



The effect of L-Arginine of treatment for infertile men on semen parameters

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ABSTRACT

The aim of the study is to determine the effect of oral supplement of L-Arginine on semen parameters as a treatment for infertile men. Patients and methods: The study conducted on 15 infertile men at infertility clinic in SalahadDin general hospital and private clinics and laboratories in Tikrit city from beginning of March to the end of July 2018. Infertility is a common clinical problem affecting 13-15% of couples worldwide. The prevalence varies throughout developed and undeveloped countries, being higher in the latter in which limited resources for diagnosis and treatment exist. L-arginine was given daily and orally at a dose 1000 mg one capsule per day morning after breakfast.

Results: There was a significant increase in total sperm count after treatment with L- Arginine as compare with that before treatment. Also there was significant elevation active motility and Ejaculate volume after treatment with L- Arginine, as compare with that before treatment. However, there are significant reductions in Sluggish motility, abnormal sperm shape and non-motile sperms after treatment with L-Arginine as compare with that before treatment.

Introduction

Male infertility cases may be divided into four major types; male factors, female factors, combined factors and unexplained infertility, [1, 3]. Also, male infertility classify either as a primary infertility if no pregnancy has ever occurred or secondary type of infertility, if it occurred after one or more pregnancy approximately 15% of couples attempting their first conception meet with a failure, and 10% infertility, [4, 5, 6]. Magnesium, iron and cobalt are adverse factors in human infertility, [7]. Over the past 20 years, data available reveal that in approximately 30% - 50% of the infertility cases, the cause is found in the man alone and another 20% the causes are found in both, while in 50% - 70% the causes are found in female alone, [8]. Recently more concerns of environmental and occupational exposure, [9]. Physiology and metabolism. It is not considered essential because humans can synthesize it de novo from glutamine, glutamate, and proline. However, dietary intake remains the primary determinant of plasma arginine levels, since the rate of arginine biosynthesis does not increase to compensate for depletion or inadequate supply [10]. Arginine contains

four nitrogen atoms per molecule, making it the most abundant nitrogen carrier in humans and animals (Figure 1). Although it is not a major inter-organ shuttle of nitrogen, arginine nevertheless plays an important role in nitrogen metabolism as an intermediate in the urea cycle, making it essential for ammonia detoxification [11]. The aim of this study is see the effect of oral L- Arginine supplement on sperm parameters in infertile men in Salah al-deen governorate.

Patients and Methods

A follow up follow up study was done on 15 infertile men and 30 normal fertile married as control. Samples were obtained from infertility clinic in SalahadDin General Hospital, and private clinics from beginning of March to the end of July 2018. After sexual abstinence for at least three days, semen samples were collected from patients and control subjects. Semen samples containers were labeled (name, age, time of ejaculates and duration of abstinence).

The semen samples were allowed to liquefy in an incubator at 37°C for 30 minutes, and within half to one hour, semen parameters were analyzed, [13,14]. All semen parameters were measured according standard procedures, such as semen volume, sperm count, motility, pH, Vitality and normal morphology and abnormal shape, [15]. The blood samples were obtained from male infertile patients and normal fertile healthy as a control. Biochemical tests like GSH; MDA, IL-6, and CRP, were analyzed according standard procedures, [16, 17]. Treatment of infertile patients was done by giving with L-Arginine at dose equal to 1000 mg by one capsule per daily for four months.

Result and Discussion

In the present study, table (1) shows that there is highly significant increase in total sperm count after treatment with L- Arginine (55 ± 7.1 million/ml), as compared with that before treatment (27 ± 2.28). Also, there is significant increase in active motility of sperm after treatment with L- Arginine (35 ± 5.89 million/ml) as compared with that before treatment (15 ± 4.45), ($p \leq 0.05$). Moreover, there is also, a significant increase in Ejaculate volume after treatment with L-Arginine (3.15 ± 0.84 ml) as compared with that before treatment (2.2 ± 0.52), ($p \leq 0.05$) [18].

