

Infertility, Megalocystic and Polycystic Ovaries: Differential Response to LHRH Therapy

M. Tucker, J. Adams,* W. P. Mason and H. S. Jacobs

Cobbold Laboratories, Middlesex Hospital, London W1, England

ABSTRACT

A group of anovulatory women have been identified as being particularly difficult to treat with pulsatile luteinising hormone releasing hormone (LHRH). Further investigation shows that sub-division into two groups is possible on the basis of ovarian morphology on ultrasound imaging. Ovulation can be successfully induced in women with megalocystic ovaries and 14 of those women treated conceived.

INTRODUCTION

Normal cumulative conception rates can be achieved in infertile women with hypogonadal hypogonadism when they are treated with pulsatile subcutaneous LHRH (2). Another group of women with anovulatory infertility is that with the Polycystic Ovary (Stein Leventhal) Syndrome. Characteristically, the serum luteinising hormone (LH) concentration is elevated in these women as is the serum testosterone concentration. We have studied a group of women whose biochemical results are similar but who can be further sub-divided on the basis of their ovarian morphology on ultrasound imaging. The response to treatment with luteinising hormone releasing hormone (LHRH) in the two groups is quite different.

PATIENTS AND METHODS

Twenty-three women who failed to respond predictably to our standard therapy were identified from within our LHRH programme. These women were investigated with serum LH, FSH and testosterone measurements and ovarian ultrasound imaging was also performed. Physical characteristics of height and weight were documented. All patients were treated initially with subcutaneous LHRH (Hoechst) at a dose of 15 micrograms every 90 minutes. Those who failed to respond to subcutaneous treatment were given either the same dose intravenously or double the dose (30 micrograms) subcutaneously, using the same pulse interval.

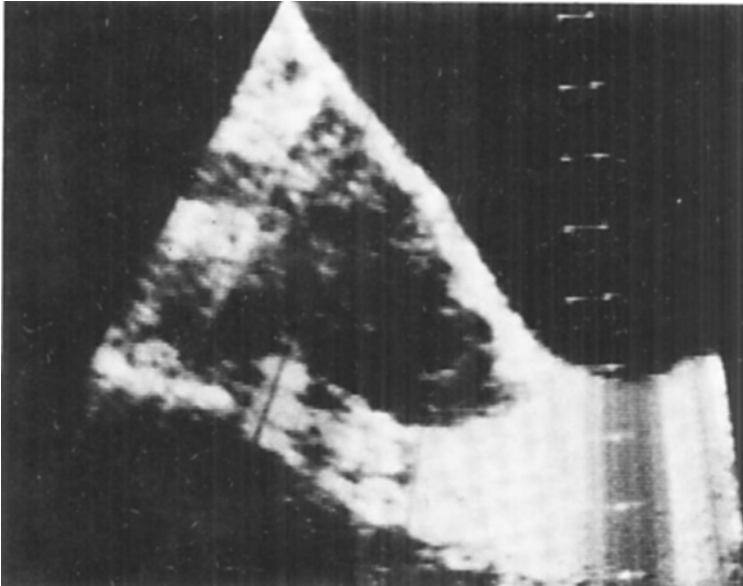
Response to therapy was evaluated by alternate day pelvic ultrasound examinations of uterine and ovarian appearances. The rate of uterine growth was used as a bio-assay of follicular oestradiol production. The formation and development of the dominant ovarian follicle was also observed. Ovulation was considered to occur between the appearance of the largest follicular diameter and the subsequent demonstration of the ultrasonic features of the corpus luteum. Confirmation of ovulation was inferred from normal luteal phase progesterone concentrations. Pregnancy was confirmed by the appearance of HCG in blood and by a demonstrable gestation sac on ultrasound.

