

Do Infections Cause Oligospermia and Could Empiric Antibiotics Antiprotozoal and Antifungal Treat Oligospermia?

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OBJECTIVE: Previous studies have shown some factors that contribute to the idiopathic oligospermia which is not significantly enough to have a definite treatment for oligospermia. Our aim is to study the effect of fungal, trichomonal and bacterial infections as causes of oligospermia and to find possible treatment for it.

STUDY DESIGN: This study was carried out prospective observational study at out-patients clinics in Amman, Jordan. Seventy five men who were diagnosed with idiopathic oligospermia were evaluated in this study. Medical history and thorough physical examination with hormonal assay and semen analysis were done before the use of antifungal, antiprotozoal and antibacterial treatment. Semen analysis with WHO regulations was used.

RESULTS: We found significant increase in the semen analysis parameters of the patients compared before and after treatment.

CONCLUSIONS: We have proved that idiopathic oligospermia is caused by fungal, trichomonal and bacterial infections, and treatment of these infections treats oligospermia with less probability to use IVF and also offers a great advantage for the couples to conceive.

Key Words: Oligospermia, Sperm morphology, Infections, Semen analysis

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Introduction

Infertility primarily refers to the biological inability of a person to contribute to conception about 40 percent of the issues involved with infertility are due to the man, another 40 percent due to the woman, and 20 percent result from complications with both partners.^{1,2} Male infertility is commonly due to deficiencies in the semen, and semen quality is used as a surrogate measure of male fecundity.³

Oligospermia refers to semen with a low concentration of sperm and is a common finding in male infertility. Semen with a decreased sperm concentration often may also show significant abnormalities in sperm morphology, motility and liquefaction.^{4,5}

In about 30% of infertile men, no causative factor is found for their decrease in sperm concentration or quality by common clinical, instrumental, or laboratory means, and the con-

dition is termed "idiopathic". In most cases of oligospermia including its idiopathic form, there is no direct medical or surgical intervention agreed to be effective.

In this study, we aimed to confirm the hypothesis that fungal, trichomonal and bacterial infections might cause oligospermia.

Material and Method

This study was carried out a prospective observational study from 1995-2010, for which approval was obtained from the hospital ethics board. We recruited healthy married couples aged between 18 and 45, who had been actively trying to reproduce for at least one year prior to being seen.

Those meeting criteria had a thorough fertility-focused history and physical exam, as well as two consecutive abnormal semen samples for the males. Exclusion criteria included patients who had likely causes of infertility in the medical history, had allergy to the antibiotic regimen, or refusal to participate. Patients were recruited consecutively, and those who completed treatment were included in the study.

Blood samples were taken for hormonal assay from males. Semen samples were taken for analysis and some of them for culture, after which patients were placed on the treatment

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listed in (Table 1) which includes antifungal, antiprotozoal, and antibacterial agents along with antiprostatic agent for 28 days. Intercourse was forbidden during treatment. Post-treatment semen analysis was conducted.

All of the women underwent an HSG, and those that had fimbrial and/or corneal blockage were therapeutically hydrotubated. Hydrotubation was done in an effort to open the fallopian tubes. Successful hydrotubation was done by instillation of a solution via vaginal Foley catheter on two subsequent days, and prescription of a 21-day oral and vaginal regimen. Details are given Table 1.

Differences between pre- and post- treatment variables were calculated using the student's t-test, with significance set at lower than 0.05. Statistical analysis was performed using Microsoft Excel.

Results

Seventy-five couples qualified for inclusion during the study period. The mean age of the women was 36.0 (range: 23-40) years. The World Health Organization's (WHO) reference values for semen parameters are presented in Table 2.

Table 1: Evaluation of the treatments

Male treatment	Hydrotubation wash	Female treatment
1. Itraconazol 100mg tablet 1X4 for 1 week then rest 3 weeks then same treatment for another week 2. Itraconazol powder (topical) 3. Oxytetracycline 100mg tablet OD for 28 days 4. Cefuroxime 500 mg tablet BD for 28 days 5. Metronidazole 500mg tablet 1x3 for 10 days then rest for 10 days and then the same treatment for another 10 days 6. Prostatonin 1x1 for 28 days	1. Hydrocortisone 2. Streptomycin 3. Analgesics 4. Dextrose	1. Fluconazole one tablet 150 mg 2. Fluconazole vaginal suppositories for 10 days 3. Metronidazole 500 mg tablet 1x3 for 1 week 4. Oxytetracycline 100 mg 1x1 for 28 days 5. (amoxicillin+clavulanic acid) 1g BD for 21 days 6. Serratiopeptidase 1x3 for 28 days

Table 2: Reference values for semen parameters, as published in consecutive WHO manuals

Semen parameters	WHO, 1992	WHO, 1999	WHO, 2010 ¹
Volume	≥ 2 mL	≥ 2 mL	1.5 mL
Sperm concentration/mL	≥ 20 × 10 ⁶ /mL	≥ 20 × 10 ⁶ /mL	15 × 10 ⁶ /mL
Total sperm concentration	≥ 40 × 10 ⁶	≥ 40 × 10 ⁶	39 × 10 ⁶
Total motility (% motile)	≥ 50%	≥ 50%	40%
Progressive Motility ²	≥ 25% (grade a)	≥ 25% (grade a)	32% (a + b)
Vitality (% alive)	≥ 75%	≥ 75%	58%
Morphology	≥ 30% ³	14% ⁴	4% ⁵
Leukocyte count	< 1.0 × 10 ⁶ /mL	< 1.0 × 10 ⁶ /mL	< 1.0 × 10 ⁶ /mL

WHO = World Health Organization.

