

**Pregnancy Rate by Intrauterine Insemination (IUI)
with Controlled Ovarian Hyperstimulation (COH)**

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=Abstract=

The effectiveness of intrauterine insemination (IUI) combined with controlled ovarian hyperstimulation (COH) in the treatment of infertility with various etiologies was compared in a total of 152 cycles. Patients received a maximum of three IUI cycles for the treatment. Severe male (< 2 X 10⁶ motile sperm) or age factor (> 39 y) patients were excluded in this study. Pregnancy was classified as clinical if a gestational sac was seen on ultrasound. The overall clinical pregnancy rate was 7.9% per cycle (12/152) and 9.7% per patient (12/124). The pregnancy rates were 0% in unstimulated natural (0/18), 7.5% in CC (3/40), 8.2% in CC+hMG (4/49), 5.9% in GnRH-a ultrashort (1/17), 5.9% in GnRH-a long (1/17) and 27.3% in dual suppression cycles (3/11), respectively. The pregnancy rate was higher in dual suppression cycle than other stimulated cycles, but this was not significant. The multiple pregnancy rates were 25.0% (2 twins and 1 triplet). No patient developed ovarian hyperstimulation. Abortion rates were 66.7% in CC (2/3) and 100% in ultrashort cycles (1/1). The livebirth rate was 5.9% per cycle (9/152) and 7.3% per patient (9/124). There were no differences in age, duration of infertility, follicle size, total ampules of gonadotropins and days

of stimulation between pregnant and non-pregnant groups. However, significant ($P < 0.05$) differences were observed in the level of estradiol (E_2) on the day of hCG injection ($3,266.6 \pm 214.2$ vs $2,202.7 \pm 139.4$ pg/ml) and total motile sperm count (212.1 ± 63.4 vs $105.1 \pm 9.9 \times 10^6$) in pregnant group than in non-pregnant group. These results suggest that IUI combined with successful ovarian stimulation tends to improve the chance of pregnancy as compared to IUI without COH and a total motile sperm count may be considered predictive of the success for pregnancy.

Key Words : Infertility, Controlled ovarian hyperstimulation, IUI, Pregnancy rate, Multiple pregnancy

가 (assisted reproductive technology , ART) 가 , (GIFT) (ZIFT) - (IVF-ET) 가 (artificial insemination by husband, AIH) (intravaginal insemination , IVI), (intracervical insemination , ICI), (intraperitoneal insemination , IPI), (intrauterine insemination, IUI), (fallopian sperm perfusion, FSP) (intrafollicular insemination, IFI) 가 . (cervical factor), (coital problem), (oligozoospermia) (asthenozoospermia) (male factor), (antisperm antibody) , (endometriosis) (unexplained infertility) . 가 5-30% (Chaffkin et al., 1991; Dodson & Haney, 1991; Mackenna et al., 1992; Arici et al., 1994; Campana et al., 1996), clomiphene citrate(CC), hMG, FSH GnRH agonist (GnRH-a) hMG/FSH (Chaffkin et al., 1991; Aboulghar et al., 1993; , 1996).

, , ,
, E₂ ,
(Dodson et al., 1991; Mills et al., 1992; Zikopoulos et al., 1993;
Tomlinson et al., 1996)가 , 5-30% (Chaffkin et al.,
1991; Mackenna et al., 1992; Arici et al., 1994; Campana et al., 1996).

가 가
, 가 40
(Agarwal & Buyalos, 1996; Campana et al., 1996; Corsan et al., 1996;
Magarelli et al., 1996; Tomlinson et al., 1996; Brzechffa & Buyalos, 1997).
가 (atresia),
(quality) , (endometrial receptivity)
가 (Abdalla et al., 1990;
Levrán et al., 1991; Navot et al., 1991a).

33 , 가
5.9-27.3% 가 가
, 12 11 가
33 1 39 23
, 가 .

Tomlinson (1996)
6 , 6

,
4-5 가 , Tomlinson (1996)

6

.

