

## Clomiphene Citrate

### Pregnancy Rate by Intrauterine Insemination (IUI) or Timed-Intercourse Combined with Clomiphene Citrate and Gonadotropins

Jeong-Eui Hong and Ji-Sam Lee

*Infertility Clinic, Hong's OB/ GYN, Taejeon, Korea*

=Abstract=

To evaluate the effectiveness of intrauterine insemination (IUI) in the treatment of infertility, timed-intercourse and intrauterine insemination by husband combined with clomiphene citrate and gonadotropins were compared in a total of 105 cycles. Patients received 100mg of clomiphene citrate daily for 5 days starting on day 3 of the menstrual cycle followed by hMG or FSH. Doses of exogenous gonadotropins were adjusted by the follicular development and concentrations of serum estradiol ( $E_2$ ). More than 3 follicles reaching  $>16\text{mm}$  were present in the ovary, 5,000 IU of hCG was administered intramuscularly. Patients received a maximum of three intercourse or IUI cycles for the treatment. Severe male ( $< 10 \times 10^6$  motile sperm) or age factor ( $> 39$  y) patients were excluded in this study. Pregnancy was classified as clinical if a gestational sac or fetal cardiac activity was seen on ultrasound. The overall clinical pregnancy rates were 17.1% per cycle (18/105) and 21.2% per patient (18/85). The pregnancy rates (per cycle) were 17.5% (11/63) in intercourse and 16.7% (7/42) in IUI groups, respectively. IUI had no significant improvement in pregnancy rate compared with timed-intercourse. The multiple pregnancy rates were

11.1%(1 twin and 1 triplet). No patient developed ovarian hyperstimulation. Abortion rate was 28.6%(2/7) in IUI group only. The delivery and ongoing pregnancy rates were 15.2% per cycle(16/105) and 18.8% per patient(16/85). There were no differences in age, duration of infertility, follicle size and level of estradiol(E<sub>2</sub>) on the day of hCG injection in pregnant and non-pregnant groups. However, total doses of gonadotropins were higher in pregnant group than in non-pregnant group(P<0.01). Pregnancy rate was not affected by ovulatory status at the time of insemination. These results indicate that well timed-intercourse combined with clomiphene and gonadotropins is as effective as IUI for infertile couples.

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Key Words : Infertility, Clomiphene citrate, hMG, FSH, Pregnancy rate,  
Multiple pregnancy

가

(sexual intercourse) 가 ,  
(fimbria)  $10^5 - 10^6$   
(Mortimer & Templeton, 1982) (IUI)

Kirby (1991)

, Martinez

(1990) Karlstrom (1993) Zikopoulos (1993)

가

(Serhal et al., 1988;

Chaffkin et al., 1991; Crosignani et al., 1991; Ho et al., 1992; Nan et al.,  
1994; Chung et al., 1994, 1995; Guzick et al., 1998; Zeyneloglu et al., 1998).

( ,

1996; & , 1998)

clomiphene citrate(CC) (Arici et al., 1994; Van der  
Westerlaken et al., 1998) CC hMG FSH

(Aboulghar et al., 1993; Depypere et al., 1994; Barandi et al., 1998; Brzechffa  
et al., 1998) hMG/FSH

(Chaffkin et al., 1991; Balasch et al., 1994; Mascarenhas et al., 1994;

, 1996) , CC hMG(Mills et al., 1992; Aboulghar et al.,

1993; Dickey et al., 1993; Depypere et al., 1994; Ransom et al., 1996; Barandi  
et al., 1998; Brzechffa et al., 1998) CC FSH (Sheldon et al., 1988;

Tzeng, 1996; Zayed et al., 1997)

CC+hMG/FSH

(OHSS) (multiple pregnancy)

(Dickey et al., 1993; Lu et al., 1996; Ransom

et al., 1996). Sheldon (1988) CC+hMG CC+FSH

22-27% , Dickey (1993) Barandi (1998)

CC+hMG hMG

, Zayed (1997) CC+FSH

28.6% .

