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Original Research Article

Interventional study to find out effect of human chorionic gonadotropin and antioxidants on idiopathic male infertility

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ABSTRACT

Background: Male contributes about 50% for cases with combined male and female infertility. When the cause is not known, it is term as idiopathic infertility. It affects 25% of men. Many advances have been made in reproductive medicine which provides great opportunities, couples which were considered untreatable now have got chance to have their own babies. Various ART procedures like ICSI have been proven as an efficient therapy in severe male factor infertility. However, the cost per cycle and complications such as multiple gestations cannot be ignored. Medical management of infertility can be specific or empirical depending on etiology. Specific medical management is use when certain etiology is identified. However, in absence of specific etiology use of empirical medical treatment can be attempted in order to improve treatment results. In this study our aim is to evaluate the effect of human chorionic gonadotropin (hCG) and antioxidants on semen parameters in men with idiopathic male infertility.
Methods: Thirty men with abnormal semen parameters were included in study. Patients were treated with injection hCG-2000 IU three times a week for three months along with the antioxidants. After 3 months of treatment repeat semen analysis were performed and results were compared with pre-treated seminal parameters.
Results: Results showed significant increase in sperm count (p value ≤ 0.001), total motility (p value=<0.001), and progressive forward motility (p value = <0.001), while no significant difference is seen in rest of the parameters.
Conclusions: Use of hCG and antioxidants in idiopathic male infertility can significantly improve seminal parameters in idiopathic male infertility.

Keywords: ART, ICSI, Male infertility, Sperm

INTRODUCTION

Infertility is defined as failure of a couple to achieve spontaneous pregnancy even after regular unprotected sexual intercourse in one year.[1] Affects about 15% of couples.[2] Both male and female contributes to infertility. Male factor is responsible for 30% of cases and contributes to an additional 20% in combination with female factor. Thus 50% of cases of infertility can be explained by combined male and female factors.[2,3]

When the cause of infertility cannot be identified, the condition is termed idiopathic. It is seen in 25% of men.[2]

Men with idiopathic infertility present with no significant history and have normal physical examination and hormonal profile. However, semen analysis reveals a decreased sperm concentration, decreased sperm motility, and increase abnormal forms of sperm. These sperm abnormalities when occur together are called oligo-astheno-teratozoospermia (OAT) syndrome.

Medical management of male infertility is divided into two categories: specific and empirical. Specific treatments are used for certain conditions like hypogonadotropic hypogonadism, hyperprolactinemia, genital tract infection, ejaculatory dysfunction etc.[4] In contrast empirical treatment consist of gonadotropins, antiestrogens, and aromatase inhibitors and support with antioxidant supplements such as carnitine, lycopene, glutathione, and vitamin E etc. when no specific cause of infertility is found.[5] However, scientifically acceptable evidence of empirical treatment efficacy is limited because of the lack of large, randomized, controlled studies.[2]

With the advance of ART techniques many infertile men have got fortune to father a child. Even in severe oligospermia, couple can achieve pregnancy with the help of ICSI. Though all this seems fascinating other side of mirror cannot be neglected. That is complications of ART procedures like multiple gestations followed by fetal reduction, miscarriages, preterm delivery and last but not the least cost of procedure. All this has drained many couples emotionally and economically. In this study, we have treated infertile men with human chorionic gonadotropin (hCG) and antioxidants in an attempt to reduce complication and economical burden of the couple.

METHODS

This study was designed as a prospective interventional study. Thirty infertile men with abnormal semen analysis attending an andrology outpatient clinic at 21st century hospital Surat, Gujarat within period of 6 months from March to August 2016 were enrolled in this study. Their age ranged from 25-45 years, mean duration of infertility was 6.5 years including a minimum of 1 year of regular unprotected sexual activity without achieving pregnancy. All men were informed about the details of study and in particular about treatment protocol at different stages of study design and about the possibility of undergoing assisted reproductive techniques during this period.

Inclusion criteria

Consisted of history of at least 1 year infertility with semen analysis showing oligo-astheno-terato-zoospermia on at least three separate occasions. Sperm concentration less than 15 million, sperm total motility was less than 40%, sperm forward progressive motility less than 32%, normal sperm morphology was greater than 4%.

Exclusion criteria

Included cases with azoospermia. Couples with combined male and female factors infertility, varicocele, hernia, and trauma were excluded.

The study was reviewed and approved by our institutional review board. All patients provided a written informed consent explaining the nature of study, the possibility of treatment failure. They underwent a clinical evaluation including history taking, general examination and genital examination for possible causes of infertility. Investigation for male partner included semen analysis according to World Health Organization criteria, hormonal profile (serum FSH, total testosterone, estrogen, prolactin), and karyotype in those who needed. Semen analyses were performed at least thrice before commencing treatment and once after completion of three months of treatment. All men with abnormal semen analysis were treated with injection hCG 2000 IU three times a week for three months along with antioxidants. After 3 months of treatment repeat semen analysis were performed and results were compared with previous parameters.

