Original Article

Effect of intrauterine administration of human chorionic gonadotropin (hCG) before embryo transfer on biochemical pregnancy rate, implantation rate, and clinical pregnancy rate in in vitro fertilization/intracytoplasmic sperm injection cycles: Prospective and interventional randomized comparative study

Imlesh Meena, Rashmi Sharma, Abhishek Baldawat, Fizayur Rehman, Ankita Gupta, Divya Chauhan

Origyn Fertility and IVF Centre, New Delhi, India
Sawai Mansingh Hospital, Jaipur, India
University College Of Medical Sciences, New Delhi, India

Abstract

Objective: To study the effect of intrauterine administration of human chorionic gonadotropin (hCG) before embryo transfer (ET) on biochemical pregnancy rate, implantation rate, and clinical pregnancy rate in in vitro fertilization/intracytoplasmic sperm injection cycles. **Design:** Prospective and interventional randomized comparative study. **Setting:** Origyn Fertility & IVF, 4th floor, HB Twin towers, Netaji Subhash Place, Above Max Hospital Pitampura, New Delhi. **Patients:** All patients aged 23 to 38 years undergoing fresh or frozen ET or planned for in vitro fertilization/intracytoplasmic sperm injection cycle are included in the study. Intervention: From August 2019 to March 2020, 80 patients were included in the study who were divided into two subgroups viz group "A" (Case group) and group "B" (control group). Group "A" patients were given 500 IU of hCG intrauterine 7 min prior to ET and in group "B" patients, the embryo was transferred directly. Outcome measure: Biochemical pregnancy rate, clinical pregnancy rate, and implantation rate. **Results:** Clinical pregnancy rate was 52.5% in the case group and 45% in the control group. Biochemical pregnancy rate was 57.5% in the case group and 52.5% in the control group. Mean implantation rate was 30.41 ± 36.57 in the case group and 24.57 ± 30.42 in the control group. **Conclusion:** The intrauterine instillation of 500 IU of hCG 7 min before ET did not show any significant difference in clinical pregnancy rate, biochemical pregnancy rate, and implantation rate. However, as this study was performed on a small group, its reliability in clinical practice needs further studies on a larger study group.

Keywords: embryo transfer, human chorionic gonadotropin, in vitro fertilization, intracytoplasmic sperm injection

Address for correspondence: Dr. Imlesh Meena, Origyn Fertility And Ivf Centre, New Delhi, India.
E-mail: saviaims@gmail.com
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INTRODUCTION

About 10% to 15% of couples today are facing infertility.[1] Infertility is defined as an inability to bear children after 12 months of regular intercourse by a non-contracepting sexually active couple.[2]

Assisted reproductive technology (ART) has been a boon for such couples. It has come a long way since the birth of Louise Brown, the first baby conceived by in vitro fertilization (IVF). ART allows us to influence the fertilization process so that we can overcome the pathological barriers such as low sperm count, blocked vas deferens in males, and nonfunctional ovaries and blocked fallopian tubes in females.[3] In spite of so many years after Louise Brown birth and millions of babies worldwide since 1978, ART has many challenges that still need to be understood and improved upon.

One such challenge is implantation failure. "Implantation is a highly complex process in which a developing embryo attaches itself to uterine wall and invades the endometrial stroma and vasculature to form the placenta and develop there until birth." These events have been called apposition, adhesion, invasion, and immune regulation.[4]

"Prior to the commencement of implantation, however, both embryo and endometrium should get on an elaborated process in a very time and location-specific manner." The crosstalk between a receptive and a competent blastocyst can only take place during a limited time span, referred to as "window of implantation."[5]

Implantation is an incredibly intricate procedure that is regulated by a variety of mediators, such as cytokines, cell adhesion molecules, growth factors, and so forth.[6]

One very important mediator among these is human chorionic gonadotropin (HCG) secreted by the early embryo.[7]

Of all the pregnancies attempted using ART only 30% per cycle are successful and more than half of the failed pregnancies using ART is due to implantation failure.[8] These data tell us how little we know and understand about this process and the vast scope for improvement.