CC hMG

가

가 ( & , 1998).

CC hMG

FSH

.

, ,  
15-30% (Dodson & Haney,  
1991; Aboulghar et al., 1993; Omland et al., 1998).

Martinez (1991)

,  
Karlstrom (1993) Zikopoulos (1993)

(Melis et al., 1987;  
Chaffkin et al., 1991; Aboulghar et al., 1993; Arici et al., 1994; Chung et al.,  
1994, 1995; Zeyneloglu et al., 1998)

가 .

15-25%(Chaffkin et al., 1991; Dodson & Haney, 1991; Calhaz-  
Jorge et al., 1994; Brzechffa et al., 1998; , 1996),  
15% (Chaffkin et al., 1991; Dodson & Haney, 1991;  
Calhaz-Jorge et al., 1994). Kirby (1991) Ho (1992)  
Nan (1994) 가

, Zayed (1997)

, (1992) 20%  
Martinez (1990, 1991) Arici (1994) Van der Westerlaken (1998)  
가 ,

(Hewitt et al., 1985; Yovich & Matson, 1988; Francavilla et al., 1990)

, (1996) (1998)

2 1  
1 ml (hypospermia) .

가

가  
 (pick-up) 가  
 (Aboulghar et al., 1989) , 가 (Abbasi et al., 1987; Dodson & Haney, 1991) 가 .  
 (prostaglandins,  
 )  
 (Blumenfeld & Nahhas, 1989) ,  
 가(Kerin & Quinn, 1987)  
 . 가 가  
 ,  
 . tenaculum catheter  
 prostaglandins (PGs)  
 가 (Hurd et al., 1993), 가  
 가 ,  
 가 (Dodson & Haney, 1991).  
 , 가  
 E<sub>2</sub>가 가 , E<sub>2</sub> 가 (quality)  
 (Moghissi, 1972; Farhi et al., 1995) 가  
 가 가  
 (Dodson & Haney, 1991).  
 (Fredricsson & Bjokr, 1977) , ,  
 (Insler et al., 1980) .  
 가 (te  
 Velde et al., 1989; Chaffkin et al., 1991; Martinez et al., 1993; Nulsen et al.,  
 1993; Plosker et al., 1994; Barandi et al., 1998; , 1996; &  
 , 1998) , Zikopoulos (1993) Karlstrom (1993)

E<sub>2</sub>

가 (Check et al., 1991) ,

CC (FSH/hMG)

가 .

( & , 1998) ,

가

가

Nan (1994) (1996)

hCG 가

Zikopoulos (1993)

hCG

가 22 mm

가 17-29 mm 가 .

가 가 가 .

(OHSS)

(multiple pregnancy) (Shelden et al., 1988; Dodson & Haney, 1991;

Navot et al., 1991) . 5-46 %

(Gagliardi et al., 1991; Aboulghar et al., 1993; Karlstrom et al., 1993;

Zikopoulos et al., 1993; Calhaz-Jorge et al., 1994; Tomlinson et al., 1996;  
Ajossa et al., 1997; Goldfarb et al., 1997) ,

(preovulatory follicle) (Dodson et al., 1988;

Ben-Nun et al., 1993),

(Dickey et al., 1991; Navot et al., 1991; Farhi et al., 1996; Goldfarb et al.,  
1997) , Zikopoulos (1993) Valbuena (1996)

E<sub>2</sub> Dodson (1988)

Dickey (1991) Navot (1991) .

가 1 ,

(1998) E<sub>2</sub>

가 , Sheldon (1988) Tur (1997)

, Dodson (1988) , E<sub>2</sub>

, Goldfarb (1997)

.

,

.



1.

1997 2 1998 10

(hysterosalpingography, HSG)

85

105

,

가 40

가  $10 \times 10^6$

(severe oligozoospermia)

.

2.

1)

TSH prolactin

,

3

LH, FSH estradiol(E<sub>2</sub>)

.

