

## The Efficacy of Recombinant Human Follicle Stimulating Hormone (rhFSH) in Human IVF-ET Program

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**Objectives:** Recently, recombinant FSH (rFSH) has been manufactured using a Chinese hamster ovary cell line transfected with the gene encoding human FSH. Both rFSH and urinary gonadotropin (uFSH) could be used for controlled ovarian hyperstimulation (COH). However, uFSH implies a number of disadvantages, such as batch-to-batch inconsistency, no absolute source control, dependence on large amounts of urine, low specific activity, and low purity. The purpose of this study was to evaluate the efficacy of rFSH in human IVF-ET program.

**Materials and Methods:** A total of 508 infertile women was enrolled in this study. They are classified into rFSH group (n=177) or uFSH group (n=331), and all of them were matched by age and cause of infertility in same period. The Puregon® (Organon, Holland) was used as rFSH, and the Metrodin-HP® (Serono, Switzerland) and Humegon® (Organon, Holland) was used as uFSH. We subdivided the patients into three age groups. The outcomes of IVF-ET program were analyzed using the statistical package for social sciences (SPSS).

**Results:** There was no significant differences in the level of estradiol on hCG injection day, the numbers of retrieved oocytes, matured oocytes, fertilized oocytes, transferred embryos, frozen embryos between the two groups. The total dose (IU) of gonadotropin for COH was significantly lower in the rFSH group compared to uFSH group (1339 ±5491.1 vs 2527.8 ±1075.2 IU,  $p<0.001$ ). Clinical pregnancy rate per embryo transfer in the rFSH group showed increasing tendency, compared to the uFSH group, but there was no statistical significance (35.2% vs 29.3%). Our results demonstrated that the relative efficiency of rFSH compared with uFSH is higher in older patients.

**Conclusions:** The ovarian stimulatory effect and clinical outcome of recombinant FSH was similar to that of the urinary gonadotropin. The IVF-ET cycles with significantly lower dose of gonadotropin in rFSH group showed comparable results. Therefore, we suggest that recombinant FSH is more potent and effective than urinary gonadotropin.

**Key Words:** Recombinant human follicle stimulating hormone (rFSH), Urinary gonadotropin (uFSH), IVF-ET, Total dose of gonadotropin, Pregnancy rate

(in vitro fertilization, IVF) . 1-4

(follicle stimulating hormone, FSH) .

(glycoprotein) .

human menopausal gonadotropin ( HMG, menotropin) 가 IU 가 1 mg 10,000 recombinant 가

hormone, LH) (luteinizing hormone, LH) . 15,16 rhFSH

5-8 monoclonal . 17 가 uhFSH

(urinary human FSH, uhFSH, urofollitropin)가 . rhFSH 가

(highly purified uhFSH, highly purified urofollitropin) 20,21 가

HMG 8-10 가

1960 가 rhFSH

1988 Chinese hamster ovary (CHO) cell line a β subunit encoding expression vector

가 1. binant human FSH, rhFSH, follitropin alpha and 1999 5 2001 5



48~72 가 3~4 matching 177 rhFSH  
HMG 331 uhFSH  
2 (16.7%), 11  
(luteal phase support) (26.8%) 13  
(proge-  
sterone in oil, Progest®, Samil Phar., Korea) 50  
mg (Utroge-  
stan®, Hanwha Phar., Korea) 300 mg  
가  
12 β- 12 (6.8%)  
hCG 3 mIU/ml 41 (12.4%)  
β-hCG  
(gestational sac)  
가  
가  
SPSS (statistical package for social science) 10.0 가 (Table 1).  
Student's t-test, chi-square 93 (52.5%), 194 (59.3%) 84  
test Fisher's Exact test (47.5%), 133 (40.7%) 가  
(efficacy criteria) 가  
, p 0.05 35.6%, 29%  
( )  
가 (Table 2).  
가  
508 가 (9.1 ±1.9 vs 9.3 ±1.7).  
2:1 1339.5 ±491.1

**Table 1.** Characteristics of patients

	rhFSH (n=177)	HMG+uhFSH-HP (n=331)	p value
Age of patients (yrs)	32.7 ± 3.8	33.0 ± 4.3	NS
Age of husbands (yrs)	35.2 ± 4.9	35.9 ± 5.0	NS
Duration of infertility (months)	50.7 ±39.5	52.4 ±38.8	NS
Endocrine profile			
Basal FSH (mIU/ml)	7.7 ± 2.6	8.4 ± 5.0	NS
Basal LH (mIU/ml)	3.5 ± 2.1	3.4 ± 1.9	NS
Basal E2 (mIU/ml)	18.4 ± 8.0	19.6 ± 9.3	NS