, ,
, 가

1-2% (Hull et al., 1985)

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

Karlstrom (1993)

Zikopoulos (1993)

Melis (1987), Chaffkin (1991), Aboulghar (1993)

Arici (1994) 가

, Zayed (1997)

20% (Chaffkin et al., 1991; Dodson

& Haney, 1991), (1992)

60%, (1996) 22.2% .

(1996)

25.0% 가 .

12 6 (50%), 5

(41.7%), 1 (8.3%) (mild

endometriosis), (1992)

25%, (1995)

GnRH - a

26.8% . (1996) 가

가 ,

가

, (pick-up) 가

(Aboulghar et al., 1989), 가 (Abbasi et

al., 1987; Dodson & Haney, 1991) 가 .

(Blumenfeld &

Nahhas, 1989)

가(Kerin & Quinn, 1987)

. CC (Arici et al., 1994; Depypere et al., 1994; , 1996) CC hMG (Mills et al., 1992; Depypere et al., 1994), hMG(Chaffkin et al., 1991; Dodson & Haney, 1991; Nan et al., 1994; Burr et al., 1996; Goldfarb et al., 1997)

FSH (Balasch et al., 1994; , 1996) GnRH- a FSH/hMG (Gagliardi et al., 1991; Zikopoulos et al., 1993; Tomlinson et al., 1996; Ajossa et al., 1997) , CC FSH/hMG CC hMG

가 . CC (Gonen & Casper, 1990; Nelson et al., 1990) hMG FSH (gonadotropins) CC 가 가 가(Ritchie, 1985) , CC (Melis et al., 1987; Karlstrom et al., 1993). CC CC+hMG 7.5-8.2% hMG , CC가 hMG가 가 . CC 66.7%(2/3) , Dickey (1996) CC , (Boue & Boue, 1973) 가 . hMG 30% (premature luteinization)가 (Nisker et al., 1993; Manzi et al., 1995) , (quality) , (Silverberg et al., 1991; Schoolcraft et al., 1991).

GnRH- a GnRH- a . Dodson (1991) GnRH- a 가

Gagliardi (1991) GnRH - a 가 가
, Manzi (1995) Ajossa (1997) 가
, Nan (1994)
LH (surge) 가 , Manzi (1995)
hMG 가 11.1%
. Dodson (1991) GnRH - a 가
, GnRH - a
. 가
E₂ 가 , (OHSS)
가 (Gelety et al., 1992) GnRH - a
(, 1995; Rosenwaks, 1996) ,
(1995) 가
. (PCOS)
GnRH - a 27.3%
,
GnRH - a가 LH (Elkind-Hirsch et al., 1995)
,
. 가
5 - 10% 2 , CC 35 - 60%
가, 80%
가 (Ritchie, 1985),
Nan (1994) hCG 18 mm
가 Zikopoulos (1993) Pittrof (1996)
, Tomlinson (1996) GnRH - a
hMG FSH 가 1
7.6%, 2 26.0%, 3 37.0% 4

44.0% , (1996) 16 mm 가 3 가
가 .

E₂ Zikopoulos (1993)
Manzi (1995) Ajossa (1997) hCG E₂ GnRH - a
가 , .

GnRH - a
hCG E₂ GnRH - a 가
, GnRH - a
recruitment가 가 (Meldrum et al., 1985)
. GnRH - a

E₂
(& , 1997). E₂
, 가
(Abbasi et al., 1987; Dodson & Haney, 1991)

가 가 , 가 .

(OHSS) (multiple pregnancy) (Dodson & Haney, 1991;
Navot et al., 1991b) . 5-
46%(Gagliardi et al., 1991; Aboulghar et al., 1993; Karlstrom et al., 1993;
Zikopoulos et al., 1993; Tomlinson et al., 1996; Ajossa et al., 1997; Goldfarb
et al., 1997) , (preovulatory follicle)
(Dodson et al., 1988; Ben-Nun et al., 1993),

