cognitive and functional abilities is possible when a social care approach rather than a bio-medical approach is adopted.

- **Josephsson et al[17, 18] (1993)** report a landmark study. The purpose of the study was to examine the effects of an intervention program on ADLs in dementia. The study had 4 subjects who had an individualized program of training in one area of instrumental ADL which was relevant to them. Response to the intervention was assessed using the Assessment of Motor and Process Skills (AMPS). 3 subjects showed some improvement, in 2 cases this was dependent on continued environmental support, and 1 subject who was very anxious did not improve. The results were replicated by Josephsson et al (1995), which also evaluated the level of support needed for ADL performance, showing decrease in need for support in some subjects following training.

- **Bach et al[7] (1995)** carried out a landmark study on the effects of two different therapy strategies on 2 samples of 22 long-term patients with mild-moderate dementia. The control group received a 24 week functional rehabilitation (FR) program of Occupational Therapy (OT), Physiotherapy and Speech Therapy. The study group received this program and an additional OT activity program

for 24 weeks. A variety of psychometric tests were carried out at baseline, 12 weeks & 24 weeks by a psychologist who was blind to the group distributions. Both groups showed a significant improvement in most areas assessed, with the study group showing significantly higher scores than the control group. The authors conclude that the application of an OT activity program in addition to FR is significantly more effective than FR alone.

- **Holm et al[14] (1995)** evaluated an in-patient rehabilitation program designed to reduce behavioral problems in geriatric patients with dementia. Each patient had an individualized treatment plan, including behavioral, environmental and psychological components. The study concluded that the multi-disciplinary approach used in the study was effective in significantly reducing behavioral problems and preserving or enhancing patient's cognitive and functional abilities.

- **Zanetti et al[27, 28] (1997)** report an experimental study with 10 subjects with mild-moderate AD which involved ADL training. Patients were evaluated following a training program, which covered 10 activities. Performance on the 10 trained activities and 10 not-trained activities was compared with baseline performance. A significant improvement was found in the time taken to perform the trained activities. There was also an improvement in performance on not-trained activities, suggesting a degree of generalization of the training effects. Zanetti et al (2001) replicated this study, including a control group. The trained group showed a significant decrease in the time taken to perform the activities, while the control group showed a non-significant increase. Both studies support the conclusion that training in ADLs is an appropriate rehabilitation strategy in mild-moderate AD. This is supported by a study by Farina et al (2002) which compared cognitive training and training in ADLs in AD. Both groups showed significant improvements but the results suggested that training in ADLs may be more effective than memory stimulation.

- **Linda Clare[8] (1999)** developed a cognitive rehabilitation approach for people with early stage dementia. Her aim was to help people deal with everyday difficulties arising from their memory problems. The goals of this program are: Learning names of familiar people, learning to use a memory aid (e.g. calendar), remembering family information, managing new washing machine, identifying different types of coins to facilitate shopping, maintaining the skill of telling the time.

- **Arkin[6] (2001)** reports a study of 11 AD patients who had a rehabilitation program implemented by students, involving exercise and volunteer work with all patients and memory and language stimulation exercises with an experimental group of 7 patients. The experimental group performed better than the experimental group on some cognition and language measures but both groups showed no change in most areas measured, both groups maintained or improved the quality of spontaneous discourse, improved on measures of mood and improved on measures of physical fitness.

- **Clare L., Woods RT, et al[9] (2003)** reviewed 6 studies reporting cognitive training interventions. They found that none of the 6 studies showed any statistically significant effects in any domain, although there were indications of some modest, non-significant effects in various domains of cognitive functioning. The authors concluded that though the findings do not provide strong support for the use of cognitive training interventions for people with early-stage AD or Vascular dementia, these findings should be viewed with caution due to the limited number of RCTs available and to the methodological limitations identified.

- **Grandmaison & Simard[12] (2003)** report a critical review of studies on memory stimulation in AD, using a qualitative approach to review the evidence. Their findings suggest that errorless learning, spaced retrieval, vanishing cues and the dyadic approach, used alone or in combination, are

effective. Visual imagery, support with encoding & retrieval and external memory aids was less effective.

- **Snowdon DA[19] (Sept 2003)** conducted the Nun Study which is a longitudinal study of 678 Catholic sisters 75 to 107 years of age who are members of the School Sisters of Notre Dame congregation. Data collected for this study include early and middle-life risk factors from the convent archives, annual cognitive and physical function evaluations during old age, and postmortem neuropathological evaluations of the participants' brains. The case histories presented include a centenarian who was a model of healthy aging, a 92-year-old with dementia and clinically significant Alzheimer disease neuropathology and vascular lesions, a cognitively and physically intact centenarian with almost no neuropathology, and an 85-year-old with well-preserved cognitive and physical function despite a genetic predisposition to Alzheimer disease and an abundance of Alzheimer disease lesions. These case histories provide examples of how healthy aging and dementia relate to the degree of pathology present in the brain and the level of resistance to the clinical expression of the neuropathology.

- **Spector A, Thorgrimsen L, Woods B, et al[26] (2004)** conducted a study, to prove the efficacy of an evidence-based cognitive stimulation therapy (CST) program for people with dementia. They selected 201 people (158 women and 43 men) diagnosed with dementia according to DSM-IV criteria. Participants receiving cognitive stimulation therapy took parting twice weekly sessions, based on reality orientation and cognitive stimulation. Sessions began with gentle non-cognitive exercises to provide continuity and orientation and included multi-sensory stimulation where possible and encouraged use of information processing. Control group participants (86 people) took part in other usual activities. The results showed that Cognitive stimulation significantly improves cognition and quality of life in older people

with dementia. Improvements in cognition with CST were comparable for those seen in studies of acetylcholiesterse inhibitors.

- **A study was conducted by Lustig and Buckner[29] in June 2004**, which examined a type of implicit memory that helps people act faster on items they have previously worked on than new items. In this study, participants were shown words and asked to judge if they represented something living, or something non living. This study suggests that with early cognitive impairment can still be taught to recall important information and to better perform daily tasks.

- **In a July 2004 report, researchers in Miami, FL[29]**, found mildly impaired AD patients who had participated in 3-to-4 months of cognitive rehabilitation had a 170 percent improvement, on an average, in their ability to recall faces and names and a 71 percent improvement in their ability to provide proper change for a purchase. The participants also could respond to and process information more rapidly and were better oriented to time and place compared to a similar group of AD patients who did not receive this targeted intervention. These improvements were still evident 3 months after the cognitive training ended.

- **David A. Loewenstein, Amarilis Acevedo, Sara J. Czaja, Ranjan Duara[21], in August 2004**, evaluated the efficacy of a new cognitive rehabilitation program on memory and functional performance of mildly impaired Alzheimer's disease (AD) patients receiving a cholinesterase inhibitor. They selected 25 participants in the cognitive rehabilitation (CR) group and 19 participants in the mental stimulation group (MS). The CR training included Face-Name association tasks, object recall training, functional tasks, orientation to time and place, visuo-motor speed of processing, and the use of a memory notebook. While the MS group consisted of interactive memory games involving memory, concentration, and problem solving skills. It was

found that compared with the MS group, participants in the CR group demonstrated improved performance on tasks that were similar to those used in training. Gains of face-name associations, orientation, cognitive processing speed were present post-intervention and at a 3 month follow-up. It was concluded that a systematic program of cognitive rehabilitation can result in maintained improvement in performance on specific cognitive and functional tasks in mildly impaired AD patients.

- **Jacqueline Abrisqueta-Gomez, et al.[16] (Sept. 2004)** studied the duration of the benefits derived from a neuropsychological rehabilitation program (NRP) for dementia patients. They selected 3 patients diagnosed as probable Alzheimer's disease in the initial-to-moderate phase; the 3 were taking anticholinesterases. They were submitted to a neuropsychological evaluation (NE) before the NRP and then revaluated after 12 an 24 months of treatment. The aim of the intervention was to do practical work with implicit and explicit residual memory by training them in everyday life activities, and using compensatory strategies and their intact cognitive abilities. Analysis of quantitative NE data after the first year of NRP showed cognitive improvement, functional stabilization and fewer behavioral problems. However, this improvement did not continue in the second year, and the disease maintained its characteristic progression.

- **Patircia Heyn, Beatrice C.Abreu and Kenneth J. Ottenbacher[13], in Oct. 2004** did a meta-analytic study on the effects of exercise training on elderly persons with cognitive impairment and dementia. In this study, a total of 2020 subjects participated in the 30 trials that met the inclusion criteria. It was concluded that exercise training increases fitness, physical function, cognitive function, and positive behavior in people with dementia and related cognitive impairments.

