

## **Carnitine supplement: Does it worth trial to improve semen quality among infertile Sudanese men?**

Abdulhadi N. H<sup>1\*</sup>, Hoyam B<sup>2</sup>

### **Abstract:**

Carnitine supplement proves to upgrade the quality of semen by increasing sperm count and motility. In this study we have determined the level of L – carnitine in the seminal plasma of men with normal and abnormal seminal analysis. L – carnitine levels among the normal group was significantly higher than the abnormal group. We recommend trials of carnitine supplements to evaluate its usefulness in correcting some infertility cases.

### **Subjects and methods:**

A total of 52 men, recruited from fertility centers in Khartoum, were included in this study. Colorimetric carnitine determination kits were used for estimation of L – carnitine in seminal plasma.

### **Results:**

Collectively, men with normal values of semen analysis had significantly higher mean seminal plasma carnitine levels compared to abnormal values ( $p = 0.028$ ). Oligospermic men had significantly lower levels of carnitine compared to normal ( $p = 0.046$ ).

### **Conclusion:**

Seminal plasma carnitine level seems to correlate with seminal quality and its deficiency may be a reason for infertility among some Sudanese men.

**Key words:** seminal plasma, infertility.

**L**-Carnitine ( $\gamma$ -trimethylamino- $\beta$ -hydroxybutyrate) is synthesized *in vivo* from methionine and lysine<sup>1</sup>. Normally, the biosynthesis of L-carnitine is sufficient to meet metabolic requirements, though for newborns and in several disease situations, oral L-carnitine supplements may be necessary as therapy<sup>2</sup>. The primary function of L-carnitine is to act as a carrier for translocation of long-chain fatty acids from the cytosol into mitochondria for  $\beta$ -oxidation, hence sustaining the supply of energy<sup>3</sup>. Moreover, L-carnitine plays a role in other physiological processes in humans and animals. L-carnitine and its acyl esters are known to have immunomodulatory properties in mammals<sup>4</sup>. Idiopathic oligoasthenoteratozoospermia (iOAT) is defined as defective spermatogenesis of unknown etiology<sup>5</sup>.

Some eitiological factors include: age,<sup>6</sup> Chlamydia trachomatis infection<sup>7</sup>, low seminal concentration of prostate-specific antigen, zinc, fructose<sup>8</sup>, prostatic acid phosphatase<sup>9</sup>, and low seminal activity of neutral alpha-glucosidase are linked to isolated asthenospermia as well as to increased viscoelasticity<sup>10</sup>, and osmolarity of seminal plasma<sup>11</sup>. Mitochondrial DNA oxidative damage has been observed in asthenospermic infertile men<sup>12</sup>. A decreased LH pulse frequency has been found to occur in iOAT men whose amplitude parallels the severity of the disorder<sup>13</sup>. Carnitine deficiency may also be implicated since it can enhance sperm motility through its positive effects on sperm energy production and probably through its antioxidant property<sup>14-16</sup>.

### **Subjects and Methods:**

The study was ethically approved by the committee of the institute of endemic diseases, University of Khartoum. Participants were recruited from Sudan fertility and tube baby's centre and Ashmaig

1. College of pharmacy, The National Rebat University, Khartoum, Sudan.

2. M. Sc student, Graduate College, University of Khartoum, Sudan.

\* Corresponding Author

centre for tube babies, Khartoum, Sudan. A total of 52 males of 24 – 46 years age range were enrolled. With the following baseline sperm selection criteria: sperm concentration of  $>20 \times 10^6/\text{mL}$ , sperm forward motility  $>50\%$ , and normal sperm morphology  $>30\%$ , 14 were classified as normal and 38 abnormal. A questionnaire form including personal data, occupational hazards, clinical history, family history and previous achievement of pregnancy were recorded. Semen samples were obtained from each participant, after signing a consent form, by masturbation after 3 days or more of sexual abstinence. Samples were analyzed immediately for viscosity, sperm count, motility and morphology. Seminal plasma was obtained by centrifugation at 500 G for 5 minutes and stored at  $-20^\circ\text{C}$ . For measurement of carnitine, seminal plasma was thawed and deproteinized using equal volume of 0.6M perchloric acid and the supernatant was neutralized by adding 1:4

volumes of 1.2M potassium bicarbonate solution. L – carnitine was determined using carnitine colorimetric kit (Biosentic, Germany). Welch two sample t – test was used for statistical comparison.

