

## 불임 환자의 치료에서 Mild Ovarian Hyperstimulation을 이용한 Single IUI와 Double IUI의 비교

중앙대학교 의과대학 산부인과학교실, 청주 성모병원 산부인과\*

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### A Comparison Study of Single with Double Intrauterine Insemination with Mild Ovarian Hyperstimulation for Infertility Patients

Young-Soo Son\*, Sang Hoon Lee

*Department of Obstetrics and Gynecology, Chung-Ang University,*

*\*Department of Obstetrics and Gynecology, Cheong-Ju St. Marys' Hospital*

**Objective:** To compare the clinical efficacy of double intrauterine insemination with single intrauterine insemination in GnRH antagonist combined ovarian hyperstimulation (Mild ovarian hyperstimulation)

**Materials and Methods:** From Jan. 2001 to Jul. 2004, a retrospective clinical analysis was done of a total of 295 cycles in 170 patients who underwent ovarian hyperstimulation for ART (assisted reproductive technique). Subjects were divided into three groups; only clomiphene citrate ovarian hyperstimulation (n=55, 95cycles), GnRH antagonist combined ovarian hyperstimulation (soft ovarian hyperstimulation) (n=66 99cycles), and GnRH agonist combined ovarian hyperstimulation (short protocol) (n=49, 101cycles) Each group were randomly divided into two subgroups. One group underwent single IUI and the other group underwent double IUI.

**Results:** GnRH antagonist group and GnRH agonist group had similar pregnancy rate. In GnRH antagonist Group, pregnancy rate was 36.1% in single IUI subgroup and was 36.6% in double IUI subgroup. These finding were not statistically significant. And Pregnancy rate was 20.8% in single IUI subgroup and was 19.3% in double IUI subgroup in single clomiphene citrate group, and 36.3% in single IUI subgroup and was 33.3% in double IUI subgroup in GnRH agonist group. These finding were not statistically significant, too.

**Conclusion:** Pregnancy rate of GnRH antagonist was high and complication rate such as OHSS and multiple pregnancy was lower. In GnRH antagonist group, to compare with single IUI and double IUI, the result do not statistically differ. So GnRH antagonist single injection with single IUI was relatively comparable ART in infertility patient.

**Key Words:** Mild controlled ovarian hyperstimulation, Single IUI, Double IUI

가 가  
가 1 (anatomical factor infertility),  
10~15% 가 (unexplained infertility), (male fac-

tor infertility), factor infertility), fertility) 가

(cervical (anovulatory in- GnRH agonist GnRH antagonist GnRH

5~30% 2~3

1

가

double IUI가 single IUI가

double IUI Random single IUI 8

Clomi- phene citrate (CC) 2 CC Silverberg 9

double IUI가 double IUI

가

GnRH 가

(premature LH surge)가 가 3

1984 Porter 4 GnRH ago- single IUI double IUI GnRH antagonist mild ovarian hyperstimulation single IUI double IUI

nist GnRH agonist GnRH agonist

1.

2001 1 2004 7

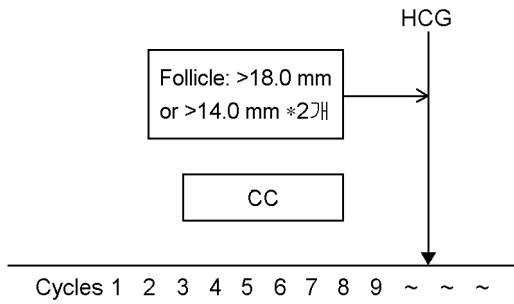
GnRH agonist GnRH antago- 170 CC single IUI 23

nist 55 , 95 , double IUI 32 53

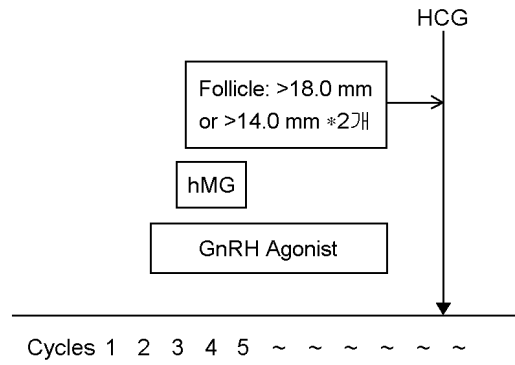
42 , GnRH agonist Short

Diedrich 5 3 GnRH antagonist protocol 49 , 101 single

cetorelix, ganirelix가 IUI 23 49 , double IUI 26



**Figure 1.** CC single ovarian hyperstimulation



**Figure 2.** GnRH agonist combined Short protocol

52 가 , GnRH antago-  
nist Mild ovarian hyperstimulation  
66 , 99 single IUI 33  
46 , double IUI 33 53  
single IUI double IUI

2.