- **R. Avila, C.M.C. Bottino, I.A.M. Carvalho, C.B.Santos, C. Seral and E.C. Miotto[22], in Nov. 2004**, tested the effects of neuropsychological rehabilitation through memory training- motor movements, verbal association, and categorization- and activities of daily living (ADL) training. A sample size of 5 elderly out-patients, mild AD along with their care givers was selected. All patients had been taking Rivastigmine for at least 3 months before being assigned to the rehabilitation sessions, and they continued to take the medication during the whole program. The results showed a statistically significant improvement in ADL measured by functional test, and only a small improvement in memory and psychiatric symptoms. The results support the view that weekly stimulation of memory and training of ADL is of great value in AD, not only to delay the progress of the disease, but also to improve some cognitive functions and ADL, even though AD is a progressively degenerative disease.

- **J. Olazaran, R. Muniz[15], et al, in 2004,** compares the efficacy of a cognitive-motor intervention with psychosocial support for patients with early Alzheimer's disease (AD) who are treated with a cholinesterase inhibitor. The cognitive-motor intervention (CMI) consisted of a 1-year structured program of 103 sessions of cognitive exercises, plus social and psychomotor activities. The results showed that the patients in the CMI group had maintained their cognitive status at the end of 6 months whereas patients in the control group had significantly declined at that time. Cognitive response was higher in the patients with fewer years of formal education. In addition, more patients in the experimental group maintained or improved their affective status at the end of 12 months.

- **In a Case Western Reserve study[32]** of 550 people, those more mentally and physically active in middle-age were three times less likely to later get the mind-robbing disease. Increased intellectual activity during adulthood was especially protective. Examples included reading, doing puzzles, playing a

musical instrument, painting, woodworking, playing cards or board games, and performing home repairs.

- **Kawashima R**.[20] **(2005 Nov)** proposed a new intervention program, the concept of which is derived from the knowledge of both brain science and clinical studies. They had set up a hypothesis that activation of the association cortices by cognitive tasks may well improve the function of these cortices. To choose effective cognitive tasks for activation of the association cortices, they reviewed previous neuroimaging studies. Then, they prepared two tasks in arithmetic and Japanese language, which were systematized basic problems in reading and arithmetic, for the training program. Sixteen experimental and 16 control subjects participated. The subjects of the experimental group were asked to perform a training program using learning tasks in reading and arithmetic. The function of the frontal cortex of the subjects was assessed by FAB (frontal assessment battery at bedside). After six months of training, the FAB score of the experimental group showed a statistically significant improvement. They also observed the restoration of communication and independence, and improvement in relationships with the clinical staff in the experimental group. Their results indicate that learning tasks of reading aloud and arithmetic calculation can be used for cognitive rehabilitation, which improves frontal functions, of dementia patients.
- **Kathryn P. Riley, David A. Snowdon, Mark F. Desrosiers, and William R. Markesbery[19] (2005)** examined the relationships between early life variables, cognitive function, and neuropathology in participants in the Nun Study who were between the ages of 75 and 95. Their early life variable was idea density, which is a measure of linguistic ability, derived from autobiographies written at a mean age of 22 years. Six discrete categories of cognitive function, including mild cognitive impairments, were evaluated, using the CERAD battery of cognitive tests. Neuropathological data included Braak staging, neurofibrillary tangle and senile plaque counts, brain weight, degree of cerebral atrophy, severity of atherosclerosis, and the presence of

brain infarcts. Early-life idea density was significantly related to the categories of late-life cognitive function, including mild cognitive impairments: low idea density was associated with greater impairment. Low idea density also was significantly associated with lower brain weight, higher degree of cerebral atrophy, more severe neurofibrillary pathology, and the likelihood of meeting neuropathological criteria for Alzheimer's disease.

- **Fernandez AL**, **Manoiloff LM**, **Monti A[11] (2006 Feb)** evaluated the effects of long-term treatment in a demented patient in this study. One individual diagnosed with Alzheimer's dementia (AD) was treated with neuropsychological rehabilitation techniques as well as drugs for a period of 2 years and 10 months. An A-B-A-B design was performed for the cognitive treatment. Neuropsychological treatment consisted of a combination of direct re-training and training in activities of daily living. Cognitive performance was monitored with the Mattis Dementia Rating Scale. Results showed improvement and a slower decline during the treatment phases (A) as compared to the no-treatment phases (B). The Conceptualization and Attention subscales benefited most followed by the Memory subscale. Long-term treatment was shown to be effective in AD. Although cognitive drugs may have been beneficial neuropsychological rehabilitation played an important role in the success of this treatment, appearing as a necessary condition.

METHODOLOGY

The study was conducted on patients diagnosed as mild Alzheimer's dementia who were divided into two groups (GrP I and GrP II), which consisted of 15 patients each.

- **GrP I** consisted of patients who received Cholinesterase inhibitors (Rivastigmine) and cognitive rehabilitation therapy. The medications were started concurrently with the cognitive rehabilitation therapy.
- **GrP II** consisted of patients who received only cognitive rehabilitation therapy and were not on any Cholinesterase inhibitors. These patients had voluntarily chosen not tot take any cholinesterase inhibitors.

INCLUSION CRITERIA:

- Patients diagnosed as a c/o mild Alzheimer's dementia on the basis of DSM-IVTR criteria, Mini Mental Status Examination (scores ranging from 20-24) and Clinical Dementia Rating scale (score 1).
- Patients over 60 yrs of age.
- Patients who literate in English upto at least high school level.

EXCLUSION CRITERIA:

- Patients having associated neurological problems, like, head injury, stoke, Parkinson's disease.
- Patients having associated psychiatric problems. Like, hallucinations, delusions, etc.
- Patients with associated depression.

DURATION AND DOSING OF THE THERAPY:

- The cognitive rehabilitation therapy was given to both the groups for a total of 40 sessions.
- For the 1st 16wks, the therapy was given twice/week, and was then tapered down to once/week sessions for the next 8wks.
- Each session lasted for about 1hr.

OUTCOME MEASURES:

The following scales were used to assess the patients in both the groups:

- **Alzheimer Disease Assessment Scale- Cognitive version (ADAS-COG):** this scale was used to assess the cognitive status of the participants. It is a highly sensitive scale which has 11 items as: Word Recall task, Naming Objects and Fingers, Commands, Constructional Praxis, Ideational Praxis, Orientation, Word Recognition, Language, Comprehension of Spoken Language, Word Finding Difficulty and Remembering Test Instructions. This scale is scored from 0-70, with 0 being no problems in cognition and 70 being severe cognitive deficits.
- **Functional Assessment and Staging Tool (FAST):** This scale was used to assess the functional status of the participants. This scale is scored from 1-7, with 1 being the lowest score or the best functional status, and 7 being the highest or the worst functional status.
- **Quality Of Life- Alzheimer's disease (QOL-AD):** This scale is used for the subjective evaluation of the quality of life of the participants. From this scale the participant's quality of life can be rated as: Poor (1), Fair (2), Good (3), and Excellent (4).

Assessment of the participants on these outcome measures were done at:

- Baseline; i.e. before starting the therapy.
- After the completion of 16wks of therapy.
- After the completion of 24wks of therapy.

- The therapy was discontinued after completion of 24wks. The patients were assessed again 4wks after the therapy was discontinued.

Material and methods: Memory notebooks, black-board, pocket calendars, stationary, mazes, scanning sheets with letters, numbers and symbols, 10 common objects, pictures of 10 people.

Treatment: The cognitive rehabilitation was given as a group activity and included activities based on the cognitive remediation and functional approaches. The cognitive rehabilitation protocol included the following activities:

1. **REALITY ORIENTATION:** Every session, the participants are required to take turns in writing on the black-board, that day's date, day of the week, month and year, time of starting the session and his name. Accordingly, the other participants are required to write the information in their memory notebooks. The memory notebook is any small notebook with divisions made each for: orientation, appointments, things to be remembered, and homework.
2. **FACE-NAME ASSOCIATION TASK:** Initially for the first few sessions this task involves addressing a fellow participant or the therapist by the name. The purpose is to help the participants remember names of the fellow participants and the therapist. This task is included in the treatment as inability to remember names is the basic complaint of people with mild Alzheimer's dementia. Hence, every time, a name is repeated, it gets consolidated in the brain and facilitates the recall process. Later, as the therapy progresses, the participants are presented with 10 pictures of different people. The participants are given 3 learning trials during which the pictures are presented in different order. The participants are required to detect the characteristic facial feature of the people in the picture and try to remember that person's name through this feature. E.g., a picture of a smiling person named SAM. In this case, the person is given the name of 'Smiling SAM'.

