

## The Efficacy of Low-dose Aspirin Therapy for Controlled Ovarian Hyperstimulation in IVF-ET

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**Objective:** To evaluate the efficacy of low-dose aspirin on IVF outcome and endometrium in patients undergoing IVF-ET.

**Materials and Methods:** From February, 2001 to Jun, 2001, 60 infertile patients were randomly divided into study group (28 cycles) and control group (32 cycles). The study group received a daily oral dose of 25 mg of aspirin for at least 2 weeks from first visiting day. Controlled ovarian hyperstimulation was initiated in all patients with the GnRH agonist starting in the midluteal phase of the previous cycle.

**Results:** There were no significant differences in age of the patients, basal serum E2, LH, FSH level and endometrial thickness among two groups. There were no statistically significant differences between the study group and the control group respectively in dosage ( $26.5 \pm 4.8$  vs  $26.2 \pm 5.3$  amples) and duration ( $10.4 \pm 4.2$  vs  $9.8 \pm 5.3$  days) of gonadotropin administration, serum E2 level on the hCG administration day ( $1823 \pm 342$  vs  $1854 \pm 543$ ), LH ( $14.5 \pm 2.7$  vs  $14.8 \pm 3.1$ ), FSH ( $16.7 \pm 3.4$  vs  $18.3 \pm 4.7$ ), the number of follicles  $> 15$  mm ( $13.2 \pm 6.3$  vs  $12.8 \pm 5.9$ ), the number of oocytes retrieved ( $9.2 \pm 2.4$  vs  $8.4 \pm 1.7$ ), the number of embryos transferred ( $4.7 \pm 2.0$  vs  $4.7 \pm 2.0$ ), fertilization rate (68.4% vs 64.5%), implantation rate (21.3% vs 17.6%), and clinical pregnancy rate (28.4% vs 26.2%).

The endometrial thickness and the percentage of endometrial trilaminar pattern on hCG day were significantly higher in study group than control group ( $12.9 \pm 3.7$  mm vs  $10.4 \pm 2.8$  mm, 78.3% vs 64.5%).

**Conclusion:** Many reports suggest that low-dose aspirin improve ovarian response, implantation rate, fertilization rate, implantation rate, and pregnancy rate by increasing the blood flow, but we couldn't prove the significant effect of low-dose aspirin on the IVF outcome except on endometrium. This may be affected by dose of aspirin, duration, and number of patients studied. This trial is small, so our results highlight the need for a large randomized controlled trial to identify the effect of low-dose aspirin on IVF-ET outcome.

**Key Words:** Low-dose aspirin, Controlled ovarian hyperstimulation, IVF-ET, Endometrium

1897 Felix Hoffman

1899 Hermann Dreser

1971 Vane

enzyme cyclooxygenase

가 arachidonic acid prosta-

glandin

2001 2 2001 6

arachidonic acid Thrombox-

ane A<sub>2</sub> (TXA<sub>2</sub>) Prostaglandin I<sub>2</sub> (PGI<sub>2</sub>) (IVF-ET) 60

60 cycles

TXA<sub>2</sub>

PGI<sub>2</sub>

80%

high-dose, 324 mg

PGI<sub>2</sub>

TXA<sub>2</sub>

FSH 가 20 mIU/ml

가

가

가

25 mg

28 cycles 32 cycles

가

(receptivity) 가

(implantation rate) 가

(pregnancy rate) 가

1)

oocyte donation

recipients estrogen stimulation en-

dometrial thickness 가 8 mm

가

가

2)

가

3) estradiol (E2), luteinizing hormone (LH), fo-

llicular stimulating hormone (FSH)

gonadotropin-

releasing hormone agonist (GnRH agonist) Lucrin

(Leuprolide acetate, Abbott, France, 2 ml/ample, 14.0 mg/

ample) 0.2 cc (1.4 mg)

가 , estradiol (E2) 30 pg/ml

10 mm human

menopausal gonadotropin (hMG) (Merional, IBSA, Swi-

tzerland, 75 I.U./ample) GnRH agonist

combined long protocol

6.5 MHz

(SonoAce, Medison, Korea) , 4)

18 mm IVF media (Medicult, Copenhagen, Denmark)

16 mm 가 2 4 6 가

human chorionic gonadotropin (hCG) (Choriomon, IBSA, Switzerland) 10,000 IU hCG 23~35

E2, LH, FSH . 가 1 가

2) 16~18

hCG 34~36 - -

demerol, valium (oocyte-cumulus-corona complex, OCCC)

, lidocaine 2 (2 pronuclei, 2 PN) 200

2 ml Dulbelcco's phosphate buffered saline ( D-PBS ) IVF

, 2 ml D-PBS 가 24~28

D-PBS 가 5)

(#3002, Falcon Plastics, USA) 6.5

(dissecting microscope) MHz (SonoAce, Medison, Korea)

, 가 (longitudinal view)

(inverted microscope) 가 3

(immature), hCG trilaminar pattern Gogen

(mature), (postmature), (degenerative) C

3) 'triple-line'

3~5 6)

, 37 30 가 , ,

(1992) 가 (strict 48 가 , 가

morphology criteria) .

tube Isolate kit 15 가

ml 1.5 ml 가 14 ml conical tube .