RESULTS

The results were expressed as mean ± SD. Analysis was done with help of SPSS version 20. Paired t test was applied to study difference between semen parameters before and after medical intervention. Mean age of the patients was 33±5.0 years (mean±SD). The average infertility duration was 6.5 years.

Table 1: Seminal parameters before and after treatment.

	Before treatment					After treatment				
	Count	**Volume (ml)**	**TM (%)**	**FPM (%)**	**ABF (%)**	**Count**	**Volume (ml)**	**TM (%)**	**FPM (%)**	**ABF (%)**
Mean	8.30	3.33	35.33	25.17	3.23	17.23[a]	2.37	75.67[b]	60.33[c]	3.67
S D	4.550	5.473	5.561	5.796	0.504	7.099	0.669	11.198	10.334	0.547
Mini	1	0	25	15	2	6	1	50	40	3
Max	17	3	40	35	4	34	4	90	80	5

Note: TM = total motility, FPM = forward progressive motility, ABF = abnormal forms. Ap = <0.001; bp = <0.001; cp = <0.001.

Sperm concentration was significantly improved from 8.3 × 106±4.5 baseline to 17.2 × 106±7 after treatment (p = <0.001; Table 1). Total motility and forward progressive motility of sperm also showed significant improvement (p = <0.001) while rest of the seminal parameters failed to show any significant difference.

DISCUSSION

Idiopathic male infertility affects almost 25% of men in reproductive age group.[2] And medical therapy for these patients is still not accepted because of lack of significant evidence. Therefore, at many centre management of male infertility consist of assisted reproduction with intra-cytoplasmic sperm injection (ICSI). Though these ART treatments provide great opportunities to couple with infertility, potential hazards like multiple gestation and cost cannot be ignored.

In this study our aim was to evaluate the effect of hCG and antioxidants on semen parameters in men with idiopathic male infertility. Thirty men with abnormal semen analysis (according to WHO criteria) were included in the study.6 All were treated with injection hCG 2000 IU three times a week for three months along with antioxidants. After 3 months of treatment repeat semen analysis were performed and results were compared with previous parameters. Sperm concentration was significantly improved (p = <0.001) along with total motility and forward progressive motility.

The hypothalamo-pituitary-ovarian axis is involved in process of spermatogenesis. Hypothalamus releases gonadotropin releasing hormones (GnRH) which acts on pituitary gland and to produce FSH and LH. FSH acts on sertoli cell while LH acts on leydigs cell to produce testosterone. Testosterone is responsible for spermatogenesis. Human chorionic gonadotropin is known to have LH like activity due to cross-reaction with β subunit of LH.7,8 Mechanism of action of hCG is same as LH. Structurally β subunit of both this glycoprotein hormones exhibit 80% of homology. Hence both binds on same receptor and therefore have same mechanism of action. In short hCG mimics the activity of LH the only difference being longer half-life of hCG.[9]

According to AACE clinical guideline hCG alone can initiate sperm production and it should be initial therapy of choice for at least 6 to 12 months. Therapy with hCG is generally started at 1000 to 2000 IU intramuscularly two to three times a week. Both testosterone levels and sperm counts should be monitored monthly. If sperm concentration is not improve after 6 months of treatment, then FSH can be added in the dose of 75 IU intramuscularly three times a week along with hCG.[10]

Reactive oxygen species (ROS) have been described as a potential cause of male infertility.[11] An imbalance between ROS and physiologic antioxidant level can cause oxidative stress with subsequent detrimental effect on of spermatogenesis. Elevated reactive oxygen species have been found in 30-80% of infertile males and can cause abnormalities of seminal parameters like sperm morphology, motility, concentration, and DNA integrity, resulting in difficulties achieving pregnancy. The impact of ROS on fertilisation and pregnancy is controversial.[12] Many studies were done to evaluate effect of antioxidants therapy in men with idiopathic infertility but its exact role is still poorly understood due to lack of controlled trials.[13] A recent Cochrane Collaboration which included pooled analysis of 34 randomized controlled trials, have noticed a significant increase in pregnancy and live-birth rates in the couples treated with antioxidant therapy, but no difference was seen in seminal parameters.[14] However, when therapeutic efficacy and the cost of the treatment is concern, oral antioxidant supplementation may be a reasonable treatment regimen before proceeding with more expensive treatments such as IVF or ICSI.

CONCLUSION

In our study though we have found that medical treatment with hCG and antioxidants for period of 3 months have significantly improved seminal parameters, results of this treatment in terms of overall pregnancy rates may have differ if observation period would have been long enough. We proposed that treatment of idiopathic male infertility with hCG and antioxidants may prove cost effective and one can achieve pregnancy naturally without ART related complication. Further trials would be informative.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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