3. **ORIENTATION TASK:** This task is subdivided into:
    a) **Temporal Orientation:** In this task, the concept of using pocket calendars to remember dates is introduced. In the first session, the participants are given pocket calendars and are asked to mark that day's date by copying it from the board. In the next session they are required to mark that day's date by looking at the previous marking. The participants are asked to follow this practice at home also. The participants are required to write the details of each session, like, the time of starting the session, place, date of the next appointment, that day's home-work etc.
    b) **Topographical Orientation:** The participants are required to solve mazes of increasing degrees of complexity. They are also required to describe in details, the way to the therapy room from their home and back.
4. **ATTENTION TASK:** The participants are required to cancel a target number, letter, or symbol from the scanning sheets provided. The results of their performance are provided at the end for self-evaluation and development of competency.
5. **MEMORY TRAINING STRATEGIES:** Here, the participants are presented with 10 objects for 30 sec. They are required to recall these objects across 3 learning trials. The participants are taught the following techniques to facilitate recall of these objects:
    a) **Rehearsal:** The participants are required to repeat silently or loudly, the names of the objects to be remembered.
    b) **Elaborating:** The participants are asked to look at each object and relate it to what he knows about the object from his past experiences.
    c) **Self reference:** The participants are asked to judge how the objects are related to them.
    d) **Visual imagery:** The participants are asked to form a visual image in their mind of the objects to be recalled.

e) **Mnemonics:** The participants are asked to form a phrase of the first letters of the objects.

f) **Story method:** The participants are asked to form a story about the objects to be recalled.

6. MAKING A SHOPPING LIST: Here the participants are required to make a shopping list of all necessary items, in their memory notebooks and calculate the approximate total.

RESULTS AND STATISTICAL ANALYSIS

For the purpose of statistical analysis, the following variants are allotted to the data:

- Cognition, as measured by ADAS-COG scale was evaluated at baseline, 16wks, 24wks, and 4wks post intervention. Accordingly these evaluations are ascribed the variants as: C base, C at 16wks, Cat 24wks and C- at 4wks post intervention.
- Functional status, as measured by FAST scale was also evaluated at baseline, 16wks, 24wks, and 4wks post intervention. These evaluations are given the variants as: FS base, FS at 16wks, FS at 24wks, and FS at 4wks post intervention.
- Quality of life, as measured by the scale, QOL-AD, was evaluated at baseline, 16wks, 24wks, and 4wks post intervention. These evaluations are given the variants as: QOL base, QOL at 16wks, QOL 24wks, and QOL at 4wks post intervention.
- The 11 items of ADAS-COG scale are abbreviated as WRT, NOF, C, CP, IP, O, WR, L, CSL, WFD, and RTI.

For the purpose of statistical analysis, Paired Student's t-test was used for comparisons of the data within 1 group, while Unpaired Student's t-test was used for comparison of the data between the 2 groups.

PAIRED t-Test:

Formula: $t = \frac{\bar{x}}{s/\sqrt{n}}$

Where; $\bar{x}$ = mean of the data under consideration.

S = standard deviation of the data.

n = No. of the observations in the group.

- mean is calculated as: $\bar{x} = \frac{\sum x}{n}$

Where; $\sum x$ = summation of the data in the group.

n = No. of observations in the group.

- Standard deviation is calculated as:

$$s = \sqrt{\frac{\sum(X-\bar{X})^2}{n-1}}$$

Accordingly, paired t-test for comparison between the total scores of ADAS-COG, FAST, and QOL- AD, of GrP I and GrP II are as follows:

GrP I: With Cholinesterase Inhibitors

Table 1a) This table shows the mean, standard deviation, standard error of the ADAS-COG scores of participants of GrP I from baseline to 16wks of therapy and from baseline to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	C Base	18.13	15	1.96	.51
	C at 16 wks	14.47	15	1.81	.47
Pair 2	C at 16 wks	14.47	15	1.81	.47
	C at 24 wks	12.53	15	1.68	.43
Pair 3	C at 24 wks	12.53	15	1.68	.43
	C Post Intervention	12.07	15	1.87	.48
Pair 4	C Base	18.13	15	1.96	.51
	C Post Intervention	12.07	15	1.87	.48

Table 1b) This table shows the significant difference in the ADAS-COG scores of GrP I from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	C Base - C at 16 wks	13.569	14	.000
Pair 2	C at 16 wks - C at 24 wks	7.790	14	.000
Pair 3	C at 24 wks - C Post Intervention	2.432	14	.029
Pair 4	C Base - C Post Intervention	19.215	14	.000

Table 2a) This table shows the mean, standard deviation, standard error of the FAST scores of GrP I from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	FS Base	3.13[a]	15	.35	9.09E-02
	FS at 16 wks	2.13[a]	15	.35	9.09E-02
Pair 2	FS at 16 wks	2.13	15	.35	9.09E-02
	FS at 24 wks	1.53	15	.52	.13
Pair 3	FS at 24 wks	1.53[a]	15	.52	.13
	FS Post Intervention	1.53[a]	15	.52	.13
Pair 4	FS Base	3.13	15	.35	9.09E-02
	FS Post Intervention	1.53	15	.52	.13

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 2b) This table shows the significant difference in the FAST scores of GrP I from intervention baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

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Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 2	FS at 16 wks - FS at 24 wks	4.583	14	.000
Pair 4	FS Base - FS Post Intervention	12.220	14	.000

Table 3a) This table shows the mean, standard deviation, standard error, of the QOL-AD scores from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

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Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	QOL Base	2.00	15	.00	.00
	QOL at 16 wks	2.93	15	.26	6.67E-02
Pair 2	QOL at 16 wks	2.93	15	.26	6.67E-02
	QOL at 24 wks	3.20	15	.41	.11
Pair 3	QOL at 24 wks	3.20[a]	15	.41	.11
	QOL Post Intervention	3.20[a]	15	.41	.11
Pair 4	QOL Base	2.00	15	.00	.00
	QOL Post Intervention	3.20	15	.41	.11

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 3b) This table shows the significant difference in the QOL-AD scores of GrP I from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	QOL Base - QOL at 16 wks	-14.000	14	.000
Pair 2	QOL at 16 wks - QOL at 24 wks	-2.256	14	.041
Pair 4	QOL Base - QOL Post Intervention	-11.225	14	.000

GrP II: Without Cholinesterase Inhibitors:

Table 4a) This table shows the mean, standard deviation, standard error of ADAS-COG scores of GrP II from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	C Base	17.73	15	1.33	.34
	C at 16 wks	14.73	15	.96	.25
Pair 2	C at 16 wks	14.73	15	.96	.25
	C at 24 wks	13.27	15	.96	.25
Pair 3	C at 24 wks	13.27	15	.96	.25
	C Post Intervention	13.07	15	1.03	.27
Pair 4	C Base	17.73	15	1.33	.34
	C Post Intervention	13.07	15	1.03	.27

Table 4b) This table shows the significant difference in the ADAS-COG scores of GrP II from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	C Base - C at 16 wks	12.550	14	.000
Pair 2	C at 16 wks - C at 24 wks	5.735	14	.000
Pair 3	C at 24 wks - C Post Intervention	1.382	14	.189
Pair 4	C Base - C Post Intervention	11.377	14	.000

Table 5a) This table shows the mean, standard deviation, standard error of the FAST scores of GrP II from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	FS Base	3.00	15	.00	.00
	FS at 16 wks	2.47	15	.52	.13
Pair 2	FS at 16 wks	2.47	15	.52	.13
	FS at 24 wks	1.93	15	.59	.15
Pair 3	FS at 24 wks	1.93[a]	15	.59	.15
	FS Post Intervention	1.93[a]	15	.59	.15
Pair 4	FS Base	3.00	15	.00	.00
	FS Post Intervention	1.93	15	.59	.15

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 5b) This table shows the significant difference between the FAST scores of GrP II from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	FS Base - FS at 16 wks	4.000	14	.001
Pair 2	FS at 16 wks - FS at 24 wks	4.000	14	.001
Pair 4	FS Base - FS Post Intervention	6.959	14	.000

Table 6a) This table shows the mean, standard deviation, standard error of QOL-AD scores of GrP II from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	QOL Base	2.00	15	.00	.00
	QOL at 16 wks	2.40	15	.51	.13
Pair 2	QOL at 16 wks	2.40	15	.51	.13
	QOL at 24 wks	2.93	15	.26	6.67E-02
Pair 3	QOL at 24 wks	2.93	15	.26	6.67E-02
	QOL Post Intervention	2.87	15	.35	9.09E-02
Pair 4	QOL Base	2.00	15	.00	.00
	QOL Post Intervention	2.87	15	.35	9.09E-02

Table 6b) This table shows the significant difference between the QOL-AD scores of GrP II from baseline to 16 wks, 16wks to 24 wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	QOL Base - QOL at 16 wks	-3.055	14	.009
Pair 2	QOL at 16 wks - QOL at 24 wks	-4.000	14	.001
Pair 3	QOL at 24 wks - QOL Post Intervention	1.000	14	.334
Pair 4	QOL Base - QOL Post Intervention	-9.539	14	.000

