# Treatment of idiopathic asthenozoospermia and oligoasthenozoospermia with Alpha lipoic acid: a placebo-controlled, cross over study.

**Thesis**

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# List of Abbreviations

| | |
|---|---|
| ALA | alpha lipoic acid |
| ALH | Amplitude lateral head displacement |
| ART | assisted reproductive techniques |
| ATP | adenosine triphosphate |
| AZF | azoospermia factor |
| AZS | asthenozospermia |
| BCF | Beat-cross frequency (Hz) |
| CAD | coronary artery disease |
| cAMP | cyclic adenosine monophosphate |
| CASA | computer assisted semen analysis |
| CASMA | computer-aided sperm morphometric Assessment |
| CFTR | cystic fibrosis transmembrane conductance regulator |
| C-max | concentration maximum |
| CRLA | controlled release alpha lipoic acid |
| DEPs | differentially expressed proteins |
| DHLA | dihydrolipoic acid |
| DMSA | dimercaptosuccinic acid |
| FSH | follicle stimulating hormone |

| | |
|---|---|
| G3PD | glyceraldehyde- 3-phosphate dehydrogenase |
| GSH-Px | glutathione peroxidase |
| IBT | Immuno beed test |
| IVOS | Integrated video optical system |
| KS | kartagener syndrome |
| LH | leutinizing hormone |
| LIN | Linearity |
| MAD | Mean angular displacement (degrees) |
| MAGI | male accessory gland infection |
| NO | nitric oxide |
| NOS | nitric oxide synthase |
| NTSC | National Television Standards Committee standard |
| ODAs | outer dynin arms |
| OSF | oral submucous fibrosis |
| PAL | phase alternating line |
| PCD | primar ciliary dyskinesia |
| PCOs | polycystic ovary syndrome |
| PDH | pyruvate dehydrogenase |
| PRM1 | protamine 1 |
| PRM2 | protamine 2 |
| R-ALA | R lipoic acid |

| | |
|---|---|
| **ROS** | **reactive oxygen species** |
| **S-ALA** | **S lipoic acid** |
| **SFA** | **Seminal fluid analysis** |
| **Se** | **Selenium** |
| **SNPs** | **Single-nucleotide polymorphisms** |
| **SQA-V** | **Sperm Quality Analyzer** |
| **STR** | **Straightness** |
| **TNF** | **tumor necrosis factor** |
| **TRP** | **transient receptor potential** |
| **VAP** | **The average path velocity** |
| **VCL** | **The curvilinear velocity** |
| **VSL** | **The straight line velocity** |
| **WHO** | **world health organization** |
| **WOB** | **Wobble** |

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# ABSTRACT

In the first section of the study 60 patients complaining of infertility, with the chief etiology is idiopathic asthenozoospermia (either isolated or associated with oligozoospermia) group I received 600 mg/day of alpha lipoic acid as an antioxidant ( Alpha lipoic acids were selected for this purpose for their efficient free radical scavenging properties, and solubility in lipid and aqueous phases.

ALA does not cause a major shift of pH into acidic regions, because the acid is categorized as a weak acid. Recent findings have also indicated that ALA is able to enter the Krebs cycle, thus assisting in the production of ATP, which is required in viable sperm.), while group II received placebo for 3 months duration, and semen was assessed monthly using CASA.

The study had been conducted in a double blind, placebo controlled; after wash out period for 3 months, the crossover section of the study started by 41 patients. All the 3 main semen parameters (count, motility &abnormal forms) monitored and compared for every patient and between both groups pretreatment, after 3$^{rd}$ month and after the second section.

The results revealed improvement with active drug intake regarding total motility (group I), after cross over section placebo improved both progressive & total motility.

While group II received placebo; there was improvement in count, progressive & total motility, but when active drug was taken for 3 months later, there was no more improvement in the cross over section and all the results regressed.

**Conclusion:** From the results of this study, alpha lipoic acid adds no more than placebo in idiopathic asthenoozospermia. We recommend further study on larger group of patients to reach final conclusions.

**Key words:** Asthenozoospermia - Alpha lipoic acid – Antioxidants – CASA.

# INTRODUCTION

Infertility is an important human health problem that affects ~15% of couples worldwide (Infertility touches 1 in 6 couples), and the underlying cause in half of these cases can be traced to men **(Flaherty, 2014**).

The infertile population has been increasing over the past few decades. However, treatment efficacy is poor because the underlying causes are unknown in 40-50% of cases **(Kretser & Baker, 1999**).

Oxidative stress is a common feature of compromising factors such as environmental pollutants, chemicals, drugs, smoke, toxins, radiation, and diseases related to infertility **(Smith et al, 2006**). In such conditions, vital cell components, such as proteins, lipids, and DNA, are oxidized (**Halliwell et al, 2007**).

Reactive oxygen species (ROS) - mediated damage to sperm is a significant contributing factor in 30-80% of infertile men **(Agarwal et al, 2006**), DNA fragmentation and oxidation of bases**,** low mitochondrial membrane potential (**Gallon et al, 2006**).

The oxidative stress, a condition resulting of an excessive production of ROS and/or a decrease in the antioxidant defense system, may cause serious cell injury and even cell death **(Halliwell et al, 2007**).