

# Estimation Of Serum Levels Of Alanine Transaminase, Aspartate Transaminase, Alkaline Phosphatase In Donepezil Therapy Of Alzheimer's Patients In A Tertiary Care Hospital

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**Abstract:** Neurodegenerative diseases are incurable and debilitating conditions that result in progressive degeneration and /or death of nerve cells. This causes problems with movement (called ataxia), or mental functioning (called dementia). Alzheimer's is a chronic neurodegenerative disease of the brain, that causes problems with memory, thinking and behavior. It is not a normal part of aging. The cause of Alzheimer's disease is poorly understood. The risk factors include a history of head injuries, depression or hypertension. The medication used to treat Alzheimer's disease are acetyl cholinesterase inhibitors and NMDA receptor antagonists. Donepezil is a cholinesterase inhibitor. It works by increasing the amount of acetylcholine in the brain, which may help reduce the symptoms of dementia in patients with Alzheimer's disease. The administration of Donepezil causes marked elevation in the serum liver enzymes like alanine transaminase, aspartate transaminase, alkaline phosphates.

**Keywords:** Neurodegenerative, alzhiemers, acetylcholinesterase NMDA receptor antagonists

## I. INTRODUCTION

Alzheimer's is a type of dementia that causes problems with memory, thinking, and behavior. Symptoms usually develop slowly and get worse over time becoming severe enough to interfere with daily tasks. Alzheimer's disease accounts for 60-80 percent of dementia cases. Alzheimer's is not a normal part of aging, although the greatest known risk factor is increasing age and the majority of people with Alzheimer's are 65 and older. The most common early symptom of Alzheimer's is difficulty in remembering newly learned information. Because Alzheimer's changes typically begin in the part of brain that affects learning. As Alzheimer's advances through the brain it leads to increasingly severe symptoms, including disorientation, mood and behavior changes, deepening confusion about events, time and places;

unfounded suspicions about family, friends, and professional caregivers; more serious memory loss and behavior changes; and difficulty speaking, swallowing and walking.

There are two types of medication used to treat Alzheimer's disease:

Acetyl cholinesterase inhibitors and NMDA receptor antagonists.

Cholinesterase inhibitors are a type of drug that boosts the amount of acetylcholine available to nerve cells by preventing its breakdown in the brain. The generic names for the cholinesterase inhibitors are donepezil, rivastigmine and galantamine.

- ✓ Donepezil was originally patented as the brand name Aricept, but is more widely available now as just generic Donepezil.

The NMDA receptor antagonist is memantine. It was originally patented as Ebixa and is now also available as generic memantine. Other UK brand names for memantine include Maruxa and Nemdatine. Donepezil is used to treat confusion (dementia) related to Alzheimer's disease. It does not cure Alzheimer's disease, but it may improve memory, awareness, and the ability to function. This medication is an enzyme blocker that works by restoring the balance of natural substance (neurotransmitter) in the brain.

Alzheimer disease is associated with a cholinergic deficiency in the cerebral cortex, and the increase in concentration of acetylcholine with acetyl cholinesterase inhibition is associated with improvement in cognitive function in patients with Alzheimer dementia. Donepezil has selective activity for acetyl cholinesterase in the central nervous system with little effect on the enzyme in peripheral tissue. Donepezil was approved for use in the United States in 1996 and is currently the most commonly used acetyl cholinesterase inhibitor used for management of Alzheimer disease. Donepezil is available as regular tablets of 5 and 10 (and recently 23 mg) and as orally disintegrating tablets of 5 and 10 mg in generic forms and under the brand name Aricept. Donepezil is also available as an solution of 1 mg/mL for oral administration. The usual maintenance dosage is 5 to 10 mg once daily. Patients who tolerate the 10 mg daily dose may benefit from a higher dose of 23 mg daily. Common side effects include diarrhea, nausea, vomiting, dizziness, fatigue, insomnia, vivid dreams, anxiety, restlessness, blurred vision, dry mouth and pruritus, symptoms common to cholinergic stimulation. Donepezil binds and inactivates reversibly the cholinesterase, thus inhibiting hydrolysis of acetylcholine. This results in an increased acetylcholine concentrations at cholinergic synapses.

Donepezil marketed under the trade name Aricept, is a medication used in the palliative treatment of Alzheimer's disease. Donepezil is used to improve cognition and behavior of people with Alzheimer's, but does not slow the progression of or cure the disease.

Donepezil binds and reversibly inactivates the cholinesterases, thus inhibiting hydrolysis of acetylcholine. This results in an increased acetylcholine concentrations at cholinergic synapses.