*Department of Ultrasonography

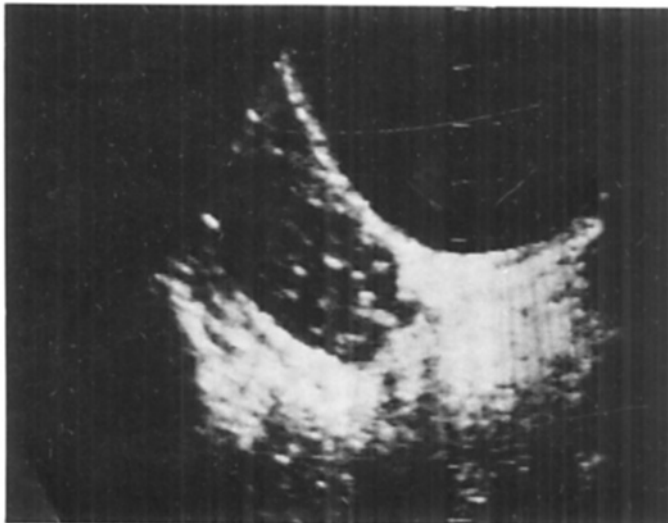
RESULTS

On the basis of ultrasound ovarian imaging prior to therapy, it was possible to sub-divide the patients into two groups on the basis of their intra-ovarian appearance. Both groups had multiple intra-ovarian cystic structures but it was on the size and distribution of these cysts that sub-division was possible.

The first group of women - those with megalocystic ovaries - were found to have cystic structures which measured 6-10 mm throughout the ovarian stroma (Figure 1).



The second group of women - those with polycystic ovaries - were also found to have intra-ovarian cystic structures, but these were smaller (measuring 2-5 mm) and more numerous than those in women with megalocystic ovaries (Figure 2).



On the basis of this ultrasonic classification, fifteen women had the ovarian features of the megalocystic type and in eight, features of the polycystic appearance were observed. The response to therapy with subcutaneous and intravenous LHRH in both groups of women is shown in Table 1 and Table 2. All the women with megalocystic ovaries responded with ovulatory cycles to LHRH treatment although more than half required intravenous therapy. In those with polycystic ovaries the response rate was 43 per cent when treated intravenously and only 12 per cent with subcutaneous therapy. Four women (two with megalocystic ovaries, two with polycystic ovaries) failed to respond to 20 days' treatment with 15 micrograms of LHRH subcutaneously and were treated for a further 20 days with 30 micrograms of LHRH subcutaneously. Despite doubling the dose of LHRH, no ovarian or uterine response was observed.

TABLE 1

Subcutaneous LHRH

	Megalocystic Ovaries	Polycystic Ovaries
Women treated	15	8
Treatment cycles	34	17
Ovulatory cycles	18	2
Pregnancies	6	1

TABLE 2

Intravenous LHRH

	Megalocystic Ovaries	Polycystic Ovaries
Women treated	9	4
Treatment cycles	13	7
Ovulatory cycles	13	3
Pregnancies	8	0

DISCUSSION

The ultrasonic classification described here has enabled us to predict the response of women with multiple intra-ovarian follicular structures to LHRH therapy. Those patients with megalocystic ovaries respond satisfactorily to pulsatile LHRH although 50 per cent eventually need intravenous therapy to conceive.

Study of a larger group of women with ovarian enlargement on ultrasound in our gynaecology clinics has revealed that measurement of gonadotrophins and testosterone fails to predict this sub-division. Evaluation of the differences in body habitus reveals that many of the patients with megalocystic ovaries have low ponderal indices and represent cases of partially recovered weight related amenorrhoea (1). The megalocystic pattern also appears to be a feature of the ovarian appearance in the peripubertal period prior to the evolution of regular ovulatory cycles and we have also observed it during lactation.

In this series, the response of the polycystic (Stein Leventhal) group to treatment with LHRH has been disappointing. Although one patient conceived following subcutaneous therapy, the overall response was poor. Increasing the subcutaneous dose of LHRH did not appear to cause desensitisation of the

pituitary response, yet failed to induce follicular maturation and even with intravenous therapy four of the seven cycles remained anovulatory (Table 2). The results reported here emphasise the value of routine ultrasound assessment of the ovaries and uterus in the diagnosis and management of women with anovulatory infertility. Ovarian imaging provides instantly available information complementary to endocrine evaluation and helps to predict the response to therapy.

REFERENCES

- 1 Knuth, U.A., Hull, M.G.R. & Jacobs, H.S.: Amenorrhoea and loss of weight. Br. J. Obstet. Gynaecol. 84:801, 1977.
- 2 Mason, W.P., Adams, J. & Jacobs, H.S.: In: Summaries of 23rd British Congress of Obstetrics and Gynaecology.

Address for reprints:

M. Tucker

Cobbold Laboratories

Middlesex Hospital

LONDON W1

United Kingdom