

## Prolactin

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### Comparison of Expression of Endometrial Prolactin in Infertile Women with Luteal Phase Defect According to Clomiphene Citrate Administration

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**Objective:** Clomiphene citrate is one of the most commonly used drugs in the treatment of infertility, but the pregnancy rate achieved with clomiphene citrate is significantly lower than the ovulation rate due to its antiestrogenic effect on the endometrium. Endometrial prolactin is considered to be a marker and an inducer of predecidualization that is characteristic of secretory endometrium. The purpose of this study was to evaluate the association of clomiphene citrate and unsatisfactory endometrial differentiation to secretory endometrium by examining the endometrial expression of prolactin in clomiphene citrate-treated infertile women with luteal phase defect.

**Methods:** The endometrial samples from infertile women with luteal phase defect (n=27) were examined. Five cases during secretory phase and six cases during proliferative phase were obtained by biopsy. Sixteen cases were obtained by biopsy during secretory phase after clomiphene citrate treatment. By immunohistochemical staining for prolactin, all obtained endometrial tissues were examined. The differences in the endometrial expression of prolactin were evaluated between proliferative phase and secretory phase, and between clomiphene citrate treated group and no treatment group during secretory phase.

**Results:** The staining of endometrial prolactin was significantly more intense in the glandular epithelial cells and stromal cells in the secretory endometrium than in the proliferative endometrium. The glandular expression of prolactin in the secretory endometrium was not significantly different between the clomiphene citrate-treated group and no treatment group (p=0.719), but the staining of prolactin in the stromal cells was significantly less intense in the clomiphene citrate-treated group than no treatment group (p=0.019).

**Conclusion:** In this investigation, we demonstrated that the endometrial stromal expression of prolactin in the secretory phase was significantly lower in the clomiphene citrate-treated group compared with no

treatment group in infertile women with luteal phase defect. And our finding suggests that clomiphene citrate may have an adverse effect on the endometrial predecidualization in infertile women.

**Key Words:** Endometrial prolactin, Clomiphene citrate, Luteal phase defect

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**Table 1.** Clinical characteristics

	Proliferative phase without CC (n=6)	Secretory phase without CC (n=5)	Secretory phase with CC (n=16)
Age (years)	29.9 ±3.3	31.6 ±3.7	29.0 ±4.6
Parity	0.3 ±0.7	0.1 ±0.3	0.1 ±0.3
Duration*	2.7 ±1.5	3.3 ±1.3	3.3 ±2.2
Biopsy date**	5.4 ±1.9	26.7 ±1.8	25.6 ±2.8
Pathologic date	-	22.7 ±1.1	23.4 ±2.7