Comparison between the sub items of ADAS-COG scores of group I and group II:

GrP I: With Cholinesterase Inhibitors:

Table 7a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG from baseline to 16 wks.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT Base	6.73	15	1.03	.27
	WRT at 16 wks of Intervention	5.8	15	1.01	.26
Pair 2	NOF Base	.27	15	.46	.12
	NOF at 16 wks of Intervention	.13	15	.35	.09
Pair 3	C Base	.00 [a]	15	.00	.00
	C at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 4	CP Base	.60	15	.51	.13
	CP at 16 wks of Intervention	.07	15	.26	.07
Pair 5	IP Base	.00 [a]	15	.00	.00
	IP at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 6	O Base	2.87	15	.35	9.09E-02
	O at 16 wks of Intervention	2.00	15	.00	.00
Pair 7	WR Base	6.60	15	.51	.13
	WR at 16 wks of Intervention	5.9	15	.64	.16
Pair 8	L Base	.00 [a]	15	.00	.00
	L at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 9	CSL Base	.00 [a]	15	.00	.00
	CSL at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 10	WFD Base	.87	15	.35	9.09E-02
	WFD at 16 wks of Intervention	.53	15	.52	.13
Pair 11	RTI Base	.20	15	.41	.11
	RTI at 16 wks of Intervention	.07	15	.26	.07
Pair 12	Total Base	18.13	15	1.96	.51
	Total at 16 wks of Intervention	14.47	15	1.81	.47

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 7b) This table shows the significant difference between the sub items of ADAS-COG scores from baseline to 16wks of intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 2	NOF Base - NOF at 16 wks of Intervention	1.47	14	.164
Pair 4	CP Base - CP at 16 wks of Intervention	4	14	0.001
Pair 6	O Base - O at 16 wks of Intervention	9.4	14	.000
Pair 7	WR Base - WR at 16 wks of Intervention	6.20	14	.000
Pair 10	WFD Base - WFD at 16 wks of Intervention	2.65	14	.019
Pair 11	RTI Base - RTI at 16 wks of Intervention	1.47	14	0.164
Pair 12	Total Base - Total at 16 wks of Intervention	13.569	14	.000

Table 8a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG scale from 16wks to 24wks of intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT at 16 wks of Intervention	5.8	15	1.01	.26
	WRT at 24 wks of Intervention	5.13	15	.83	.21
Pair 2	NOF at 16 wks of Intervention	.13	15	.35	.09
	NOF at 24 wks of Intervention	.07	15	.26	.06
Pair 3	C at 16 wks of Intervention	.00 [a]	15	.00	.00
	C at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 4	CP at 16 wks of Intervention	.07	15	.26	6.67E-02
	CP at 24 wks of Intervention	.07	15	.26	6.67E-02
Pair 5	IP at 16 wks of Intervention	.00 [a]	15	.00	.00
	IP at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 6	O at 16 wks of Intervention	2.00	15	.00	.00
	O at 24 wks of Intervention	1.47	15	.52	.13
Pair 7	WR at 16 wks of Intervention	5.9	15	.64	.16
	WR at 24 wks of Intervention	5.33	15	.72	.19
Pair 8	L at 16 wks of Intervention	.00 [a]	15	.00	.00
	L at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 9	CSL at 16 wks of Intervention	.00 [a]	15	.00	.00
	CSL at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 10	WFD at 16 wks of Intervention	.53	15	.52	.13
	WFD at 24 wks of Intervention	.4	15	.51	.13
Pair 11	RTI at 16 wks of Intervention	.07	15	.35	.09
	RTI at 24 wks of Intervention	.07	15	.35	.09
Pair 12	Total at 16 wks of Intervention	14.47	15	1.81	.47
	Total at 24 wks of Intervention	12.53	15	1.68	.43

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 8b) This table shows the significant difference in the sub items of ADAS-COG of GrP I from 16wks to 24wks of intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	WRT at 16 wks of Intervention - WRT at 24 wks of Intervention	5.29	14	.000
Pair 2	NOF at 16 wks of Intervention - NOF at 24 wks of Intervention	1.00	14	.334
Pair 4	CP at 16 wks of Intervention - CP at 24 wks of Intervention	1.000	14	.334
Pair 6	O at 16 wks of Intervention - O at 24 wks of Intervention	4.000	14	.001
Pair 7	WR at 16 wks of Intervention - WR at 24 wks of Intervention	2.646	14	.019
Pair 10	WFD at 16 wks of Intervention - WFD at 24 wks of Intervention	1.871	14	.082
Pair 11	RTI at 16 wks of Intervention - RTI at 24 wks of Intervention	-1.000	14	.334
Pair 12	Total at 16 wks of Intervention - Total at 24 wks of Intervention	7.790	14	.000

Table 9a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG of GrP I from 24wks to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT at 24 wks of Intervention	5.13	15	.83	.21
	WRT at 4 wks after Intervention	4.93	15	.8	.2
Pair 2	NOF at 24 wks of Intervention	.13 [a]	15	.35	9.09E-02
	NOF at 4 wks after Intervention	.13 [a]	15	.35	9.09E-02
Pair 3	C at 24 wks of Intervention	.00 [a]	15	.00	.00
	C at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 4	CP at 24 wks of Intervention	.07[a]	15	.26	6.67E-02
	CP at 4 wks after Intervention	.07[a]	15	.26	6.67E-02
Pair 5	IP at 24 wks of Intervention	.00 [a]	15	.00	.00
	IP at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 6	O at 24 wks of Intervention	1.47	15	.52	.13
	O at 4 wks after Intervention	1.33	15	.49	.13
Pair 7	WR at 24 wks of Intervention	5.33	15	.72	.19
	WR at wks after Intervention	5.20	15	.77	.20
Pair 8	L at 24 wks of Intervention	.00 [a]	15	.00	.00
	L at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 9	CSL at 24 wks of Intervention	.00 [a]	15	.00	.00
	CSL at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 10	WFD at 24 wks of Intervention	.4	15	.51	.13
	WFD at 4 wks after Intervention	.33	15	.49	.13
Pair 11	RTI at 24 wks of Intervention	.07	15	.26	.07
	RTI at 4 wks after Intervention	.07	15	.26	.07
Pair 12	Total at 24 wks of Intervention	12.53	15	1.68	.43
	Total at 4 wks after Intervention	12.07	15	1.87	.48

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 9b) This table shows the significant difference between the sub items of ADAS-COG scores of GrP I from 24wks to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	WRT at 24 wks of Intervention - WRT at 4 wks after Intervention	1.87	14	.082
Pair 6	O at 24 wks of Intervention - O at 4 wks after Intervention	1.47	14	.164
Pair 7	WR at 24 wks of Intervention - WR at wks after Intervention	1.468	14	.164
Pair 11	RTI at 24 wks of Intervention - RTI at 4 wks after Intervention	1.47	14	.164
Pair 12	Total at 24 wks of Intervention - Total at 4 wks after Intervention	2.432	14	.029

Table 10a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG of GrP I from baseline to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT Base	6.73	15	1.03	.27
	WRT at 4 wks after Intervention	4.93	15	.80	.21
Pair 2	NOF Base	.27	15	.46	.12
	NOF at 4 wks after Intervention	.13	15	.35	9.09E-02
Pair 3	C Base	.00 [a]	15	.00	.00
	C at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 4	CP Base	.60	15	.51	.13
	CP at 4 wks after Intervention	6.67E-02	15	.26	6.67E-02
Pair 5	IP Base	.00 [a]	15	.00	.00
	IP at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 6	O Base	2.87	15	.35	9.09E-02
	O at 4 wks after Intervention	1.33	15	.49	.13
Pair 7	WR Base	6.60	15	.51	.13
	WR at wks after Intervention	5.20	15	.77	.20
Pair 8	L Base	.00 [a]	15	.00	.00
	L at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 9	CSL Base	.00 [a]	15	.00	.00
	CSL at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 10	WFD Base	.87	15	.35	9.09E-02
	WFD at 4 wks after Intervention	.33	15	.49	.13
Pair 11	RTI Base	.2	15	.35	.09
	RTI at 4 wks after Intervention	.07	15	.26	.07
Pair 12	Total Base	18.13	15	1.96	.51
	Total at 4 wks after Intervention	12.07	15	1.87	.48

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 10b) This table shows the significant difference between the sub items of the ADAS-COG of GrP I from baseline to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	WRT Base - WRT at 4 wks after Intervention	10.311	14	.000
Pair 2	NOF Base - NOF at 4 wks after Intervention	1.000	14	.334
Pair 4	CP Base - CP at 4 wks after Intervention	4.000	14	.001
Pair 6	O Base - O at 4 wks after Intervention	7.990	14	.000
Pair 7	WR Base - WR at wks after Intervention	7.359	14	.000
Pair 10	WFD Base - WFD at 4 wks after Intervention	4.00	14	.001
Pair 11	RTI Base - RTI at 4 wks after Intervention	1.47	14	.164
Pair 12	Total Base - Total at 4 wks after Intervention	19.215	14	.000

