

Hyperprolactinemia and Luteal Phase Defects

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The role of bromocriptine in restoring ovulation in anovulatory hyperprolactinemic women is well established. The role of hyperprolactinemia in luteal phase defects (LPD) is less clear and, therefore, the importance of bromocriptine in its treatment is less certain. The mere coexistence of hyperprolactinemia and LPD does not necessarily establish cause and effect.

There have been several anecdotal reports of correction of LPD and subsequent conception following treatment with bromocriptine.^{1,2} However, Vanrell³ found that only 6.6% of hyperprolactinemic patients had LPD, compared with 17.4% of normoprolactinemic women. To assess fully the relationship of hyperprolactinemia and LPD, it is necessary to distinguish two basic types: LPD associated with the formation of a mature dominant follicle (pure LPD) and LPD associated with an immature dominant follicle. Our data suggest that mild hyperprolactinemia best correlates with LPD associated with immature follicles and that bromocriptine is effective in correcting this condition, but not pure LPD.

Studies

Three different groups of patients with infertility of at least 18 months' duration were studied. Study 1 looked at patients with ovulation problems and mild hyperprolactinemia (maximum prolactin level, 59 ng/mL) to determine if they had pure LPD, LPD secondary to immature follicles, or anovulation, and to document their response to bromocriptine. The initial dose of bromocriptine—2.5 mg daily—was increased to twice daily if the prolactin level was still elevated one month later.

The purpose of study 2 was to determine the incidence of hyperprolactinemia in patients with pure LPD and to see if treatment with progesterone vaginal suppositories was effective if their prolactin levels were not lowered with bromo-

criptine. Administration of the suppositories (25 mg twice a day) was started four days after formation of a mature follicle.

Study 3 was done to determine the incidence of LPD and other ovulation disorders in regularly menstruating infertility patients and to distinguish those with normal ovulation and ovulation problems characterized as LPD secondary to immature follicles, pure LPD, or luteinized unruptured follicle syndrome. The patients were told the benefits and side effects of therapy with clomiphene citrate and bromocriptine and were allowed to choose.

Results

Bromocriptine corrected the follicular maturation defects in 20 of 23 patients (87%) with LPD and immature follicles, and 11 (48%) conceived within six months. Eleven of the 20 patients (55%) in whom bromocriptine had corrected follicular maturation conceived. Three of the 11 patients (27%) aborted in the first trimester. Bromocriptine was effective in only three of ten patients with pure LPD, based on the results of endometrial biopsy. Only one patient conceived. This study showed that mild hyperprolactinemia is associated with LPD more commonly than with anovulation (84.6% v 15.4%) and that LPD due to immature follicles is more common than pure LPD (70% v 30%). The results suggest that the worse the ovulation problem the better the response to bromocriptine.

In study 2, 35 of 50 patients receiving progesterone (70%) achieved a pregnancy within six months. All four hyperprolactinemic patients conceived without bromocriptine therapy. Five patients (14.7%) had first trimester spontaneous abortions.

In study 3, 16 of 44 patients (36%) had LPD associated with immature follicles, and 14 of these (87%) achieved a pregnancy within eight months of therapy with either clom-

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iphenone citrate or bromocriptine. Seven of the 16 (16% of the total) had hyperprolactinemia, and six of them (85.7%) conceived. All four patients who were treated with bromocriptine and two of the three treated with clomiphene conceived. One of the 14 pregnant patients (7%) treated with supplemental progesterone and one of two untreated women aborted.

Conclusions

These studies suggest that bromocriptine is not effective in treating pure LPD, although progesterone therapy is. We did not study the effectiveness of progesterone in treating women with LPD and immature follicles, but suspect it would not be useful. El-Mahgoub⁴ found progesterone therapy to be ineffective and bromocriptine effective for women with LPD and hyperprolactinemia, leading us to wonder whether his subjects may have had LPD associated with immature follicles.

Hyperprolactinemia does not appear to inhibit the

response to progesterone therapy in women with pure LPD. Both bromocriptine and clomiphene were effective in treating patients with immature follicles, but we prefer bromocriptine because it has no adverse effects on cervical mucus. Studies 1 and 3 suggest that the most common ovulation defect in mild hyperprolactinemia is LPD associated with immature follicles. Unfortunately, no studies of bromocriptine and LPD, including our own, provide adequate controls.

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