Ovarian Hyperstimulation during Chronic Pulsatile GnRH Therapy

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Chronic pulsatile administration of gonadotropin-releasing hormone (GnRH) is now being used successfully for ovulation induction in infertile women with hypothalamic amenorrhea [1, 2]. The physiological approach and the minimal risk of ovarian hyperstimulation have been claimed as the obvious advantages of this therapy. As illustrated by the following case, however, proper clinical monitoring remains a prerequisite.

The present article reports a 32-year-old woman suffering from primary oligomenorrhea with intervals of up to 4 months and primary infertility for 15 years. The physical and endocrine examinations revealed no abnormalities, follicle-stimulating hormone was 4.3 IU/l, luteinizing hormone 9.8 IU/l and prolactin 10.7 µg/l; laparoscopy showed ovaries of normal appearance and patent tubes. Since clomiphene in various doses between 50 and 150 mg daily for 5 days failed to induce adequate follicular maturation, treatment with human menopausal gonadotropins and human chorionic gonadotropin was performed, resulting in ovulatory cycles, but not in pregnancy. Despite close monitoring repeated ovarian hyperstimulation was noted. It was therefore decided to use GnRH as an alternative, but presumably less risky therapy. The pulsatile administration was started on the 5th day of a spontaneous menstruation by means of a preprogrammed portable pump (Zyklomat). Every 90 min the patient received a pulse of 20 ng GnRH via a catheter placed into the left antecubital vein. Follicular development was monitored by daily ultrasonography and hormone analyses. In the first 3 days after initiation of therapy a very high release of luteinizing hormone was observed. The serum levels ranged between 30.8 and 78.0 IU/l, while the increase in follicle-stimulating hormone was rather moderate. This exaggerated response was most likely due to an unusual pituitary sensitivity and reserve and might explain the subsequent ovarian enlargement. Further follow-up revealed fairly normal gonadotropin patterns and apparently adequate stimulatory effects until the 14th day of the cycle, when there was a dominant follicle of 24 mm in the right ovary and a serum estradiol level of 1,250 pmol/l. Presumably shortly afterwards ovulation occurred as indicated by a rise in

the basal body temperature and in the serum progesterone values. On the 18th day, still under GnRH infusion, ultrasonography showed multiple cysts measuring up to 45 mm in diameter in the right and up to 35 mm in the left ovary, whereas estradiol and progesterone values remained within normal limits, i.e. 750 pmol/l and 66 nmol/l, respectively. No additional symptoms, such as abdominal distension, nausea, vomiting or ascites were observed. Treatment was discontinued immediately and on the 30th day a menstrual bleeding occurred; the diameter of the cysts was below 30 mm at this time.

Although one of the main criteria of the hyperstimulation syndrome, i.e. excessive estrogen values, was missing, there is no doubt that cyst formation was due to the chronic intermittent GnRH application. So far no similar observations have been published, except by Skarin et al. [3]. Ovarian enlargement seems therefore to be a rather rare complication of pulsatile stimulation therapy. Nevertheless it must be concluded that peri-ovulatory monitoring is not fully dispensable and should be performed in a similar manner as in clomiphene-treated cycles.

References

- Reid, R.L.; Leopold, G.R.; Yen, S.S.C.: Induction of ovulation and pregnancy with pulsatile luteinizing hormone releasing factor: dosage and mode of delivery. *Fert. Steril.* 36: 553 (1981).
- Leyendecker, G.; Wildt, L.; Hansmann, M.: Pregnancies following chronic intermittent (pulsatile) administration of GnRH by means of a portable pump (Zyklomat): a new approach to the treatment of infertility and hypothalamic amenorrhea. *J. clin. Endocr. Metab.* 51: 1214 (1980).
- Skarin, G.; Nillius, S.J.; Wide, L.: Pulsatile low dose luteinizing hormone-releasing hormone treatment for induction of follicular maturation and ovulation in women with amenorrhea. *Acta endocr., Copenh.* 101: 78 (1982).