### Results:

According to the seminal analysis results, 14 (29.9%) were normal, 11 (21.2%) oligoastheno/ oligospermic, 14 (29.9%) asthenospermic and 13 (25%) azospermic. Data of these groups are shown in table 1. There were no cases of teratozoospermia. Seven out of the 38 abnormal men (18.4%) were sub fertile, had achieved previous pregnancies with the same or another partner. Six of the latter were asthenospermic. Men with normal values of semen analysis had significantly higher mean seminal plasma carnitine levels compared to abnormal ( $p = 0.022$ ). Oligospermic men had significantly lower levels of carnitine compared to normal ( $p = 0.046$ ).

Table1: Carnitine levels and other semen parameters among normal and abnormal men.

Parameter	Normal	Abnormal	Abnormal		
	N= 14	N= 38	O(N= 11)	As(N=14)	Az(N=13)
Previous Pregnancy Achievement, n (%)	7 (50%)	7 (18.4%)	1 (9.1%)	6 (42.8%)	0 (0%)
Sperm count(millions) (Mean±SEM)	55.1±12.1	17.9±3.2	11.5±2.0	39.5±3.9	0.0
Decreased Motility (<40% motile)	0 (0.0%)	33 (87%)	63.6%	100%	0.0
Carnitine (umol/l) (Mean±SEM)	190±15.9	142.9±11.3	136.6±19.7	54.35±14.6	36.07±24.6

O= Oligozoospermic, As= Asthenozoospermic, Az= Azoospermic

### Discussion:

Carnitine accumulates in the spermatozoa by passive diffusion from the epididymal plasma<sup>17</sup>. The concentration of L-carnitine in epididymal plasma and spermatozoa varies from 2 to 100 mM, which is nearly 2000-fold greater than circulating levels (10–50  $\mu\text{M}$ ). Its role in improving motility of sperms has been documented<sup>18</sup>. Carnitine supplements can modulate the Pro-inflammatory and oxidative

stress pathways which compromise sperm motility and survival<sup>19</sup>, and may improve the sperm count<sup>20</sup>. In general, results of this study may indicate the importance of carnitine for the improvement of the quality of semen, especially the motility and count of sperms, since individuals with abnormal seminal analysis had significantly lower levels of carnitine than normal. Asthenospermic

individuals in this study had none significantly lower levels, probably due to small number of samples, of seminal plasma carnitine compared to normal. Twenty (6 sub fertile and 14 infertile) out of the thirty eight males are asthenospermic, a condition that proves to respond to carnitine supplements<sup>18</sup>. Moreover, our results showed significantly lower levels of seminal plasma carnitine among oligospermic individuals compared to normal, a condition that can also be corrected by carnitine supplements<sup>20</sup>.

In conclusion, carnitine supplement seems to be worth trying in treatment of, at least, some cases of oligospermia and asthenospermia. Azoospermia, though associated with lower carnitine levels than normal, may need further investigation.

#### Acknowledgements:

We gratefully acknowledge the cooperation of Dr. M. Sidique who provided the lab facilities for collection and processing of samples at Khartoum fertility centre. This work was supported by the Ministry of higher education, Sudan.

