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The Effect of Intrauterine Injection of Human Chorionic Gonadotrophin on Implantation Rate During ICSI Cycles: Systemic Review and Meta-Analysis

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Abstract

Background: Failed implantation is a major limiting factor in assisted reproduction. Therefore, a better understanding of the molecular mechanisms responsible for implantation may help clinicians to treat infertility and early pregnancy loss.

Aim of Study: The aim of the present work was to perform a systemic review and meta-analysis to evaluate: The effects of intrauterine injection of the human chorionic gonadotrophin hormone and evaluate its significance prior to the embryo transfer. The effect of the different doses of human chorionic gonadotrophin (hCG) to be injected and their beneficial effects on the endometrial environment, implantation rate and pregnancy rate in in vitro fertilization (IVF) outcomes.

Subjects and Methods: We searched the PubMed, European clinical trial database (EuCLiD), Science direct (EMBASE), any randomized controlled trials (RCTs) that compared the intrauterine injection of HCG at the time of embryo transfer with nonintervention group were included, and data were extracted independently by two reviewers. The meta-analysis was performed by Revman 5.3 software. Eleven RCTs (3112 patients) were included in this meta-analysis.

Results: PubMed: Searching strategy: [Human chorionic gonadotropin or human chorionic gonadotrophin (hCG)] or recombinant human chorionic gonadotrophin (hCG) or recombinant human chorionic gonadotropin (r-hCG) and (intrauterine or intrauterine injection or endometrial infusion) and (assisted reproductive techniques or ART or in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) or in vitro fertilization or intracytoplasmic sperm injections or embryo transfer).

ScienceDirect (EMBASE): Searching strategy: [Human chorionic gonadotropin or human chorionic gonadotrophin (hCG)] and (intrauterine injection or endometrial infusion) and (assisted reproductive techniques or in vitro fertilization or intracytoplasmic sperm injections or embryo transfer). Filters: Medical journals only, open access, keyword in title "intrauterine".

CENTRAL: Searching strategy: (Human chorionic gonadotropin or human chorionic gonadotrophin (hCG) or recombinant human chorionic gonadotrophin (hCG) or recombinant human chorionic gonadotropin (r-hCG)) and (intrauterine or intrauterine injection or endometrial infusion) and (assisted reproductive techniques or ART or in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) or in vitro fertilization or intracytoplasmic sperm injections or embryo transfer).

Conclusion: Intrauterine injection of 500IU human chorionic gonadotrophin (hCG) at embryo transfer (ET) increases implantation and pregnancy rates. These findings suggest that intrauterine injection of human chorionic gonadotrophin (hCG) could be considered an adjuvant to traditional embryo transfer (ET) protocols.

Key Words: *Intrauterine injection – Human chorionic gonadotrophin – Implantation rate during ICSI cycles.*

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Introduction

IT is estimated that one out of seven couples worldwide and 15% of the couples in developed countries are suffering from infertility. In vitro fertilization (IVF) as the main treatments in infertile couples. It is a highly complex technique that involves the use of standardized protocols for a controlled ovarian stimulation, oocyte retrieval under ultrasound guidance, fertilization of gametes in the laboratory, embryo culturing, and embryo transfer [1]. The first step in IVF/intracytoplasmic sperm injection (ICSI) treatment is controlled ovarian stimulation with gonadotropins during each cycle [2].

The success rate for IVF reported range between 40.1% (in women <35 years) and 20.6% (in women in the 41-42 years) [3]. Successful implantation after IVF and ICSI cycles depends on various factors and requires precise synchronization between the embryo and the uterine environment [4]. Inappropriate implantation is the cause of two-thirds of IVF failures [5]. Implantation is regulated by many factors, the most important of which is the human chorionic gonadotrophin (hCG) concentration [3].