hCG is a type of heterodimeric glycoprotein found in placenta that is essential for maintaining pregnancy. The heterodimeric glycoprotein that is placental "human chorionic gonadotropin" that consist tow subunits namely α and β. These subunits are bound by a noncovalent hydrophobic and ionic interactions. hCG have many isoforms chiefly hCG, free beta-subunit-hCG, pituitary hCG, hyperglycoslated-hCG, all of these are produced by different cells for different function in the body. Villous syncyntiotroblast in early developing embryo is responsible for secreting most predominant form of hCG.[9]

This hCG helps in rescuing corpus luteum with continued progesterone production, vital for maintenance of pregnancy. In the uterine arteries receptors for hCG/LH are present and they stimulates angiogenesis in uterine vasculature ensuring adequate nutrition to developing embryo.[10]

Its role in fusion of cytotrophoblast cells and formation of syncytiotrophobalst has also been elucidated in various studies. "Hyperglycosylated hCG an autocrine hormone promotes cytotrophoblast cells growth and hCG also encourages the differentiation of cytotrophoblast cells to syncytiotrophoblast cells."[11,12]

It is also helpful in immune modulation during early pregnancy, important for maternal acceptance of embryo by promoting an antimacrophage inhibitory factor or a macrophage migration inhibitory factor.[13]

There is also evidence of direct enhancement of innate immunity by stimulating macrophage function.[14]

There is evidence to suggest that hCG is secreted by unimplanted blastocyst which signals the endometrium through hCG/LH receptors on endometrium about forthcoming implantation and encourages angiogenesis and immune tolerance at maternal fetal interface.[15]

A number of researches have demonstrated that when 500 IU of hCG is administered in uterus, it leads to marked suppression of macrophage colony stimulating factor, insulin like growth factor-binding protein 1, furthermore leukemia inhibiting factor, an important cytokine required for implantation, vascular endothelial growth factor that promotes angiogenesis and matrix metalloproteinase 9 (MMP-9) that regulates tissue modeling, these were indicated as important factors.[16,17]

To improve implantation and endometrial response in IVF cycles several modalities are understudy such as endometrial injury, sildenafil, low dose aspirin, heparin, corticosteroids, granulocyte–colony stimulating factors, intrauterine injection of hCG, and intrauterine

administration of autologous peripheral blood mononuclear cells.[18]

"On the basis of the hypothesis that instillation of hCG inside the uterine cavity (IC-hCG) before embryo transfer (ET) enhances implantation, this clinical trial aimed to investigate the effect of intrauterine hCG administration before ET on pregnancy outcome in infertile couples."

Objective

"To study the effect of intrauterine administration of hCG before ET on Biochemical pregnancy rate, implantation rate, and clinical pregnancy rate in vitro fertilization/intracytoplasmic sperm injection cycles."

METHODOLOGY

The study was conducted at Origyn Fertility & IVF, 4th floor, HB Twin towers, Netaji Subhash Palace, Above Max Hospital, Pitampura, New Delhi. Patients who underwent fresh and frozen ET at our center were considered for the study. This study was a prospective and Interventional Randomized Comparative Study. Patients in age group of 23 to 38 years undergoing fresh or frozen ET planned for IVF/intracytoplasmic sperm injection (ICSI) cycle were included in the study. Patients with history of ovum donation, thin endometrial thickness, poor quality embryos, and severe endometriosis were excluded from the study. Base line parameters such as age, BMI, anti-Mullerian hormone (AMH) level, number of embryos, and quality were matched in study and control group.

Sample Size

The study of Osman *et al.* observed that RR of clinical pregnancy rate in Wirleitner *et al.* was 0.91 for intrauterine HCG administration versus no HCG.[19,20] Taking these values as reference, the minimum required sample size with 95% power of study and 5% level of significance is 32 patients in each study group. To reduce margin of error, total sample size taken is 80 patients (40 patients per group).

Formula used was:

$$n \geq (2 \times (Z\alpha + Z\beta)^2)/(ES)^2$$

where $Z\alpha$ is value of Z at two-sided alpha error of 5% and $Z\beta$ is value of Z at power of 95% and ES is effect size.

Calculations:

$$n \geq ((2 \times (1.96+1.645)^2)/(0.91)^2$$

$$\geq 31.39 = 32 \text{ (approximately)}$$

Statistical Analysis

Descriptive statistics were elaborated in the form of means/standard deviations and medians/interquartile ranges for continuous variables, and frequencies and percentages for categorical variables. Data were presented in a graphical manner wherever appropriate for data visualization using histograms/Box-and-Whisker plots/column charts for continuous data and bar charts/pie charts for categorical data.