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

E₂ Dodson
(1988) Navot (1991b) . CC+hMG
1 , 가 1 ,

E₂ 1,768-2,073 pg/ml GnRH - a

2,664 pg/ml . Dodson (1988) Navot
(1991b) E₂
가 .
(Kossoy et al., 1988) ,
LH hCG ,
hCG 36 (Mills et al., 1992; Zikopoulos et
al., 1993; Balasch et al., 1994; Matorras et al., 1995; Campana et al., 1996;
Corsan et al., 1996; Huang et al., 1996; Manzi et al., 1995; Brzechffa &
Buyalos, 1997; Goldfarb et al., 1997). Mackenna
(1992) (AID)
, Kelly (1997) ,
가 , Brook (1994)
(insemination window)가 24
가 , (1996) LH
.
Centola (1990) Silverberg (1992) 2
가 , Ransom (1994) Brook (1994)
Anderson (1996) 2 가
, (1996) hCG 18 42 2
8.9% .
LH 가 hCG 24 ,
36-37
, 39 2
가 2 Ransom (1994) Brook
(1994) Anderson (1996) 2
.
1-2 가
(Burr et al., 1996), 3-4

(Chaffkin et al., 1991; Dodson & Haney, 1991; Karlstrom et al., 1993; Agarwal & Buyalos, 1996; Campana et al., 1996; & , 1992; , 1996), Tomlinson (1996) 1 22.3% 가 , Burr (1996) 1 21.4%, 2 11.5% 3 8.2% , Huang (1996) 96%가 3 . (1992) (1996) 가 4 , 3 . 3-4 - (IVF-ET) . 15% (Chaffkin et al., 1991; Dodson & Haney, 1991) , Ho (1992) Nan (1994) 가 , Zayed (1997) , (1992) 20% . Arici (1994) 3.9% , (1996) . 1-3 X 10⁶ (Brasch et al., 1994; Campana et al., 1996; Huang et al., 1996; Pittrof et al., 1996) , (Dodson & Haney, 1991; Karlstrom et al., 1993; Zikopoulos et al., 1993; Burr et al., 1996; Pittrof et al., 1996) 가 Brasch (1994) Huang (1996) 가 , Nan (1994) , Tomlinson (1996) 가 10 X 10⁶/ml . 가 가 (P<0.05) , Brasch (1994)

Huang (1996)

가

가

. Burr (1996)

가

가

, Lindheim (1996)

. Matorras

(1995)

가

가 $2.8 - 11.5 \times 10^6$

(1996)

,

.

가

,

(

)

가

,

가

.

1.

1993 10 1998 2

(hysterosalpingography, HSG)

124

152

,

가

40

가 2×10^6

(severe oligozoospermia)

.

2.

1)

TSH prolactin

,

3

LH, FSH estradiol(E₂)

.

3-5

(tubal patency)

,

(preovulatory period)

(postcoital test, PCT)

,

가

WHO(1992)

.

2)

(15 / 18), CC (28 / 40), CC+hMG

(40 / 49), GnRH-a

(ultrashort protocol; 14 / 17),

GnRH-a

(long protocol; 16 / 17)

GnRH-a

(dual suppression protocol; 11 / 11)

.

가 16 mm

urinary LH kit(Conceive, Quidel, San Diego, CA, USA)

LH
 Switzerland) 5,000- 10,000 IU 24
 , LH 가 10 hCG 5,000-
 10,000 IU 36-37 .
 CC 3-5 CC
 (Clomifene, ,) 100 mg 5 , CC hMG
 3-5 CC 100 mg 5
 hMG(hMG, IBSA, Switzerland) 75- 150 IU
 가 18 mm LH
 hCG 5,000- 10,000 IU ,
 .
 GnRH- a
 (1997) 2 21
 Decapeptyl(Triptorelin, Ferring, Germany) nafarelin(Synarel,
 가 ,) GnRH- a 3 FSH(FSH,
 IBSA, Switzerland) hMG 150IU ,
 (oral contraceptive pill) GnRH- a (dual
 suppression protocol) (1995) Rosenwaks(1996)
 1 ethinylestradiol 0.03mg levonorgestrel 0.15mg
 (Minivlar, Schering, Germany) 1 1 25
 21 GnRH- a nafarelin
 200µg 1 2 3
 hMG 150 IU 가 18 mm
 16 mm 가 3 10 hCG 5,000- 10,000 IU
 36-37 .
 hCG 36-37 24 (hCG 60
) 1 .