Support of the luteal phase is routinely administered worldwide to women undergoing IVF. a significantly higher pregnancy rate in the luteal phase support is reported compared with the pregnancy rates with no support. The most commonly used types of supplementation for the luteal phase support include the administration of the progesterone and/or hCG. It is still unclear whether progesterone alone, hCG alone, or a combination of both will provide the optimal degree of support [6].

hCG is a heterodimeric placental glycoprotein hormone that is required to maintain pregnancy and is initially produced by the blastocyst 6-8 days after fertilization [7]. HCG is one of the early embryonic signals in primates that is secreted by the embryo before its implantation and is the most important factor to control implantation [8].

Correlation between implantation rate and the beta-hCG concentration in IVF cycles is assessed in some studies. One study reported a positive correlation between the beta-hCG concentration and the implantation rate; also, other studies showed a positive correlation and significant increase in the clinical pregnancy rate after intrauterine injection of hCG before the embryo transfers [4].

Several studies have shown that the LH and hCG receptors are present in the human endometrium. In consideration of these reports, it seems that hCG that is used in luteal support might have a direct effect on the endometrium at implantation [9].

A positive correlation has been found between hCG concentration in embryo culture medium and implantation rate, suggesting that hCG secreted by embryos may be a useful biomarker for embryo selection in IVF [7]. Early embryonic hCG secretion is beneficial to implantation [10].

In his work, Licht et al., [11], stated that intrauterine injection of hCG (500IU/ml) significantly inhibits insulin-like growth factor binding protein 1 and macrophage colony-stimulating factor, while leukaemia inhibitory factor, vascular endothelial growth factor and matrix metallopeptidase 9 are significantly stimulated. These multiple effects appear to precede the classical endocrine role of hCG, and may be directly involved in the regulation of implantation.

Another prospective study trial to evaluate the intrauterine injection of lower doses of hCG below 500IU/hCG before the embryo transfer. In this clinical trial doses of 100IU/hCG, and 200IU/hCG were injected intrauterine in two different study randomized groups respectively but no significant difference had been reported versus the control group [4].

More clinical trials are suggested to evaluate the effect of intrauterine injection of hCG before the embryo transfers in IVF cycles in infertile women in a higher dose than 500IU/hCG. Injection of 700IU/hCG of intrauterine hCG but no significant difference against the study using 500IU/hCG is observed in this study [12].

The aim of the present work was to perform a systemic review and meta-analysis to evaluate: The effects of intrauterine injection of the human chorionic gonadotrophin hormone and evaluate its significance prior to the embryo transfer. The effect of the different doses of hCG to be injected and their beneficial effects on the endometrial environment, implantation rate and pregnancy rate in IVF outcomes.

Subjects and Methods

Search strategy:

human chorionic gonadotropin OR hcg OR recombinant hcg OR rhcg) AND (intrauterine OR intrauterine injection OR endometrial infusion) AND (assisted reproductive techniques OR art OR ivf OR icsi OR in vitro fertilization OR intracytoplasmic sperm injections OR embryo transfe were used as the keywords for PubMed, European clinical trial database (EuCLiD), Science direct (EMBASE) and any randomized controlled trials (RCTs) that compared the intrauterine injection of HCG at the time of embryo transfer with nonintervention group were included. The retrieval time was from the first publication of the journal to the end of December 2018. References included in the studies were also searched.

Inclusion criteria:

1- Retrospective RCT.
2- Or prospective RCT.
3- Before embryo transfer.
4- Comparative study.
5- Control group have placebo or no treatment.
6- Data regarding pregnancy outcomes were reported.

Exclusion criteria:

1- Experimental group containing other therapy.
2- Data unavailable for meta-analysis.
3- Review articles.

Data extraction and quality assessment:

Studies were screened by two reviewers (MA. and AA) independently, and any debate was solved by the opinion of the third reviewer (AF). First, the title and abstract of each study was read carefully to exclude the studies that clearly did not meet the inclusion criteria. Then, the full text of the remaining studies was read to determine which studies would be included in this study. The quality assessment of RCTs was compiled using modified GADAD scale which included sequence generation, allocation concealment blinding of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias.