1)

(1) Clomiphene citrate group

3 5 clomiphene citrate 100  
mg , 8

(E2)

18.0 mm

14.0 mm

가 2

hCG 10,000 IU (Figure 1).

(2) GnRH agonist ovarian hyper-  
stimulation (Short protocol)

2 leuprolide acetate  
0.2 cc (1.4 mg) 3 , 4

hMG 150 IU/d

가 7 hMG  
group 18.0

mm 14.0 mm

가 2 hCG 10,000 IU

(Figure 2).

(3) GnRH antagonist ovarian hyper-  
stimulation (Mild ovarian hyperstimulation)

3 5 clomiphene  
citrate 100 mg , 6

hMG 150 IU/d 5~6

가 100~150 pg/ml

12.0~14.0 mm Cetorelix (GnRH anta-  
gonist) 3.0 mg

18.0 mm

14.0 mm

가 2

hCG 10,000 IU

(Figure 3).

2)

2~3

20~30

2 ml

(Ham's F=10;

Sigma, St. Louis, MO)

300 ×g

5~10

2 ml

300 ×g

5

1 ml

가 45

1

single IU hCG 34

double IUI

hCG 12

hCG 34

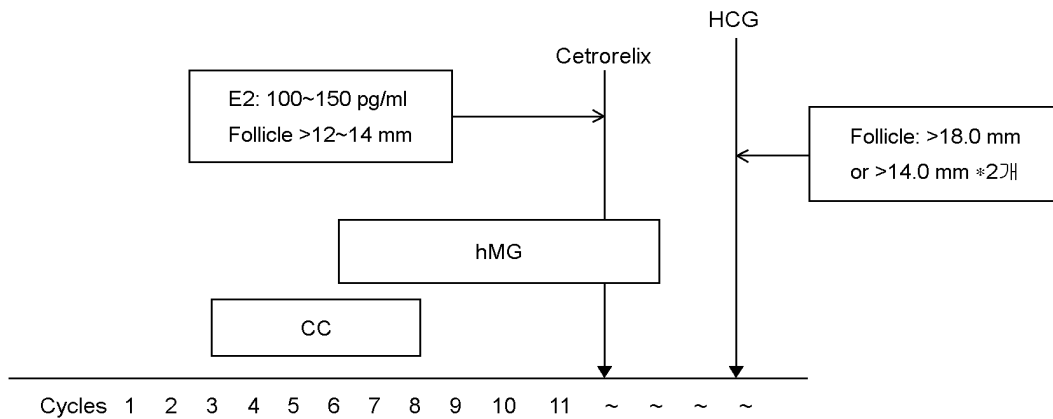


Figure 3. GnRH antagonist Mild ovarian hyperstimulation

|            |                 |                       |  |                       |                       |
|------------|-----------------|-----------------------|--|-----------------------|-----------------------|
| 3)         |                 |                       |  | 10.4%, double IUI     | 19.3%,                |
| 가          |                 |                       |  | 12.7%                 | GnRH agonist          |
| 12         | $\beta$ -hCG    | (>10                  |  | 36.3%,                | 17.0%, double IUI     |
| mIU/mL)    | 2~4             |                       |  | 33.3%,                | 16.7%                 |
|            |                 |                       |  |                       | GnRH antagonist       |
|            | 3               |                       |  | 36.1%,                | 22.4%, double IUI     |
|            |                 |                       |  | 36.6%,                | 26.8%                 |
|            |                 |                       |  |                       | single IUI double IUI |
| 4)         |                 |                       |  |                       |                       |
|            | chi-square test | student's t-test      |  | CC                    | GnRH agonist          |
|            | , p<0.01        |                       |  | GnRH antagonist       | p-value <0.01, <0.01  |
|            |                 |                       |  | GnRH agonist          | GnRH antagonist       |
|            |                 |                       |  |                       | 가                     |
| 1.         |                 |                       |  | CC                    | GnRH antagonist       |
| CC         |                 | 31.4±5.9              |  |                       | GnRH agonist 15       |
|            | 3.8±2.5         | , GnRH agonist        |  | 1                     |                       |
|            |                 | 33.4±5.8              |  | CC                    | 11 2                  |
|            | 4.8±3.2         | , GnRH antagonist     |  | GnRH agonist          | 15 5, GnRH            |
| 32.5±4.7   |                 | 4.7±2.4               |  | antagonist 24         | 1                     |
|            |                 |                       |  |                       | GnRH ago-             |
| 2.         |                 |                       |  | nist                  | GnRH antagonist       |
|            |                 |                       |  | (Table 1).            |                       |
| 1)         |                 | single IUI double IUI |  | 2)                    |                       |
|            |                 |                       |  | single IUI double IUI |                       |
|            | CC              |                       |  |                       | CC                    |
| single IUI |                 | 20.8%,                |  | single IUI            | 10%,                  |

