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Pelvic Sonography to Help Determine the Appropriate Therapy for Luteal Phase Defects

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ABSTRACT

Check, Jerome H., M.D., Goldberg, Barry B., M.D., Kurtz, Alfred, M.D., Adelson, Harriet G., B.S., and Rankin, Amy, R.D.M.S. (Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Department of Radiology, Division of Ultrasound. The Jefferson Medical College of Thomas Jefferson University. Philadelphia, Pennsylvania 19107. U.S.A.). *Pelvic sonography to help determine the appropriate therapy for luteal phase defects.*

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In some series the most appropriate therapy for luteal phase defects is supplemental progesterone in the luteal phase. Clomiphene's efficacy is more controversial since in one series only 8% achieved a successful pregnancy versus 45% in another study. Pelvic sonography was used to evaluate follicular development and release of the ovum in 50 infertile women with luteal phase defects. The results showed that only 40% had "pure" luteal phase defects whereas 52% had immature follicles and 8% had unruptured follicles. Sixty-two percent of the patients had previous therapy for a luteal phase defect and failed to conceive. Sixty-eight percent of this group did conceive when ultrasound was used to determine the appropriate therapy.

Thus ultrasound can be employed to determine if the women with a luteal phase defect should be treated with a fertility drug, e.g., clomiphene or just with luteal phase progesterone support. Supplemental progesterone might still be needed with clomiphene based on repeat endometrial biopsy results.

INTRODUCTION

The appropriate therapy of luteal phase defects is still controversial. In some series progesterone supplementation has had a 50% pregnancy rate (1). Clomiphene in one series was found to be very ineffective for treating luteal phase defects resulting in only two successful pregnancies out of 26 patients (2). However, a more recent study claimed a fertility rate of 45% (31 of 69 patients) using clomiphene to treat luteal phase deficiencies (3).

In the past we have arbitrarily added fertility drugs such as clomiphene if no successful pregnancy occurs following 4-6 months of luteal phase support with progesterone based on the assumption that perhaps the reason for the poor progesterone was the inability to form a mature follicle. Also the possibility of failure secondary to an unruptured follicle would exist.

Recently ultrasound has been used for monitoring follicular development (4, 5). A size between 17 and 25 mm diameter seems to be appropriate and release of the ovum is considered with a decrease in follicular size by at least 5 mm three days after the ideal size has been attained. We found only 2 pregnancies in 500 treatment cycles with a follicle of a 16 mm diameter or less in our own unpublished study. We decided to evaluate 50 infertile women with luteal phase deficiencies with pelvic sonography to determine what percentage have pure luteal phase deficiencies and what percentage have problems with follicular development. Subsequent fertility rates were then evaluated.

MATERIALS AND METHODS

Fifty women with luteal phase deficiencies were selected. The criteria for selection was that they had a serum progesterone level in the mid-luteal phase of over 8 ng / ml and had an endo-

metrial biopsy in two consecutive cycles in the late luteal phase that dated at least three days early. They also had a minimum of one year infertility. Each patient was required to have a normal laparoscopy, a good post-coital test (over 5 or more sperm per high-powered field with good linear progressive motion) and a semen specimen of the husband with a minimum of 30×10^6/sperm cc with 70% actively motile sperm.

Serial pelvic ultrasounds were performed beginning 17 days before the expected menses and were performed at least every other day until the third day of the rise of the basal body temperature chart. A normal size follicle was considered with a size between 17 and 25 mm. Release of the ovum from the follicle was considered if the follicle disappeared or reduced in size by at least 5 mm three days after attaining a normal size follicle. Three cycles were evaluated.

RESULTS

Fifty-two percent of these 50 infertile women with luteal phase defects released the ovum before a 17 mm follicle was achieved. A mature follicle was not achieved in 20 patients in any one of the three observed cycles. An immature follicle was demonstrated in 6 patients in 2 of 3 cycles. A pure luteal phase defect was found in 40% of the patients in that they did make a mature follicle in the majority of instances. Seventeen patients formed and released mature follicles in each of the three cycles while in 3 patients a mature follicle was found in 2 of 3 cycles. Eight percent of the patients produced a mature follicle but release of the ovum did not occur. Nevertheless, the BBT did rise and the mid-luteal phase progesterone levels were over 8 ng/ml.

