

가 Gonadotropin Releasing Hormone Agonist Stimulation Test (GSAT)

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Objectives : The aims of this study are 1) to determine if GAST is a better indicator in predicting ovarian response to COH compared with patient's age or basal FSH level and 2) to evaluate its role in detecting abnormal ovarian response.

Design: Prospective study in 118 patients undergoing IVF-ET using GnRH-a short protocol during May-September 1995.

Materials and Methods: After blood sampling for basal FSH and estradiol (E<sub>2</sub>) on cycle day two, 0.5ml(0.525mg) GnRH agonist (Suprefact, Hoechst) was injected subcutaneously. Serum E<sub>2</sub> was measured 24 hours later. Initial E<sub>2</sub> difference (ΔE<sub>2</sub>) was defined as the change in E<sub>2</sub> on day 3 over the baseline day 2 value. Sixteen patients with ovarian cyst or single ovary or incorrect blood collection time were excluded from the analysis. The patients were divided into three groups by E<sub>2</sub>; group A (n=30): E<sub>2</sub><40 pg/ml, group B (n=52): 40 pg/ml ≤ E<sub>2</sub> < 100 pg/ml, group C (n=20): E<sub>2</sub> ≥ 100 pg/ml. COH was done by GnRH agonist/HMG/hCG and IVF-ET was followed. Ratio of ΔE<sub>2</sub> on day of hCG injection over the number of ampules of gonadotropins used (ΔE<sub>2</sub>/hCGday/Amp) was regarded as ovarian responsiveness. Poor ovarian response and overstimulation were defined as ΔE<sub>2</sub>/hCGday less than 600 pg/ml and greater than 5000 pg/ml, respectively.

Results : Mean age (±SEM) in group A, B and C were 33.7±0.8\*, 31.5±0.6 and 30.6±0.5\*, respectively (\*P<0.05). Mean basal FSH level of group A (11.1±1.1 mIU/ml) was significantly higher than those of B (7.4±0.2 mIU/ml) and C (6.8±0.4 mIU/ml) (P<0.001). Mean ΔE<sub>2</sub>/hCGday of group A was significantly lower than those of group B or C, i.e., 1402.1±187.7 pg/ml, 3153.2±240.0 pg/ml, 4078.8±306.4 pg/ml respectively (P<0.0001). The number of ampules of gonadotropins used in group A was significantly greater than those in group B or C : 38.6±2.3, 24.2±1.1 and 18.5±1.0 (P<0.0001). The number of oocytes retrieved in group A was significantly smaller than those in group B or C : 6.4±1.1, 15.5±1.1 and 18.6±1.6, respectively (P<0.0001). By stepwise multiple regression, only ΔE<sub>2</sub> showed a significant correlation (r=0.68, P<0.0001) with ΔE<sub>2</sub>/hCGday/Amp, while age or basal FSH level were not significant. Likewise, only ΔE<sub>2</sub> correlated significantly with the number of oocytes retrieved (r=0.57, P<0.001). All four patients whose COH was canceled due to poor ovarian response belonged to group A only (Fisher's exact test, P<0.01). Whereas none of 30 patients in group A (0%) had overstimulation, 14 patients among 72 patients (19.4%) in group B and C had overstimulation

(Fisher's exact test,  $P < 0.01$ ).

Conclusions: These data suggest that initial  $E_2$  difference after GAST may be a better prognostic indicator of ovarian response to COH than age or basal FSH level. Since initial  $E_2$  difference demonstrates significant association with abnormal ovarian response such as poor ovarian response necessitating cycle cancellation or overstimulation, GAST may be helpful in monitoring and consultation of patients during COH in IVF-ET cycle.

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Key words: GnRH Agonist stimulation test, Ovarian reserve, Controlled ovarian hyperstimulation.