#### References:

- Bremer J. Carnitine metabolism and functions. *Physiol Rev* 1983; 63:142-80.
- Famularo G, Marticardi F, Nucera E et al. Carnitine deficiency: Primary and secondary syndromes. In: De Simone C and Famularo G, Editors, *Carnitine Today*, Landes Bioscience and Chapman & Hall, New York 1977; 120-61.
- Foster DW. The role of the carnitine system in human metabolism. *Ann NY Acad Sci* 2004; 1033:1-16.
- Buyse J, Swennen Q, Niewold TA et al. Dietary l-carnitine supplementation enhances the lipopolysaccharide-induced acute phase protein response in broiler chickens. *Veterinary Immunol Immunopathol* 2007; 118:154-9.
- Bonanomi N, Lucente G, Silvestrini B. Male fertility: core chemical structure in pharmacological research. *Contraception* 2002; 65: 317-20
- Eskenazi B, Wyrobeck A.J, Slotter E et al. The association of age and semen quality in healthy men. *Hum Reprod* 2003; 18: 447-54
- Veznik Z, Pospisil L, Svecova D et al. Chlamydiae in the ejaculate: their influence on the quality and morphology of sperm. *Acta Obstet Scand* 2004; 83: 656-60
- Elzanaty S, Richthoff J, Malm J et al. The impact of epididymal and accessory gland sex function on sperm motility. *Hum Reprod* 2002; 17: 2904-11.
- Carpino A, Sisci D, Aquila S et al. Adnexal gland secretion markers in unexplained asthenozoospermia. *Arch Androl* 1994; 32: 37-43
- Elzanaty S, Malm J, Giwerkman A. Viscoelasticity of seminal fluid in relation to the epididymal and accessory sex gland function and its impact on sperm motility. *Int J Androl* 2004; 27: 94-100
- Rossato M, Balercia G, Lucarelli G et al. Role of seminal plasma osmolarity in the reduction of human sperm motility. *Int J Androl* 2002; 25: 230-5.
- Sharma RK, Said T, Agarwal A. Sperm DNA damage and its clinical relevance in assessing reproductive outcome. *Asian J Androl* 2004; 6: 139-48.
- Sharma RK, Pasqualotto AE, Nelson DR et al. Relationship between seminal white blood cell count and oxidative stress in men treated at an infertility clinic. *J Androl* 2001; 22: 575-83.
- Kumar R, Gautam G, Gupta NP: Drug therapy for idiopathic male infertility: rationale versus evidence. *J Urol* 2006; 176: 1307-1312.
- Abd - Allah AR, Al-Majed AA, Al-Yahya AA et al. L-Carnitine halts apoptosis and myelosuppression induced by carboplatin in rat bone marrow cell cultures (BMC). *Arch Toxicol* 2005; 79:406-13.
- Liu J, Head E, Kuratsune H et al. Comparison of the effects of l-carnitine and acetyl-l-carnitine on carnitine levels, ambulatory activity and oxidative stress biomarkers in the brain of old rats. *Ann NY Acad Sci* 2004; 1033:117-31.
- Jeulin C and LM Lewin. Role of free L-carnitine and acetyl-L-carnitine in postgonadal maturation of mammalian spermatozoa. *Hum Reprod Update* 1996;2: 87-102.
- Balercia G, Regoli F, Armeni T et al. Placebo-controlled double-blind randomized trial on the use of L-carnitine, L-acetylcarnitine, or combined L-carnitine and L-acetylcarnitine in men with idiopathic asthenozoospermia. *Fertil Steril.* 2005;84(3):662-71.
- Abd - Allah AR., Helal G, Al-Yahya AA et al. Pro-inflammatory and oxidative stress pathways which compromise sperm motility and survival may be altered by L-carnitine. *Oxidative Medicine and Cellular Longevity*, April/May/June 2009, 2(2): 73-81.
- Costa M, D Canale, M Filicori et al. L-Carnitine in idiopathic asthenozoospermia: a multicentre study—Italian study group on carnitine and male infertility. *Andrologia* 1994, 26: 155-159.