Grp II: Without Cholinesterase Inhibitors:

Table 11a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG of GrP II, from baseline to 16wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT Base	6.87	15	.74	.19
	WRT at 16 wks of Intervention	6.2	15	.56	.14
Pair 2	NOF Base	.20	15	.41	.11
	NOF at 16 wks of Intervention	.07	15	.26	.07
Pair 3	C Base	.00 [a]	15	.00	.00
	C at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 4	CP Base	.67	15	.49	.13
	CP at 16 wks of Intervention	0	15	0	0
Pair 5	IP Base	.00 [a]	15	.00	.00
	IP at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 6	O Base	2.80	15	.56	.14
	O at 16 wks of Intervention	2.00	15	.00	.00
Pair 7	WR Base	6.40	15	.51	.13
	WR at 16 wks of Intervention	5.9	15	.5	.13
Pair 8	L Base	.00 [a]	15	.00	.00
	L at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 9	CSL Base	.00 [a]	15	.00	.00
	CSL at 16 wks of Intervention	.00 [a]	15	.00	.00
Pair 10	WFD Base	.73	15	.46	.12
	WFD at 16 wks of Intervention	.6	15	.51	.13
Pair 11	RTI Base	6.67E-02	15	.26	6.67E-02
	RTI at 16 wks of Intervention	0	15	0	0
Pair 12	Total Base	17.73	15	1.33	.34
	Total at 16 wks of Intervention	14.73	15	.96	.25

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 11b) This table shows the significant difference between the sub items of ADAS-COG of GrP II from baseline to 16wks of intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	WRT Base - WRT at 16 wks of Intervention	3.16	14	.007
Pair 2	NOF Base - NOF at 16 wks of Intervention	1.00	14	.334
Pair 4	CP Base - CP at 16 wks of Intervention	5.29	14	0.00
Pair 6	O Base - O at 16 wks of Intervention	5.53	14	.000
Pair 7	WR Base - WR at 16 wks of Intervention	2.48	14	.027
Pair 10	WFD Base - WFD at 16 wks of Intervention	1.47	14	.164
Pair 12	Total Base - Total at 16 wks of Intervention	12.550	14	.000

Table 12a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG of GrP II from 16wks to 24wks of intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT at 16 wks of Intervention	6.2	15	.56	.14
	WRT at 24 wks of Intervention	5.67	15	.49	.13
Pair 2	NOF at 16 wks of Intervention	6.67E-02	15	.26	6.67E-02
	NOF at 24 wks of Intervention	.00	15	.00	.00
Pair 3	C at 16 wks of Intervention	.00 [a]	15	.00	.00
	C at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 4	CP at 16 wks of Intervention	0 [a]	15	0	0
	CP at 24 wks of Intervention	0 [a]	15	0	0
Pair 5	IP at 16 wks of Intervention	.00 [a]	15	.00	.00
	IP at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 6	O at 16 wks of Intervention	2.00	15	.00	.00
	O at 24 wks of Intervention	1.60	15	.51	.13
Pair 7	WR at 16 wks of Intervention	5.87	15	.52	.13
	WR at 24 wks of Intervention	5.60	15	.63	.16
Pair 8	L at 16 wks of Intervention	.00 [a]	15	.00	.00
	L at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 9	CSL at 16 wks of Intervention	.00 [a]	15	.00	.00
	CSL at 24 wks of Intervention	.00 [a]	15	.00	.00
Pair 10	WFD at 16 wks of Intervention	.6	15	.51	.13
	WFD at 24 wks of Intervention	.4	15	.51	.13
Pair 11	RTI at 16 wks of Intervention	0 [a]	15	0	0
	RTI at 24 wks of Intervention	0 [a]	15	0	0
Pair 12	Total at 16 wks of Intervention	14.73	15	.96	.25
	Total at 24 wks of Intervention	13.27	15	.96	.25

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 12b) This table shows the significant difference in the sub items of ADAS-COG of GrP II from 16wks to 24wks of intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	WRT at 16 wks of Intervention - WRT at 24 wks of Intervention	4.000	14	.001
Pair 2	NOF at 16 wks of Intervention - NOF at 24 wks of Intervention	1.000	14	.334
Pair 6	O at 16 wks of Intervention - O at 24 wks of Intervention	3.055	14	.009
Pair 7	WR at 16 wks of Intervention - WR at 24 wks of Intervention	1.468	14	.164
Pair 10	WFD at 16 wks of Intervention - WFD at 24 wks of Intervention	1.871	14	.082
Pair 12	Total at 16 wks of Intervention - Total at 24 wks of Intervention	5.735	14	.000

Table 13a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG from 24wks to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT at 24 wks of Intervention	5.67	15	.49	.13
	WRT at 4 wks after Intervention	5.47	15	.64	.17
Pair 2	NOF at 24 wks of Intervention	.00 [a]	15	.00	.00
	NOF at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 3	C at 24 wks of Intervention	.00 [a]	15	.00	.00
	C at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 4	CP at 24 wks of Intervention	0 [a]	15	0	0
	CP at 4 wks after Intervention	0 [a]	15	0	0
Pair 5	IP at 24 wks of Intervention	.00 [a]	15	.00	.00
	IP at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 6	O at 24 wks of Intervention	1.60 [a]	15	.51	.13
	O at 4 wks after Intervention	1.60 [a]	15	.51	.13
Pair 7	WR at 24 wks of Intervention	5.60	15	.63	.16
	WR at wks after Intervention	5.53	15	.64	.17
Pair 8	L at 24 wks of Intervention	.00 [a]	15	.00	.00
	L at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 9	CSL at 24 wks of Intervention	.00 [a]	15	.00	.00
	CSL at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 10	WFD at 24 wks of Intervention	.40	15	.51	.13
	WFD at 4 wks after Intervention	.33	15	.49	.13
Pair 11	RTI at 24 wks of Intervention	0 [a]	15	0	0
	RTI at 4 wks after Intervention	0 [a]	15	0	0
Pair 12	Total at 24 wks of Intervention	13.27	15	.96	.25
	Total at 4 wks after Intervention	13.07	15	1.03	.27

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 13b) This table shows the significant difference between the sub items of ADAS-COG of GrP II from 24wks to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	WRT at 24 wks of Intervention - WRT at 4 wks after Intervention	1.87	14	.082
Pair 7	WR at 24 wks of Intervention - WR at wks after Intervention	1.000	14	.334
Pair 10	WFD at 24 wks of Intervention - WFD at 4 wks after Intervention	1.000	14	.334
Pair 12	Total at 24 wks of Intervention - Total at 4 wks after Intervention	1.382	14	.189

Table 14a) This table shows the mean, standard deviation, standard error of the sub items of ADAS-COG of GrP II from baseline to 4wks post intervention.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	WRT Base	6.87	15	.74	.19
	WRT at 4 wks after Intervention	5.47	15	.64	.17
Pair 2	NOF Base	.20	15	.41	.11
	NOF at 4 wks after Intervention	.00	15	.00	.00
Pair 3	C Base	.00 [a]	15	.00	.00
	C at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 4	CP Base	.67	15	.49	.13
	CP at 4 wks after Intervention	0	15	0	9.09E-02
Pair 5	IP Base	.00 [a]	15	.00	.00
	IP at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 6	O Base	2.80	15	.56	.14
	O at 4 wks after Intervention	1.60	15	.51	.13
Pair 7	WR Base	6.40	15	.51	.13
	WR at wks after Intervention	5.53	15	.64	.17
Pair 8	L Base	.00 [a]	15	.00	.00
	L at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 9	CSL Base	.00 [a]	15	.00	.00
	CSL at 4 wks after Intervention	.00 [a]	15	.00	.00
Pair 10	WFD Base	.73	15	.46	.12
	WFD at 4 wks after Intervention	.33	15	.49	.13
Pair 11	RTI Base	6.67E-02	15	.26	6.67E-02
	RTI at 4 wks after Intervention	0	15	0	0
Pair 12	Total Base	17.73	15	1.33	.34
	Total at 4 wks after Intervention	13.07	15	1.03	.27

a. The correlation and t cannot be computed because the standard error of the difference is 0.

Table 14b) This table shows the significant difference between the sub items of ADAS-COG of GrP II from baseline to 4wks post intervention.

