Hypogonadotropic hypogonadism: Can have multiple pregnancy and or ovarian hyper stimulation syndrome

Nisreen Aref Albezrah*
Obstetrics and Gynecology Department Head, Medical college /Taif University, Saudi Arabia

Abstract
Hypogonadotropic hypogonadism (HH) is the least common etiology of all the causes of infertility. Patients in whom fertility is desired, induction of gonadotropin secretion by pulsatile GnRH or treatment with exogenous gonadotropin is the current treatment of choice. Ovulation induction in patients with hypogonadotropic hypogonadism (HH) is a challenge to the treating physician. The ovarian response in HH cannot be predicted and may differ substantially from that of normal patients. A step-up protocol longer duration of stimulation is required in some cases to reach that threshold levels of follicle stimulating hormone, in so as to prevent multiple pregnancies and to eliminate the risk of ovarian hyper stimulation syndrome (OHSS).

Introduction
Hypogonadotropic hypogonadism (HH) is a rare cause of infertility, characterized by reduced hypothalamic or pituitary activity resulting in abnormally low serum FSH and LH levels and negligible estrogen activity and has classified as a group 1 anovulation disorder by World Health Organization (WHO) [1-4].

Irrespective of the underlying etiology, women with HH require both LH and FSH to restore normal ovarian function and override follicular growth arrest which can be achieved by either exogenous gonadotropins or pulsatile GnRH pump [5]. The average treatment duration and the number of ampules used for HH patients are higher compared with patients with other etiologies of infertility and the ovarian response in these patients may differ substantially from that established for normal patients. The success of ovulation induction is reported to be as high 60–80% with a high multiple pregnancy rate (20–50%) [6].

In order to avoid higher order pregnancies, these patients may require a longer duration of stimulation with gradually stepping up the dose in order to reach the threshold of FSH and LH [7]. Moreover assisted reproductive technology (ART) is beneficial in this group of patients to prevent higher order multiple pregnancies or to increase the chance of pregnancy whenever there is a poor response on ovarian stimulation but OHSS and multiple pregnancies still can happen and each patient should be assessed carefully and individually. We present a case with hypogonadotropic hypogonadism who developed OHSS and multifetal pregnancy after controlled ovulation-stimulating and IUI with human menopausal gonadotrophin (HMG) and human chorionic gonadotrophin (HCG)

Case report
Mrs. S.A.N, 29-year-old, was referred to as a case of primary amenorrhea with primary infertility for 3 years to Maternity and Child Hospital in Taif city / Saudi Arabia. She had not attained her menarche by 17 years of age and gave a history of withdrawal bleeding on combined oral pills only (E+P). During the evaluation of primary infertility, HH was diagnosed. Her serum hormone measurements determined the following results; follicle stimulating hormone (FSH) - 0.124mIU/ml, luteinizing hormone (LH) - 0.185mIU/ml, estradiol - 7 pg/ml and her serum thyroid stimulating hormone (TSH) and serum prolactin was within normal limits. Body mass index (BMI) was normal (20.2kg/m²) and psychogenic stress could not be ruled out. Hysterosalpingography showed blocked lift fallopian tube. The husband's semen analysis was normal. Before her referral, repeated attempts of ovulation induction were attempted in a private clinic in the last three years. All inductions were canceled due to poor responsiveness of the ovaries. In a private clinic, ovarian stimulations had commenced by Clomiphene Citrate (CC)150 mg for 3 cycles with no response when she was started on Menagon, (HMG, Ferring Pharmaceuticals) 150 IU for 12 days in one cycle and Gonal F - Gonal-P (follitropin alfa for injection.Merck Sorono) 300IU for 15 days in the second cycle; however pregnancy was not achieved. In our clinic Controlled ovarian hyper stimulation (COH) and IUI was planned. Menagon 225 IU was started on the second day of the cycle (3 amp per day for 16 days). A transvaginal scan was done on day 7, 9, 12, 14 and on day 16, it showed 2 follicles (17 mm and 18 mm in diameter). 10000 IU h-CG (Pregnyl 5000 IU amp. Organon) was given by intramuscular (IM) injection on treatment day 17, Swim-up and Percoll gradients were indiscriminately employed for insemination using her husband's sperm. Intrauterine insemination was performed 36 h after IM hCG administration. The luteal phase was supported with 100 mg/day micronized progesterone (Progestan 200 mg, KocakFarma) however she got her period after 14 days from HCG injection. COH Controlled was repeated using Menagon 300 iu (4 ampules/day) for 12 days which was followed by vaginal scan on day 7, 9, 11, and the last scan on day 14 showed 3 dominant follicles with size

*Correspondence to: Nisreen Aref Albezrah, Obstetrics and Gynecology Department Head, Medical college /Taif University, P.O BOX 15273, Jeddah 2317, Saudi Arabia, Email: nisreenare@yahoo.com

Key words: ovarian hyperstimulation syndrome, hypogonadotropic hypogonadism, ovulation induction

Received: June 03, 2019; Accepted: June 11, 2019; Published: June 15, 2019
16,17 and 18 mm in diameter in each ovary. IUI done based on the patient request and insist despite the risk of OHSS was explained. The patient was using Folic Acid, Aspirin, and cyclogest suppository. The pregnancy test was positive after 7 days of missing her period.