3)

30

80% percoll , 300 x g 30

37 ° C, 5% CO₂

10% (fetal cord serum)

Ham 's F - 10 (GIBCO, No. 430- 1200, USA) 2ml 가 250

x g 5 , 10%

Ham 's F - 10 가

0.5ml 1ml 가 Tom Cat (Sherwood

Medical, St. Louis, MO, USA) .

4)

(Aloka, Model SSD - 1700, Japan)

, (lithotomy position) (gauze)

가

30

가 , progesterone (Utrogestan

, Laboratories Besins - Iscovesco, Paris, France) 300mg

.

5)

10- 11 β- hCG 10

IU/ml (biochemical pregnancy) ,

(gestational sac) (fetal heartbeat)

(clinical pregnancy) .

6) estradiol (E₂)

hCG E₂ 5ml 1,000 x g 10

(enzyme-linked fluorescent immunoassay; ELFA)

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

, E₂ 10-4,000 pg/ml .

3.

Student's t-test x²-test

, P < 0.05 .

1.

124 1 78 (62.9%)
 , 2 46 (37.1%) 1 (Table 1).
 68 (54.8%) 가
 , 가 32 (25.8%), 가 16 (12.9%), 2가 가
 가 5 (4.0%) 3 (2.4%) ,
 가

(Table 1)

Table 1. Infertility categories in IUI patients

Categories	Natural	Controlled ovarian hyperstimulation ¹⁾				
		CC	CC+hMG	US	Long	Dual
No. of patients	15	28	40	14	16	11
Type of infertility (%)						
Primary	13 (86.7)	18 (64.3)	27 (67.5)	5 (35.7)	10 (62.5)	5 (45.5)
Secondary	2 (13.3)	10 (35.7)	13 (32.5)	9 (64.3)	6 (37.5)	6 (54.5)
Causes of infertility (%)						
Ovulatory	3 (20.0)	3 (10.7)	11 (27.5)	5 (35.7)	4 (25.0)	6 (54.5)
Endometriosis	0 (0.0)	0 (0.0)	1 (2.5)	0 (0.0)	1 (6.3)	1 (9.1)
Male	3 (20.0)	8 (28.6)	3 (7.5)	2 (14.3)	0 (0.0)	0 (0.0)
Unexplained	9 (60.0)	17 (60.7)	24 (60.0)	6 (42.9)	10 (62.5)	2 (18.2)
Combined	0 (0.0)	0 (0.0)	1 (2.5)	1 (7.1)	1 (6.3)	2 (18.2)

1) CC ; clomiphene citrate, CC + hMG ; clomiphene citrate and hMG,

US ; ultrashort protocol, Long ; long protocol, Dual ; dual suppression protocol

2.

22-39 31.6 ± 0.3 ,
 CC (32.2 ± 0.7)가 CC+hMG (30.2 ± 0.6)
 (P<0.05), GnRH- a (33.3 ± 0.9) CC+hMG
 (P<0.01). 1 12
 4.4 ± 0.3 , 가 (Table
 2).

(Table 2)

Table 2. Clinical characteristics of IUI patients

	Controlled ovarian hyperstimulation ¹⁾					
	Natural	CC	CC+hMG	US	Long	Dual
No. of patients	15	28	40	14	16	11
Age(Years)	31.1 ± 0.8 ^{ab}	32.2 ± 0.7 ^a	30.2 ± 0.6 ^{bA}	32.9 ± 1.3 ^a	33.3 ± 0.9 ^{abB}	31.8 ± 0.9 ^{ab}
Duration of infertility (Years)	4.0 ± 0.7 ^a	4.6 ± 0.5 ^a	4.1 ± 0.4 ^a	4.0 ± 0.5 ^a	5.1 ± 0.6 ^a	4.7 ± 0.9 ^a

- 1) CC ; clomiphene citrate, CC + hMG ; clomiphene citrate and hMG,
 US ; ultrashort protocol, Long ; long protocol, Dual ; dual suppression protocol.
 2) Values are mean ± SEM.
 3) a, b ; P < 0.05, A, B ; P < 0.01.