Paired Samples Test

		t	df	Sig. (2-tailed)
Pair 1	WRT Base - WRT at 4 wks after Intervention	5.735	14	.000
Pair 2	NOF Base - NOF at 4 wks after Intervention	1.871	14	.082
Pair 4	CP Base - CP at 4 wks after Intervention	2.779	14	.015
Pair 6	O Base - O at 4 wks after Intervention	6.000	14	.000
Pair 7	WR Base - WR at wks after Intervention	5.245	14	.000
Pair 10	WFD Base - WFD at 4 wks after Intervention	1.47	14	.164
Pair 12	Total Base - Total at 4 wks after Intervention	11.377	14	.000

Unpaired t-test:

Formula: $t = \dfrac{\overline{x_1} - \overline{x_2}}{SE}$

Where, $\overline{x_1}$ = Mean of the observations of Group I

$\overline{x_2}$ = Mean of the observations of Group II

$SE = \delta \sqrt{\dfrac{1}{n_1} + \dfrac{1}{n_2}}$

Standard deviation, $\delta = \sqrt{\dfrac{\sum (x - \overline{x})^2}{n - 1}}$

Accordingly the unpaired t-test was applied for comparison between the ADAS-COG, FAST and QOL-AD scores, as follows:

Table 15a) This table shows the comparison between the means, standard deviation, standard error of the baseline scores of ADS-COG, FAST, QOL-AD of GrP I and GrP II.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
C Base	With Choline	15	18.13	1.96	.51
	Without Choline	15	17.73	1.33	.34
FS Base	With Choline	15	3.13	.35	9.09E-02
	Without Choline	15	3.00	.00	.00
QOL Base	With Choline	15	2.00	.00[a]	.00
	Without Choline	15	2.00	.00[a]	.00

a. t cannot be computed because the standard deviations of both groups are 0.

Table 15b) This table shows the significant difference in the ADAS-COG and FAST scores at baseline of GrP I and GrP II.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
C Base	.654	28	.519
FS Base	1.468	14.000	.164

Table 16a) This table shows the comparison between the means, standard deviations, and standard errors of the scores of ADAS-COG, FAST, and QOL-AD at 16wks of GrP I and GrP II.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
C at 16 wks	With Choline	15	14.47	1.81	.47
	Without Choline	15	14.73	.96	.25
FS at 16 wks	With Choline	15	2.13	.35	9.09E-02
	Without Choline	15	2.47	.52	.13
QOL at 16 wks	With Choline	15	2.93	.26	6.67E-02
	Without Choline	15	2.40	.51	.13

Table 16b) This table shows the significant difference between the ADAS-COG, FAST and QOL-AD scores at 16 wks of GrP I and GrP II.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
C at 16 wks	-.505	28	.618
FS at 16 wks	-2.066	24.695	.049
QOL at 16 wks	3.630	20.802	.002

Table 17a) This table shows the comparison between the means, standard deviations, and standard errors of the ADAS-COG, FAST, and QOL-AD scores at 24wks of intervention of GrP I and GrP II.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
C at 24 wks	With Choline	15	12.53	1.68	.43
	Without Choline	15	13.27	.96	.25
FS at 24 wks	With Choline	15	1.53	.52	.13
	Without Choline	15	1.93	.59	.15
QOL at 24 wks	With Choline	15	3.20	.41	.11
	Without Choline	15	2.93	.26	6.67E-02

Table 17b) This table shows the significant difference between the ADAS-COG, FAST and QOL-AD scores of GrP I and GrP II.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
C at 24 wks	-1.464	22.241	.157
FS at 24 wks	-1.969	28	.059
QOL at 24 wks	2.117	23.458	.045

Table 18a) This table shows the comparison between the means, standard deviations, and standard errors of ADAS-COG, FAST, QOL-AD of GrP I and GrP II at 4 wks post intervention.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
C Post Intervention	With Choline	15	12.07	1.87	.48
	Without Choline	15	13.07	1.03	.27
FS Post Intervention	With Choline	15	1.53	.52	.13
	Without Choline	15	1.93	.59	.15
QOL Post Intervention	With Choline	15	3.20	.41	.11
	Without Choline	15	2.87	.35	9.09E-02

Table 18b) This table shows the significant difference between the ADAS-COG, FAST, and QOL-AD scores at 4 wks post intervention of GrP I and GrP II.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
C Post Intervention	-1.813	21.817	.084
FS Post Intervention	-1.969	28	.059
QOL Post Intervention	2.376	28	.025

Similarly, unpaired t-test was applied for the comparison between the sub items of ADAS-COG scores between GrP I and GrP II

Table 19a) This table shows the comparison of the means, standard deviations, and standard errors of the sub items of ADAS-COG of GrP I and GrP II at baseline.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
WRT Base	With Choline	15	6.73	1.03	.27
	Without Choline	15	6.87	.74	.19
NOF Base	With Choline	15	.27	.46	.12
	Without Choline	15	.20	.41	.11
C Base	With Choline	15	.00	.00[a]	.00
	Without Choline	15	.00	.00[a]	.00
CP Base	With Choline	15	.60	.51	.13
	Without Choline	15	.67	.49	.13
IP Base	With Choline	15	.00	.00[a]	.00
	Without Choline	15	.00	.00[a]	.00
O Base	With Choline	15	2.87	.35	9.09E-02
	Without Choline	15	2.80	.56	.14
WR Base	With Choline	15	6.60	.51	.13
	Without Choline	15	6.40	.51	.13
L Base	With Choline	15	.00	.00[a]	.00
	Without Choline	15	.00	.00[a]	.00
CSL Base	With Choline	15	.00	.00[a]	.00
	Without Choline	15	.00	.00[a]	.00
WFD Base	With Choline	15	.87	.35	9.09E-02
	Without Choline	15	.73	.46	.12
RTI Base	With Choline	15	.20	.41	.11
	Without Choline	15	6.67E-02	.26	6.67E-02
Total Base	With Choline	15	18.13	1.96	.51
	Without Choline	15	17.73	1.33	.34

a. t cannot be computed because the standard deviations of both groups are 0.

Table 19b) This table shows the significant difference between the sub items of ADAS-COG of GrP I and GrP II at baseline.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
WRT Base	-.406	28	.688
NOF Base	.418	28	.679
CP Base	-.367	28	.716
O Base	.390	28	.699
WR Base	1.080	28	.289
WFD Base	.894	28	.379
RTI Base	1.058	28	.301
Total Base	.654	28	.519

Table 20a) This table shows the comparison of the means, standard deviations, and standard errors of the sub items of ADAS-COG of GrP I and GrP II at 16 wks of intervention.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
WRT at 16 wks of Intervention	With Choline	15	5.8	1.01	.26
	Without Choline	15	6.2	.56	.14
NOF at 16 wks of Intervention	With Choline	15	.13	.35	.09
	Without Choline	15	0.07	.26	0.07
C at 16 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
CP at 16 wks of Intervention	With Choline	15	.1	.3	9.09E-02
	Without Choline	15	0	0	0
IP at 16 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
O at 16 wks of Intervention	With Choline	15	2.00	.00 [a]	.00
	Without Choline	15	2.00	.00 [a]	.00
WR at 16 wks of Intervention	With Choline	15	5.9	.6	.2
	Without Choline	15	5.9	.5	.1
L at 16 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
CSL at 16 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
WFD at 16 wks of Intervention	With Choline	15	.53	.52	.13
	Without Choline	15	.06	.51	.13
RTI at 16 wks of Intervention	With Choline	15	.1	.35	0.1
	Without Choline	15	0	.26	0
Total at 16 wks of Intervention	With Choline	15	14.47	1.81	.47
	Without Choline	15	14.73	.96	.25

a. t cannot be computed because the standard deviations of both groups are 0.

Table 20b) This table shows the significant difference between the sub items of ADAS-COG of GrP I and GrP II at 16 wks of intervention.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
WRT at 16 wks of Intervention	-1.34	28	.19
NOF at 16 wks of Intervention	0.59	28	.56
CP at 16 wks of Intervention	1.0	28	.33
WR at 16 wks of Intervention	0.000	28	1
WFD at 16 wks of Intervention	0.357	28	.72
RTI at 16 wks of Intervention	1.00	28	.33
Total at 16 wks of Intervention	-.505	28	.618

Table 21a) This table shows the comparison of the means, standard deviations, and standard errors of the sub items of ADAS-COG of GrP I and GrP II at 24wks of intervention.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
WRT at 24 wks of Intervention	With Choline	15	5.13	.83	.21
	Without Choline	15	5.67	.49	.31
NOF at 24 wks of Intervention	With Choline	15	.07	.26	.06
	Without Choline	15	.00	.00	.00
C at 24 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
CP at 24 wks of Intervention	With Choline	15	1	.26	0.1
	Without Choline	15	.0	0	0
IP at 24 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
O at 24 wks of Intervention	With Choline	15	1.47	.52	.13
	Without Choline	15	1.60	.51	.13
WR at 24 wks of Intervention	With Choline	15	5.33	.72	.19
	Without Choline	15	5.60	.63	.16
L at 24 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
CSL at 24 wks of Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
WFD at 24 wks of Intervention	With Choline	15	.4	.51	.13
	Without Choline	15	.4	.51	.13
RTI at 24 wks of Intervention	With Choline	15	.1	.3	.1
	Without Choline	15	0	0	0
Total at 24 wks of Intervention	With Choline	15	12.53	1.68	.43
	Without Choline	15	13.27	.96	.25

a. t cannot be computed because the standard deviations of both groups are 0.

