

Efficacy of follicle-stimulating hormone as a treatment of severe idiopathic oligospermia: A retrospective study

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Abstract

Introduction: About 15% of couples are infertile, with the male factor being responsible for about 50% of these cases of infertility. Idiopathic oligospermia (IO) is a dilemma that faces every andrologist and yet is one of the most common causes of male infertility. Although studies have shed some light on multiple treatment modalities and their effectiveness, one of the most fascinating ones is follicle-stimulating hormone (FSH).

Methodology: This is a single tertiary center retrospective study; all patients with severe IO (sperm count of <5 million/ml) from January 2016 till January 2018 were included in the study. We divided our retrospective population into 2 groups, Group 1 who received FSH 75 IU (Menogon[®]) twice a week and Group 2 who received FSH 150 IU (Menogon[®]) twice a week. Semen parameters were recorded pretreatment and posttreatment.

Results: Number of the patients included in the study was 32. Group 1 included 16 patients who received FSH 75 IU. Group 2 included 16 patients who received FSH 150 IU. After 4 months of treatment, the mean sperm count in Group 1 increased to 4.745 million/ml (pretreatment was 1.235 million/ml), while in Group 2, it was 1.516 million/ml (pretreatment was 0.578 million/ml). The mean total motility in Group 1 was 20.3%, while Group 2 mean total motility was 27.5%.

Conclusion: In conclusion, our study elicited that a dose of FSH as low as 75 IU can improve sperm count significantly in patients with severe IO.

Keywords: Follicle-stimulating hormone, idiopathic oligospermia, infertility

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INTRODUCTION

About 15% of couples are infertile, with the male factor being responsible for about 50% of these cases of infertility.^[1] The majority of these cases are idiopathic and can happen even with normal semen parameters. Even with

the presence of a semen abnormality, it is not unusual that the cause is not identified or explained.^[2] While identifiable causes of infertility have been targeted either by medical or surgical therapy with good success rates, idiopathic infertility is still a challenging issue in modern medicine. In

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such cases, the literature holds a good number of empirical therapies and trials trying to tackle idiopathic infertility.

Idiopathic oligospermia (IO) is a dilemma that faces every andrologist and yet is one of the most common causes of male infertility.^[3] With various studies in the literature suggesting multiple empirical treatment modalities that could increase sperm count and motility, none is yet established to be the standard of care.^[4] When it comes to the treatment of IO, we still have a long way to go. Although studies have shed some light on multiple treatment modalities and their effectiveness, one of the most fascinating ones is follicle-stimulating hormone (FSH). FSH is a hormone secreted by the anterior pituitary gland which plays a major role in spermatogenesis by acting on Sertoli cells; it also plays an important role in sperm DNA integrity.^[5] Multiple studies have shown that FSH improves sperm quality, with different doses and on multiple populations.^[6-8] The exact dose of FSH is yet to be established; Ding *et al.*^[9] suggested that high doses of FSH (at least 200 IU) would yield the highest effect on sperms' quality.

We believe that low doses of FSH can be also effective. In our study, we aim to prove that small doses of FSH can be effective in cases of IO. Furthermore, our study will try to elucidate the effect of FSH in patients with severe IO (sperm count of <5 million/ml) which would solidify the effectiveness of FSH as a treatment modality of IO.

METHODOLOGY

This is a single tertiary center retrospective study; all patients with severe IO from January 2016 till January 2018 were included in the study. We excluded patients with abnormal hormonal profile (high FSH), low volume ejaculate, sperm count more than 5 million/ml, varicocele, abnormal karyotype, and patients undergoing or received other treatment modalities for severe IO. We divided our retrospective population into 2 groups, Group 1 who received FSH 75 IU (Menogon®) twice a week and Group 2 who received FSH 150 IU (Menogon®) twice a week; both groups received the treatment regularly for 4 months. A baseline semen before initiation of treatment and another one after 4 months were collected. Data collected included age, sperm count and total motility before treatment, and sperm count and total motility 4 months after treatment. Data were entered using an excel sheet; data analysis was done using The IBM SPSS® software. Descriptive analysis was done, and *t*-test was used to compare the mean between the groups.

RESULTS

Number of the patients included in the study was 32.