Outcome measures:

The main efficacy outcome measures included the implantation rate, clinical pregnancy rate (defined as the presence of a gestational sac on ultrasound or gestational sac with fetal heart tones), the ongoing pregnancy rate (determined as pregnancies with over 12 weeks of gestation), and the live birth rate. The secondary outcome measures were biochemical pregnancy rate, miscarriage rate and ectopic pregnancy rate.

Statistical analysis:

All statistical analyses were performed using Revman 5.3 software. Dichotomous outcomes were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Heterogeneity was evaluated using the Q-test and I^2-index values, and reported for each outcome as a p-value and percentage, respectively. If heterogeneity was adopted (I^2<25% or >50% with p>0.1), meta-analysis used a fixed-effects model. Otherwise (I^2›_50% or I^2>25% with p<0.1), meta-analysis used a random-effects model. Sensitivity analysis was used to determine the stability of the results. Begg's funnel plot and Begg's test were used to assess publication bias.

Results

Study Question (in PICOS):

Participant	Intervention	Control	Outcome	Study design
Patients intended to undergo embryo transfer	Intrauterine hCG injection	Placebo or no injection	*Pregnancy outcomes:* - Pregnancy rate - Implantation rate - Miscarriage rate	Retrospective and prospective RCT

PRISMA system:

1- Identification: From databases.
2- Screening: Duplicates excluded.
3- Eligibility: Add full article, remove abstracts.
4- Included: NO of Qualitative synthesis, NO of Quantitative synthesis.

1- *Identifaction:*

A- PubMed:

Searching strategy: [Human chorionic gonadotropin or human chorionic gonadotrophin (hCG) or recombinant human chorionic gonadotrophin (hCG) or recombinant human chorionic gonadotropin (r-hCG)] and (intrauterine or intrauterine injection or endometrial infusion) and (assisted reproductive techniques or ART or in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) or in vitro fertilization or intracytoplasmic sperm injections or embryo transfer).

B- EULC:

Intrauterine hcg injection.

C- ScienceDirect (EMBASE):

Searching strategy: (Human chorionic gonadotropin or human chorionic gonadotrophin (hCG)) and (intrauterine injection or endometrial infusion) and (assisted reproductive techniques or in vitro fertilization or intracytoplasmic sperm injections or embryo transfer).

Filters: Medical journals only, open access, keyword in title "intrauterine".

D- CENTRAL:

Searching strategy: [Human chorionic gonadotropin or human chorionic gonadotrophin (hCG) or recombinant human chorionic gonadotrophin (hCG) or recombinant human chorionic gonadotropin (r-hCG)] and (intrauterine or intrauterine injection or endometrial infusion) and (assisted reproductive techniques or ART or in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) or in vitro fertilization or intracytoplasmic sperm injections or embryo transfer).

