Serum Prolactin Levels during Ovulatory Menstrual Cycle and Menstrual Disorders in Women

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Synopsis

The changes in the serum prolactin levels during 8 ovulatory cycles, 3 anovulatory cycles, 3 clomiphene treated cycles, 4 premarin treated cycles and 2 cycles which had just become pregnant were measured by our heterologous radioimmunoassay.

Serum prolactin levels showed an increase in the ovulatory phase in 6 out of 8 ovulatory women and in the luteal phase in 5 out of 8 ovulatory women respectively. No definite increase of serum prolactin in the ovulatory phase was observed in 2 out of 8 ovulatory and 3 anovulatory women. Oral administration of 1.25 mg of premarin for 7, 10, 14 days slightly increased serum prolactin levels in 4 ovulatory women. Treatment with clomiphene increased serum prolactin in the ovulatory phase in 2 ovulatory women, but did not increase it in one woman who failed to ovulate.

Serum prolactin levels in 2 women who became pregnant during the investigation were determined. The rise of serum prolactin was observed in the ovulatory phase. But no marked increase of serum prolactin was demonstrated in the early pregnant luteal phase.

Our present results demonstrated ovulatory rise of serum prolactin. It is too early to conclude that human prolactin may have luteotrophic action in man.

Remarkable progress has been shown recently in the research on secretion of human pituitary hormones such as ACTH, GH, TSH, FSH, and LH except prolactin, because of development of radioimmunoassay. The reason why only human prolactin showed poor development in the research lies in both lack of sensitivity in prolactin bioassay and undevelopment of human prolactin radioimmunoassay. Recently Bryant et al. (1971) and Friesen et al. (1972) succeeded in human prolactin radioimmunoassay using purified human prolactin and anti human prolactin serum, but these precious antigen and antisera are not available yet. Quite recently Jacobs et al. (1972) devised a new heterologous radioimmunoassay of human prolactin using purified porcine prolactin and anti-ovine prolactin sera. Our new modification (Tamura and Igarashi, 1973) simplified the original Jacobs et al.'s method in omitting bioassay of prolaction standard.

The purpose of the present paper is to study the secretion of human prolactin in normal ovulatory women and other pathological states untreated or treated, using our modified heterologous radioimmunoassay.

Materials and Methods

Blood samples were collected about 10:30 A.M. daily or every two days or every three days in 8 normal menstruating women, 3 anovulatory women, 3 anovulatory and clomiphene-treated women, and 4 premarin-treated ovulatory women. Two women,
one in spontaneous ovulation and the other in clomi-
phene-premarin treated cycle, became pregnant during
the investigation. Blood samples were centrifuged and
the sera were stored at -20°C until radioimmunoassay.

Our method of radioimmunoassay for human
prolactin was previously reported (Tamura and
Igarashi, 1973). Purified porcine prolactin kindly
provided by Dr. Eppstein, Upjohn Company was
used for iodination and standard. 20 μg of purified
porcine prolactin was iodinated with 1mCi of 131I-Na.
Anti ovine prolactin guinea pig serum was kindly
provided by Dr. Johke of the National Institute of
Animal Industry. The slope of the dose response curve

using the purified porcine prolactin was demonstrated
to be parallel to that using diluted sera of post-partum
lactating women.

Results

Serum prolactin levels during ovulatory
menstrual cycle

Serum prolactin levels in 8 ovulatory wo-
men were assayed at 10: 30A.M. every two
days. As shown in Figure 1, ovulatory increase

![Graph 1: Changes of serum prolactin during 8 ovulatory menstrual cycles. Day 0, the last day of the low phase in B.B.T.](image1)

![Graph 2: Changes of serum prolactin during 3 anovulatory cycles.](image2)
of serum prolactin levels was observed in 6 out of 8 women. This ovulatory peak corresponds to the day zero (the last day of low phase of BBT) in 4, one day prior to the day zero in one woman, and one day after the day zero in one woman.

