

**Serum Insulin-like growth factor binding proteins profiles
during the normal ovulatory menstrual cycle**

Jung Jae Hun and Jung Gu Kim

Department of Obstetrics & Gynecology, College of Medicine,
Seoul National University, Seoul 110-744, Korea

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1996

(:2- 96- 92)

=Abstract=

The insulin-like growth factor(IGF)s are believed to one of several growth factors that play an adjunctive role in ovarian follicular development. These factors circulate bound to a family of IGF-binding protein(IGFBP)s. It is known that circulating IGFBPs are involved in the transport of IGFs to tissues and modulate IGFs actions at local tissue. The purposes of this study were to evaluate changes in serum IGFBPs profiles during normal ovulatory menstrual cycle and to compare serum IGFBPs profiles in periovulatory phase of between normal ovulatory menstrual cycle and controlled hyperstimulated cycle. Fasting blood samples were obtained from 15 normal healthy women throughout normal ovulatory menstrual cycle and on the day of aspiration of oocyte from 10 patients undergoing ovarian hyperstimulation for in vitro fertilization-embryo transfer. Serum IGFBP-1 - IGFBP-4 were measured by western ligand blot and immunoprecipitation. Serum 17β -estradiol was determined by radioimmunoassay. Type and molecular weight of serum IGFBP did not changed during normal ovulatory menstrual cycle. No significant variation in the relative proportion and level of each IGFBP was found throughout normal ovulatory menstrual cycle. Also, the relative proportion and level of each IGFBP did not correlated with serum 17β -estradiol level. There was no significant difference in the relative proportion and level of each serum IGFBP between on the day of ovulation in normal ovulatory menstrual cycle and on the day of aspiration of oocyte in controlled hyperstimulated cycle. Our data indicate that IGFBPs have regulatory functions in ovary through an paracrine and autocrine rather than endocrine mechanism during normal ovulatory menstrual cycle.

Key Words: IGFBP, 17β -estradiol, Normal ovulatory menstrual cycle, Controlled hyperstimulated cycle

(insulin-like growth factor: IGF)

,

(Giudice, 1995). IGF-I

IGF-I

가 (Rabinovici et al.,1990; Hamori et al.,1991). IGF-I

(messenger ribonucleic acid; mRNA) 가

(El-Roiey et al.,1993,1994; Zhou & Bondy,1993). IGF-I 가 IGF-I

가 . 가 IGF-I

(Wang et al.,1995; Van Dessel et al.,1996; Blake et al.,1997).

IGF IGF I(IGF binding protein: IGFBP

) IGFBP-1 - IGFBP-6 6 . IGFBP가 IGF

IGF 가 IGF (storage

IGFBP) (transport/shuttle IGFBP)

(Jones & Clemmons,1995) IGF가

IGFBP 가 .

IGFBP-1 IGFBP-3

가 (Wang et al.,1995; Van Dessel et al.,1996; Blake et al.,1997; Helle et al.,1998). IGFBP-3 IGFBP, IGFBP-2,

IGFBP-4 (Jones & Clemmons, 1995) IGFBP

IGF

IGFBP .

IGFBP-1 - IGFBP-4

IGFBP

IGFBP

(1)

3 (27-30)
가 15
10
D-Trp-6-LHRH (Decapeptyl, Ferring Malmö, Sweden) 0.1
mg 17β-estradiol 가 30pg/ml
10mm human menopausal gonadotropin(hMG)/follicle
stimulating hormone(FSH) 150 unit
27-35 20-30
10 , 가 5 Western ligand blot

(2) ,

가 3
7-9 1-2 3,5 mHz realtime sector scanner
2-3 , 9-10 가
7 9 -70 ° C 가
3
-70 ° C
가

(3) IGFBP

IGFBP
Western ligand blot

(Kim & Lee,1996)

9

5 ° C 5 가 sodium dodecyl sulfate(SDS) polyacrylamide
 semidry -electrotransfer (Pharmacia, LKB, Sweden)
 . 3% Nonidet P-40, 1% (bovine serum albumin;
 BSA), 0.1% Tween-20 1%
 BSA, 0.1% Tween-20 ¹²⁵I-IGF-I(10⁶cpm) 4 ° C 18
 . BAS (imaging plate)
 BAS 2040 24 IGFBP
 Bio-imaging analyzer system (BAS 2000, Fuji Film Co.Ltd.,Japan) Tina 2.0
 . Western ligand blot IGFBP-3
 , IGFBP-2 . IGFBP
 interassay variation 5.1% . *IGFBP*
 (Kim & Lee,1996)
 (*Immunoprecipitation*) .

(4) 17β -estradiol

가 1-4 25
 estradiol kit(Sereno Diagnostics,Switzerland) 17β-estradiol
 . 20-2000pg/ml estrone 1.3%, estriol
 0.4% intrassay variance 5.5% .

(5)

±
 . SAS program repeated measures ANOVA test,
 student's t-test p < 0.05 .

가 37/43kDa, 31kDa, 26kDa, 24kDa
 IGFBP IGFBP-1 , IGFBP-2 , IGFBP-3 ,
 IGFBP-4 37/43kDa IGFBP가
 IGFBP-3, 31kDa IGFBP가 IGFBP-2, 26kDa IGFBP가 IGFBP-1, 24kDa IGFBP가 IGFBP-4

IGFBP

가 (Fig. 1). IGFBP

Western ligand blot

10 IGFBP 1
 IGFBP-1, IGFBP-2, IGFBP-3,
 IGFBP-4 가 (Table 1).

IGFBP

IGFBP

IGFBP

Table 2

가 (Table 2).