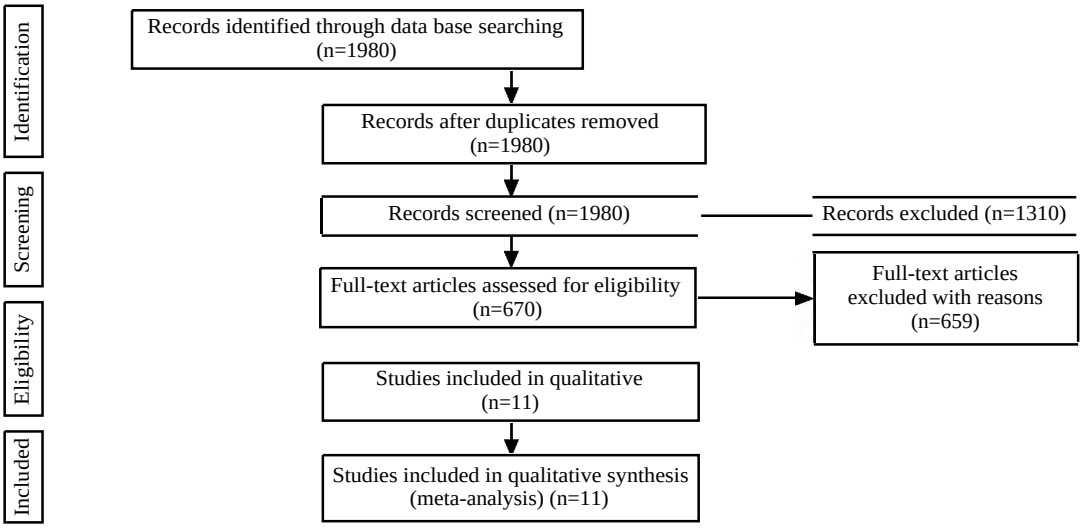

Fig. (1): Literature screening flow diagram.