¹Lower reference limit obtained from the lower fifth centile value.

²Grade a = rapid progressive motility (> 25 μm/s); grade b = slow/sluggish progressive motility (5–25 μm/s); Normal = 50% motility (grades a + b) or 25% rapid progressive motility (grade a) within 60 min of ejaculation.

³Arbitrary value.

⁴No actual value given, but multicenter studies refer to > 14% (strict criteria) for *in vitro* fertilization (IVF).

⁵Normal shaped spermatozoa according to Tygerberg (Kruger) strict criteria.

More than half of the male study population had a sperm count below the critical reference value of 15 million/ml. Mean motility initially was 35%, which subsequently dropped to a mean of 17% at 6 hours.

After treatment, men sperm count increased in 84% of all cases. Improved with 76% of patients demonstrating a count of 15 million sperm/ml or greater. Average motility for all time points increased significantly and normal morphology as well.

Ninety-five percent of the women had partial or total corneal and/or fimbrial obstruction by HSG. Infertility was primary in 80%. Four patients had hydrosalpinx, which partially or completely resolved with treatment. No complications occurred during the study period including adverse antibiotic reactions (beyond occasional GI distress).

Discussion

After we obtained a fertility-focused history from patients, this was followed by physical exam we found that the testicles were painful with presence of symptoms and signs of fungal infection such as itching and lacerations on the groin area. In some cases, scrotum was severely hyperemic. These cases

were moderate. In severe cases, the testicles were very soft and with treatment they start to become firmer.

This study didn't include 20 azoospermic men. We found that the circumcision was not done properly for them and there was a lot of fungal cottage cheese material under the prepuce, when we did the circumcision for them properly and the treatment was given the cases improved clearly.

In many cases were improved in the number of sperms, motility and liquefaction but with no improvement in the morphology of sperms, after that we examine the female partner we found that she had trichomonal infection so we started treatment of metronidazole for the couple and the morphology started to improve and became normal.

As we know there is no benefit of doing varicocele repairing for patients with varicocele as the results of semen analysis will not be changed after this operation.^{6,7,8}

Along with the treatment the patients should be aware about their personal hygiene especially in the groin area and should avoid the use toilet papers for drying and also avoid the use of nylon underwear, because it induces sweating which in turn offers a good environment for the growth of fungi.^{9,10}

Because the cases we are dealing with are chronic cases, the treatment should be given for 28 days, and if there is no improvement, the treatment can be repeated for another 28 days and this depends on how much aware is the patient about his personal hygiene.

In order to treat male infertility, we have to treat both the man and the woman concurrently because our aim is to treat this couples to be able to conceive and have babies. We have proved that this infections are transmitted to the woman and the trichomonas causes cervical ulcers and the infection can ascend to the fallopian tubes and cause tubal obstruction by edema. So we also treat the woman for these infections at the same time we treat the men.

Once the easily identifiable and correctable causes have been eliminated, treating the remaining infertile with ART can be prohibitive. The average cost of IVF in Jordan ranges from \$6,000-\$7,000, with a per capita income of \$5,900. This is so financially exhausted for the patients as long as the psychosocial stressors.^{11,12}

IVF also had many complications including ovarian hyperstimulation syndrome due to repeated induction of ovulation and sometimes those may develop temporary menopause and their FSH and LH values became high, then by time this will resolve spontaneously approximately in 6 months.¹⁴ IVF has high rate of failure due to the high percentage of abnormality in the morphology of sperms in patients with oligosper-

mia, and by our study we introduce a treatment for oligospermia which in turn makes the treatment of infertility using IVF and other ART easier and more reliable.

Some new theories say that in order for the IVF to be successful in women with obstructed tubes, the doctor have to do salpingectomy, we see this is disastrous for the woman and the couple especially if they encounter a failure in IVF, but with our treatment we open the tubes by hydrotubation and in the same time we treat the man for oligospermia.¹⁵

In our study the treatment was offered to the couples and none of the pregnancies achieved was ectopic all were normal pregnancies. By this study we offer a cheap, short-term and already used treatment for male infertility, so this will make the treatment of infertility around the world more easier with less costs and exhaustion.

The approach we used in the present study treats men with so-called "idiopathic" infertility for chronic, subacute infection. The empiric treatment of infertility is not a new concept; everything from steroids, to nutritional supplements and aromatase inhibitors has been studied in an attempt to improve rates of conception. However, several clinical features point to our rationale as being based on more than pure empirical science. Female partners in this cohort had a high rate of tubal obstruction, also suggestive of an inflammatory process, either independent of their partners or as a transmitted result of chronic infection.

Weaknesses in this study include the non-randomized, observational nature of its design, as well as the difficulty with obtaining long-term follow-up of our patients. Our clinic treats a large number of people who then return to their countries, which makes for challenging continuity of care. However, the relatively high success rate we have demonstrated warrants further study, as a means to bringing fertility treatment to those without the option of ART at their disposal.

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