The Influence of the Prolactin-Inhibitor Bromocriptin (CB 154) on Human Luteal Function in vivo

K.-D. Schulz¹, W. Geiger¹, E. Del Pozo², K. H. Lose¹, H. J. Künzig¹, I. Lancranjan²

¹ Department of Obstetrics and Gynecology, University of Cologne, Kerpener Straße 34, D-5000 Köln 41, Federal Republic of Germany
² Department for Therapeutic Research, Sandoz Ltd., Basel, Switzerland

Summary. Five volunteers with normal ovarian cycles received oral doses of 2 x 2.5 mg or 3 x 2.5 mg bromocriptin (CB 154)/day respectively. The treatment started at the onset of menstruation and lasted one complete cycle. In addition to the decrease of prolactin secretion, a reduction of plasma progesterone concentrations during the corpus luteum phase was demonstrated. This fall of progesterone seemed to be preferentially due to bromocriptin-induced hypoprolactinaemia and not to direct ovarian effects of the drug.

In various animal species, prolactin has been shown to act directly on the ovary, displaying luteolytic as well as luteotrophic properties. Little however, is known regarding the role of this lactogenic hormone in the regulation of human ovarian function. It has been recently observed that in some patients corpus luteum insufficiency is accompanied by hyperprolactinaemia [5]. In these cases prolactin-inhibiting therapy abolished promptly the disturbance of luteal function. Other investigations demonstrate that a rise of pituitary prolactin secretion induced by sulpiride exerts luteolytic effects in man [6]. The present study was undertaken in an attempt to elucidate the role of hypoprolactinaemia in human corpus luteum function.
Subjects and Methods

Five clinically healthy volunteers without endocrine abnormalities or menstrual disorders, aged 24—28 years, comprised the study. Normal cycles were defined as cycles having a complete length of 26—29 days and a luteal phase of at least 13 days. Serial daily blood samples were withdrawn between 8 and 10 A.M. during the postovulatory stage of the menstrual cycle. The plasma was separated immediately by centrifugation and frozen at -20 °C until assay. Details of the radioimmunological techniques required for assaying plasma concentrations of prolactin [4, 8], progesterone [9], FSH and LH [7] were described previously. After measurement of untreated control levels test persons received 2.5 mg bromocriptin (2-bromo-alpha-ergocryptine, Parlodel®, CB 154, Sandoz Ltd.) twice daily for the duration of the next cycle starting at the onset of menstruation. The synthetic drug has been shown before to be an effective inhibitor of prolactin secretion in man [1, 2]. In two volunteers the treatment was continued for one additional cycle using a higher dose of 3 x 2.5 mg CB 154/day. As at the dose range tested the ovulation was maintained in regularly cycling women [11], the measurement of plasma hormone concentrations under therapy was again restricted to the luteal phase. Using these test conditions each subject served as its own control. Test results were evaluated by unpaired Student's t-test.

Results

As shown in Fig. 1, the continuous administration of 2 x 2.5 mg or 3 x 2.5 mg bromocriptin/day for the duration of one cycle resulted in a significant reduction of plasma progesterone concentrations on day 5, 6, and 7 during the luteal phase. The fall in progesterone secretion was however not extreme. Corpus luteum insufficiency became clinically evident only in individuals treated with the higher dose of CB 154. This observation explains possibly the repeated occurrence of a statistically significant decrease of luteal progesterone levels on day 10 post ovulationem.

The overall mean of the basal prolactin plasma concentrations during the secretory phase of control cycles was 10.8 ± 1.9 ng/ml as compared to 2.2 ± 0.2 ng/ml during bromocriptin treatment.

As demonstrated in Table 1, no statistically significant differences in FSH and LH levels measured on post-ovulatory days 3, 6, and 9 were noted between treated and untreated volunteers.

![Fig. 1. Progesterone plasma concentrations (x ± S.E.M.) in regularly cycling women before and under bromocriptin therapy](image-url)