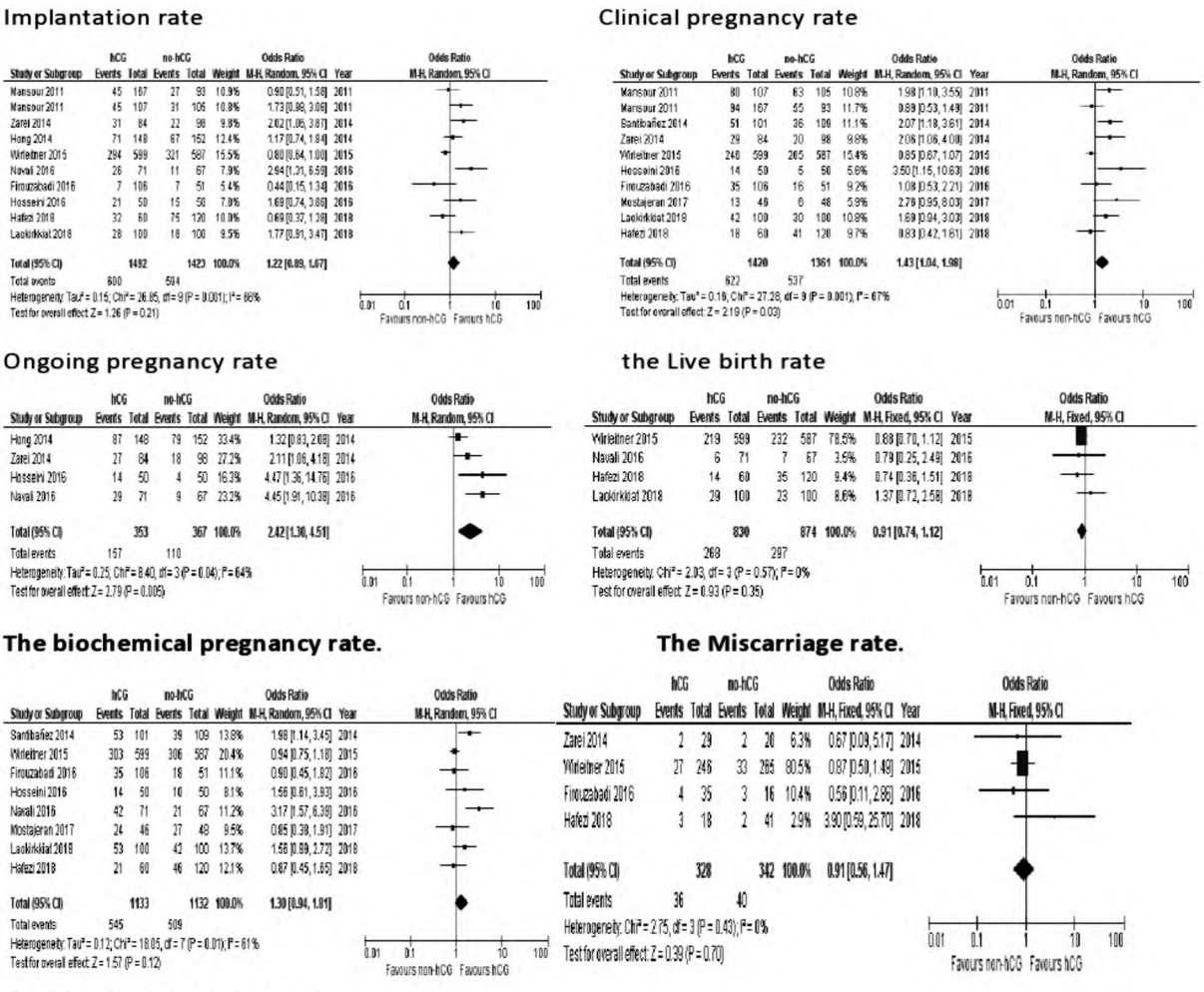

Fig. (2): Forest plots of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on implantation rate, clinical pregnancy rate, ongoing pregnancy rate, Live birth rate, Biochemical pregnancy rate, miscarriage rate and ectopic Pregnancy rate.

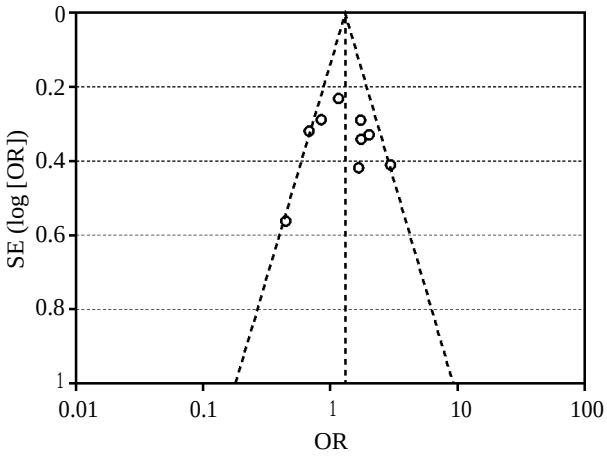

Fig. (3): Funnel plot after exclusions of studies with large effect sizes shows no study bias.

2- *Screening: Duplicates excluded:*

DB code	A	B	C	D	E	F	G
Data base	Pubmed	EULC	EMBASE	CENTRAL	Web of Science	SCOPUS	EBSCO
Found	573	32	1,261	114	0	0	0
After first examining		2		52			
Full article	417	0	240	13			
Free	105	0	21	13			
Related	16		2	13			
Total				31			
Removing Duplicates				23			
Eligible to criteria(Inclusion)				11			
Excluded by Exclusion Criteria				1 no data 1 case control study (not RCT) 3 reviews			

Eligibility:

Included:

- Retrospective RCT
- Or prospective RCT.
- Before embryo transfer.
- Comparative study.
- Control group have placebo or no treatment.
- Data regarding pregnancy outcomes were reported.

Excluded:

- Experimental group containing other therapy.
- Data unavailable for meta-analysis.
- Review articles.

4- *Included for Quantitative Synthesis:*

No.	Title	Author	Year
1	- Intrauterine administration of hCG immediately after oocyte retrieval and the outcome of ICSI: A randomized controlled trial.	Navali et al.	2016
2	- Effect of intrauterine injection of human chorionic gonadotropin before embryo transfer on pregnancy rate: A prospective randomized study.	Mostajeran et al.	2017
3	- The effect of intrauterine human chorionic gonadotropin injection before embryo transfer on the implantation and pregnancy rate in infertile patients: A randomized clinical trial.	Firouzabadi et al.	2016
4	- Intrauterine administration of human chorionic gonadotropin does not improve pregnancy and life birth rates independently of blastocyst quality: A randomised prospective study.	Wirleitner et al.	2015
5	- Endometrial infusion of human chorionic gonadotropin at the time of blastocyst embryo transfer does not impact clinical outcomes: A randomized, double-blind, placebo-controlled trial.	Hong et al.	2014
6	- Intrauterine administration of recombinant human chorionic gonadotropin before embryo transfer on outcome of in vitro fertilization/ intracytoplasmic sperm injection: A randomized clinical trial.	Zarei et al.	2014
7	- Effect of intrauterine injection of human chorionic gonadotropin before embryo transfer on clinical pregnancy rates from in vitro fertilisation cycles: A prospective study.	Santibañez et al.	2014