At 6 week, the scan showed five intrauterine gestational sacs. Both ovaries are enlarged with 5-6 cysts (30-50 mm in diameter with fluid behind the uterus and renal angles. Her vital signs were stable. Liver function (LF), renal function (RF) and coagulation profile were all normal. She was advised for admission but refused and individual approach for ovulation induction should be applied in order to decrease the incidence these complications and if a step-up protocol is used to decrease the incidence of multiple pregnancies, it will lead a longer duration of stimulation.

Our case emphasizes that OHSS and multiple pregnancies can be seen in patients with HH after ovulation induction with HMG and IUI who was stimulated before two times and failed to respond. We should know how high a dose of hMG to give and for how long to give this dose before give up or end in up in risk of complication.

We conclude that patients with HH undergoing ovarian stimulation for IVF should be carefully assessed, on a trial and error basis, for the ovarian response before we give up on obtaining fertilizable oocytes [8-12].

**Conclusion**

Treating patient with HH using ovulation induction drug is a challenge to the treating physician. Ovarian reserve is difficult to assess in these patients and very little information is available on the high-risk groups and prophyaxis of OHSS in HH patients. When planned for ovulation induction we must be prepared for a longer duration of stimulation which does not affect the quality of oocytes and embryo and the pregnancy rate. The treating physician and the patient need a lot of patience and motivation to continue the treatment for a longer duration. And counselling for the complication should always be explained and stressed.

**Conflict of interest**

There are no conflicts of interest.

**Author’s contributions**

Authors manage the patient and wrote all the manuscript.

**References**

1. Practice Committee of the American Society for Reproductive Medicine (1998) Induction of Ovarian Follicle Development and Ovulation with Exogenous Gonadotropins: Practice Committee Report. A Technical Bulletin, (pp 1-12).
2. Legro RS, Barnhart HX, Schlaff WD, Carr BR, Diamond MP, et al. (2007) Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. N Engl J Med 356: 551-566. [Crossref]
3. Crowley WF, Filicori M, Spratt DI, Santoro NF (1985) The physiology of gonadotropin-releasing hormone (GnRH) secretion in men and women. In Proceedings of the 1984 Laurentian Hormone Conference (pp. 473-531).
4. Santoro N, Filicori M, Crowley WF Jr (1986) Hypogonadotropic disorders in men and women: diagnosis and therapy with pulsatile gonadotropin-releasing hormone. Endocr Rev 7: 11-23. [Crossref]
5. Reame NE, Sauder SE, Case GD, Kelch RP, Marshall JC (1985) Pulsatile gonadotropin secretion in women with hypothalamic amenorrhea: evidence that reduced frequency of gonadotropin-releasing hormone secretion is the mechanism of persistent anovulation. J Clin Endocrinol Metab 61: 851-858. [Crossref]
6. Silveira LF, MacColl GS, Bouloux PM (2002) Hypogonadotropic Hypogonadism. Semin Reprod Med 20: 327-338.
7. Allabbadia G (2001) 1st ed. Rotunda Medical Technologies PVT. LTD. Manual of Ovulation Induction (pp 93-94).
8. Kumbak, B., & Kahraman, S. (2006). Women with hypogonadotropic hypogonadism: cycle characteristics and results of assisted reproductive techniques. Acta Obstet Gynecol Scand 85: 1453-1457. [Crossref]
9. Pandurangi M, Tamicharasi M, Reddy NS (2015) Pregnancy outcome of assisted reproductive technology cycle in patients with hypogonadotropic hypogonadism. J Hum Reprod Sci 8: 146. [Crossref]
10. Šimněr M, Žížen B, Atabekoglu CS, Papuccu EG, Ozkavukcu S (2012) Serum anti-Mullerian hormone levels correlate with ovarian response in idiopathic hypogonadotropic hypogonadism. J Assist Reprod Genet 29: 597-602. [Crossref]
11. Burgues ST (2001) The effectiveness and safety of recombinant human LH to support follicular development induced by recombinant human FSH in WHO group I anovulation: evidence from a multicentre study in Spain. Hum Reprod 16: 2525-2532. [Crossref]
12. Spitz IM, Rosen E, Ben-Aderet N, Polichuk W, Jaffe-H (1977) Isolated hypogonadotropic hypogonadism: induction of ovulation with exogenous gonadotropins. Fertil Steril 28: 535-540. [Crossref]