## II. REVIEW OF LITERATURE

- ✓ Etsuro Mori *et al*; (2016) conducted a study on Increased plasma donepezil concentration improves cognitive function in patients with dementia with Lewy bodies: An exploratory pharmacokinetic/ pharmacodynamic analysis in a phase 3 randomized controlled trial. The aim of the study was to investigate whether increasing plasma donepezil concentration further improves cognitive function and neuropsychiatric symptoms without compromising safety in patients with dementia with Lewy bodies (DLB). We analyzed data from a 12-week phase 3 trial of donepezil (5 and 10 mg/day) in patients with DLB. The contribution of factors affecting plasma donepezil concentration was evaluated using multivariate regression analysis. The relationships between plasma donepezil concentration and efficacy. The data of 87 patients were used in the analyses. Plasma donepezil concentration increased proportionally with increasing dose from 5 to 10 mg/day. Plasma donepezil concentration correlated positively with change in cognitive function without affecting safety, and was affected mainly by dose and to a lesser extent by age. Therefore, for patients in whom safet.
- ✓ Ramón Cacabelos *et al*; (2007) conducted a study on Donepezil in Alzheimer's disease: From conventional trials to pharmacogenetics. Donepezil is the leading compound for the treatment of Alzheimer's disease (AD) in more than 50 countries. As compared with other conventional acetylcholinesterase inhibitors (AChEIs), donepezil is a highly selective and reversible piperidine derivative with AChEI activity that exhibits the best pharmacological profile in terms of cognitive improvement, responders rate (40%–58%), dropout cases (5%–13%), and side-effects (6%–13%) in AD. The result of the study concludes that the main causes of therapeutic failure with AChEIs in general and donepezil in particular in AD are the following: (1) the central cholinergic deficit in AD is not the cause of the disease but the consequence of neurodegeneration associated with complex pathogenic mechanisms involving many different genomic, proteomic, and metabolomic cascades; (2) pharmacokinetic and pharmacodynamic weaknesses of the AChEIs.
- ✓ Ronald.c.petersen *et al*; (2005) conducted a study on vitamin E and Donepezil for the treatment of mild cognitive impairment. In a double-blind study evaluated subjects with the amnesic subtype of mild cognitive impairment. Subjects were randomly assigned to receive 2000IU of vitamin E daily, 10 mg of donepezil daily, or placebo for three years. A total of 769 subjects were enrolled and possible or probable Alzheimer's disease developed in 212. The overall rate of progression from mild to cognitive impairment to Alzheimer's disease was 16 percent per year. As compared with placebo group, there were no significant differences in the probability of progression to Alzheimer's disease in the vitamin E group or the donepezil group during the three years of treatment. By this study it is concluded that vitamin E had no benefit in patients with mild cognitive impairment.
- ✓ Seltzer B *et al*; (2004) conducted a study on Efficacy of donepezil in early-stage Alzheimer disease: a randomized placebo-controlled trial. The aim of the study was to evaluate the efficacy of donepezil in patients with early-stage Alzheimer disease. Multicenter, randomized, double-blind, 24-week, placebo-controlled study that enrolled patients with early-stage Alzheimer disease. Patients were randomized in an approximately 2:1 ratio to donepezil, 5 mg/d, for the first 6 weeks, with a forced escalation to 10 mg/d thereafter (n = 96), or placebo (n = 57). The result of the study shows that These data suggest significant treatment benefits of donepezil in early-stage Alzheimer disease, supporting the initiation of therapy early in the disease course to improve daily cognitive functioning.

- ✓ Steven.m.greenberg *et al*: (2000) was conducted a study based on the Donepezil therapy in clinical practice. The objective of study was to determine the efficacy of Donepezil hydrochloride for the treatment of alzheimer's disease in patients drawn from clinical practice. It is a Two- centre, randomised, placebo- controlled, double-masked cross over study. Sixty individuals with probable Alzheimer's disease and scores of 20 or less on information – memory- concentration subscale of the Blessed Dementia Scale. Among patients completing treatment and testing for both periods (n=48) subscale scores improve during donepezil therapy relative to placebo therapy. This independent confirmation of data from phase 3 trials suggests that Donepezil therapy modestly improves cognition in patients with alzheimers disease who are encountered in clinical practice.
- ✓ Rogers SL, *et al*; (1998) conducted a study on the Efficacy and Safety of Donepezil in Patients with Alzheimer's Disease: Results of a US Multicentre, Randomized, Double-Blind, Placebo-Controlled Trial. This study evaluated the efficacy and safety of donepezil in patients with mild to moderately severe Alzheimer's disease, and examined the relationships between plasma donepezil concentration, red blood cell acetylcholinesterase (AChE) activity and clinical response. The trial was of a multicenter, double-blind, parallel-group design and patients were randomised to once-daily treatment with either donepezil (1, 3 or 5 mg) or placebo. The 12-week double-blind phase was followed by a 2-week single-blind placebo washout. 161 patients (55-85 years of age) entered the study and 141 completed treatment. Patients treated with donepezil showed dose-related improvements in the Alzheimer's Disease Assessment Scale - cognitive subscale score (ADAS-cog) and in MMSE scores. The improvements in ADAS-cog were statistically significantly greater with donepezil 5 mg/day than with placebo.
- ✓ R. S. Doody, *et al* ; ( 1998) conducted a study on A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease .The efficacy and safety of donepezil as a treatment for patients with mild to moderate Alzheimer's disease (AD) was investigated in a multicenter, double-blind study. Patients were randomly assigned to treatment with placebo (n = 162), 5 mg/d donepezil (n = 154), or 10 mg/d donepezil (n = 157) for 24 weeks followed by a 6-week, single-blind placebo washout. The primary efficacy measures were the cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-cog) and the Clinician's Interview Based Assessment of Change-Plus (CIBIC plus), with the Mini-Mental State Examination (MMSE), Clinical Dementia Rating Scale-Sum of the Boxes (CDR-SB), and patient rated Quality of Life (QoL) used as secondary measures. Cholinergic side effects (primarily diarrhea, nausea, and vomiting) were reported more often in the 10-mg/d group than either the 5-mg/d or placebo groups. Side effects were transient and generally mild in severity. These data indicate that donepezil is a well-tolerated drug that

improves cognition and global function in patients with mild to moderate AD.

### III. CONCLUSION

The studies regarding the effect of drug Donepezil on liver enzymes are of much important and are very rare. It is important to monitor liver function test while taking Donepezil. The study will be very informative to the patients and medical practitioner.

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