No.	Title	Author	Year
8	- Intrauterine injection of human chorionic gonadotropin before embryo transfer significantly improves the implantation and pregnancy rates in in vitro fertilization/intracytoplasmic sperm injection: A prospective randomized study (The 100 and 200 IU group).	Mansour et al.	2011
8	- Intrauterine injection of human chorionic gonadotropin before embryo transfer significantly improves the implantation and pregnancy rates in in vitro fertilization/intracytoplasmic sperm injection: A prospective randomized study (The 500 IU group).	Mansour et al.	2011
10	- The effect of intrauterine human chorionic gonadotropin flushing on live birth rate after vitrified-warmed embryo transfer in programmed cycles: A randomized clinical trial.	Hafezi et al.	2018
11	- Effect of Intrauterine Injection of Human Chorionic Gonadotropin Before Frozen-Thawed Embryo Transfer on Implantation and Clinical Pregnancy Rate: A Randomized Controlled Trial.	Hosseini et al.	2016
12	- Increased implantation rate after intrauterine infusion of a small volume of human chorionic gonadotropin at the time of embryo transfer: A randomized, double-blind controlled study.	Laokirkkiat et al.	2018

Data Analysis

Table (1): Summary of the methodologies of the RCTs included in the meta-analysis.

Study	Country	Age (≤)	No. of Participants		Treatment Details		Transfer type	M. Jaddad Scale
			Hcg	Control	hCG	Control		
1	Iran	41	71	67	- 500 IU: 0.1 ml (500 IU hCG) and 0.4 ml normal saline were given via insulin syringe immediatey after oocyte retrieval	0.5ml normal saline	4-8 cell embryos	5
2	Iran	37	46	48	- 700 IU of intrauterine hCG 10 min before embryo transfer	No treatment	Embryo transfer	5
3	Iran	34	106	51	- 500 or 1000 IU of hCG before ET.	No treatment	Embryo transfer	6
4	Austria	43	599	587	- 500 IU HCG (urinary) in 0.04 ml of culture media, cohort an infusion carried out 48 h before transfer, cohort B infusion 3 min beforeTransfer	0.04 ml culture media without HCG	Day 5 blastocyst	5
5	USA	43	148	152	- 500 IU of hCG diluted in ET media	Sham infusion of ET media	Fresh or frozen ET	7
6	Iran	40	84	98	- 250 mg (0.5 ml) of rhCG	0.5 ml normal saline	Fresh embryos	6
7	Mexico	40	101	109	- 500 IU HCG (urinary) in 0.02 ml culture media given 4 min before transfer	0.02 ml culture media without HCG	Day 3 fresh or frozen	6
8	Egypt	40	167	93	- 100 or 200 IU intrauterine infusion of hCG	No hCG	Fresh embryo transfer	6
8*	Egypt	40	107	105	- 500 IU of hCG	No hCG	Fresh embryo transfer	6
9	Iran	37	60	120	- 7-10 min before embryo transfer, 500 IU of hCG with a 40 μL of culture Medium	40 μL of culture medium Intrauterine and no treatment	Fresh embryo transfer	6
10	Iran	40	50	50	- 500 IU of hCG	No hCG	Fresh embryo transfer	6
11	Thailand	43	100	100	- 500 IU of hCG in 1 0μL culture medium	10 μL of culture medium	Fresh embryo transfer	6

Table (2): Frequency of events reposted in the included RCTs regarding pregnancy outcome parameters.