1-4

IGFBP

IGFBP

estradiol

가 .

가

IGFBP

(Fig. 2)

IGFBP

IGFBP

(Fig. 3)

가

가 .

IGF IGF
 IGF IGF 가
 IGFBP-2, IGFBP-4 가
 IGFBP .
 IGFBP IGF 가 .

IGFBP-1 가 가 (diurnal fluctuation) 가 가

(Jones & Clemmons,1995).

IGFBP-1 9

IGFBP Western ligand blot

IGFBP ,

가 .

IGFBP-1, IGFBP-3

IGFBP-1

가

1 IGFBP-1 (peak) Wang (1995)

(Van Dessel et al,1996; Helle et al.,1998) .

IGFBP

. IGFBP-1

IGFBP-1 (Lee et al.,1993)

IGFBP-1 가 IGF

가 (Tiitinen et al.,1993). IGFBP-3

Wang (1995), Van Dessel (1996) . IGFBP-3가

가 Helle (1998) . IGFBP-3

IGFBP (growth hormone; GH)

(Jones & Clemmons,1995) GH

Juul (1997) .

IGFBP-3 IGF 150kDa

IGFBP, IGFBP-2, IGFBP-4

(Jones & Clemmons,1995) IGFBP IGF

IGFBP-2, IGFBP-4

IGFBP 가가 IGF

(Cataldo & Giudice, 1992; San Roman & Magoffin, 1993). (Kim &

Lee,1996) 가

IGFBP-2 가 가 IGFBP-2

IGFBP-2
 가 IGFBP-2, IGFBP-4

IGFBP-1
 (gonadotropin releasing hormone agonist) hMG
 IGFBP-1 가
 (Martikainen et al.,1991; Arthur et al.,1994) 가

IGFBP
 가
 IGFBP IGFBP 가

IGFBP-1 - IGFBP-5 mRNA가 (El-Roiey et al.,1993,1994)
 IGFBP-1 - IGFBP-4
 (, 1996). IGFBP-1 -
 IGFBP-4 가 IGFBP가
 (paracrine) (autocrine) IGF
 가 IGF IGFBP
 IGF , pH
 (vascular permeability)
 가

IGFBP-1 - IGFBP-4
 가 15
 10 IGFBP-1 - IGFBP-4 17 β -estradiol Wetern ligand
 blot, , IGFBP
 17 β -estradiol
 IGFBP
 IGFBP , ,
 가 IGFBP 17 β

- Maturitas 1998, 28, 259-265.
- Jones JI, Clemmons DR: Insulin-like growth factors and their binding proteins : Biological actions. Endo Rev 1995, 16, 3-34.
- Juul A, Scheika T, Pedersen AT, Main KM, Andersson AM, Pedersen LM, Skakkebek NE: Changes in serum concentrations of growth hormone, insulin, insulin-like growth factor and insulin-like growth factor-binding protein 1 and 3 and urinary growth hormone excretion during the menstrual cycle. Hum Reprod 1997, 10, 2133-2128.
- Kim JG, Lee JY: Serum insulin-like growth factor binding protein profiles in postmenopausal women: their correlation with bone mineral density. Am J Obstet Gynecol 1996, 174, 1511-1517.
- 1996, 39, 261-278.
- Lee PDK, Conover CA, Powell DR: Regulation and function of Insulin-like growth factor binding protein-1. Proc Soc Exp Biol Med 1993, 204, 4-29.
- Martikainen H, Tapanainen J, Ronnberg L, Kauppila A, Selenius P, Seppala M: Insulin-like growth factor binding protein-1 and ovarian stimulation. Hum Reprod 1991, 6, 1220-1222.
- Rabinovici J, Dandekar P, Angle MJ, Rosenthal S, Martin MC: Insulin-like growth factor I (IGF-I) levels in follicular fluid from human preovulatory follicles : correlation with serum IGF-I levels. Fertil Steril 1990, 54, 428-433.
- San Roman GA, Magoffin DA: Insulin-like growth factor-binding proteins in healthy and atretic follicles during normal menstrual cycles. J Clin Endocrinol Metab 1992, 76, 625-632.
- Tiitinen AE, Laatikainen TJ, Seppala MT: Serum levels of insulin-like growth factor binding protein-1 and ovulatory response to clomiphene citrate in women with polycystic ovarian disease. Fertil Steril 1993, 60, 58-62.
- Van Dessel HJHM, Chandrasekher Y, Stephanie GW, Lee PDK, Hintz RL, Faessen GHJ, Braat DDM, Fauser BCJM, Giudice LC: Serum and follicular levels of insulin-like growth factor I(IGF-I), IGF-II and IGF- binding protein-1 and -3 during the normal menstrual cycle. J Clin Endocrinol Metab 1996, 81, 1224-1231.
- Wang HS, Lee JD, Soong YK: Serum levels of insulin-like growth factor I and

insulin-like growth factor binding protein-1 and -3 in women with regular menstrual cycle. *Fertil Steril* 1995, 63, 1204-1209.

Zhou J, Bondy CA: Anatomy of the human ovarian insulin-like growth factor system.

Biol Reprod 1993, 48, 467-482.