ISSN: 2753-359X

Journal of Sexual Medicine & Research

SCIENTIFIC Research and Community

Research Article

Open Access

Treatment Protocols For Isolated Asthenospermia Among A Group of Patients Scheduled for an Intrauterine Insemination (IUI) Procedure: Results of a Prospective Study

Nicola Arrighi[1]* and Carlo Gastaldi[2]

[1]Urologist-FECSM, ART Center Atheneum, Brescia, Italy

[2]Gynecologist, ART Center Atheneum, Brescia Italy

ABSTRACT

Intrauterine Insemination (IUI) is a largely used, also debated, technique. We tried to standardize a treatment protocol before IUI, to obtain an increase in motile sperm, expressed as Total Motile Sperm Cell (TMSC) with the aim of avoiding overtreatment in "large amount of spermatozoa" patients.

A group of 97 patients was enrolled for a prospective study and underwent the assumption of the dietary supplement based on 100 mg ORISOD, 11 mg Extremely (SOD=154 IU), 50 mg lipoic acid, 30 mg glutathione, 1.5 mg zinc, 36 mg niacin, 25 mg riboflavin, 9.5 mg vitamin B6, 400 mcg folic acid, 33 mcg vitamin B12 for 90 day, with encouraging results. An increase in TMSC was detected in 77 patients with a.statistical significance (TMSC average increase from 10.7 to 15.2). Even considering this study a preliminary one, our results give a relevant contribution in a field that lack strong evidences and requires more randomized controlled trails (RCT).

***Corresponding author**

Nicola Arrighi, Urological Surgeon-FECSM Expert in Sexual Medicine and Human Reproduction, Salò, Lombardy, Italy.

Received: August 27, 2023; **Accepted:** September 02, 2023; **Published:** September 08, 2023

Introduction

The use of intrauterine insemination (IUI) in the treatment of couple infertility is widely debated, No clear indications are available and the results are disputed [1]. At the same time, it is particularly preferred by patients in light of its less invasiveness, (it is an outpatients procedure) and the less-stringent "ethical" limits in the religious sphere. The quality of sperm is a limiting condition for the technique and, in particular, sperm motility is a major limitation [2].

Asthenospermia is a frequent condition in the male population, of which there is no true validated treatment scheme. Moreover, being expressed in percentage, it is affected by the total number of sperm cells present in the sample [3]. To overcome this limitation, it is proposed to use the total motile sperm count (TMSC), which is calculated by multiplying the total number of spermatozoa by the percentage of motile spermatozoa. In the context of this study, a series of patients were prospectively enrolled who had expressed willingness to undergo an IUI procedure but had a clinical picture of isolated asthenospermia. Before undergoing the IUI procedure, we proposed a treatment scheme to increase the number of motile spermatozoa, in order to improve the chance of pregnancy [4-6].

Materials and Methods

Between 2018 and 2023, 97 patients referred to our Center for Couple Infertility were prospectively selected. All of these patients had a clinical picture of couple infertility according to the International Guidelines. Female partners had an AMH value above 3 and did not show major causes of infertility on first- and second-level investigations or had an indication to undergo second-level techniques of Medically Assisted Procreation. None of the patients had a smoking habit or BMI > 30. The average age was 33 years (with the range between 27 and 35).

Male partners had a spermiogram (performed at a different Center than ours) with an isolated alteration in sperm motility, associated with an insufficient total sperm count to offset in absolute value. Specifically the cut-off considered was 20 milions TMSC. Baseline values and motility were assessed using the WHO 5th Edition Manual methodology, which was in use at the beginning of the study.

Patients underwent the same sperm analysis at our Center, and were enrolled in the study if the total motility value was reduced (<40%) and TMSC was low (<20 millions). Pivotal requirement for recruiting was couples' willingness to undergo an IUI procedure, for clinical or ethical reasons.

Couples expressed consent to participate while waiting to be entered into the IUI protocol, this being a prospective observational study that would not involve changing the timing of the IUI. Male partners were then started on a treatment regimen with the following dietary supplement dosage: 100 mg ORISOD, 11 mg Extremely (SOD=154 IU), 50 mg lipoic acid, 30 mg glutathione, 1.5 mg zinc, 36 mg niacin, 25 mg riboflavin, 9.5 mg vitamin B6, 400 mcg folic acid, 33 mcg vitamin B12 (available in Italy under the trade name FertiPlus® SOD) for 90 days.

