

Evaluation of Combined Effect of Alpha Lipoic Acid and Sertraline on Primary Efficacy In Comparison to Sertraline Alone in Depressive Patients

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Abstract: The aim of the study was to assess the therapeutic benefits, response pattern with sertraline alone to that of combined effect of alpha lipoic acid with sertraline in depressive disorder patients. 31 patients included in the study, of which 14 patients were given sertraline alone (Control group) and 17 patients with sertraline and alpha lipoic acid for a duration of 8 weeks after taking informed consent. The demographic and hematological data was collected. Drugs were administered dose dependently for 8 weeks. Patients were asked to visit psychiatry out-patient department every 2 weeks to measure Hamilton Depression Rating Scale (HDRS) score. The collected data was analyzed by student 't' test for statistical significance. After 2 weeks of administration of drugs the control groups showed 1.93 and test showed 1.88 as week's progress the score was decreased but test group showed significant decrease compared to control group. Same results were observed at 2nd, 4th visit. In this study combined administration of alpha lipoic acid with sertraline decreased the HDRS score, learned helplessness, suicidal tendency dose dependently. Alpha lipoic acid was used to treat depression along with standard anti-depressant drugs.

Keywords: Anti-depressant, Depression, Hamilton Depression Rating Scale, Sertraline, Alpha -lipoic acid

Introduction

Depression is a most common symptom associated with several systemic as well as psychiatric disorders. Major depressive disorder (MDD) commonly seen in nursing home resident, old age, patients suffering from chronic disorders and disability¹. Several classes of anti-depressant drugs were used to treat the depression. These medications can develop several unwanted side effects that may impair patients quality of life and reduce the compliance². The Major classes of drugs used are Tricyclic antidepressants (TCA), Selective serotonin reuptake inhibitors (SSRI) and atypical antidepressants. According to growing research and database support, The Selective serotonin reuptake inhibitors are effective in the treatment of MDD in humans. Several studies have been reported on sertraline³. But fewer studies had showed combination therapy of this drug. Not only neurotransmitter deficiency is a cause for depression. Depletion of essential omega-3 fatty acids in the diet is linked to chronic diseases and the huge increase in the rate of depression⁴. These fatty acids are the sources for the formation of CNS membrane and decrease the synthesis of several pro-inflammatory mediators in brain. Co-administration of omega-3 fatty acids along with standard anti-depressant drugs can improve the depressive

patient. Alpha lipoic acid is a source of omega-3 fatty acids⁵. The present study planned to find the combined effect of alpha lipoic acid with sertraline in depression patient.

Materials and Methods

Inclusion criteria:

- Male or female age between 18-65 years.
- The patients full fill the DSM-IV criteria for depression.
- Patients have base line HDRS score of 18 on 24 items⁶.
- No CNS disorders.

Exclusion criteria:

- Those not meeting DSM-IV criteria for depression.
- Pregnant and lactating women.
- Hypertension.
- Diabetes mellitus.
- Hepato-renal diseases.
- History of any other psychiatric or neurological disorders⁷.

Design of the study:

Group-I (Control): Sertraline (50-150mg/orally)⁸

Group-II (Test): Sertraline (50-150mg/orally) + Alpha lipoic acid (200mg/orally)⁹

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Procedure:

The patients satisfy the inclusion and exclusion criteria was selected and randomly allocated in to two groups. Control group (n=14) and Test group (n=17).

Dosage regimen:

Control group: Patients were given tablet Sertraline (50mg) initially to be taken once daily after breakfast. The dose was titrated and raised up to maximum 150mg once daily at subsequent fortnight visits, depending upon the persistence of symptoms and response on HDRS score at each visit during the entire study period¹⁰.

Test group: Patients were given Sertraline 50mg initially to be taken once daily after breakfast along with capsule ALA-100mg twice daily. The dose of sertraline was titrated and increased up to a maximum of 100mg daily at subsequent biweekly visits, depending on HDRS score and persistent of symptoms during entire study period¹¹.

During study period all the patients were advised to visit outpatient department once in every two weeks. The patients in test and control groups were advised to bring empty strips of the tablets sertraline and capsules ALA-100 depending on the group they belong to. The tablets or capsules taken were counted at each visit and recorded in evaluation proforma against each visit. Patients attenders were involved and entrusted to monitor medication intake by the patient and were asked into the details of any missing doses. HDRS scores were measured for all visits^{12, 13}. The study was ethically cleared by Institutional Human Ethical Committee (Gandhi Medical College, Secunderabad). The patients were permitted to take benzodiazepine, lorazepam as and when required for sleep disturbances. Patients with established Acid peptic disease were allowed to continue the use of proton pump inhibitors, H₂- blockers and were advised to take antacids on manifestation of gastrointestinal upset.

Statistical analysis:

The primary safety variables data was analyzed by Student "t" test for statistical significant. P-value less than 0.05 considered statically significant¹⁴.