Table (1) : The mean & standard deviation of semen parameters of infertile men before & after treatment with L- Arginine.

Semen parameters	Before	After	P value
Total count (mil/ml)	27 ± 2.88	55 ± 7.1	0.01
Active %	15 ± 4.454	35 ± 5.89	0.05
Sluggish Motility %	37 ± 6.454	17 ± 2.88	0.05
Non Motile %	40 ± 7.072	15 ± 4.67	0.01
Normal Sperms %	30 ± 4.782	60 ± 4.08	0.05
Abnormal Sperms %	50 ± 6.342	25 ± 3.23	0.05
PH	7.3 ± 1.02	6.9 ± 6.8	ns
Viability %	33.77 ± 14.3	75.5 ± 6.4	0.01
Ejaculate Volume ml	2.2 ± 0.52	3.15 ± 0.84	0.05

However, there is significant reduction in Sluggish, abnormal sperm shape and non-motile sperm count after treatment with L-Arginine, as compared with that before treatment ($p \leq 0.05$). In the present study there was a low sperm count in infertile men compared with control group. These results agreed with previous result which found that a reduction in sperm count, sperm motility & morphology of sperm in semen of infertile men than healthy control subjects, [14]. Also the present study agrees with previous study done in Tikrit on infertile men, [15].

and in Mosul city which stated that a reduction in semen quality, [16, 17 ,18]. Table (2) show In the present study, there is significant elevation in the concentration of GSH in the serum of infertile men after treatment with L-Arginine as compared with the value of GSH before treatment, ($P \leq 0.05$). Also, there are significant reductions in the concentration of MDA, IL-6, and C- Reactive protein (CRP). In the serum of infertile patients after treatment with L- Arginine as compared with values before treatment, (table 2).

Table (2): The mean & standard deviation of serum (GSH, MDA, IL-6, CRP) of infertile men before & after treatment with L- Arginine.

Parameters	Before treatment	After treatment	P value
GSH ($\mu\text{mol/l}$)	0.369 ± 0.8980	0.524 ± 2.018	0.01
MDA ($\mu\text{mol/l}$)	0.4890 ± 1.4700	0.412 ± 0.8020	0.01
IL-6 (pg/ml)	2.073 ± 9.432	1.231 ± 6.100	0.05
C.R.P (mg/l)	0.7200 ± 0.238	0.368 ± 0.113	0.05

L-arginine which provides protection against oxidative stress which is likely to act as an antioxidant, [19,20]. L-arginine may protect spermatozoa against lipid peroxidation by increased the release of nitric oxide gas, (NO production), [21, 22, 23]. Supplement of 500 mg arginine per day to infertile men for 8-12 weeks markedly increased sperm count and motility in a majority of patients,

and resulted in reduction of MDA level, and increased testosterone hormone concentration, [24, 25]. Sperm cells from infertile men with oligospermia have a significantly higher activity of arginase enzyme than fertile men. The study found a positive relationship between motility of sperm and the activity of the enzyme, [26,27].

