META-ANALYSIS OF DOUBLE-BLIND PLACEBO
CONTROL TRIALS EVALUATING THE ROLE OF COENZYME Q10 ON SEMEN PARAMETERS
Ashok Agarwal, PhD., 1 Aditi Sharma, MSc., 1 Kruyanshi Master, MSc., 1 Rakesh Sharma, PhD., 1 and Ralf Henkel, PhD.1,2
1American Center for Reproductive Medicine, Department of Urology, Cleveland Clinic, OH, USA
2Department of Medical Bioscience, University of the Western Cape, Bellville, 7535, South Africa

Introduction
Oxidative stress (OS) is prevalent in a number of conditions including male genital tract infections, varicocele, and obesity. It is also an important cause of sperm DNA damage. OS is a result of an imbalance between excessive production of reactive oxygen species (ROS) and the available antioxidants to scavenge these ROS. A number of enzymatic and non-enzymatic antioxidants exist to maintain a favorable redox potential. Co-enzyme Q10 (Co-Q10) is an essential antioxidant that is ubiquitous to almost all body tissues and is highly concentrated in the sperm mitochondria where it plays an integral role in energy production.

The antioxidant properties of Co-enzyme Q10 are carried by its reduced form - ubiquinol, which can neutralise ROS through donating electrons. The administration of Co-enzyme Q10 as a supplement may have a positive role in treating men with infertility as suggested by few studies reporting significant improvement in sperm motility after antioxidant therapy.

We aimed to perform a meta-analysis of double-blind randomized placebo-controlled clinical trials examining the effect of Co-enzyme Q10 supplementation on semen parameters in infertile men with idiopathic oligo-astheno-teratozoospermia and idiopathic asthenozoospermia.

Materials and Methodology
A literature search was carried out using the key words Co-enzyme Q10, semen parameters, motility, male infertility and sperm quality was conducted using Google Scholar, MedLine, PubMed and Wiley Online Library. The search was filtered to only include clinical trials and human studies over the past 15 years. No language limits were used. We screened the reference lists of all of the relevant articles and reviews.

The literature review was carried out based on double-blind, placebo trials done on antioxidants, vitamins and other minerals used in the treatment of male infertility. The outcome obtained from this search was four studies on Co-enzyme Q10, and fewer on vitamins. Co-enzyme Q10 antioxidants was selected because of its effective outcomes in sperm motility.

Study Design
The study design included 395 patients with idiopathic infertility who received 100-200 mg of Co-enzyme Q10 or placebo for 3-9 months. Semen samples were compared at baseline and after the completion of the treatment period. Co-enzyme Q10 levels were also measured in the seminal plasma. Improvement in sperm concentration and total sperm motility were the two parameters that were common in all four studies.

Based on Co-enzyme Q10 antioxidants, we decided to collect all the data from the four studies obtained from our literature search and conduct a review. This was difficult as the time duration of the treatment varied among all the four studies. It was necessary to carry out the meta-analysis as a standard statistical measure in conducting this review based on four double-blind placebo controlled trials.

Statistical Analysis
Statistical Analysis was done using MedCalc: Statistical Software version 18.2.2 (MedCalc Software bvba, Ostend, Belgium). The continuous measures and 95% confidence interval was calculated for the two common semen parameters: concentration and motility. Statistical analysis was based on the mean and SD of the referred studies. The mean and SD between the semen parameters before the treatment and after the baseline and after the treatment were used to analyze the data. A P-value < 0.05 was considered statistically significant (Ross et al., 2010).

Results
1. The results of sperm concentration and motility for each study are shown before and after treatment in Figures 1 and 2.

2. Two studies represent significant differences in sperm concentration before and after treatment, while other two showed no differences (Figures 3).

3. No improvement in mobility was seen in any of the 4 studies. Two studies showed a significant decline in mobility after treatment (Figure 4).

4. Meta-analysis result showed significant improvement in total motility and sperm concentration (P<0.0001) after Co-enzyme Q10 supplementation (Figure 4).

5. Patients with a lower baseline value of sperm count had a significantly higher probability to respond to the treatment (Figure 4).

6. Mobility also showed significant improvement (P<0.0001) (Figure 5).

Conclusion
1. Our study examined the meta-analysis on double-blind, placebo controlled trials for Co-enzyme Q10 and its effects on sperm concentration and sperm motility.

2. Co-enzyme Q10 shows significant improvement in sperm concentration and sperm motility. It can be used as an effective therapy in the treatment of male infertility.

3. Patients presenting with poor motility before Co-enzyme Q10 supplementation respond better to antioxidant therapy.