Results

Patients administered standard drug with alpha lipoic acid showed visit depend decrease in the HDRS score at 24-item compared to control group. The difference is found to be statistically significant at all the visits between control and test

groups (Table.1). There was a significant difference observed in helplessness score between sertraline alone and sertraline with Alpha lipoic acid administered groups (Table.2). HDRS 24-worthlessness score observations showed significant difference at 2nd, 3rd, 4th and 5th visit and no significant difference was observed at 1st visit (Table.3). The suicidal ideations score also showed significant difference between control and test. Statistically insignificant results observed at 1st visit in HDRS 24-suicidal ideations score (Table. 4).

Table.1: Comparison of 24-item total HDRS scores in test and control at each visit

Groups	First visit (HDRS1) (MEAN±SD)	Second visit (HDRS2) (MEAN±SD)	Third visit (HDRS3) (MEAN±SD)	Forth visit (HDRS4) (MEAN±SD)	Fifth visit (HDRS5) (MEAN±SD)
Test	35.65±7.14	21.82±6.42	14.24±7.37	7.53±4.09	3.06±1.39
Control	42.21±7.56*	32.43±8.13*	26.50±9.34*	17.50±7.55*	9.71±4.79*

(*P<0.05 significant compared test group with control)

Table.2: Comparison of HDRS subscale item 23- helplessness in test and control at each visit

Groups	First visit (HDRS1) (MEAN±SD)	Second visit (HDRS2) (MEAN±SD)	Third visit (HDRS3) (MEAN±SD)	Forth visit (HDRS4) (MEAN±SD)	Fifth visit (HDRS5) (MEAN±SD)
Test	2.00±0.50	1.18±0.64	0.71±0.59	0.18±0.39	0.08±0.24
Control	1.79±0.89	1.43±1.02	1.36±0.84*	0.86±0.66*	0.57±0.65*

(*P<0.05 significant compared test group with control)

Table.3: Comparison of HDRS subscale item 24- worthlessness in test and control at reach visit

Groups	First visit (HDRS1) (MEAN±SD)	Second visit (HDRS2) (MEAN±SD)	Third visit (HDRS3) (MEAN±SD)	Forth visit (HDRS4) (MEAN±SD)	Fifth visit (HDRS5) (MEAN±SD)
Control	1.94±1.03	0.94±0.66	0.65±0.49	0.24±0.44	0.00±0.00
Test	2.07±0.92	1.71±0.91*	1.43±0.94*	0.86±0.77*	0.43±0.51*

(*P<0.05 significant compared test group with control)

Table.4: Comparison of HDRS subscale item 24- suicidal ideations in test and control at reach visit

Groups	First visit (HDRS1) (MEAN±SD)	Second visit (HDRS2) (MEAN±SD)	Third visit (HDRS3) (MEAN±SD)	Forth visit (HDRS4) (MEAN±SD)	Fifth visit (HDRS5) (MEAN±SD)
Control	2.00±1.66	0.88±1.05	0.35±0.61	0.16±0.24	0.00±0.00
Test	2.57±0.94	1.64±0.93*	1.29±1.14*	0.86±0.66*	0.50±0.52*

(*P<0.05 significant compared test group with control)

Discussion

Depression is common mental disorder observed in all the age groups. Though the complex pathophysiology of major depression remain unknown, studies have shown the role of Monoamine neuro-transmitters like Serotonin(5HT), Noradrenalin, and dopamine, dysfunction or deficiency in neurons in the causation of major depressive disorders. Increase this neuro-transmitters in synaptic cleft may improve the symptoms of depression. Several classes of drugs

are used in the treatment of depression. Almost all anti-depressant drugs increase the release or inhibit the reuptake of neurotransmitter at neurons. Antidepressant drugs produce the several severe adverse effects in the patients. There is requirement of adjuvant drugs to treat the major depressive disorders. Lipoic acid is present in almost all foods and naturally occurring lipoic acid is always covalently bound and readily available from dietary source. The several studies and clinical trials proved that lipoic acids have many health benefits like organ protection, prevent cardiovascular disorders, improve the wound healing, decrease the iron toxicity, improve the cognitive function and slow down the disease progression in dementia. The present study conducted to find the dose dependent effect of the alpha lipoic acid effect on major depressive disorder. In this study combined administration of alpha lipoic acid with Sertraline showed significant results in HDRS scores in the areas of learned helplessness, worthlessness, and suicidal ideations at every visit. Alpha lipoic acid administration has been shown to increase the brain derived neurotrophic factor in the hippocampus and cortex. This neurotrophic factor involved in neurogenesis, cell survival, neuronal plasticity and neuro protection. Preclinical studies showed anti-depressant activity leading, researchers to conclude that therapeutic effect of alpha lipoic acid would have similar anti-depressant effects in the humans suffering from depression. Present study showed positive results in the depression patients. Therefore, the natural alpha lipoic acid should be studied as an alternative or add on therapy to treat major depressive disorder.

Conclusion

Our results suggested that combined administration of Sertraline and alpha lipoic acid can improve the patient's behavior and cognitive functions in short time compared to mono therapy. There are several clinical trials required to study more on this combination therapy.

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