3.

estradiol(E₂)
 (FSH/hMG)
 75IU GnRH- a 가 24.3 ± 1.8
 19.1 ± 1.1 (P<0.05),
 가 (Table 3). hCG CC
 (20.9 ± 0.4 mm)가 CC+hMG (19.0 ± 0.5 mm) (P<0.01),
 GnRH- a (19.5 ± 0.5 mm)

(P<0.05), 가 22 mm 가 . hCG
 E₂ GnRH-a (2,664.1 ± 213.6 pg/ml)가
 (2,038.6 ± 141.3 pg/ml) (P<0.05)
 (2,073.7 ± 307.0 pg/ml) 가 .
 (Table 3)

Table 3. Ovarian responses after controlled ovarian hyperstimulation (COH) in IUI patients

	Controlled ovarian hyperstimulation ¹⁾					
	Natural	CC	CC+hMG	US	Long	Dual
No. of patients	15	28	40	14	16	11
No. of cycles	18	40	49	17	17	11
No. of FSH/hMG (Ampules)	---	---	---	22.5 ± 1.2 ^{ab}	24.3 ± 1.8 ^a	19.1 ± 1.1 ^b
Days of stimulation	---	---	---	10.6 ± 0.5 ^a	11.1 ± 0.5 ^a	10.1 ± 0.4 ^a
Follicle size (mm)	20.1 ± 0.4 ^{ab}	20.9 ± 0.4 ^{AA}	19.0 ± 0.5 ^{BB}	19.5 ± 0.5 ^b	19.8 ± 0.8 ^{ab}	19.5 ± 0.7 ^{ab}
E ₂ on day of hCG (pg/ml)	320.3 ± 18.0	599.1 ± 72.2	1768.5 ± 124.3	2038.6 ± 141.3 ^a	2664.1 ± 213.6 ^b	2073.7 ± 307.0 ^{ab}

- 1) CC ; clomiphene citrate, CC + hMG ; clomiphene citrate and hMG, US ; ultrashort protocol, Long ; long protocol, Dual ; dual suppression protocol.
- 2) Values are mean ± SEM.
- 3) a, b ; P < 0.05, A, B ; P < 0.01.

4.

27-43 34.2 ± 0.5
 , 2.8-525 X 10⁶ 111.6 ± 10.3 X 10⁶
 , 가 (Table 4).

(Table 4)

가 15.6%(5/32) , 8.8%(6/68)

, .

CC 가 66.7%(2/3) , GnRH - a

가 100%(1/1) , , CC

6-7 , GnRH - a 23

.

CC 가 2.5%(1/40), 3.6%(1/28)

, CC+hMG 가 8.2%(4/49), 10.0%(4/40) , GnRH - a

가 5.9%(1/17), 6.3%(1/16) .

27.3%(3/11) .

(take home baby) 9 CC 가

1 , CC+hMG 3 (twin) 1 , GnRH - a

1 , ,

(triplet)가 1 . (Table 5)

Table 5. Clinical pregnancy and birth rates after IUI

	Controlled ovarian hyperstimulation ¹⁾					
	Natural	CC	CC+hMG	US	Long	Dual
Clinical pregnancy (%)						
Per cycle	0/18(0.0)	3/40(7.5)	4/49(8.2)	1/17(5.9)	1/17(5.9)	3/11(27.3)
Per patient	0/15(0.0)	3/28(10.7)	4/40(10.0)	1/14(7.1)	1/16(6.3)	3/11(27.3)
Abortion/pregnancy (%)						
	0/0(0.0)	2/3(66.7)	0/4(0.0)	1/1(100)	0/1(0.0)	0/3(0.0)
Livebirth (%)						
Per cycle	0/18(0.0)	1/40(2.5)	4/49(8.2)	0/17(0.0)	1/17(5.9)	3/11(27.3)
Per patient	0/15(0.0)	1/28(3.6)	4/40(10.0)	0/14(0.0)	1/16(6.3)	3/11(27.3)
Single	0	1	3	0	1	1
Twin	0	0	1	0	0	1
Triplet	0	0	0	0	0	1

1) CC ; clomiphene citrate, CC + hMG ; clomiphene citrate and hMG,
 US ; ultrashort protocol, Long ; long protocol, Dual ; dual suppression protocol.