Group comparisons for continuously distributed data were made using independent sample "*t*" test when comparing two groups. If data were found to be non-normally distributed, appropriate nonparametric tests in the form of Wilcoxon-Mann-Whitney U test were used for these comparisons.

Chi-squared test was used for group comparisons for categorical data. In case the expected frequency in the contingency tables was found to be <5 for >25% of the cells, Fisher's exact test was used instead.

A *P* value of <0.05 will be considered statistically significant.

The data were entered in MS Excel spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 23 (IBM Corp).

Block Randomization

In block randomization with sealed envelope system, we prepared 10 randomly generated treatment allocations within sealed opaque envelopes assigned A and B in five envelopes each, where "A" represented Group A receiving hCG and "B" represented Group B not receiving HCG. Once patient gave consent to enter the trial an envelope was opened and the patient were allocated group. In this technique, patients were randomized in a series of blocks of 10.

Method of Recruitment

All women of age group 23 and 38 years and with BMI between 18 and 30 kg/m^2 who were suffering from primary or secondary infertility attending Origyn fertility & IVF Centre and who were planned for IVF/ICSI cycles asked to participate in the study. They were fully informed about the study objectives and procedures. Only women who signed a consent form were enrolled into the study. Patient information sheet was given to the patient.

For all the patient's complete history evaluation and physical examination was done.

Baseline clinical and hormonal parameters of all patients noted. Age, BMI, and AMH levels were matched in the case and control group.

Data Collection

All the data were collected by the investigator on a predesigned Performa.

Procedure

The data collection was proelective. Patients were randomly allocated to either intervention group (cases) or control group.

On the day of transfer in intervention group (cases) 500 IU of hCG was instilled 7 min before ET, whereas direct ET was performed without hCG instillation in the control group

The preparation of intrauterine injection vial consisting of 5000 IU of hCG was dissolved in 0.1 ml of culture media and from this solution, we took around 10 µl or 500 IU hCG.

At the time of the Embryo transfer, the patients of both groups were put in lithotomy position and cervix was visualized by Cusco's speculum. Cervical mucus was gently cleaned with the help of cotton swabs. The ET was guided by abdominal ultrasound with a full bladder.

In intervention group (cases), soft outer catheter was put just beyond the internal os, then 10 µl of culture media with 500 IU of hCG was loaded in inner catheter and introduced through outer catheter just beyond the internal os and gently the hCG solution was pushed inside the uterine cavity.

The hCG preparation was injected in the uterine cavity under transabdominal USG guidance then soft outer catheter was drawn out. It was reinserted after 7 min interval and previously loaded embryo was transferred after 7 min of intrauterine injection of hCG.

In the control group, ET was carried out as usual with soft catheter without prior instillation of hCG.

Patients who underwent ET, beta hCG levels were calculated after 12 days to confirm pregnancy followed by TVS which was done for localization of gestation sac 1week later. The collected data included age, BMI, duration of infertility, and type of infertility (whether primary or secondary), causes of infertility, AMH, method of fertilization (IVF or ICSI), whether fresh or frozen ET, number, and stage of embryos transferred and pregnancy rates.

Outcome Variables

Biochemical Pregnancy rate, Clinical Pregnancy Rate, Implantation Rate

Biochemical pregnancy rate was observed by quantitative values of a serum test of B-hCG level according to standard values that are used in laboratory.

Clinical pregnancy rate is defined as presence of gestational sac, embryo, and fetal heart rate at the time of USG evaluation.

Implantation rate is defined as the number of gestation sacs observed at 6 weeks of pregnancy divided by no of embryos transferred.

Number of gestation sac observed divided by number of embryos transferred × 100 = Implantation Rate.

ETHICAL CONSIDERATIONS

Ethical issues were addressed as follows:

(1) Informed written consent were taken from all couple. No pressurewas exerted on subjects for participation in the study.
(2) Confidentiality and privacy was ensured at all levels.
(3) The subject was free to leave the study at any time and no questions were asked further. However, they were not debarred from getting any medical services as being provided to the other participants.