3-5

(tubal patency)

,

(preovulatory period)

(postcoital test, PCT)

,

가

WHO(1992)

.

2)

CC

hMG

FSH

,

3-5

CC(Clomifene,

,

) 100 mg

5

hMG(IVF-M, LG , )

FSH-HP(Fostimon, IBSA, Switzerland) 75-

150 IU

가 18 mm

16 mm

가 3

LH (Conceive, Quidel, CA, USA)

hCG(IVF-C, LG , )

5,000 IU

24

1

,

LH 가

10 hCG 5,000 IU 36-37 1  
LH 가 hCG 5,000 IU  
, LH 가  
hCG 30 .

3)

30  
80% percoll (Pharmacia, Uppsala, Sweden) ,  
300 x g 30 .  
Quinn(1995) modified human tubal fluid  
(mHTF) 10% 가 37 ° C, 5% CO<sub>2</sub>  
2ml 가 , 250 x g 5  
10% mHTF  
가 0.5ml 1ml  
가 TomCat (Sherwood Medical, MO, USA) .

4)

(Aloka, Model SSD-1700, Japan)  
, (dorsal lithotomy position)  
(gauze) 가  
. 30  
가 , progesterone  
(Utrogestan , Laboratories Besins-Iscovesco, France) 300mg

5)

10-11  $\beta$ -hCG

10 mIU/ml

(biochemical pregnancy)

,

(gestational sac)

(fetal heart-beat)

(clinical pregnancy)

.

6) estradiol(E<sub>2</sub>)

hCG

E<sub>2</sub>

5ml

1,000 x g 10

(enzyme-linked fluorescent immunoassay; ELFA)

mini-VIDAS ELFA counter(bio Merieux Vitek, Inc., France)

, E<sub>2</sub>

10-4,000pg/ml

.

3.

Student's t-test    x<sup>2</sup>-test

, P < 0.05

.

1.

85 1 39 (45.9%) , 2  
 46 (54.1%) 2 (Table 1).  
 60 (70.6%) 가 ,  
 가 20 (23.5%), 가 2 (2.4%), 2가 가  
 가 2 (2.4%) 1 (1.1%) ,  
 (1998)  
 가 가  
 .  
 (Table 1 )

Table 1. Infertility categories in intercourse and IUI patients

Items	Intercourse	IUI
No. of patients	55	30
Type of infertility (%)		
Primary	25 (45.5)	14 (46.7)
Secondary	30 (54.5)	16 (53.3)
Categories of infertility (%)		
Ovulatory	14 (25.5)	6 (20.0)
Endometriosis	1 ( 1.8)	0 ( 0.0)
Male	0 ( 0.0)	2 ( 6.7)
Unexplained	39 (70.9)	21 (70.0)
Combined	1 ( 1.8)	1 ( 3.3)

2.

21-39 30.4 ± 0.3 ,

(31.4 ± 0.5 ) (29.7 ± 0.4 ) 가  
 (p<0.05). 1 15 3.4 ±  
 0.3 , (3.0 ± 0.3 vs 4.0 ± 0.3 ) 가

(Table 2).

(Table 2 )

Table 2. Ovarian responses after ovulation induction in intercourse and IUI patients

Items	Intercourse	IUI	P value
No. of patients	55	30	
No. of cycles	63	42	
Age(Years)	29.7 ± 0.4	31.4 ± 0.5	P < 0.05
Duration of infertility (Years)	3.0 ± 0.3	4.0 ± 0.3	NS
No. of FSH/hMG(Ampules)	6.1 ± 0.4	7.7 ± 0.7	P < 0.05
Follicle size(mm)	21.5 ± 0.4	20.9 ± 0.3	NS
E <sub>2</sub> on day of hCG(pg/ml)	1444.1 ± 306.6	1592.0 ± 264.7	NS

1) Values are mean ± SEM. NS : Not significant.

