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Research Article

Difference in IVF outcome and pregnancy rate in triggering ovulation by rHCG vs uHCG

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Abstract: Historically, urinary human chorionic gonadotropin (uHCG) has been used as an alternative to LH to induce final oocyte maturation in women undergoing IVF. This retrograde chart review study was done at Medcare Fertility Center, Dubai, UAE between April 2016 to July 2017 to know the difference in IVF outcome and pregnancy rate in triggering ovulation by rHCG vs uHCG.

Total 117 women with poor ovarian response were included in this study. Embryo transfer rate for the recipient of Pregnyl and Ovitrelle was 50.77% and 51.92% respectively. The clinical pregnancy rate for Pregnyl vs Ovitrelle was 15.38% and 16.92% respectively. Positive βHCG was noted in 22.22% participants.

Large-scale multi-center RCT is required to predict the outcomes more accurately.

Keywords: IVF, Triggering ovulation, rHCG , uHCG, PREGNANCY

Introduction

The Luteinizing hormone (LH) surge promotes ovulation via activation of multiple signaling networks in the ovarian follicle. In addition, the LH surge is essential for forming an active corpus luteum. Due to structural similarity, the urine-derived Human Chorionic Gonadotrophin (uHCG) has been used for about 4 decades in assisted conception to mimic LH surge. But, uHCG has many limitations such as batch to batch inconsistency, urinary protein contamination, post-injection side-effects experienced by few patients, a movement to avoid human source materials, and limited availability of BioSource. Recombinant HCG does not have aforementioned shortcomings and is produced in a Chinese hamster ovary cell line expressing the genes for the alpha and beta subunits of HCG; the protein is purified using stepwise chromatography. The pharmacokinetic properties of rHCG is comparable to that of uHCG with linearity over a dose range of 500–20,000 IU and a terminal elimination half-life of approximately 30 hours. A recent Cochrane review and metanalysis reported no significant differences between rHCG and uHCG regarding ongoing pregnancy rate (OR = 0.98; 95% CI, 0.69-1.39), miscarriage rate and the incidence of ovarian hyperstimulation syndrome in GnRH agonist protocol. This study was undertaken to know which type of HCG (uHCG or rHCG) provides better IVF outcome in both GnRH antagonist and long agonist protocols.

Materials and methods

Study design

This retrospective chart review study was conducted in Medcare Fertility Clinic – Dubai. All patients with a poor ovarian response (POR) attended the clinic for IVF during the study period (April 2016 to July 2017) was included in this study. Bologna criteria definition of poor ovarian response was used to form the selection criteria for the study. This study was reviewed and approved by the institutional review board and Ethics Committee of Medcare Fertility Centre and all volunteers for participation in this study were informed regarding the purpose and method of the study. Institutional review board approval was not collected because this was not an interventional study.

Inclusion criteria

Poor ovarian responders with following criteria were included in this study:

- Age $\geq$ 38 years.
- Basal Follicular Stimulation Hormone (FSH) $\leq$ 16 IU/L.
- Low ovarian reserve based on antral follicle count $\leq$ 5.
- Low Anti-mullerian Hormone (AMH) $\leq$ 0.8 ng/mL.

The study did not have any exclusion criteria. After considering the inclusion criteria patients were divided into two groups according to the treatment they received:

- Group A for those who received I/M 10,000 IU uHCG
- Group B for the others who received S/C 250µg rHCG

Oocyte retrieval

Monitoring of cycle was done by serial vaginal ultrasonography and measurement of serum Estradiol level. In both groups, Transvaginal ultrasound-guided oocyte retrieval by using a 17-gauge needle was performed 35 hours after HCG injection. The numbers of retrieved oocytes were recorded. Standard laboratory protocols were followed and approximately two hours after retrieval the cumulus cells were removed and an assessment of Oocyte maturity under an inverted microscope (germinal vesicle, metaphase I, metaphase II, atretic or degenerative) were made. Metaphase

II oocytes (mature oocytes) were characterized by the presence of the first polar body, metaphase I oocytes was characterized by the absence of both germinal vesicle and first polar body and prophase I oocytes was characterized by its distinct germinal vesicle.

Research objectives

Primary objective

- Difference in pregnancy rate in triggering ovulation by rHCG vs uHCG

Secondary objective

- Difference in IVF outcomes in triggering ovulation by rHCG vs uHCG

Statistical analysis

Continuous variables were presented in mean ± SD, descriptive statistics were used to analyze categorical variables.
Analysis was performed using Statistical Package for Social Science (SPSS), version 20 (IBM, Armonk, NY, USA).