OBSERVATION AND RESULTS

This prospective study was conducted in the Origyn fertility & IVF Centre, New Delhi with effect from August 1, 2019 to March 31, 2020. During this study period, a total of 80 patients were selected. Out of these, 40 patients were selected as case group in whom intrauterine instillation of hCG was instilled prior to ET and in other 40 patients directly embryo instilled as per standardised protocol. No patient was lost to follow-up.

The observations made during the study are described in Table 1.

DISCUSSION

In our trial, we found that IU hCG instillation 7 min prior to ET did not improve implantation rate, clinical

Table 1: Baseline parameters

Parameters	Group		*P* value
	Case (*n*=40)	Control (*n*=40)	
Age (Years)***	31.35 ± 3.29	31.48 ± 3.82	0.6501
Age			0.2482
25–29 Years	17 (42.5%)	10 (25.0%)	
30–34 Years	16 (40.0%)	20 (50.0%)	
35–38 Years	7 (17.5%)	10 (25.0%)	
BMI (Kg/m^2)	26.32 ± 2.12	26.52 ± 1.67	0.5413
BMI			0.2172
18.5–24.9 Kg/m^2	14 (35.0%)	9 (22.5%)	
25.0–29.9 Kg/m^2	26 (65.0%)	31 (77.5%)	

Parameters	Group		*P* value
	Case (*n*= 40)	Control (*n*=40)	
Type of Infertility			0.0752
Primary	26 (65.0%)	33 (82.5%)	
Secondary	14 (35.0%)	7 (17.5%)	
Duration of Infertility (Years)	5.33 ± 2.52	5.05 ± 2.04	0.8033
Factor of Infertility			0.6884
Tubal Factor	13 (32.5%)	13 (32.5%)	
PCOD	11 (27.5%)	9 (22.5%)	
Male Factor	6 (15.0%)	10 (25.0%)	
Poor Ovarian Reserve	4 (10.0%)	5 (12.5%)	
Unexplained Infertility	6 (15.0%)	3 (7.5%)	
Number of Previous IVF Cycles			0.3712
0	22 (55.0%)	18 (45.0%)	
1	18 (45.0%)	22 (55.0%)	

Parameters	Group		*P* value
	Case (*n*=40)	Control (*n*=40)	
Number of Oocytes Retrieved	15.90 ± 5.56	16.30 ± 6.14	0.7611
Response			1.0004
Poor Responder (1-8)	3 (7.5%)	3 (7.5%)	
Normal Responder (8-15)	16 (40.0%)	17 (42.5%)	
Hyper-Responder (>15)	21 (52.5%)	20 (50.0%)	
Technique of Fertilisation			0.4852
ICSI	24 (60.0%)	27 (67.5%)	
IVF	16 (40.0%)	13 (32.5%)	
Number of Oocytes Fertilised	13.95 ± 4.80	14.25 ± 5.69	0.8001
Fertilization Rate	86.72 ± 8.19	86.64 ± 6.05	0.7733
Endometrial Thickness (mm)	8.92 ± 1.23	8.99 ± 0.98	0.6233
Endometrial Thickness			0.2192
7.1–8 mm	10 (25.0%)	8 (20.0%)	
8.1–9 mm	14 (35.0%)	12 (30.0%)	
9.1–10 mm	7 (17.5%)	15 (37.5%)	
>10 mm	9 (22.5%)	5 (12.5%)	
Day of Embryo Transfer			0.6542
Day 3	17 (42.5%)	14 (35.0%)	
Day 4	14 (35.0%)	18 (45.0%)	
Day 5	9 (22.5%)	8 (20.0%)	
Type of Embryo Transfer			0.2282
Fresh	10 (25.0%)	15 (37.5%)	
Frozen	30 (75.0%)	25 (62.5%)	
Number of Embryos Transferred			0.4204
1	3 (7.5%)	1 (2.5%)	
2	20 (50.0%)	25 (62.5%)	
3	17 (42.5%)	14 (35.0%)	
AMH (ng/mL)	5.22 ± 3.99	4.38 ± 2.91	0.4623
AMH			0.4774
0.5–1.1 ng/mL	3 (7.5%)	6 (15.0%)	
1.2–3.5 ng/mL	16 (40.0%)	12 (30.0%)	
>3.5 ng/Ml	21 (52.5%)	22 (55.0%)	

Outcome Variables: - ***Significant at $P < 0.05$, (1) *t* test, (2) chi-squared test, (3) Wilcoxon-Mann-Whitney U Test, (4) Fisher exact test.