가 (receptivity)  
 (controlled ovarian hyperstimulation, COH)  
 가 ovarian reserve ovarian age  
 가  
 stimulating hormone, FSH),<sup>4-10</sup> (Estradiol) ,<sup>11</sup> Clomiphene citrate  
 challenge test( CC challenge test) <sup>12-16</sup> (Follicle  
 Winsolw <sup>17</sup> (provocative test) GnRH agonist stimulation test  
 ( GAST)  
 GAST GnRH  
 E<sub>2</sub>  
 GAST  
 (initial E<sub>2</sub> difference)

FSH GAST

1.  
 1995 5 1995 9 GnRH agonist  
 118  
 41 , 42 , 13 , 10  
 12 .

2.  
 1) GnRH agonist stimulation test (GAST)  
 2 FSH (E<sub>2</sub>) ,  
 GnRH agonist (Buserelin acetate, Suprefact , Hoechst, Germany) 0.525 mg  
 24 E<sub>2</sub> . 24 가 E<sub>2</sub>  
 (initial E<sub>2</sub> difference) 가 40  
 pg/ml A , 40 pg/ml 100 pg/ml B , 100  
 pg/ml C . 28  
 FSH E<sub>2</sub> interassay coefficient  
 of variance intraassay coefficient of variance 5% .

2)

GnRH agonist 0.525 mg  
FSH(Metrodin, Serono, Switzerland) human menopausal gonadotropin(Pergonal, Serono, Switzerland)  
18 mm (hCG, Profasi, Serono)  
hCG E<sub>2</sub> 가 600 pg/ml (poor responder)  
, 5,000 pg/ml (overstimulation) . hCG 34-36  
, 2-3 .  
progesterone in oil 50 mg 12  
 $\beta$ -HCG 10  
(gestational sac) .

3)

E<sub>2</sub> 가 GnRH agonist  
24 16 98  
test , P < 0.05 , Fisher's exact

1. GnRH agonist stimulation test

GAST A 30 B 52 C 20 . ( 1)  
 A 33.7 ± 0.8 B 31.5 ± 0.6 C 30.6 ± 0.5 A  
 C (P<0.05).  
 FSH A 11.1 ± 1.1 mIU/ml, B 7.4 ± 0.2  
 mIU/ml, C 6.8 ± 0.4 mIU/ml A B C  
 (P<0.0001). 2 E<sub>2</sub> A 24.8 ± 2.2 pg/ml, B 20.8 ± 0.9  
 pg/ml, C 21.4 ± 0.9 pg/ml  
 (P>0.05).

2. GAST , FSH  
 , hCG E<sub>2</sub> ,  
 2 .  
 B C A hCG E<sub>2</sub> 가 ( A :1402.1 ±  
 187.7 pg/ml B : 3153.2 ± 240.0 pg/ml C : 4078.8 ± 306.4 pg/ml, p<0.0001)  
 ( A : 6.4 ± 1.1 B : 15.5 ± 1.1 C : 18.7 ± 1.6 ,  
 p<0.0001) 가 ( A : 4.3 ± 0.6 B : 9.0 ± 0.8 C  
 : 8.3 ± 1.2 , p<0.0001) ( A : 38.6 ±  
 2.3 B : 24.2 ± 1.1 C : 18.5 ± 1.0 , P<0.0001).  
 ( A : 8.5 ± 0.2 B : 8.4 ± 0.3 C 9.0 ± 1.0  
 ). A 12.5% (4/32), B 27.5% (11/20), C  
 25% (5/20) .  
 hCG E<sub>2</sub> (E<sub>2</sub> on hCG/ampules)  
 E<sub>2</sub> on hCG/ampules FSH  
 (stepwise multiple  
 regression, r=0.68, p<0.001).  
 (stepwise multiple  
 regression, r=0.57, p<0.001) ( 1,2).