References

- [1] WHO Manual for the Standardised Investigation and Diagnosis of the Infertile Couple. Cambridge: Cambridge University Press, 2000 .
- [2]-Kollettis PN , (2003). Evaluation of the subfertile man Am Fam Physician; 67: 2165-73.
- [3] - Forti , G., Krausz, C,(1998) . Evaluation and Treatment of the Infertile Couple. *The J.of Clin Endocr. And Metab.*;83 (12):4177-4188.
- [4] Jeulin C, Lewin ML, (1996). Role of L-Arginine in postgonadal maturation of mammalian spermatozoa. Hum. Reprorepost. Update; 2: 87-102.
- [5] Guzick DS , Overstreet JW, Litvak PM, Brazil CK , Steven T, Nakajima , *et al*, (2001). Sperm morphology, motility and concentration in fertile and infertile men . *N Engl J med* .; 345: 1388-93 .
- [6] Geidam AD, tawe kdt, Adebayo AEA,(2008). hormonal profile of men nvestigated for infertility at the university of Maiduguri in northern Nigeria. *Singaporemed J.*; 49: 538-541.
- [7] Ekwere Pd, Archibong EE, Bassey EE *et a,l*(2007). Infertility among Nigerian couples as seen in calabar. *Port. Harcourt. Med J.*; 2: 35-40.
- [8] Mathur N, pandey G and jain GC,(2010). male reproductive toxicity of some selected metals: a review. *J bio sci.*;10: 396-404.
- [9] Wiersema, N.; Drukker, A.Dung, M.(2006). Consequences of infertility in developing countries: results of a questionnaire and interview survey in the South of Vietnam. *J. Trans. Med.* 4: 54.
- [10] Martens-Lobenhoffer J, Bode-Boger SM,(2014). Mass spectrometric quantification of L-arginine and its pathway related substances in biofluids: the road to maturity. *J Chromatogr B Analyt Technol Biomed Life Sci*;964:89–102.
- [11] Hupertan, V., Neuzillet, Y., Stücker, O., Pons, C., Leammel, E., Leuret, T,(2012). Effects of Nucleotides Adenosine Monophosphate and Adenosine Triphosphate in Combination with L-Arginine on Male Rabbit Corpus Cavernosum Tissue. *International Journal of Andrology.* 35 (6): 860-866.
- [12] Baker HWG, Burger HG , de krester DM Hudson B,(1986). Relative incidence of etiological disorder for male infertility infertility ,in : R.J. Santen, R.S. Swerdl off (Eds.), male Reproductive Dysfunction, Marcel Dekker, New York ,p.350.[13] - world Health Organization. WHO,(1999). laboratory manual for the examination of human semen and sperm –cervical mucus interaction . 4th ed. Cambridge University Press. Cambridge. England.
- [14] Marbut MM. Ihsan, M. Ezedeem, F. Abdul-Ghani, M. (2006). Elemental Analysis of Human Semen. *Tikrit Med. J.*; 12(1):47-52.
- [15] Agarwal, A., Sharma, R,(2007). Automation is the key to standardized semen analysis using the automated SQA-V sperm quality analyzer. *Fertility and Sterility* Vol. 87, No. 1, January
- [16] Botsoglou N A, Fletouris D J, Papageorgiou G E,(1994), Vassilopoulos V N, Mantis A J, Trakatellis A G Rapid, Sensitive And Specific Thiobarbituric Acid Method for measuring lipid peroxidation in animal tissue, food and feedstuff samples. *Agric Food Chem* 42: 1931–37
- [17] Agarwal, A., Sharma, R,(2007). Automation is the key to standardized semen analysis using the automated SQA-V sperm quality analyzer. *Fertility and Sterility* Vol. 87, No. 1, January
- [18] Menkveld, R.(2001).Semen parameters including WHO and strict criteria morphology in a fertile and sub-fertile population: An effort towards standardization of in-vivo thresholds. *Human reproduction*; 16 (6):1165-1171.
- [19] - Husein, RH., Ahmed, MO., and Muhammed, SM, (2011). Effects of L-Arginine, Vitamin E and Their Combinations on Sperms Morphology in Albino Male Mice. *Journal of Al-Nahrain University.* 14 (2): 137-143.
- [20] Balercia G, Regoli F, Armeni T, *et al*, (2005). 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: 662–671.
- [21] Sheweita SA, Tilmisany AM, Al-Sawaf H,(2005). Mechanisms of male infertility: role of antioxidants. *Curr Drug Metab.*; 6: 495-501.
- [22] Fafula, RV., Iefremova, UP, Olena K. Onufrovych, (2018). Alterations in Aeginase -NO-Synthase system of spermatozoa of in human subjects with different fertility potential. *J. Med. Biochem.* 37: 134 –140.
- [23] O Flaherty C, De Lamirande E, Gagnon C, (2004). Phosphorylation of the Arginine –X-X- (Serine-Threonine) motif in human sperm proteins during A dependency. *Molecular Human Reproduction.*; 10: 355-363.
- [24] Srivastava S, Desai P, Coutinho E, Govil G, (2006). Mechanism of action of L- arginine on the vitality of spermatozoa is primarily through increased biosynthesis of nitric oxide . *Biol Reprod*, 74: 954-958.
- [25] Srivastava S, Desai , Coutinho E, Govil G, (2006). St. Louis: The CV Mosby.
- [26] Elgun S, Kacmaz M, Sen I *et al*. (2000). Seminal arginase activity in infertility. *Urological Research*, 28: 20-23.
- [27] Hassan, HY,(2019) .Role of varicocelectomy in improving fertility in infertile male with varicocele. *J. of Madent Alelem College*; 11(1): 19-26.