Values are mean ±SD, NS : not significant

(IU) 2527.8 ±1075.2 (IU) (p<0.005).  
 (p<0.001).  
 (p<0.001). , hCG ,  
 71.9%, 65.6%

**Table 2.** Indication of infertility

	rhFSH (n=177)	HMG+uhFSH-HP (n=331)	p value
Tubal factor	63 (35.6%)	96 (29% )	NS
Male factor	56 (31.6%)	94 (28.4%)	NS
Endometriosis	24 (13.6%)	54 (16.3%)	NS
Immune factor	2 ( 1.1%)	4 ( 1.2%)	NS
Peritoneal factor	10 ( 5.6%)	20 ( 6.0%)	NS
Old age	3 ( 1.7%)	14 ( 4.2%)	NS
Uterine factor	3 ( 1.7%)	5 ( 1.5%)	NS

NS: not significant

**Table 3.** Results of controlled ovarian hyperstimulation, and in vitro fertilization

	rhFSH (n=177)	HMG+uhFSH-HP (n=331)	p value
E2 on hCG injection day (pg/ml)	2105.3 ±1377.1	2536.9 ±3061.2	NS
Days of stimulation	9.1 ±1.9	9.3 ±1.7	NS
Total dose used (IU)	1339.5 ±491.1	2527.8 ±1075.2	p<0.001
Gonadotropin units per oocyte (IU)	217.7 ±295.6	435.8 ±716.9	p<0.001
Mean fertilization rate per cycle (%)	71.9	65.6	p<0.005
Cancellation rate (%)	6.8	12.4	p<0.05
hCG positive rate (%)	40	34.1	NS
Clinical pregnancy rate (%)	35.2	29.3	NS

Values are mean ±SD, NS: not significant

**Table 4.** Results of retrieved oocytes and embryo parameters

	rhFSH (n=177)	HMG+uhFSH-HP (n=331)	p value
Mean number of retrieved oocytes	12.2 ±8.8	11.9 ±8.1	NS
Mean number of mature oocytes	10.2 ±6.0	9.1 ±5.1	NS
Mean number of fertilized oocytes	8.7 ±6.2	7.9 ±5.2	NS
Mean number of high quality embryo	1.7 ±1.4	1.6 ±1.3	NS
Mean number of embryos transferred	3.6 ±1.4	3.4 ±1.7	NS
Mean number of embryos frozen	8.4 ±6.3	8.1 ±4.5	NS

Values are mean ±SD, NS: not significant



(Table 4).  
Table 5

(maturation rate)  
69.9%, 62.5%  
( $p < 0.001$ ).

( $p < 0.001$ ).

, 35 39 , 40

가 가  
가

( $p < 0.05$ ).  
35

rhFSH  
17,30-33

가

lenton  
rhFSH

26-29

34

(Table 6).

uhFSH HMG rhFSH 가  
 Out 17 rhFSH rhFSH  
 uhFSH rhFSH 가  
 rhFSH 가  
 uFSH Bennink 31  
 22-24 Lenton 25 가  
 150 (IU) rhFSH 가  
 rhFSH 가 uFSH  
 가 rhFSH uhFSH  
 HMG hCG ,

rhFSH 가 40

rhFSH uFSH 35 39

rhFSH (1490.9 IU vs 1535.7 IU)

가 rhFSH

가 40

가 32-35

Daya<sup>8</sup> pub-med rhFSH meta-analysis 가

uhFSH rhFSH 가

uhFSH rhFSH 가

Raga<sup>39</sup> De Placido uFSH rFSH 가

(ICSI)

2 (16.7%), 11 (26.8%)

가

uFSH Ravhon<sup>30</sup> rFSH

가

Out<sup>37</sup> 30 rhFSH

33 (250 IU vs 150 IU, )

가

rhFSH

rhFSH (200 IU vs 100 IU, )

가

35

38

35

rhFSH follitropin alpha (Gonal-F<sup>®</sup>) follitropin beta (Puregon<sup>®</sup>)

가

uFSH follitropin alpha

가





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