3. GAST

6 A (Fisher's exact test, p<0.01).  
 A 30 (0/30) B C  
 72 14 (19.4%) . C

, 가 ,  
 .  
 ovarian reserve  
 1-3 , 4-10 11  
 18 가 CC challenge  
 test 12-16 GAST 17 가가  
 .  
 19  
 (chronological age) 가  
 가 .  
 FSH ovarian reserve 가 .  
 , (inhibin) -  
 가 가 20  
 21  
 가 CC challenge test .  
 . CC challenge test  
 (E2) inhibin FSH  
 . CC challenge test FSH reserve가  
 . CC challenge test  
 reserve 가  
 , clomiphene citrate FSH  
 100%  
 22  
 Scott FSH 가 FSH 가 2.6 ±  
 0.2 mIU/ml FSH 가 7.4 ± 0.9 mIU/ml 가  
 23 FSH 가 FSH가  
 가  
 FSH 가 reserve가  
 .  
 FSH CC challenge test  
 가 .  
 . FSH Scott 25mIU/m ,<sup>9</sup> CC challenge  
 test Navot 26mIU/ml,<sup>12</sup> Tanbo 12mIU/ml,<sup>14</sup> Loumaye  
 13mIU/ml,<sup>13</sup> Scott 10mIU/ml 가 .<sup>15</sup>  
 GAST - 가 . GnRH

E<sub>2</sub> GAST - -  
 (initial E<sub>2</sub> difference)  
 GAST가  
 GnRH  
 E<sub>2</sub> GAST  
 (initial E<sub>2</sub> difference)  
 E<sub>2</sub> FSH GAST  
 가  
 GAST 가 hCG E<sub>2</sub>가  
 (Table 2) GAST  
 FSH  
 가 (Table 1, P<0.0001).

<sup>24-25</sup> hCG E<sub>2</sub>  
 GAST가  
 P<0.001). Winslow GnRH agonist (Fig. 1,2 stepwise multiple regression,  
 E<sub>2</sub> E<sub>2</sub> pattern 2 3 4  
 가 .<sup>17</sup>  
 4 GAST (4/4, 100%),  
 100%) GAST A 6 (6/6,  
 GnRHa pure FSH <sup>26</sup> GnRHa  
<sub>27-28</sub>

GAST  
 A  
 B C 가  
 overstimulation 가  
 GAST 가  
 GAST dose-response correlation  
 가가

GAST 24 가 E<sub>2</sub>  
 가 hCG E<sub>2</sub>가  
 (Table 2). hCG E<sub>2</sub>  
 (E<sub>2</sub> on hCG/ampule) E<sub>2</sub> on  
 hCG/ampule  
 (stepwise multiple regression, r=0.68, p<0.001).  
 (stepwise multiple regression, r=0.57, p<0.001)( 1,2).  
 GAST  
 GAST

가



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Table 1. Initial E difference (E) after GnRH agonist stimulation test (GAST)

	Group A (E < 40 pg/ml)	Group B (40 pg/ml < E < 100 pg/ml)	Group C (100 pg/ml > E)
No. of Patients	30	52	20
Age*	33.7 ± 0.8	31.5 ± 0.6	30.6 ± 0.5
Basal FSH† (mIU/ml)	11.1 ± 1.1	7.4 ± 0.2	6.8 ± 0.4
Initial E (pg/ml)	248 ± 22	208 ± 0.9	214 ± 19

\*  $P < 0.05$  Group A versus C

†  $P < 0.0001$  Group B and C versus A

Table 2. Ovarian stimulation outcomes by initial E<sub>2</sub>

	Group A (E <sub>2</sub> <100pg/ml)	Group B (100pg/ml E <sub>2</sub> <1000pg/ml)	Group C (1000pg/ml E <sub>2</sub> )
No. of hMGFSH ampules used	386 ± 23	242 ± 1.1*	185 ± 1.0*
Duration of COH (days)	85 ± 02	84 ± 03	90 ± 1.0
E <sub>2</sub> on hCG day (pg/ml)	1402.1 ± 187.7	3153.2 ± 240.0*	4078.8 ± 306.4*
Total no. of oocytes retrieved	64 ± 1.1	155 ± 1.1*	187 ± 1.6*
Total no. of embryos	43 ± 0.6	90 ± 0.8*	83 ± 1.2*
Clinical PR	4/32 (12.5%)	11/40 (27.5%)*	5/20 (25.0%)*

\* P<0.0001, Group B and C versus A