Group 1 included 16 patients who received FSH 75 IU. Group 2 included 16 patients who received FSH 150 IU. The mean age in Group 1 was 36.6 years and Group 2 was 37 years. The mean sperm count before treatment in Group 1 was 1.235 million/ml and in Group 2 was 0.578 million/ml. The mean total sperm motility before treatment in Group 1 was 23.9%, while in Group 2, it was 21.8% [Table 1].

After 4 months of treatment, the mean sperm count in Group 1 increased to 4.745 million/ml, while in Group 2, it was 1.516 million/ml. The mean total motility in Group 1 was 20.3%, while Group 2 mean total motility was 27.5% [Table 1].

When comparing Group 1 before treatment and posttreatment in regard to sperm count, posttreatment sperm count had an improvement which was statistically significant (*P* = 0.006). Furthermore, comparing total motility prior and posttreatment, there was no statistically significant improvement (*P* = 0.5) [Table 2].

In Group 2, sperm count showed a significant improvement after treatment compared to pretreatment with a statistically significant *P* value (*P* = 0.009). When it comes to total motility, there was not a significant difference prior or posttreatment (*P* = 0.25) [Table 3].

Comparing the two groups who received FSH 75 IU and 150 IU, sperm count before treatment, there was no statistically significant difference between the two

Table 1: The means of the 2 groups

Variables/means	Group 1	Group 2
Age (years)	36.6	37
Sperm count (million/ml) before treatment	1.235	0.578
Sperm count (million/ml) posttreatment	4.745	1.516
Total motility (%) before treatment	23.9	21.8
Total motility (%) posttreatment	20.3	27.5

Table 2: The means of Group 1 before treatment and posttreatment with *P* value comparing the means using *t*-test

Semen parameter	Mean	<i>P</i>
Sperm count (million/ml) before treatment	1.235	0.006
Sperm count (million/ml) posttreatment	4.745	
Total motility (%) before treatment	23.9	0.5
Total motility (%) posttreatment	20.3	

Table 3: The means of Group 2 before treatment and posttreatment with *P* value comparing the means using *t*-test

Semen parameter	Mean	<i>P</i>
Sperm count (million/ml) before treatment	0.578	0.009
Sperm count (million/ml) posttreatment	1.516	
Total motility (%) before treatment	21.8	0.251
Total motility (%) posttreatment	27.5	

groups ($P = 0.162$). When comparing the same groups after treatment, Group 1 showed better improvement than Group 2 after receiving FSH 75 IU with a significant P value ($P = 0.04$). When it comes to total motility, the two groups showed no difference before treatment ($P = 0.736$). After treatment, the total motility showed no significant difference between the two groups ($P = 0.334$) [Table 4].

DISCUSSION

FSH plays an important role in spermatogenesis and DNA integrity of the sperms.^[5] It is a hormone that is secreted by the anterior pituitary gland and acts on Sertoli cells on the testicular level. Multiple studies have demonstrated the importance of FSH for sperms' DNA integrity and the positive effect of spermatogenesis,^[9] yet, its role in idiopathic infertility is poorly demonstrated. Giving the scare literature when it comes to the use of FSH as a treatment of idiopathic infertility or IO, the exact dose and protocol of FSH administration is still unclear. Keeping in mind that spermatogenesis is a long and complex process that takes up to 74 days to be completed,^[10] it is rational to propose that the effects of FSH would take up to 3 months to be apparent.

The notion of such a treatment modality is that patients who are having normal FSH levels and severe IO thought to be having a lazy pituitary gland, as the logical response of having a severe IO is to increase FSH secretion, while in such patients, FSH is normal. By giving FSH, we are challenging the testes to promote spermatogenesis.

In a randomized control trial, Ding *et al.*^[6] were able to demonstrate the efficacy of FSH as a treatment for IO; the effect was proportional to the dose of FSH which was at least 200 IU and to the duration of treatment. In the mentioned trial, it was found that doses of 300 IU and longer duration of therapy were associated with improvement in total motility and morphology as well, a finding that was not reported previously in the literature and not found in our study.