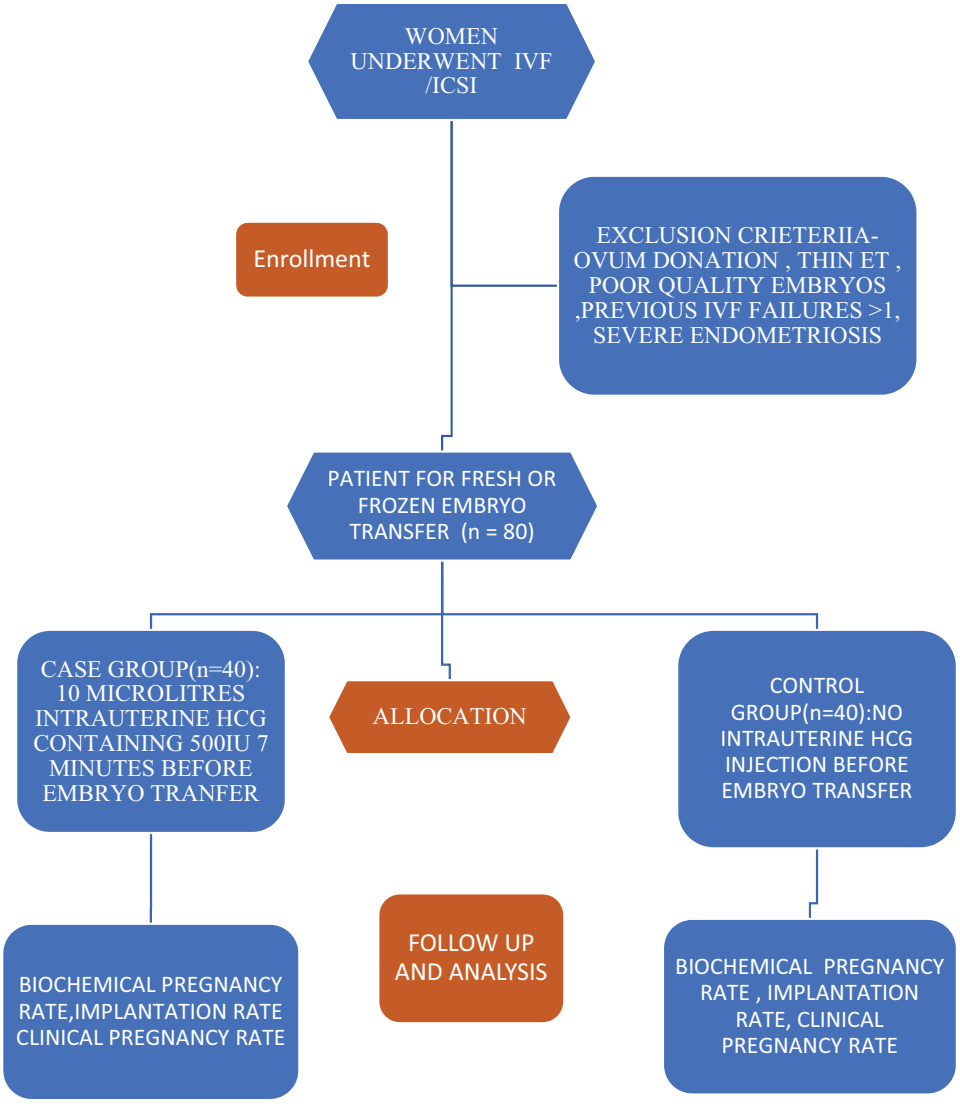

Figure 1: Alogrithm of methodology

pregnancy rate, or biochemical pregnancy rate was a little higher in hCG group Figure 1.

Implantation failure is one of the major roadblocks in assisted reproductive technology (ART). In spite of major advances in clinical and laboratory ART live birth rates remain low. Out of all IVF failures it is estimated that 50% to 75 % are due to implantation failure.[18,21]

In ART successful implantation is dependent on the following three main factors:
(1) Embryo quality
(2) Endometrial receptivity (ER)
(3) Embryo-endometrium synchronization.