Table 1: Age, no. of matured follicles, no. of oocytes and M2 of all respondents (n = 117)

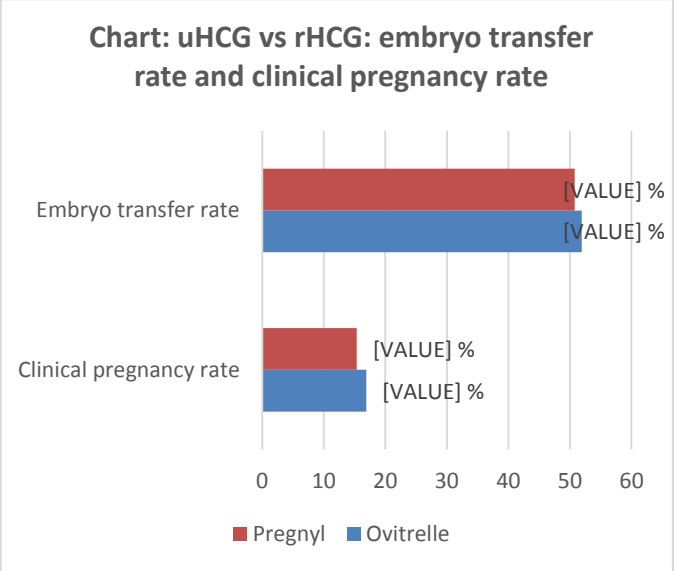
	Age (years)	No. of follicles > 14 mm	No. of oocytes	M2
Mean	41.45	7.15	6.12	4.76
Standard error	0.23	0.40	0.37	0.30
Median	42	7	5	4
Standard deviation	± 2.49	± 4.29	± 3.99	± 3.29
Minimum	38	1	0	0
Maximum	46	18	17	14

Table 2: Age, no. of matured follicles, no. of oocytes and M2 of patients received Pregnyl (n = 65)

	Age (years)	No. of follicles > 14 mm	No. of oocytes	M2
Mean	41.37	7.75	7.06	5.63
Standard error	0.29	0.55	0.52	0.43
Median	42	8	7	5
Standard deviation	± 2.31	± 4.40	± 4.16	± 3.48
Minimum	38	1	1	1
Maximum	46	18	17	14

Table 3: Age, no. of matured follicles, no. of oocytes and M2 of patients received Ovitrelle (n = 52)

	Age (years)	No. of follicles > 14 mm	No. of oocytes	M2
Mean	41.56	6.40	4.94	3.67
Standard error	0.38	0.56	0.56	0.37
Median	42	6	5	3
Standard deviation	± 2.72	± 4.06	± 3.47	± 2.69
Minimum	38	1	0	0
Maximum	46	17	16	14



Results

Total 117 poor ovarian responders were included in this single centered retrospective chart-review study. The mean ± SD age of all respondents was 41.45 ± 2.49 years. The number of matured follicles for patients who received Pregnyl vs who received Ovitrelle was 7.75 ± 4.40 vs 6.40 ± 4.06. The number of oocytes retrieved for group A patients was 7.06 ± 4.16 and for group B patients was 4.94 ± 3.47. Matured oocyte count was 5.63 ± 3.48 for Pregnyl recipients and 3.67 ± 2.69 for Ovitrelle recipients. (Table 1, 2 and 3)
The rate of positive βHCG was 22.22%. Embryo transfer rate for the recipient of Pregnyl and Ovitrelle was 50.77% and 51.92% respectively. The clinical pregnancy rate for Pregnyl vs Ovitrelle was 15.38% and 16.92% respectively. (Chart 1)

Discussion:

There was no significant difference in age of the respondents between two groups. This study showed the number of matured follicles, the number of oocytes retrieved and number of matured oocytes are higher if ovulation is triggered by Pregnyl instead of Ovitrelle. This is contradictory to a previous study. In terms of embryo transfer rate and clinical

pregnancy rate, recombinant HCG was suggested better than urinary HCG. A study by E.G. Papanikolaou also suggested a similar outcome.

A large-scale randomized controlled trial is needed to give the final verdict.

Conclusion

uHCG and rHCG both have effect on triggering ovulation but in this study, rHCG was proven superior to uHCG for pregnancy rate. But, Pregnyl showed superiority in triggering ovulation and oocyte maturation. This study can act as a starting point for a large scale RCT in this topic so that the outcomes can be generalized and possibly come into future guidelines.

Limitations

- Study was done in one fertility center
- Observational study
- Certain medical conditions like endometrioma, ovarian surgery, elvic infections, genital tuberculosis, chlamydial infections, smoking, obesity, ethnicity etc. were not considered.

Recommendation

This study can act as a baseline for future large scale complex randomised control trial which may ultimately declare the efficacy of one treatment is significantly superior than other with greater precision.

Acknowledgement

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