Table 21b) This table shows the significant difference between the sub items of ADAS-COG of GrP I and GrP II at 24wks of intervention.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
WRT at 24 wks of Intervention	-2.14	28	.041
NOF at 24 wks of Intervention	1.00	28	.33
CP at 24 wks of Intervention	1.00	28	.33
O at 24 wks of Intervention	.74	28	.481
WR at 24 wks of Intervention	-1.07	28	.292
WFD at 24 wks of Intervention	.00	28	1
RTI at 24 wks of Intervention	1.00	28	.33
Total at 24 wks of Intervention	-1.464	28	.157

Table 22a) This table shows the comparison of the means, standard deviations, and standard errors of the sub items of ADAS-COG of GrP I and GrP II at 4 wks post intervention.

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
WRT at 4 wks After Intervention	With Choline	15	4.93	.80	.21
	Without Choline	15	5.47	.64	.165
NOF at 4 wks after Intervention	With Choline	15	.07	.26	.06
	Without Choline	15	.00	.00	.00
C at 4 wks after Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
CP at 4 wks after Intervention	With Choline	15	6.67E-02	.26	6.67E-02
	Without Choline	15	.13	.35	9.09E-02
IP at 4 wks after Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
O at 4 wks after Intervention	With Choline	15	1.33	.49	.13
	Without Choline	15	1.60	.51	.13
WR at wks after Intervention	With Choline	15	5.20	.8	.20
	Without Choline	15	5.53	.64	.2
L at 4 wks after Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
CSL at 4 wks after Intervention	With Choline	15	.00	.00 [a]	.00
	Without Choline	15	.00	.00 [a]	.00
WFD at 4 wks after Intervention	With Choline	15	.33	.49	.13
	Without Choline	15	.33	.49	.13
RTI at 4 wks after Intervention	With Choline	15	.1	.3	0.1
	Without Choline	15	0	0	0
Total at 4 wks after Intervention	With Choline	15	12.07	1.87	.48
	Without Choline	15	13.07	1.03	.27

a. t cannot be computed because the standard deviations of both groups are 0.

Table 22b) This table shows the significant difference between the sub items of ADAS-COG of GrP I and GrP II at 4 wks post intervention.

Independent Samples Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
WRT at 4 wks after Intervention	-2.02	28	.053
NOF at 4 wks after Intervention	.1	28	.33
CP at 4 wks after Intervention	1	28	.33
O at 4 wks after Intervention	-1.468	28	.153
WR at wks after Intervention	-1.28	28	.21
WFD at 4 wks after Intervention	0.00	28	1.00
RTI at 4 wks after Intervention	1.00	28	.33
Total at 4 wks after Intervention	-1.813	28	.084

DISCUSSION

The study was conducted on a total of 30 patients who were diagnosed as mild Alzheimer's dementia. These patients were divided into 2 groups (GrP I and GrP II). GrP I received cholinesterase inhibitors in addition to cognitive rehabilitation therapy, while GrP II received only cognitive rehabilitation therapy. Evaluations were carried out at baseline, at 16wks of intervention, at 24 wks of intervention, and at 4wks post intervention.

The effects of a systematized cognitive rehabilitation protocol on the cognitive abilities of people with mild Alzheimer's dementia are well documented. This study has attempted to show that cognitive rehabilitation does help to improve the cognitive and functional abilities and the quality of life of people with mild Alzheimer's dementia. No significant correlation was found between the educational status and the cognitive abilities of the participants.

The results of the study are summarized as follows:

1. COGNITION:

Was measured with the scale ADAS-COG, and following results were obtained:

The table 15b) and Fig 1) show that there was no significant difference between the ADAS-COG scores at baseline of GrP I and GrP II. This shows that both the cognitive status of both the groups was nearly the same.

As seen in tables 1a) and 4a), there was a decrease in the means from baseline to 16wks, 16wks to 24wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention, in both GrP I and GrP II.

Accordingly, the p-value for was found to be very highly significant (i.e. $p < 0.001$) between baseline to 16wks, 16wks to 24wks and baseline to 4wks post intervention, in both GrP I and GrP II. The p-value was found to be highly significant (i.e. $p<0.01$) between 24wks to 4wks post intervention for GrP I.

p-value between 24wks to 4wks post intervention for GrP II was not found to be significant (i.e. p>0.05).

This shows that there was a significant improvement in the cognitive abilities of the participants in GrP I throughout the duration of the therapy and they continued to improve even after the therapy was discontinued. The participants in GrP II, though their cognitive abilities improved significantly, the effect became stable after the therapy was discontinued. This fact could be explained by the study conducted by Jacqueline et al[16] in Nov. 2004, in which they found that cognitive rehabilitation was effective in delaying the cognitive and functional decline in these patients, but the effects plateaued after the 1st yr of discontinuing the therapy.

As seen in table 16b), 17b), 18b) there was no significant difference in the cognitive status of the participants in GrP I and GrP II at 16wks, 24wks, and at 4wks post intervention, as the p-value was >0.05. This shows that cognitive rehabilitation alone was as effective in improving the cognitive status of people with mild Alzheimer's dementia as was cognitive rehabilitation combined with cholinesterase inhibitors.

This fact has been summarized by the study conducted by Spector A et al[26], in 2003. They have found from their study that cognitive rehabilitation is an alternate, efficacious therapy for individuals who either cannot tolerate cholinesterase inhibitors or chose not to take medications. They have also found that the results obtained in their patients were comparable to those seen with cholinesterase inhibitors.

2. FUNCTIONAL STATUS:

Was measured with the scale FAST and the following results were obtained:

The table 15b) shows that there was no significant difference in the functional status of participants of GrP I and GrP II ($p>0.05$).

Tables 2a) and 5a) and fig. 2) show that the means of the FAST scores had decreased from baseline to 16wks, 16wks to 24wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention in both GrP I and GrP II. Accordingly, the p-value for the FAST scores between 16 to 24wks and from baseline to 4wks post intervention was found to be very highly significant (i.e. $p<0.001$) for the participants in GrP I. Similarly, the p-value was found to be highly significant ($p<0.01$) between baseline to 16wks, 16 to 24wks and was very highly significant ($p<0.001$) from baseline to 24wks. This fact can also be seen in Fig. 2). This shows that cognitive rehabilitation was very effective in improving the functional status of these patients. Since most of the tasks of the cognitive rehabilitation therapy were unrelated to functional tasks, this improvement could be explained by the fact that there was a generalization of skills learned during the therapy. This fact has been stated in the study conducted by R. Avila et al[22] in Nov. 2004.

Table 16b) shows that there was a significant improvement ($p<0.05$) in the functional status of GrP I and GrP II, which shows that the functional status of the participants in GrP I had improved more than that of GrP II at 16wks of intervention.

Tables 17b) and 18b) show that on comparing the functional status of participants in GrP I and GrP II, there was no significant improvement ($p>0,05$) at 24 wks and 4 wks post intervention. This could be explained by the fact that Rivastigmine is effective in improving the functional status of the patients in the 1st 3 months and the effects of the drugs become stabilized after that and therefore (stated in the study conducted on the effects of neurological rehabilitation in patients with Alzheimer's disease, by

R. Avila[22]), the improvements seen in the functional status of the participants in GrP I was purely because of the cognitive rehabilitation therapy.

3. QUALITY OF LIFE:

Was measured by the scale QOL-AD, and the effect of cognitive rehabilitation on the quality of life of the participants is summarized as follows:

Table 15a) shows that the means of the QOL-AD scores of GrP I and GrP II at baseline were same, indicating that the participants in both the groups had the same perceived quality of life.

Table 3a) and fig. 3) show that the mean QOL-AD scores of the participants of GrP I, had increased from baseline to 16wks, 16 to 24wks, and 24wks to 4wks post intervention and from baseline to 4wks post intervention. Accordingly table 3b) shows that the p-value was very highly significant ($p<0.001$) from baseline to 16wks and from baseline to 4wks post intervention and it was significant ($p<0.05$) from 16wks to 24wks.