350 G 20 6 가

2 ml 7)

300 G 10 2

1 ml (Progesterone in oil; Progest, Samil Pharma, Korea) 30 mg

37 , 5% CO<sub>2</sub> 12 beta-hCG

swim-up . , 10.0 mIU/ml .

**Table 1.** Comparison of clinical characteristics

Variables	Study group (n=28)	Control group (n=32)	P value
Mean age	34.2 ± 5.3	35.7 ± 4.8	NS
Baseline E2 (pg/ml)	15.3 ± 6.7	15.8 ± 5.7	NS
LH (mIU/ml)	8.6 ± 2.2	8.8 ± 3.2	NS
FSH (mIU/ml)	6.8 ± 1.3	7.2 ± 1.7	NS

NS: not significant

**Table 2.** Comparison of ovarian response to COH

Variables	Study group (n=28)	Control group (n=32)	P value
No. of hMG	26.5 ± 4.8	26.2 ± 5.3	NS
Duration of hMG	10.4 ± 4.2	9.8 ± 5.3	NS
hCG day E2 (pg/ml)	1823 ± 342	1854 ± 543	NS
hCG day LH (mIU/ml)	14.5 ± 2.7	14.8 ± 3.1	NS
hCG day FSH (mIU/ml)	16.7 ± 3.4	18.3 ± 4.7	NS

NS: not significant

8) mean ± standard deviation, Fisher's exact test 5.3, Student's t-test, p < 0.05. hCG E2 1823 ± 342 pg/ml, 1854 ± 543 pg/ml. LH 14.5 ± 2.7 mIU/ml, 14.8 ± 3.1 mIU/ml. FSH 16.7 ± 3.4 mIU/ml, 18.3 ± 4.7 mIU/ml. (Table 2).

1. 34.2 ± 5.3, 35.7 ± 4.8. E2 15.3 ± 6.7 (pg/ml), 15.8 ± 5.7 (pg/ml). LH 8.6 ± 2.2 mIU/ml, 8.8 ± 3.2 mIU/ml. FSH 6.8 ± 1.3 mIU/ml, 7.2 ± 1.7 mIU/ml. (Table 1).

2. hMG 26.5 ± 4.8, 26.2 ± 5.3. 3.8 ± 0.6, 4.2 ± 0.7. 9.2 ± 2.4, 8.4 ± 1.7. 13.2 ± 6.3, 15 mm.

**Table 3.** Comparison of clinical result after controlled ovarian hyperstimulation

Variables	Study group (n=28)	Control group (n=32)	P value
No. of follicles	13.2 ± 6.3	12.8 ± 5.9	NS
No. of oocyte retrieved	9.2 ± 2.4	8.4 ± 1.7	NS
No. of embryos transferred	4.7 ± 2.0	4.7 ± 2.0	NS
Fertilization Rate (%)	68.4	64.5	NS
Implantation Rate (%)	21.3	17.6	NS
Clinical PR (%)	28.4	26.2	NS

NS: not significant

**Table 4.** Endometrial thickness on the hCG day

Variable	Study group (n=28)	Control group (n=32)	P value
Base line (mm)	4.8 ± 0.7	4.6 ± 0.5	NS
After COH (mm)	12.9 ± 3.7	10.4 ± 2.8	<0.05
Trilaminar pattern (%)	78.3	64.5	<0.05

NS: not significant

67.5%, 65.4% 가 .

14.2% , 16.2% , 가 , 가 , 3-5

29.3%, 28.7% (Table 3). hMG

4. 가

3 6-8

4.8±0.7 mm, 4.6±0.5 mm 가

hCG GnRH agonist 가 가

12.9±3.7 mm, 10.4±2.8 mm 가 , GnRH agonist ,

trilaminar pattern 78.3% , LH, FSH

64.5% LH 가

(Table 4).

가 가

가 (Meldrum et al., 1984; Palermo et al., 1988; Caspe et al., 1989).





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