Between 80 and 100 days after the start of the treatment, the patient underwent a sperm analysis at our Center, performed by the

same operator. TMSC data was recorded and then compared with the previous data. Statistical analysis of pre and post-treatment TMSC values was performed using a Wilcoxon test, in order to evaluate if the protocol exerted a significant medical effect. After this treatment, all patients, regardless of the outcome of the study, continued with the IUI treatment after a few days.

Results

Out of 97 patients, in 13 patients (12, 37%) we recorded a decrease in TMSC, 7 (7, 21%) had no improvement, while in 77 (79, 38%) TMSC values increased. The mean TMSC in the pre-treatment group was 10.76 million (SD: 2.96, median 10), while in the post-treatment group the mean was 15.07 (SD: 5.22, median: 15). Analysis of pre and post- treatment TMSC using the Wilcoxon test showed a statically significant difference. No side effects were described; none of the enrolled patients dropped out of the ongoing study. We evaluated statistical significance of results with two different tests. Z-test results demonstrated that p-value is smaller than alpha, hypothesis that two groups are similar is rejected. P-value equals 1.52045e-12, so the chance of type I error is small. The observed effect size is d large (1.02) so the difference in magnitude is large.

Wilcoxon test has similar results: p-value is smaller than alpha, so the difference between the randomly selected value of Group 1 (pretreatment) and Group 2 is big enough to be significant. The p-value equals 5.648e-10, so the type error 1 is small. The test statistic Z equals -6.1989, which is not in 95% of acceptance, so U=2290.5. Finally the observed standardized effect size is medium (0.45), with a medium difference between the two Group.

Discussion

In the Italian context, the use of IUI in the context of couple fertility treatment represents a technique that is highly debated, but at the same time often used. For this reason, it would be necessary to have validated parameters to be able to select patients who may be eligible for the technique, particularly referring to the male patients. In this context, patients with isolated asthenospermia may have reduced access to the technique, as this parameter may reduce efficacy [7]. At the same time, we do not currently have therapies with high efficacy in the treatment of isolated asthenospermia [8,9].

The use of oral antioxidants is extremely common in clinical practice, although levels of evidence are still extremely low: an estimated 43% of males scheduled for a Assisted Reproduction Technique (ART) procedure in the United States use them [10]. To our knowledge, this study represents the first study in which a group of patients with isolated asthenospermia were treated, in a prospective manner, and in which the evaluation of the treatment was extremely homogeneous, both in indication, selection, follow-up and evaluation of the results [13-18].

We decided to use the parameter of TMSC because the use of motility alone would have risked enrolling patients with low motility but high absolute sperm counts, with a significant risk of over-treatment [19]. The use of this parameter made it possible to exclude conditions of apparent asthenospermia, which is not necessarily an indication for Assisted Reproductive Techniques (ART).

The results were encouraging, with a significant change in TMSC values, assessed by 2 statistical methods. This should be considered a preliminary study, and it will be necessary to proceed with further investigation. At the same time, we hope to expand the cohort of treated patients and assess parameters that have not been included, such as IUI outcome.

Clearly, there are a number of biases present within the study. First of all, to have evaluated only the sperm-related parameter and not the IUI success rate. This choice stems from the need to exclude additional parameters confounding the clinical picture, so that the results would be more reliable.

The second bias arises from the definition of baseline values according to the WHO 5th edition Manual (not the latest one). The 5th edition was in use at the time the study protocol was filed, and it was not possible to change it during the course of the study.

Finally, the lack of a placebo control group inevitably does not allow for high methodological validity. On the other hand, if we had proceeded in such a manner, we would have risked not having high patient adherence to the study and thus insignificant total numbers. We hope that in the future there will be published studies confirming the results we have obtained, and that this may lead to the achievement of clinical goals, since there is the need for validated protocols for the asthenospermia, along with clear seminological inclusion (and exclusion) criteria as a part of IUI protocols.