Similarly, table 6a) shows that the mean QOL-AD scores of the participants in GrP II had increased from baseline to 16wks, 16 to 24wks, 24wks to 4wks post intervention and from baseline to 4wks post intervention. Accordingly, the table 6b) shows that this improvement in the quality of life was highly significant ($p<0.01$) from baseline to 16wks, very highly significant ($p<0.001$) from 16wks to 24wks and from baseline to 4wks post intervention. But it is seen that the p-value is not significant ($p>0.05$) from 24wks to 4wks post intervention. This shows that there was no significant improvement in the perceived quality of life of the participants in GrP II from 24wks to 4wks post intervention.

The improvement in the quality of life of the participants in is thus seen to be directly proportional to the improvement in their functional status and this improvement is seen to be independent of their cognitive status. This could be explained by the inclusion of functional approach in the therapy process. Since the therapy also included activities that resembled real-life problems faced by the

participants, practice in these areas improved the performance in these areas and thus improved their perceived quality of life.

Table 16a) shows that the mean of the QOL-AD score of GrP I was higher than that of GrP II at 16wks, 24wks and at 4wks post intervention. Accordingly, table 16b) shows that this difference was highly significant ($p<0.01$) at 16wks, and it was significant ($p<0.05$) at 24wks and 4wks post intervention. This indicates that the improvement in the quality of life of the participants in GrP I was more than that in GrP II. Dr. Loewenstein[21] states in his study that by combining specific cognitive rehabilitation strategies, we can help people with Alzheimer's dementia to remain engaged in daily activities and retain a connection to their family and friends and the world as a whole for a longer period of time.

4. **Similar comparison was done between the 11 items of ADAS-COG scale**, and following results were found:

Table 19a) and fig.4) show the means of the 11 items of ADAS-COG of both GrP I and GrP II at baseline and that the participants in both groups scored 0 in the items C, IP, L and CSL, which indicates that they were not affected in these areas. Also, the means of GrP I was lower (better) than GrP II on the item WRT and CP, higher than (worse) the means of GrP II on the items NOF, O, WR, WFD and RTI. Accordingly, table 19b) shows that there was no significant difference in the scores any of the 11 items of ADAS-COG between GrP I and GrP II at baseline.

- **GrP I (Cognitive rehabilitation with Cholinesterase inhibitors):**

Table 7a) shows that the means of the items, WRT, NOF, CP, O, WR, WFD, and RTI, of GrP I had decreased (improved) from baseline to 16wks. Accordingly, table 7b) shows that this improvement was very highly significant ($p<0.001$) for the items CP, O, WR, and it was highly significant ($p<0.01$) for the WFD task. For the rest of the tasks, like, WRT, NOF, RTI, the improvement in the mean scores was not found to be significant ($p>0.05$).

Table 8a) shows that the mean scores of the items WRT, NOF, O, WR, and WFD had decreased further, whole those of CP and RTI remained the same, from 16wks to 24wks of intervention in GrP I. Accordingly, table 8b) shows that this improvement in the mean scores was very highly significant ($p<0.001$) for the items WRT and O and it was highly significant ($p<0.01$) for WR. However, the improvement was not found to be significant ($p>0.05$) for the rest of the items (NOF, CP, WFD, RTI).

Table 9a) shows that there was an improvement in the means of the items WRT, O, WR, WFD, while, there was no difference in the means of the items NOF, CP, RTI from 24wks to 4wks post intervention in the participants of GrP I. Accordingly, table 9b) shows that there was no significant difference in the improvement seen in the items WRT, O, WR, WFD and RTI.

Table 10a) shows that there was an improvement in the mean scores of the items WRT, NOF, CP, O, WR, WFD, and RTI from baseline to 4wks post intervention, of GrP I. Accordingly, table 10b) shows that this improvement was very highly significant ($p<0.001$) for the items WRT, CP, O, WR, and WFD, while it was not significant for the items NOF and RTI.

- **Group II (only Cognitive rehabilitation):**

Table 11a) shows that there was an improvement in the mean scores of the items WRT, NOF, CP, O, WR, and WFD from baseline to 16wks, in the participants of GrP II. Accordingly, table 11b) shows that this improvement was very highly significant ($p<0.001$) for the items CP and O, and it was highly significant ($p<0.01$) for the items WRT and WR. However, it was not significant ($p>0.05$)for the items NOF, and WFD.

Table 12a) shows that there was an improvement in the means of the items WRT, NOF, O, WR, and WFD from 16wks to 24wks of intervention in GrP II. Accordingly, the table 12b) shows that this improvement was very highly significant ($p<0.001$) for the item WRT and highly significant ($p<0.01$) for the item O. There was no significant difference ($p>0.05$) in the items NOF, WR and WFD.

Table 13a) shows that there was an improvement in the mean scores of the items WRT, WR and WFD, while the mean of the items NOF and O remained the same from 24wks to 4wks post intervention of GrP I. Accordingly, table 13b) shows that this improvement was not significant ($p>0.05$) in any of these items.

Table 14a) shows that there was an improvement in the means of the items WRT, NOF, CP, O, WR, and WFD from baseline to 4wks post intervention of GrP II. Accordingly, this improvement was very highly significant ($p<0.001$) for the items WRT, O, and WR, while it was not significant for the items NOF, CP and WFD.

On comparing the scores of the individual items of ADAS-COG scale between the two groups, the following results were found:

Table 20a) and fig. 5) show that the means of the Grp I was lower (better) than GrP II on the items WRT and WFD, equal to GrP II on the items O and WR, and higher (worse) than GrP II on the items NOF, CP, RTI, at 16wks of intervention. Accordingly, table 20b) shows that there was no significant difference ($p>0.05$) in the means of the items WRT, NOF, CP, WR, WFD and RTI of GrP I.

Table 21a) and fig.6) show that the means of GrP I on the items WRT, O and WR were better than those for GrP II, equal to the means of GrP II on the item WFD, and worse than the means of GrP II on the items NOF, CP, and RTI, at 24wks of intervention. Accordingly, table 21b) shows that there was a significant difference ($p<0.05$) in the means of GrP I and GrP II on the item WRT. However, no significant difference ($p>0.05$) was found in the means of the items NOF, CP, O, WR, WFD, and RTI.

Table 22a) and fig. 7) show that the means of GrP I on the items WRT, CP, O, and WR were better than those of GrP II, equal to those of GrP II on the item WFD, and worse than those of GrP II on the items NOF and RTI, at 4wks post intervention. Accordingly, table 22b) shows that this difference was significant ($p<0.05$) for the item WRT, while it was not significant ($p>0.05$) for the items CP, O, NOF, WR, WFD and RTI.

Thus, through this analysis, it was attempted to show the change in the individual components of the ADAS-COG scale after intervention in the two groups. From the above analysis, it can be concluded that the participants in the two groups

scored differently on the various items of the scale throughout the study. It can be seen from the above analysis that the participants of both the groups improves steadily on the items WRT, O, WR, and that this improvement was statistically significant. This can be explained as due to the effect of the memory improving strategies taught during the therapy, use of external aids like memory notebooks and calendars.

The improvements in the individual items of ADAS-COG scale also shows that the participants have shown the ability to improve on trained as well as untrained tasks, indicating generalization of the learning that occurred from the cognitive rehabilitation therapy. Also, improvement in these tasks has been proven by the study conducted by Dr. Loewenstein[21], Lustig and Buckner [29]. They have reported from their study that it is possible to pinpoint what memory capabilities are preserved or affected in early Alzheimer's dementia and that it is also possible to target these memory functions and make the most of them.

The fact that the cognitive status of the participants in GrP II did not improve after the therapy was discontinued indicates that for the long term effect, cognitive rehabilitation has to be combined with cholinesterase inhibitors.

CONCLUSION

1. People in the early stage of Alzheimer's dementia have the ability for learning new associations.
2. Cognitive rehabilitation helps to improve the cognitive abilities of the people with mild Alzheimer's dementia, irrespective of whether they are taking cholinesterase inhibitors or not.
3. Cognitive rehabilitation helps to improve the functional status and the quality of life of the people with mild Alzheimer's dementia.
4. There is no significant statistical difference in the cognitive status of patients receiving Cholinesterase inhibitors and the patients not receiving them. This indicates that cognitive rehabilitation is equally effective in improving the cognitive status of the patients with mild Alzheimer's dementia.
5. It is possible to train the people with mild Alzheimer's dementia in specific tasks related to functional activities, like, Face-Name associations.
6. It is possible to improve the implicit memory of people with mild Alzheimer's dementia with the help of various memory training strategies like, rehearsal, elaborating, self reference, visual imagery, mnemonics and story method.
7. It is also possible to improve memory by provision of external aids like memory notebooks and pocket calendars.
8. Generalization of learning does occur in people with mild Alzheimer's dementia.
9. It is possible to train the people with mild Alzheimer's dementia in individual cognitive abilities like attention, orientation, word recall, word recognition, and face-name associations.
10. It is possible to delay the progression of Alzheimer's disease by treating the patients with a combination of cholinesterase inhibitors and cognitive rehabilitation.

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