3. estradiol(E<sub>2</sub>)

CC (FSH/hMG)  
 75IU 7.7 ± 0.7 6.1 ± 0.4  
 (P<0.05; Table 2) hCG (21.5 ± 0.4  
 mm) (20.9 ± 0.3 mm) 가 , hCG  
 가 17-29 mm  
 가 22 mm 가 . hCG  
 E<sub>2</sub> (1,444.1 ± 306.6 pg/ml) (1,592.0 ±  
 264.7 pg/ml) 가 .

4.

17.5% (11/63) ,  
20.0% (11/55) , 11 (twin pregnancy)  
(triplet pregnancy) 1 18.2% (2/11) .  
30 42 1-3  
1.4 , 16.7% (7/42)  
, 23.3% (7/30) .  
(ectopic pregnancy) (OHSS)

(Table 3).

50.0%

(9/18) 가 , 가 44.4%(8/18) , 가 5.6%(1/18)

, .

28.6%(2/7) 7

10 .

17.5%(11/63), 20.0%(11/55) , 11.9%

(5/42), 16.7%(5/30) . 16

9 , 가 1 ,

5 .

(Table 3 )

Table 3. Clinical pregnancy and delivery rates after intercourse or IUI

Items	Intercourse	IUI	P value
<b>Clinical pregnancy (%)</b>			
Per cycle	11/63 (17.5)	7/42 (16.7)	NS
Per patient	11/55 (20.0)	7/30 (23.3)	NS
<b>Abortion/Pregnancy (%)</b>	0/11 (0.0)	2/7 (28.6)	NS
<b>Delivery or Ongoing (%)</b>			
Per cycle	11/63 (17.5)	5/42 (11.9)	NS
Per patient	11/55 (20.0)	5/30 (16.7)	NS
Singleton	9	5	
Twin	1	0	
Triplet	1	0	

1) NS : Not significant.

5.

Table 4

E<sub>2</sub> 가

(P<0.01).

(Table 4 )

Table 4. Comparison of clinical characteristics between pregnant and non-pregnant groups

Items	Pregnant	Non-pregnant	P value
No. of patients	18	67	
No. of cycles	18	87	
Age(Years)	30.6 ± 0.9	30.3 ± 0.4	NS
Duration of infertility(Years)	4.2 ± 0.6	3.2 ± 0.3	NS
Follicle size(mm)	21.4 ± 0.7	21.2 ± 0.3	NS
FSH/hMG(Ampules)	8.9 ± 1.2	6.3 ± 0.4	P<0.01
E <sub>2</sub> on day of hCG(pg/ml)	1501.7 ± 329.4	1571.0 ± 264.7	NS

1) Values are mean ± SEM. NS : Not significant.



1997 2 1998 10

85 105

1. 1 39 (45.9%), 2 46 (54.1%),  
60 (70.6%)

가 , 가 20 (23.5%), 가 2 (2.4%), 가 2  
(2.4%) 1 (1.1%) .

2. 30.4 ± 0.3 3.4 ± 0.3

, 가  
(31.4 ± 0.5 ) (29.7 ± 0.4 ) (P < 0.05).

3. CC (7.7 ± 0.7 )

(6.1 ± 0.4 ) (P < 0.05), hCG

(21.5 ± 0.4 mm) (20.9 ± 0.3 mm) 가

, hCG E<sub>2</sub> (1,444.1 ± 306.6 pg/ml)

(1,592.0 ± 264.7 pg/ml) 가 .

4. 17.5% (11/63) ,

20.0% (11/55) , 16.7% (7/42), 23.3%

(7/30) . 50.0%

(9/18) 가 , 가 44.4% (8/18) , 가 5.6%

(1/18) , .

18.2% (2/11) 11 1

28.6% (2/7) .

16 9 ,

가 1 , 5 .

5. , ,

E<sub>2</sub>

가

(P < 0.01).

.

. . . . . :  
1996, 39, 1286-  
1299.

. : . . . . . 1992,  
35, 982-987.

. : . . . . . 1998, 25,  
217-231.

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