**Table 1.**

|                              | Mild ovarian hyperstimulation |        | CC     |        | GnRH agonist group (Short protocol) |        |
|------------------------------|-------------------------------|--------|--------|--------|-------------------------------------|--------|
|                              | Single                        | Double | Single | Double | Single                              | Double |
|                              | No. patient                   | 36     | 30     | 24     | 31                                  | 22     |
| No. of cycle                 | 58                            | 41     | 48     | 47     | 47                                  | 54     |
| No. of pregnancy             | 13                            | 11     | 5      | 6      | 8                                   | 9      |
| Pregnancy rate (%)           | *36.1                         | *36.6  | 20.8   | 19.3   | *36.3                               | *33.3  |
| Pregnancy rate for cycle (%) | 22.4                          | 26.8   | 10.4   | 12.7   | 17.0                                | 16.7   |
| OHSS                         | 1                             | 0      | 1      | 1      | 3                                   | 2      |
| Twin                         | 0                             | 0      | 0      | 0      | 1                                   | 0      |

\*: p-value &lt;0.01

**Table 2. Male factor infertility**

|                              | Mild ovarian hyperstimulation |        | CC     |        | GnRH agonist group |        |
|------------------------------|-------------------------------|--------|--------|--------|--------------------|--------|
|                              | Single                        | Double | Single | Double | Single             | Double |
|                              | No. of patient                | 7      | 8      | 6      | 8                  | 6      |
| No. of cycle                 | 11                            | 17     | 10     | 16     | 12                 | 16     |
| No. of pregnancy             | 3                             | 5      | 1      | 4      | 3                  | 5      |
| Pregnancy rate for cycle (%) | 27                            | 29     | 10     | 25     | 25                 | 31     |

**Table 3. Unexplained factor infertility**

|                              | Mild ovarian hyperstimulation |        | CC     |        | GnRH agonist group |        |
|------------------------------|-------------------------------|--------|--------|--------|--------------------|--------|
|                              | Single                        | Double | Single | Double | Single             | Double |
|                              | No. of patient                | 14     | 15     | 11     | 16                 | 7      |
| No. of cycle                 | 17                            | 15     | 14     | 25     | 14                 | 17     |
| No. of pregnancy             | 5                             | 4      | 2      | 1      | 3                  | 2      |
| Pregnancy rate for cycle (%) | 29                            | 27     | 14     | 4      | 20                 | 12     |

double IUI 25% GnRH 3)  
 agonist 25%, double IUI single IUI double IUI  
 31% GnRH antagonist  
 single IUI 27%, do- CC single IUI  
 double IUI 29% (Table 2) 14%, double IUI 4%  
 double IUI가 single IUI GnRH agonist 20%,  
 double IUI 12% GnRH

|                              | Mild ovarian hyperstimulation |        | CC     |        | GnRH agonist group |        |
|------------------------------|-------------------------------|--------|--------|--------|--------------------|--------|
|                              | Single                        | Double | Single | Double | Single             | Double |
|                              | No. of patient                | 12     | 10     | 6      | 8                  | 10     |
| No. of cycle                 | 18                            | 21     | 18     | 12     | 23                 | 19     |
| No. of pregnancy             | 5                             | 4      | 2      | 1      | 3                  | 2      |
| Pregnancy rate for cycle (%) | 17                            | 19     | 11     | 8      | 13                 | 11     |

antagonist single IUI , ,  
 29%, double IUI 27% , ,  
 (Table 3) single IUI가 double IUI .