Study	Sample No.		Clinical pregnancy rate (n)		Implantation rate (n)		Biochemical pregnancy rate (n)		Miscarriage rate (n)		Ongoing pregnancy rate (n)		Ectopic pregnancy rate (n)		Live birth rate (n)	
	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C
1	71	67			26	11	42	21			29	9	1	0	6	7
2	46	48	13	6			24	27								
3	106	51	35	16	7	7	35	18	4	3						
4	599	587	246	265	294	321	303	306	27	33					219	232
5	148	152			71	67			17	11	87	79				
6	84	98	29	20	31	22			2	2	27	18	1	1		
7	101	109	51	36			53	39								
8	167	93	94	55	45	27										
8*	107	105	80	63	45	31										
9	60	120	18	41	32	75	21	46	3	2			0	3	14	35
10	50	50	14	5	21	15	14	10			14	4				
11	100	100	42	30	28	18	53	42							29	23

S: Study group. C: Control group.

Table (3): The size of effect of intrauterine hCG before embryo transfer in comparison to placebo or no-treatment.

Item	No. of Studies	I2 (%)	OR	95% CI	*p*-value
Clinical Pregnancy rate	9	67	1.43	1.04-1.98	0.03 *
Implantation rate	9	66	1.22	0.89-1.76	0.21
Biochemical pregnancy rate	8	61	1.3	0.94-1.81	0.12
Miscarriage rate	4	0	0.91	0.56-1.47	0.7
Ongoing pregnancy rate	4	64	2.42	1.3-4.51	0.005*
Ectopic Pregnancy rate	3	0	0.84	0.19	3.81
Live birth rate	4	0	0.91	0.74	1.12

OR: Odd ratio. CI: Confidence interval. *: Statistically significant difference.

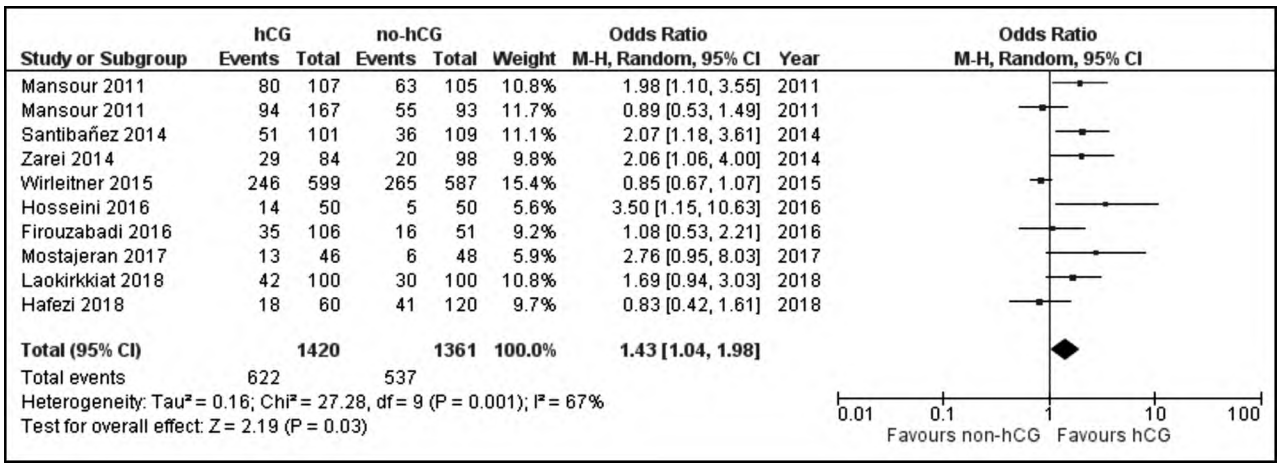

Fig. (4): Forest plot of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on clinical pregnancy rate.