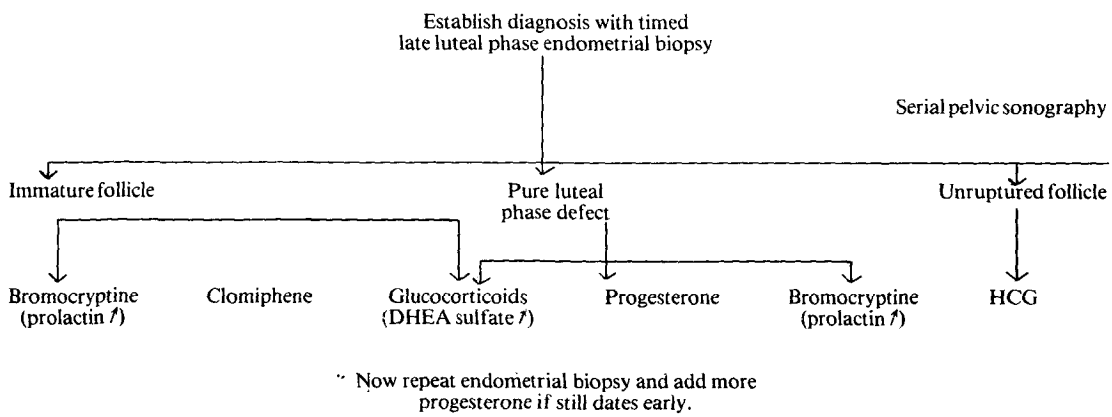
The serum progesterone level average in 54% of the patients was over 15 ng/ml for 3 cycles, thus, reconfirming the superiority of the timed endometrial biopsy over the mid-luteal phase serum progesterone level in diagnosing luteal phase defects. This good progesterone level was seen in 13 of 20

Table I. *Therapy of luteal phase defects based on ultrasound criteria and its efficacy*

	Group I (Immature follicle)		Group II (Pure luteal phase)		Group III (Unruptured follicles)	
	Total	Previous Rx	Total	Previous Rx	Total	Previous Rx
Number patients	26	18	20	11	4	2
Clomiphene Rx	17	11	0	0	0	0
Bromocryptine Rx	7	5	5	3	0	0
HMG Rx	2	2	0	0	3	1
Pregnancies	19	13	15	7	2	1

Legend: Group I = Immature follicle group with majority of cycles showing release of a follicle less than 17 mm
Group II = Pure luteal phase deficiency showing production of a mature follicle between 17-25 mm and a subsequent reduction of size 3 days later by at least 5 mm
Group III = Unruptured follicle showing the failure to decrease the follicle size by 5 mm 3 days after achieving normal size follicle.

Table II. *Evaluation and diagnosis of luteal phase defects*



patients with pure luteal phase deficiencies, 12 of 26 patients with immature follicles, and 3 of 4 patients with unruptured follicles.

Eighteeen of the 26 patients who released ova from immature follicles (Group I) had previous therapy for ovulation for at least 6 cycles (and an average of 8.5 cycles) without achieving a pregnancy. Eleven patients had been treated with clomiphene citrate and seven patients with progesterone supplementation. Thirteen of these 18 previous treatment failures conceived within 6 months when follicular maturation was governed by sonography (see Table I). In the eight patients who had no previous therapy 75% conceived within 6 months.

Group II (pure luteal phase defects) consisted of 20 patients treated with progesterone. Nine patients had been treated with clomiphene. Persistent luteal phase defects were found in 7 of the 9 clomiphene treated patients and hostile cervical mucus was found in the two patients whose endometrial biopsies dated appropriately. Three of 11 patients were found to have hyperprolactinemia and were also treated with bromocryptine. Seventy-five percent of these patients conceived within 6 months of progesterone therapy.

Two of the four patients in Group III (unruptured follicle) had previous therapy with progesterone. One finally showed ovum release with 10,000 units HCG at a 20 mm follicle size. One of the 2 previously untreated patients showed release with therapy of HMG and HCG. Both patients showing release of the ovum conceived.

DISCUSSION

The results suggest that this ultrasound technique improves the efficacy of determining appropriate therapy for luteal phase defects. Thirty-one patients in this study had previous ovulation therapy for a minimum of six months without achieving a pregnancy. Twenty-one patients in this group conceived (68%) within 6 months when the type of treatment was determined by ultrasound. Overall, 72% of the total patients conceived within 6 months. The ultrasound treatment approach is outlined in Table II.

We feel that Jones' good success with progesterone and poor results with clomiphene was probably secondary to fortuitously choosing patients who have pure luteal phase defects and this could have been demonstrated by ultrasound. Hammond's good success with clomiphene, in contrast, may be due to selection of patients with immature follicles; this may be related to selecting a higher percentage of patients with very poor progesterone levels. This hypothesis may be supported by data from Downs and Gibson who found that the patients with the worst progesterone levels responded the best to clomiphene and those with only mild progesterone deficiencies were best treated with luteal phase progesterone support (6).

We cannot be sure why 28% did not conceive. Some just needed more than 6 months since eight others did conceive within one year whereas other unknown factors might still exist in the others. The possibility also exists that the ultrasound criteria hold for the majority but not all the cases. For some women, possibly a follicle under 17 mm may still be fertilizable. However, in others who are treated by progesterone exclusively because they are making an 18 mm follicle might really need to mature that follicle to 25 mm. Another possible problem is what appears to be a follicle is really a persistent cyst and a wrong judgement could be made because of it. Nevertheless, with the above exceptions noted, we feel that ultrasound evaluation provides a more rational approach in deciding whether the initial therapy for luteal phase deficiencies should be with clomiphene or progesterone. Though, apparently safe, the theoretical possibility of future detrimental side effects of the procedure must be kept in mind and the patients should be made aware of this unlikely possibility before employing the ultrasound.

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