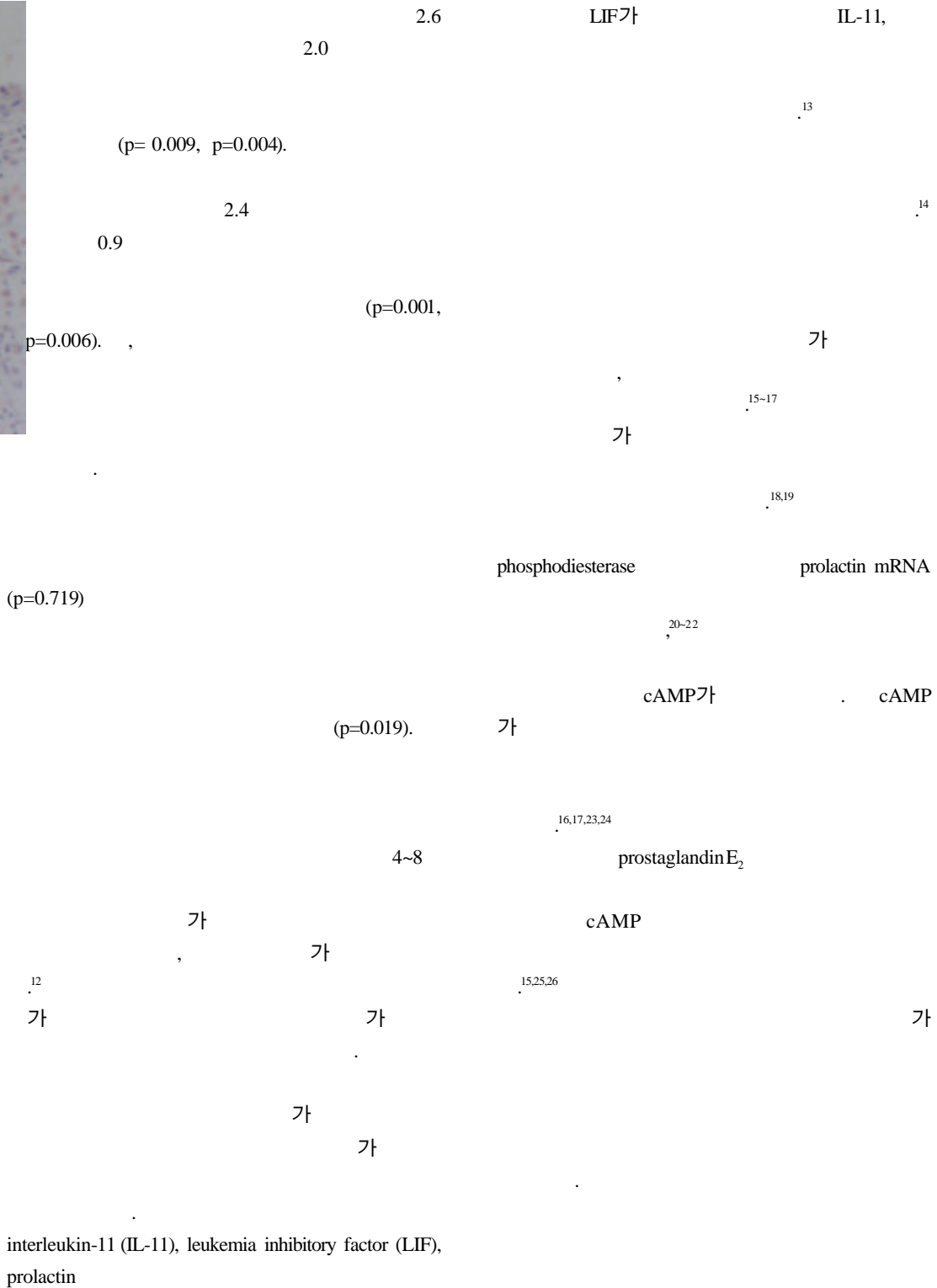
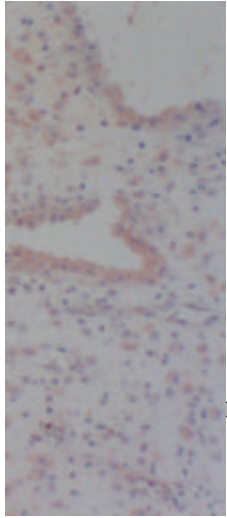
CC: clomiphene citrate, Duration\*: duration of infertility (years), Biopsy date\*\*: menstrual cycle day when endometrial biopsy was performed

**Table 2.** Mean expressions of prolactin in endometrium

	Proliferative phase without CC (n=6)	p. value*	Secretory phase without CC (n=5)	p. value**	Secretory phase with CC (n=16)	p. value***
Gland	1.17	p=0.009	2.6	p=0.001	2.4	NS (p=0.719)
Stroma	0.0	p=0.004	2.0	p=0.006	0.9	p=0.019

CC: clomiphene citrate, p. value\*: compared with proliferative phase without CC and secretory phase without CC, p. value\*\*: compared with proliferative phase without CC and secretory phase with CC, p. value\*\*\*: compared with secretory phase without CC and secretory phase with CC

10% H<sub>2</sub>O<sub>2</sub> 10 min, tris buffer, 1:50 dilution, 1. Affinity-purified goat polyclonal antibody Prolactin (C-17) (Santacruz Biotechnology, USA), Table 1, 2. N-histofine simple stain MAX PO (G) (Nichirei corporation, Japan), 15. aminoethylcarbasole (AEC), Mayer hematoxylin, 7+2, 5% (Table 1), Mil-ler 0 (absent), 1 (weak), 2 (moderate), 3 (intense), 2. Figure 2, Table 2, Figure 1, SPSS version 11.0 Mann-Whitney test, p<0.05, 0, 1, 2, 3, 1.17, 0.0



**Figure 1.** The prolactin expression in endometrium during secretory phase with clomiphene citrate. The stromal cells were weakly stained and the glandular epithelial cells were intensively stained by immunohistochemical staining for prolactin ( ×100).

**Figure 2.** The prolactin expression in endometrium during secretory phase without clomiphene citrate. The stromal cells and the glandular epithelial cells were intensively stained by immunohistochemical staining for prolactin ( ×100).

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