These factors need to be critically coordinated and are influenced by a number of elements such as cyclic adenosine monophosphate (cAMP), relaxin, gonadotropin, prostaglandin E2 (PGE2), hCG, and glycoprotein hormones that are secreted from the embryo or endometrium affect implantation.[22] Recent studies have suggested hCG is one of the chief regulators of the process. Our study aims to find out if intrauterine administration of hCG can improve chances of implantation and thus leading to clinical pregnancy.

Endometrial receptivity is largely regulated by embryo-endometrium synchronization also known as embryo-endometrium crosstalk that they achieve through a number of paracrine factors.

In a normal pregnancy, the embryo after fertilization in the fallopian tubes moves into the uterus in form of a blastocyst that is ready to hatch from its zona pellucida. This blastocyst has the potential of giving away paracrine signaling via different mediators such as hCG, interlukin-

1, and insulin-like growth factors that in turn endometrial receptivity at the implantation site.

Although the embryo is preparing for implantation, the endometrium is undergoing changes at the same time, giving rise to a number of growth factors and cytokines such as leukemia inhibitory factor, macrophage colony stimulating factor, and epidermal growth factor. These factors help to regulate the trophoblastic differentiation and embryonic development.[23]

All these various process go on at the same time between the embryo and endometrium and one function influences the other, so only when a healthy embryo giving the right paracrine signal at the right time, to prepared and receptive endometrium, a successful implantation occurs.

Role of hCG in implantation

It is well known that hCG is one of the first embryonic product released by the embryo prior to implantation. The hCG subunits are already being transcribed in the eight-celled embryos. High concentrations of this bioactive hormone is secreted by blastocyst that enables detection of hCG in maternal circulation 10 days after fertilization.[24] hCG targets several factors that are responsible for various function viz. decidualization, implantation, vascularization, and tissue remodeling such as prolactin, insulin-like growth factors binding protein-1, macrophage colony stimulating factor, leukemia inhibitory factor, vascular endothelial growth factor, matrix metalloproteinase-9, tissue inhibitors of MMP, galactin-3 and glycodelin.[17] Considering all the above acts, it is safe to assume that hCG can help with implantation process by modulating several cytokine and paracrine functions that are considered important to achieve successful implantation.

In our study, we aimed to study the effect of intrauterine instillation of 500 IU of hCG 7 min prior to ET on Clinical pregnancy rate, biochemical pregnancy rate and Implantation rate. In IU HCG group Clinical pregnancy rate, biochemical pregnancy rate and implantation rate was higher. According to results observed in our study, there was no significant difference in clinical pregnancy rate, biochemical pregnancy rate, and implantation rates in the control and intervention group. There have been several studies in which effects of hCG prior to ET were observed but these studies have failed to give a clear picture as to its significance as some of them has shown significant outcome in results where as other have negated its significance, thus more research is required to reach to definite conclusion as implantation failure is the most considerable roadblock faced in ART and in spite of major technological breakthroughs in clinical and laboratory ART, live birth rates remain low. Out of all IVF failures, it is estimated that 50% to 75% are due to implantation failure.[18,21]

In a study done by Schumacher *et al.*,[25] it was observed that early hCG during pregnancy shows number of immunologic functions and helps regulate local immune cell numbers and forces them to change their physical compositions so that they can function better in supporting and protection the pregnancy. This is beneficial as during early in pregnancy a number of functions takes place like angiogenesis, decidualization, trophoblast invasion, and placentation that are in turn regulated by the innate and adaptive immune cells.

Xiao-Yan *et al.* observed in their study while measuring hCG in human embryos in embryo cultures, that there is a positive correlation between implantation rates and beta hCG levels and embryo selection during IVF cycles. Embryos may be selected using hCG secreted by embryos as biomarker.[26]

A study similar to ours was done by Dehghani Firouzabadi *et al.*[27] in which a cohort of 159 study subjects were taken and divided in three groups of 53 each. All three groups were treated with ICSI/IVF. First group were given 500 IU of hCG intrauterine before ET, second group was given 1000 IU of hCG intrauterine before ET, and in the third group (control), ET was done without prior intrauterine hCG. It was observed that there was not significant difference in implantation rates, chemical pregnancy, and clinical pregnancy rates among the three groups. "Implantation rate in first second and third group were 18.86%, 13.52%, and 14.37% respectively, observed chemical pregnancy rates were 34%, 32.1%, and 35.3%, and clinical pregnancy rates were 34%, 32.1%, and 31.4%, respectively." Their study concluded there was no significant improvement in implantation rate, chemical pregnancy rate, and clinical pregnancy rate when patients were given intrauterine hCG 500/1000 IU before ET.

