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The Role of Subcutaneous Luteinising Hormone Releasing Hormone in the Induction of Ovulation

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ABSTRACT

Induction of ovulation using pulsatile luteinising hormone releasing hormone (LHRH) has been performed in 53 anovulatory women who had previously failed to respond to clomiphene. Pelvic ultrasound imaging prior to treatment provided an accurate means of predicting the subsequent response to subcutaneous and intravenous therapy and was of particular value in differentiating patients with ovarian enlargement due to multiple intra-ovarian follicles. Subcutaneous administration was appropriate in the majority of patients. Thirty-eight conceptions have been confirmed.

INTRODUCTION

Induction of ovulation following the pulsatile administration of LHRH is well documented (2). Conjecture remains as to whether the most appropriate mode of infusion is by the subcutaneous or intravenous route (3). The value of good quality ultrasound in the evaluation of the development of ovarian follicles has previously been confirmed and the correlation with uterine growth has been reported. Considerable insight with regard to intra-ovarian morphology can also be gained using pelvic ultrasound.

PATIENTS AND METHODS

Fifty-three anovulatory women were investigated according to the protocol of Hull and Jacobs (1). None of these patients had exhibited an ovulatory response to clomiphene citrate (200 mg daily for 5 days). All had a normal pelvic appearance on laparoscopic examination and had partners with normal semen analyses. Twenty-seven of the patients had amenorrhoea secondary to hypogonadotrophic hypogonadism. Six patients had primary amenorrhoea, which was associated with anosmia in five. Twenty-one women had secondary amenorrhoea, which was structural in one case, weight related in six and undiagnosed "functional" in 14 patients. None of the hypogonadotrophic hypogonadal patients had intra-ovarian follicular development prior to commencing treatment.

The remaining patients (24 cases) had bilateral ovarian enlargement on ultrasound associated with a reversed FSH/LH ratio. Eighteen of these women exhibited a megalocystic intra-ovarian ultrasound appearance prior to therapy and in eight the ovaries appeared polycystic in nature.

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The route of administration of LHRH was initially subcutaneous in all patients, intravenous infusion only being employed in those women who failed to exhibit an ovulatory response to subcutaneous therapy. LHRH was provided via miniaturised automatic infusion pumps specially designed for this purpose by colleagues at the National Institute of Medical Research. A total daily dose of 240 ug was infused in 16 injections of 15 ug throughout the cycle. If menstruation occurred the pulsatile LHRH was continued into the subsequent cycle.

Pelvic ultrasound imaging was performed on alternate days during therapy. The maximum diameter of the dominant ovarian follicle and the uterine dimensions were recorded. Ovulation was considered to occur in the interval between visualisation of a mature follicle on one scan and the appearance of a ruptured follicle or early corpus luteum at the next examination. Pregnancy was confirmed ultrasonically by identification of a gestation sac and by measurement of serum HCG concentration.

RESULTS

One hundred and fifty four cycles were induced in 54 women (Table 1).

Table 1

LHRH TREATMENT CYCLES		SUBCUTANEOUS		INTRAVENOUS	
HYPOGONADOTROPHIC HYPOGONADISM (27 cases)					
	Ovulatory	65	(88%)	8	(100%)
	Anovulatory	9	(12%)	0	
MEGALOCYSTIC OVARIES (18 cases)					
	Ovulatory	18	(53%)	14	(100%)
	Anovulatory	16	(47%)	0	
POLYCYSTIC OVARIES (8 cases)					
	Ovulatory	2	(13%)	3	(42%)
	Anovulatory	13	(87%)	4	(58%)

In the patients with hypogonadotrophic hypogonadism, 88 per cent of the cycles were ovulatory in nature following pulsatile subcutaneous administration of LHRH. All of the remaining patients ovulated with intravenous infusion. In the megalocystic group, 53 per cent of the subcutaneous cycles were ovulatory, the remaining patients all responding to intravenous therapy. The patients with a "polycystic" intra-ovarian appearance on pelvic ultrasound exhibited a poor ovulation rate whether LHRH was administered subcutaneously or intravenously.

Thirty-eight pregnancies were confirmed in the 54 women (Table 2). Seventeen normal infants have been delivered and 10 pregnancies are continuing. Seven first trimester spontaneous abortions have occurred and four chemical pregnancies have been detected following prolongation of the luteal phase with associated raised serum levels of HCG.

Table 2

Number of women		54
Cycles -	Subcutaneous	126
	Intravenous	28
Pregnancies		38

The cumulative conception rate of the patients with hypogonadotrophic hypogonadism is shown in Table 3.

Table 3

HYPOGONADOTROPHIC HYPOGONADISM

Cycle	Number entering cycle	Conceptions during cycle	Cumulative conception rate (%)
1	27	8	29.6
2	18	5	49.1
3	13	6	72.6
4	6	4	91.2
5	2	1	95.4
6	1	1	100

- all other infertility factors excluded

- 3 patients needed intravenous therapy

Following four cycles of treatment more than 90 per cent of these women had conceived. All of the patients with megalocystic ovaries had conceived by the sixth cycle of treatment (Table 4).

Table 4

MEGALOCYSTIC OVARIES

Cycle	Number entering cycle	Conceptions during cycle	Cumulative conception rate (%)
1	18	5	27.7
2	13	2	38.8
3	7	2	56.6
4	5	2	73.8
5	3	2	91.3
6	1	1	100

- 50% of patients required intravenous therapy

Only one of the women with "polycystic" ovaries achieved conception and this followed subcutaneous therapy.

DISCUSSION

Pulsatile LHRH therapy restored normal fertility in the women with hypogonadotrophic hypogonadism and those with megalocystic ovaries. Our experience suggests that subcutaneous administration of LHRH is appropriate in both of these groups, the majority of amenorrhoeic patients exhibiting an ovulatory response with this route of infusion.

Pelvic ultrasound imaging prior to therapy allowed prediction of satisfactory response in those patients with bilaterally enlarged cystic ovaries and high peripheral concentrations of luteinising hormone. This is the first series in which an ultrasonic subdivision of this group of patients has been attempted.

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