Serum prolactin levels were lower in the follicular phase than in the luteal phase in 5 out of 8 women. Among the other 3 women, two women showed temporary follicular rise, and the remaining one showed flat secretion except daily variation.

**Serum prolactin levels during anovulatory menstrual cycle**

As shown in Figure 2, serum prolactin levels during three anovulatory cycles did not show any significant daily variation, any ovulatory rise, and any relatively high levels in the luteal phase, as demonstrated in the ovulatory cycle.

**Effect of clomiphene citrate upon prolactin secretion in anovulatory women (Fig. 3)**

As shown in Figure 3, on the fourth day during the administration of clomiphene, a temporary rise in serum prolactin levels was observed in 2 out of 3 anovulatory women. An ovulatory increase in serum prolactin was shown in ovulation-induced cases, but no change was observed in anovulatory case.

**Effect of estrogen (premarin) upon prolactin secretion in four ovulatory women**

As shown in Figure 4, daily administration of 1.25 mg premarin induced a temporary rise of serum prolactin levels on the fourth day in 3 women and on the sixth day in 1 woman. After cessation of premarin administration, serum prolactin levels increased in 2 out of 3 women.

**Serum prolactin levels in the two women who became pregnant during investigation. (Fig. 5)**

Pregnancy was established spontaneously in one case and in the cycle treated with clomiphene and premarin in another case. In both cases ovulatory temporary rise of serum prolactin and no increase in the luteal phase were observed.

**Discussion**

Radioimmunoassay of human prolactin has been reported by Hwang et al., (1971); Bryant et al., (1971); L’Hermite et al., (1972); Jacobs et al., (1972). There have been a few reports of cyclic changes in serum prolactin during
Premarin 1.25mg/day 7days

Premarin 1.25mg/day 10days

Premarin 1.25mg/day 14days

Fig. 4  Effect of premarin on serum prolactin in ovulatory menstrual cycles.

menstrual cycles. L'Hermite et al., (1972) reported no cyclic change, especially neither midcycle peak nor mid-luteal peak. They also showed a higher tendency in the luteal phase than in the follicular phase. While Friesen et al., (1972) reported no preovulatory peak, but a midluteal peak in some women. But our present results clearly demonstrate ovulatory rise of serum prolactin in 6 out of 8 ovulatory women, in 2 clomiphene-induced ovulatory women and in 2 ovulatory women who have just become pregnant during the investigation. Moreover, there was no peak during the three anovulatory cycles.

Administration of premarin, a kind of estrogen, induced temporary rise of serum prolactin. This result coincides with the reports demonstrating that prolactin secretion from the pituitary is stimulated by the administration of estrogen in rats (Nicoll and Meites, 1962; Kanematsu and Sawyer, 1963; Ramirez and McCann, 1964; Ratner and Meites, 1964) and in man (L'Hermite et al., 1972). It is well established that estrogen secretion shows a remarkable peak in the preovulatory phase. Consequently it is conceivable that the ovu-
latory rise in serum prolactin levels may be induced by the feedback action of preovulatory increase of blood estrogen.

It is an interesting problem whether serum prolactin levels during the luteal phase are high or not, because prolactin is an established luteotrophic hormone in rats and mice, but the role of prolactin in human luteotrophic function remains obscure.

The present data show a higher tendency of serum prolactin in the luteal phase in 5 out of 8 women. However, in the two cycles in which pregnancy was established, there was no increase of serum prolactin levels in the luteal phase. From these results, it is too early to conclude that human prolactin may have luteotropic action.

L'Hermite et al. (1972) and Tyson et al. (1972) reported a sharp rise of serum prolactin levels from 8 weeks of gestation to parturition. Our data are limited to the early phase of pregnancy, so our results do not contradict with their results.

Our assay results seem to be slightly higher than the results assayed with homologous human prolactin radioimmunoassay. The reason why the assay values are different between homologous prolactin radioimmunoassay and heterologous prolactin radioimmunoassay is not clear, but the relative tendency during the normal menstrual cycle and other menstrual disorders may not be dependent on the assay method.

References

L'Hermite, M., P. Delvoye, J. Mokin,