Similarly, a prospective randomized study was done by Santibanez *et al.*[28] in Mexico City in 2010 in which a total of 210 women suffering from infertility were included who were further divided into two subgroups. The intervention group included 101 patients and the underwent intrauterine instillation of 500 IU of hCG

before ET whereas the control group of 109 patients underwent ET without any intrauterine instillation of hCG. The results were analyzed and it was found that there was a significant improvement in implantation rate that was 52.4% in intervention group and 35.7% in control group with a *P* value of 0.014. Clinical pregnancy rate also showed significant results where intervention group showed pregnancy rate of 50.4% compared to 33% of that of control group with a *P* value of 0.010.

Similar to our study, Rebolloso *et al*.[29] also in a small randomized study in 2013 did not observe any difference in implantation rates (17.53% versus 17.67%; $P = 0.78$) or ongoing pregnancy rates (26.31% versus 26.51%; $P = 0.29$) between women who received 500 IU of IU hCG (n = 38) and controls (n = 83). Transfers included both cleavage stage and blastocyst transfers.

Ribaldi *et al*.[30] in a randomized trial on women older than 35 years and with previous two or more IVF failures undergoing vitrified/warmed blastocyst transfers concluded that intrauterine administration of rhCG, 6 h before blastocyst transfer, accelerates the endometrial receptivity increasing implantation and clinical pregnancy rates when low-grade blastocysts are exclusively available for transfer.

Zarei *et al*.[31] conducted a randomized double-blind clinical trial in Iran on 182 infertile women undergoing their first IVF/ICSI cycle. The study group (n = 84) received 250 mcg of intrauterine recombinant hCG and control group (n = 98) received placebo before ET. The study result concluded that patients who received intrauterine recombinant hCG before ET had significantly higher implantation (36.9% versus 22.4%; $P = 0.035$), clinical pregnancy rates (34.5% versus 20.4%; $P = 0.044$), and ongoing pregnancy rate (32.1% versus 18.4%; $P = 0.032$) when compared to those who received placebo.

In the study conducted by Mansour *et al*.[8] in two phases with three experimental arms (phase 1: IC-hCG 100 IU versus IC-hCG 200 IU versus control; and phase 2: IC-hCG 500 IU versus control), intrauterine injection of 100, 200, and 500 IU of hCG before ET was compared to control group. In this study, 167 patients in two groups received intrauterine injection of 100 or 200 IU of hCG before ET and pregnancy rate in these groups was assessed compared to control group. They could not find any statistically significant difference between the intervention groups and control group (pregnancy rate was 54% in the 100 hCG group, 57% in the 200 IU hCG group, and 60% in the control group). The pregnancy rate in 500 IU of hCG group (75%) was significantly higher as compared to the control group (60%).

In a study conducted by Laurentius Craciunas *et al*,[32] there was an increase in clinical pregnancy rate in the subgroup of women having cleavage-stage ETs with an IC-hCG dose of 500 IU or greater compared to women having cleavage-stage ETs with no IC-hCG (RR 1.41, 95% CI 1.25 to 1.58, seven RCTs, n = 1414, $I^2 = 0\%$, moderate quality evidence).

So as seen in various studies there is variation in results obtained in different studies, the difference can be due to no of factors like type of embryo selected, quality of embryo selected, time of implantation, quantity of hCG used, type of hCG used, age of patients, history of previous cycles, technique of implantation, selection bias, and so forth.

Our study was limited in itself due to smaller patient group, follow-up only until clinical pregnancy is confirmed, as patients were then followed up by their gynaecologists after that.

So, we need more studies with a standardised protocol considering various factors that have effect on results. More studies done using similar protocols and study design done on larger study group with better patient follow-up will be much more helpful in getting more reliable results regarding the use of hCG prior to ET.

CONCLUSIONS

We observed that there was no significant improvement in patients after giving the hCG before ET. Further studies with large groups would be helpful to strengthen our conclusions. Studies with different molecular hCG types would be helpful to help to reach better understanding. Thus, we conclude that intrauterine instillation of 500 IU of hCG prior embryo transfer does not help to improve implantation of embryo.

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Conflicts of interest

There are no conflicts of interest.

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