References

1. Agarwal A, Makker K, Sharma R (2008) Clinical relevance of oxidative stress in male factor infertility: an update. Am J Reprod Immunol 59: 2-11.
2. Ombelet W, Puttemans P, Bosmans E (1995) Intrauterine insemination: a first step procedure in the algorithm of male subfertility treatment. Hum Reprod 10: 90e102.
3. WHO (2021) laboratory manual for the examination and processing of human semen, sixth edition. Geneva: CC BY-NC-SA 3.0 IGO
4. Jouannet P, Ducot B, Feneux D, Spira A (1988) Male factors and the likelihood of pregnancy in infertile couples. I. Study of sperm characteristics. Int J Androl 11: 379-394.
5. Zinaman MJ, Brown CC, Selevan SG, Clegg ED (2000) Semen quality and human fertility: a prospective study with healthy couples. J Androl 21: 145-153.
6. Larsen L, ScheikeT, JensenTK, BondeJP, ErnstE, et al. (2000) Computer- assisted semen analysis parameters as predictors for fertility of men from the general population. The Danish First Pregnancy Planner Study Team. Hum Reprod 15: 1562-1567.
7. Wainer R, Merlet F (1998) Indications des inseminations intra-uterine intraconjugales encase d'oligo-asthenospermie. In: Les treatments actuals de la sterility masculine. Paris: John Libb 103: e21
8. Nan PM, Cohlen BJ, TeVelde ER, RJ Van Kooji, JM Emers, et al. (1994) Intrauterine insemination or timed intercourse after ovarian stimulation for male subfertility. Hum Reprod 9: 2022-2026.
9. N O'Flynn (2014) Assessment and treatment for people with fertility problems: NICE guideline Br J Gen Practice 64: 50-51.
10. Palmsten K, Flores KF, Chambers CD, Weiss LA, Sundaram R, et al. (2018) Most frequently reported prescription medications and supplements in couples planning pregnancy: The LIFE study. Reprod. Sci 25: 94-101.
11. Sidorkiewicz I, Zareba K, Wolcinski S, Czerniecki J (2017) Endocrine-disrupting chemicals- mechanisms of action on male reproductive system. Toxicol Ind Health 33: 601-609.
12. Marian G Showell, Julie Brown, Anusch Yazdani, Marcin T Stankiewicz, Roger J Hart (2014) Antioxidants for male subfertility. Cochrane Database Syst Rev CD007411.

13. Smits RM, MacKenzie-Proctor R, Yazdani A, Stankiewicz MT, Jordan V, et al. (2019) Antioxidants for male subfertility. Cochrane Database Syst Rev 3: CD007411.
13. Steiner AZ, Hansen KR, Barnhart KT, Cedars MI, Legro RS, et al. (2020) The effect of antioxidants on male factor infertility: the Males, Antioxidants, and Infertility (MOXI) randomized clinical trial. Fertil Steril 113: 552-560.
14. A Kamischke, E Nieschlag (199) Analysis of medical treatment of male infertility Hum Reprod 1: 1-23.
15. Davies R, Jayasena CN, Minhas S (2023) Hormonal and non-Hormonal treatment of male infertility in "Management of Infertility" 15: 145-152. https://www.sciencedirect.com/science/article/abs/pii/B9780323899079000375?via%3Dihub.
16. Hamilton JAM, Cissen M, Brandes M, Smeenk JMJ, de Bruin JP, et al. (2015) Total motile sperm count: a better indicator for the severity of male factor infertility than the WHO sperm classification system, Hum Reprod 30: 1110-1121.
17. O Sefrioui (2023) Management of Infertility Elsevier Chap 19, page 191. https://books.google.co.in/books?id=fKVMEAAAQBAJ&pg=PA191&lpg=PA191&dq=1.+O.+Sefrioui+%E2%80%9CManagement+of+Infertility%E2%80%9D+Elsevier+2023,+Chapter+19,+page+191&source=bl&ots=duJqieF5Q8&sig=ACfU3U0AlQOlpiMZO3iJT0cYiMTL_Qo3Nw&hl=en&sa=X&ved=2ahUKEwjVmK2rnIuBAxXka2wGHdgqCNMQ6AF6BAgjEAM#v=onepage&q=1.%20O.%20Sefrioui%20%E2%80%9CManagement%20of%20Infertility%E2%80%9D%20Elsevier%202023%2C%20Chapter%2019%2C%20page%20191&f=false.
18. O Sefrioui (2023) Mangement of Infertility Elsevier 2023, Chap 19, page 202. https://books.google.co.in/books?id=fKVMEAAAQBAJ&pg=PA191&lpg=PA191&dq=1.+O.+Sefrioui+%E2%80%9CManagement+of+Infertility%E2%80%9D+Elsevier+2023,+Chapter+19,+page+191&source=bl&ots=duJqieF5Q8&sig=ACfU3U0AlQOlpiMZO3iJT0cYiMTL_Qo3Nw&hl=en&sa=X&ved=2ahUKEwjVmK2rnIuBAxXka2wGHdgqCNMQ6AF6BAgjEAM#v=onepage&q=1.%20O.%20Sefrioui%20%E2%80%9CManagement%20of%20Infertility%E2%80%9D%20Elsevier%202023%2C%20Chapter%2019%2C%20page%20191&f=false.

Copyright: ©2023 Nicola Arrighi. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.