6.

Table 6

가 E₂ 3,266.6 ± 214.2 pg/ml 2,202.7
 ± 139.4 pg/ml (P<0.05),
 212.1 ± 63.4 X 10⁶ 105.1 ± 9.9 X 10⁶ (P<0.05).

(Table 6)

Table 6. Comparison of clinical characteristics between pregnant and non-pregnant groups

	Pregnant	Non - pregnant	P value
No. of patients	12	112	
No. of cycles	12	140	
Age(Years)			
Female	30.4 ± 1.2	31.7 ± 0.4	NS
Male	33.3 ± 1.1	34.3 ± 0.5	NS
Duration of infertility (Years)	3.5 ± 0.4	4.5 ± 0.2	NS
Follicle size(mm)	19.0 ± 0.5	19.8 ± 0.2	NS
FSH/hMG (Ampules)*	21.2 ± 1.8	22.4 ± 1.0	NS
Days of stimulation*	9.8 ± 0.2	10.8 ± 0.3	NS
E ₂ on day of hCG(pg/ml)*	3,266.6 ± 214.2	2,202.7 ± 139.4	< 0.05
Motile sperm count(X 10 ⁶)	212.1 ± 63.4	105.1 ± 9.9	< 0.05

- 1) Values are mean ± SEM. NS : Not significant
 2) * ; Ultrashort, long and dual suppression groups.

1993 10 1998 2
124 152

1. 1 78 (62.9%), 2 46 (37.1%) ,
68 (54.8%)
가 , 가 32 (25.8%), 가 16 (12.9%), 가 5
(4.0%) 3 (2.4%) .
2. 31.6 ± 0.3 4.4 ± 0.3
, CC (32.2 ± 0.7) GnRH - a (33.3 ± 0.9)가 CC+hMG
(30.2 ± 0.6) (P<0.05 & P<0.01),
가 .
3. GnRH - a (24.3 ±
1.8)가 (19.1 ± 1.1) (P<0.05)
가 . hCG CC
(20.9 ± 0.4mm)가 CC+hMG (19.0 ± 0.5 mm) GnRH - a
(19.5 ± 0.5mm) (P<0.05), hCG E₂
GnRH - a (2,664.1 ± 213.6 pg/ml)가 (2,038.6 ±
141.3 pg/ml) (P<0.05).
4. 34.2 ± 0.5 ,
111.6 ± 10.3 X 10⁶ 가
.
5. 152 12 7.9% ,
124 12 9.7% ,
CC 7.5%(3/40), 10.7%(3/28) ,
CC+hMG 8.2%(4/49), 10.0%(4/40) ,
GnRH - a 5.9%(1/17), 7.1%(1/14) .

GnRH - a 5.9% (1/17), 6.3% (1/16)
, 27.3% (3/11) ,
, .
가 .
6. 33.3% (1/3) 가
, 가 15.6% (5/32) ,
8.8% (6/68) , .
7. 25% (3/12) , 12 2
, 1 .
8. CC 가 66.7% (2/3) , GnRH - a
가 100% (1/1) , , GnRH - a
23 .
9. 9 CC 가 1 , CC+hMG
가 3 1 , GnRH - a 1
, , 가 1 .
10. , ,
가 E₂ (3,266.6 ± 214.2 pg/ml)
(2,202.7 ± 139.4 pg/ml) (P < 0.05),
(212.1 ± 63.4 X 10⁶) (105.1 ± 9.9 X 10⁶)
(P < 0.05).
가
가 , GnRH - a
,
가 .
3 3-4
- (IVF - ET) .

. :
1996, 39, 1286-
1299.

. :
Gonadotropin-Releasing Hormone Agonist
1995, 38, 1030-1037.

. :
GnRH agonist 1995, 38,
1898-1908.

. :
1992,
35, 982-987.

. :
1997, 24, 361-368.

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