

Gonadotropins in Infertile Men with Idiopathic Hypogonadotropic Hypogonadism

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Abstract

Background: Stimulatory therapy with gonadotropins is an effective treatment to induce spermatogenesis in men with idiopathic hypogonadotropic hypogonadism (IHH). The aim of this study was to assess the effectiveness of human chorionic gonadotropin / human menopausal gonadotropin on hypogonadotropic infertile men.

Materials and Methods: This study included fifty-six azoospermic infertile men with IHH treated with hCG / hMG. All patients received hCG (5000 IU, IM3 times /week) for three months. After that, treatment was continued combined with hMG (75 IU, IM 3 times/week). Semen analysis was performed every 3 months. After 15 months, fine needle aspiration was performed if the patients were azoospermic. Treatment continued if mature spermatozoa were present in FNA, otherwise treatment was discontinued. In the former cases, semen analysis was requested 24months after the beginning of treatment.

Results: In this study, spermatozoa were present in the ejaculate in 50 out of 56 patients (89.2%) after combined treatment. Average time of sperm appearance was 9.2 months. Mean sperm concentration was 9.12×10^6 /ml. FNA carried out after 15 months of treatment in 23(41%) of patients with persistent azoospermia, 91.3% of these latter patients had mature spermatozoa on fine needle aspiration. Pregnancy occurred in 23 (41%) cases.

The mean sperm concentration in patients whose spouses became pregnant was 15.56×10^6 .

Conclusion: hCG/ hMG combination therapy is effective treatment for fertility in patients with IHH. FNA can be used as a safe and suitable tool to evaluate patients that remains azoospermic after 15 month of treatment.

Keywords: Fertility, Spermatogenesis, Human Chorionic Gonadotropin, Human Menopausal Gonadotropin

Introduction

Infertility is a global problem, with a prevalence of 15%. Male factor is involved in 50-60% (1). One of the endocrinologic causes of infertility is Idiopathic hypogonadotropic hypogonadism (IHH), defined by: incomplete or absent puberty, a serum testosterone level less than 100ng/dl (3.5nmol per liter) in the presence of low or normal levels of gonadotropins, otherwise normal pituitary function, and normal hypothalamus-pituitary CT-scan findings (2). Although several treatments are available for these individuals, none of them has proved to be ideal. The aim of this study was to evaluate the combination therapy [human chorionic gonadotropin and human menopausal gonadotropin (hMG/hCG)] on Idiopathic hypogonadotropic hypogonadic individuals.

Materials and Methods

From Jun 2006 to Jun 2008, 56 infertile males with

IHH were enrolled in a self-controlled clinical study in Isfahan fertility and sterility center. This study was approved by ethical committee of Isfahan fertility and sterility center. Inclusion criteria were infertile married men with, azoospermia, low serum levels of FSH, LH and testosterone, and normal levels of prolactin. The patients were treated with 5000 IU hCG intramuscularly 3 times a week for 3 months, then 75 IU hMG was added (intramuscular 3 times a week) and this combination was continued for Two years.

Semen analysis was performed, before and every 3 months after the beginning of combination therapy. Testicular FNA was carried out when the patients were still azoospermic after 15 months. In cases that mature sperm were present, treatment were continued for further 6 months, otherwise treatment was discontinued and embryo donation was proposed.

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Results

The mean age of men in this study was 31 years and ranged from 20 to 50 years. The results of semen analysis revealed presence of sperm in 50 out of 56 patients, resulting in spermatogenesis in 89% of cases by 24 months from the beginning of combined therapy. Average time of sperm appearance in this study was 9.2 months. The mean sperm concentration in these individuals was 9.12×10^6 ranging from $0.1 \text{--} 78 \times 10^6$.

Natural pregnancy was achieved in 19 couples following 2 years of treatment. Thirteen patients used assisted reproductive techniques including IUI, IVF, and ICSI. Two pregnancies were achieved by IUI, and two through ICSI, resulting in total 23 pregnancies. The average sperm count in couples with natural pregnancy was 10.8×10^6 ranging from 1.05×10^6 to 44×10^6 , respectively.

Discussion

Treatment of IHH may have two goals: induction of virility, and fertility.

First purpose can be achieved by testosterone, and second by treatment with gonadotropins or GnRH agonists (3). The results of this study reveals that combined gonadotropin therapy can induce spermatogenesis, and results in pregnancy. Our results are compatible with Burgues et al, and canal et al, that reported spermatogenesis in 80% and 87%, using this combined therapy respectively. (4) The pregnancy rate of 41.7% obtained in this study is compatible with 50% that reported by Saal W. et al (5). It is important to note that in this report 8 out of 16 couples achieved pregnancy, which is a small population relative to our study, which were 23 out of 56 couples. In most studies including this study, the mean sperm count is lower than 20×10^6 per ml which is the cut value that reported by the WHO for normospermia. Burriss et al showed that although oligospermia is common after IHH treatment sperm motility is often good. That is the reason why in contrast to other cases of oligospermia such as Idiopathic Oligospermia, most IHH patients are fertile after treatment despite having low sperm counts (6). In IHH individuals, it is important to know how long the treatment could be continued, and when the treatment should be terminated. Based on previous studies, duration of treatment is 9-24 months. The most important criteria for termination of treatment is pregnancy and another criteria is positive semen analysis and the criteria for discontinuation of treatment is absence of sperm in the ejaculate by 24 month from

the beginning of treatment (3). One of the interesting findings of this study was the results of FNA findings. Although our study was not comparative but showed that in cases with presence of mature sperm in FNA, the treatment could be continued and in cases with absence of sperm, the treatment discontinued, and this makes the approach more cost effective. Our results also showed that the FNA procedure is safe and without major complications, and may increase patient's compliance with combined treatment.

Another important factor in the treatment of IHH individuals is the time of sperm detection in semen analysis. Average time of sperm appearance in this study was 9.2 months, which was longer than 4 months on average (2-22 months) reported by Buchter D et al (3), and 5 months that reported by Burgues S. et al (4).

Conclusion

In conclusion, the results of this study reveal that hMG & hCG can induce spermatogenesis in over 90% of IHH individuals and results in approximately 50% pregnancy rate, even though not all the WHO criteria for semen parameters are achieved. Additionally, FNA can be used to evaluate continuation of the treatment in cases with no sperm in their ejaculate after 15 months of gonadotropin administration.

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