4) single , ,  
 IUI, double IUI ,  
 single IUI double IUI ,

CC single IUI , ,  
 11%, double IUI ,  
 8% GnRH agonist 2 ml , 가 20 million/  
 13%, double IUI 11% ml , 가 50% ,  
 GnRH antagonist single IUI 가 30% 가  
 17%, double IUI ,<sup>12</sup> ,  
 19% (Table 4) 가 .

agonist , CC GnRH 가 가  
 GnRH antagonist , 가  
 GnRH antagonist GnRH agonist 35  
 GnRH antagonist 가

가 1 , , ,  
 10~5%가 , 가 45~50% ,  
 가 , 가  
 1 25%, 6 70%, 1 85% ,  
 6 5~30% ,  
 1 5% 가 ,<sup>10</sup> ,

|                          |                 |      |                       |  |   |
|--------------------------|-----------------|------|-----------------------|--|---|
|                          |                 |      |                       | GnRH antagonist                        | GnRH<br>GnRH agonist                          |
| 가                        |                 |      |                       |  |   |
|                          |                 |      |                       |  | 6   |
| Clomiphene citrate (CC)  |                 | 2    |                       | GnRH antagonist<br>single dose regimen | multiple dose re-<br>multiple dose<br>regimen |
| CC                       |                 |      |                       | agonist/antagonist                     | 5~6 HCG                                       |
|                          |                 |      |                       | Cetrorelix                             | 1997  |
| GnRH                     | 가               |      |                       | Albano et al. <sup>16</sup>            | 0.5 mg, 0.25 mg, 0.1 mg cetro-<br>relix       |
|                          | 가               |      |                       |  | 0.1 mg cetrorelix                             |
|                          |                 |      |                       |  | 0.25 mg 0.5 mg                                |
|                          |                 |      | 가 가                   |  |   |
|                          |                 |      | 가                     |  | 3   |
|                          | GnRH agonist    |      |                       |  | 0.25 mg                                       |
| GnRH agonist             |                 |      |                       | GnRH                                   | Single dose regimen clomiphene citrate        |
| agonist                  |                 |      |                       | 8~9                                    | cetrorelix 3 mg                               |
|                          |                 |      |                       | Michael et al <sup>17</sup>            | 2003 multiple                                 |
|                          |                 |      |                       | dose regimen                           | single dose regimen                           |
|                          | 가               |      |                       | GnRH antagonist                        | single dose regimen                           |
|                          |                 | 3,13 |                       | cetrorelix                             |   |
| GnRH agonist             |                 |      |                       | 가 100~150 pg/ml                        | 12.0~14.0                                     |
| pian study <sup>14</sup> | GnRH agonist    |      | Euro-                 | single injection                       |   |
| 가                        |                 |      |                       |  |   |
|                          |                 |      | 가가                    |  | 18 mm 가                                       |
|                          |                 |      | 가                     |  | hCG   |
|                          | 가               |      |                       |  | 6%  |
|                          |                 |      |                       |  | 15  |
| GnRH antagonist          | GnRH agonist    |      |                       |  | 2~3   |
|                          |                 |      |                       |  | swim-up method                                |
|                          | 가 1994          |      | Diedrich              | 5                                      |   |
| 3                        | GnRH antagonist |      | cetrorelix, ganirelix |  |   |
| 가                        |                 |      |                       |  |   |

double IUI가 single IUI  
 IUI  
 single IUI가  
 가 dou-  
 ble IUI가  
 Silverberg <sup>9</sup> double IUI가  
 single IUI  
 (fertilization)  
 가 single IUI  
 가  
 hCG 36 double IUI  
 single IUI double IUI  
 가  
 10~20 <sup>9</sup> hCG 12~34 가 Silverberg <sup>9</sup> single IUI 1/4  
 frozen sperm  
 Diedrich <sup>2</sup> hCG 34~60  
 12~34 agonist CC GnRH  
 GnRH antagonist  
 agonist GnRH antagonist  
 가 GnRH antagonist  
 single GnRH agonist GnRH anta-  
 IUI hCG 34  
 double IUI  
 hCG 12 double IUI  
 34  
 single IUI double IUI  
 Saeed A.  
 single IUI  
<sup>11</sup> double IUI가  
 가  
 Ransom <sup>8</sup> single IUI가



Saeed A. <sup>10</sup>

가 single IUI가 double IUI 가 가 가 가 GnRH antagonist mild ovarian hyperstimulation GnRH agonist short protocol double IUI single IUI single IUI

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