In our study, a dose of FSH 75 IU or 150 IU for 4 months was clearly enough to produce a statistically significant improvement in sperm count, in contrast to the findings observed in Yin-man *et al.*'s trial. When it comes to the total motility, our study found no significant difference when

using either FSH 75 IU or 150 IU, a result that is similar to the previously mentioned trial or even in the literature.^[11] An interesting finding that our study elicited is that patients who received FSH 75 IU had a greater improvement of sperm count, compared to the patient who received 150 IU, a finding that might be biased by the fact that most patients who had FSH 150 IU had a lower sperm count to begin with from those who received FSH 75 IU, although this was not statistically apparent when comparing the two groups before treatment.

Our study carries its own limitations; as a retrospective study, it holds its own share of bias. Furthermore, a small sample size when compared to other randomized control trials which tackled the same subject demeans its reliability. Nevertheless, our study also has its own merits, giving the fact that our population are all having severe IO (sperm count <5 million/ml) gives it an advantage, being one the few tackling severe IO rather than IO alone. Furthermore, being able to demonstrate the efficacy of a small dose of FSH which was not established previously, also opens the door for more research in the domain of FSH as a treatment modality for severe IO.

CONCLUSION

Our study elicited that a dose of FSH as low as 75 IU can improve sperm count significantly in patients with severe IO. We also believe that we need more large and multicenter randomized control trials to truly understand the effect of FSH as a sole treatment of IO which might in the future be the gold standard for the treatment of such cases.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Irvine DS. Epidemiology and aetiology of male infertility. *Hum Reprod* 1998;13 Suppl 1:33-44.
2. Haidl G. Medical treatment of male infertility. *Male Infertil* 2007;1:333-43. [Doi: 10.3109/9780203090626-27].
3. Nieschlag E. Classification of andrological disorders. In: Nieschlag E, Behre HM, editors. *Andrology: Male Reproductive Health and Dysfunction*. 2nd ed. Berlin: Springer; 2000. p. 83-7.
4. Koukkou E, Billa E, Kapolla N, Pappa A, Venaki E, Andreou L, *et al.* An empiric treatment for idiopathic oligozoospermia revisited: A 20-year investigative saga. *Andrologia* 2012;44:337-42.
5. de Kretser DM, Loveland KI, Meinhardt A, Simorangkir D, Wreford N. Spermatogenesis. *Hum Reprod* 1998;13 Suppl 1:1-8.
6. Ding YM, Zhang XJ, Li JP, Chen SS, Zhang RT, Tan WL, *et al.* Treatment of idiopathic oligozoospermia with recombinant human follicle-stimulating hormone: A prospective, randomized, double-blind,

Table 4: The means of Group 1 and Group 2 by t-test

Semen parameters/means	Group 1	Group 2	P
Sperm count (million/ml) before treatment	1.235	0.578	0.162
Sperm count (million/ml) posttreatment	4.745	1.516	0.043
Total motility (%) before treatment	23.9	21.8	0.736
Total motility (%) posttreatment	20.3	27.5	0.334

- placebo-controlled clinical study in Chinese population. *Clin Endocrinol (Oxf)* 2015;83:866-71.
7. Nieschlag E, Simoni M, Gromoll J, Weinbauer GF. Role of FSH in the regulation of spermatogenesis: Clinical aspects. *Clin Endocrinol (Oxf)* 1999;51:139-46.
 8. Depenbusch M, von Eckardstein S, Simoni M, Nieschlag E. Maintenance of spermatogenesis in hypogonadotropic hypogonadal men with human chorionic gonadotropin alone. *Eur J Endocrinol* 2002;147:617-24.
 9. Farrag A, Manna C, Grimaldi G. Efficacy of recombinant human FSH in the treatment of idiopathic male factor infertility before ICSI. *Hum Reprod* 2006;21:27.
 10. Wong WY, Merkus HM, Thomas CM, Menkveld R, Zielhuis GA, Steegers-Theunissen RP, *et al.* Effects of folic acid and zinc sulfate on male factor subfertility: A double-blind, randomized, placebo-controlled trial. *Fertil Steril* 2002;77:491-8.
 11. Efesooy O, Cayan S, Akbay E. The efficacy of recombinant human follicle-stimulating hormone in the treatment of various types of male-factor infertility at a single university hospital. *J Androl* 2009;30:679-84.