

USE OF THE PULSATILE GnRH PUMP FOR OVULATION INDUCTION IN PATIENTS WITH FUNCTIONAL HYPOTHALAMIC AMENORRHEA (FHA): 5-YEAR EXPERIENCE FROM A SWISS UNIVERSITY HOSPITAL

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BACKGROUND: Congenital or acquired hypogonadotropic hypogonadism (HH) is an important cause of anovulatory infertility. In functional hypothalamic amenorrhea (FHA), loss of function of the hypothalamic-hypopituitary axis occurs in catabolic states induced by eating disorders, compulsive exercise and high levels of somatic or psychological stress [1]. In patients with FHA attempting to conceive, in addition to addressing the underlying cause, a subcutaneous pulsatile gonadotropin releasing hormone (GnRH) pump may be used to induce ovulation [2]. The device is FDA-approved but currently unavailable in the United States. It is available in most of Europe including Switzerland.

OBJECTIVE: To analyze the five-year experience of treating patients with FHA using the pulsatile GnRH pump at a Swiss university-based tertiary referral center.

MATERIALS AND METHODS: All patients with FHA undergoing ovulation induction using the GnRH pump between January 2014 and October 2019 were analyzed retrospectively. Baseline characteristics including age, BMI, smoking status, AMH, AFC, endocrine profiles, and lifestyle parameters including exercise were recorded in all patients. The primary outcome was the cumulative live birth rate (LBR). Secondary outcomes included ovulation rates per cycle, cumulative ovulation rates, the number of dominant follicles per cycle, clinical pregnancy rates, miscarriage rates and multiple pregnancy rates.

RESULTS: 23 patients with a diagnosis of FHA were treated using the GnRH pump during the study period. Baseline characteristics of the study population included a mean age of 33.1, mean BMI of 19.2, and a mean serum AMH concentration of 28.4 pmol/l, equivalent to 3.98 ng/ml (Table 1). The ovulation rate per cycle attempt was 95.7%. Ovulation occurred in at least one of the cycle attempts in 23/23 patients (cumulative ovulation rate 100%). Monofollicular ovulation (one follicle of ≥ 14 mm size at time of ovulation) was observed in 67% of cycle attempts (Table 2). Clinical pregnancy rates per cycle attempt were 11/23 (48%) in the first, 7/14 (50%) in the second, 2/6 (33%) in the third, and 3/3 (100%) in the fourth cycle attempt. The cumulative LBR was 19/23 (82.6%). The miscarriage rate was 4/23 (17.4%). There was one dizygotic twin pregnancy (multiple pregnancy rate $1/19 = 5.3\%$) [Table 2]. No significant adverse effects were reported by any of the patients in the study.

CONCLUSIONS: Using the subcutaneous pulsatile GnRH pump, successful monofollicular ovulation can safely be achieved in the majority of anovulatory patients with FHA, with a cumulative LBR over 80%, and a low multiple pregnancy rate. Treatment of FHA using the pulsatile GnRH pump represents a safer, more physiologic alternative to ovulation induction using injectable gonadotropins.

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Table 1. Baseline patient characteristics

Patient characteristic	Mean	Standard deviation
Age	33.1	3.0
BMI (kg/m ²)	19.2	2.1
AMH (pmol/l)	28.4	15.2
AFC	23.4	10.3
Baseline FSH (IU/l)	5.5	1.5
Baseline LH (IU/l)	3.5	2.0

Table 2. Treatment outcomes using the pulsatile GnRH pump (n=23, undergoing a total of 46 cycle attempts)

BPR= biochemical pregnancy rate (defined as positive serum hCG level)

CPR= clinical pregnancy rate (defined as the presence of a fetal heartbeat on first trimester ultrasound)

LBR= live birth rate

Clinical parameter	Outcome (n / %)
Monofollicular ovulation (one follicle of ≥ 14 mm size at time of ovulation)	31/46 (67%)
Two follicles of ≥ 14 mm size at time of ovulation	13/46 (28%)
Three or more follicles of ≥ 14 mm size at time of ovulation	2/46 (4%)
Overall BPR per cycle attempt	26/46 (56.5%)
Overall CPR per cycle attempt	23/46 (50%)
CPR 1st cycle	11/23 (48%)
CPR 2nd cycle	7/14 (50%)
CPR 3rd cycle	2/6 (33%)
CPR 4th cycle	3/3 (100%)
SAB rate	4/23 (17.4%)
Multiple pregnancy rate	1/19 (5.3%)
Adverse effects reported	0/23 (0%)
LPR per cycle	19/46 (41.3%)
Cumulative LBR	19/23 (82.6%)

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