دور وتأثير الارجنين في السائل المنوي للرجال العقيمين وعلاجهم

عبد الرحمن جهاد منصور¹ ، زيد محمد مبارك¹ ، عزوي مصطفى هادي²¹قسم علوم الحياة ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق²قسم جراحة المسالك البولية ، كلية الطب ، جامعة تكريت ، تكريت ، العراق

الملخص

تم الحصول على عينات من قسم العقم في مستشفى صلاح الدين العام ومن مختبرات خاصة في مدينة تكريت من 1-3 - 2018 إلى 1-7-2018. مجموعة الدراسة تتكون من 15 رجل عقيم. العقم مشكلة كبيرة تؤثر على الرجال والنساء. يعرف العقم بأنه فشل الزوجة في تحقيق حمل ناجح بعد سنة واحدة أو أكثر من الجماع المستمر المنتظم، والعقم مشكلة سريرية شائعة تؤثر على 13-15% من الأزواج حول العالم. و يختلف مدى انتشار المرض بين البلدان المتقدمة والبلدان غير المتقدمة، حيث يكون انتشاره أعلى في البلدان الاقل تقدماً وذلك لوجود موارد محدودة للتشخيص والعلاج. صممت هذه الدراسة لتقييم تأثير الارجنينين **L-arginine** على جودة الحيوانات المنوية و تم علاج الرجال المصابين بالعقم بعقار الارجنينين المقوي (**L- Arginine 1000mg**) كبسولة مرة واحدة يوميا صباحا بعد الفطور. و لوحظ أن مقارنة السائل المنوي للمريض المصاب بالعقم الذي يعالج بـ **L-arginine** قبل وبعد العلاج. هناك زيادة معنوية في إجمالي عدد الحيوانات المنوية بعد العلاج مع **L- أرجينين** (7.071 ± 55 مليون / مل) ، مقارنة بذلك قبل العلاج (2.286 ± 27) ، ($P \leq 0.05$) ، كما أن هناك زيادة معنوية في حركة الحيوانات المنوية النشطة بعد المعالجة بـ **L- أرجينين** (5.89 ± 35 مليون / مل) ، مقارنة بذلك قبل المعالجة ، (4.45 ± 15) ، ($P \leq 0.05$) علاوة على ذلك ، هناك زيادة معنوية في حجم السائل المنوي بعد المعالجة بـ **L- أرجينين** (0.84 ± 3.15 مل) ، بالمقارنة مع ذلك قبل المعالجة ، (0.52 ± 2.2) ، ($P \leq 0.05$) ، ومع ذلك ، هناك انخفاض كبير في شكل الحيوانات المنوية الغير الطبيعية، وشكل الحيوانات المنوية اظهرت تحسنا بعد العلاج مع **L- أرجينين** مقارنة مع ذلك قبل العلاج. ($p \leq 0.05$).