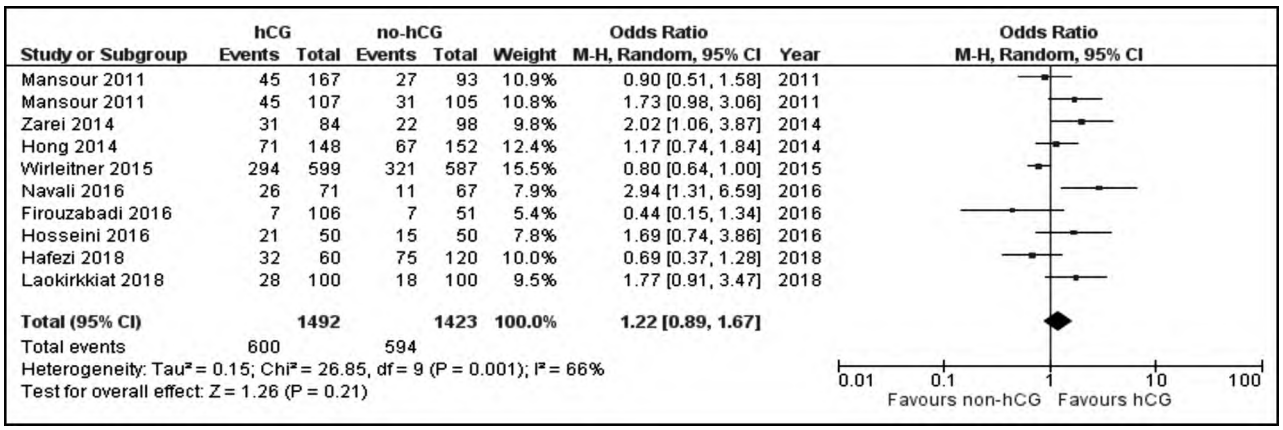

Fig. (5): Forest plot of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on Implantation rate.

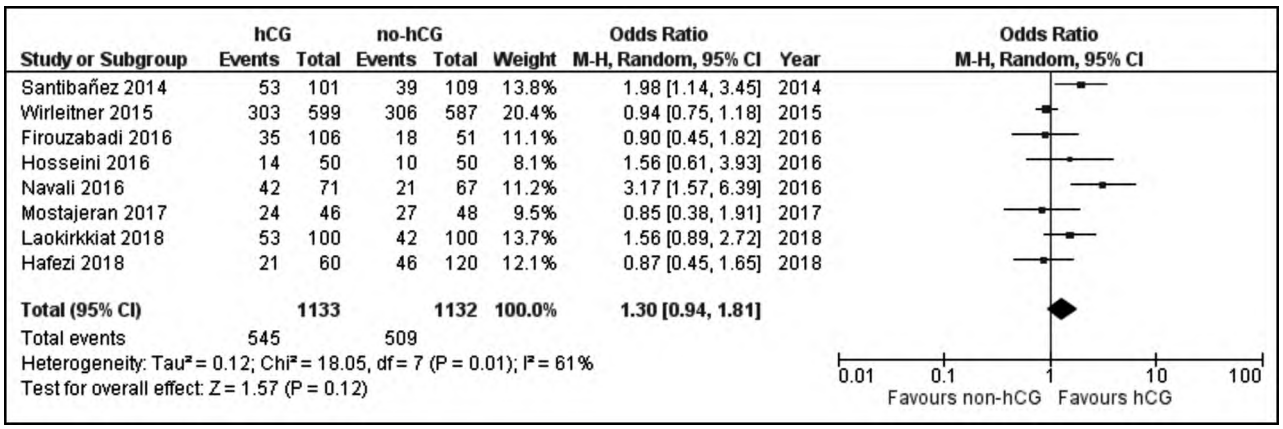

Fig. (6): Forest plot of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on Biochemical pregnancy rate.

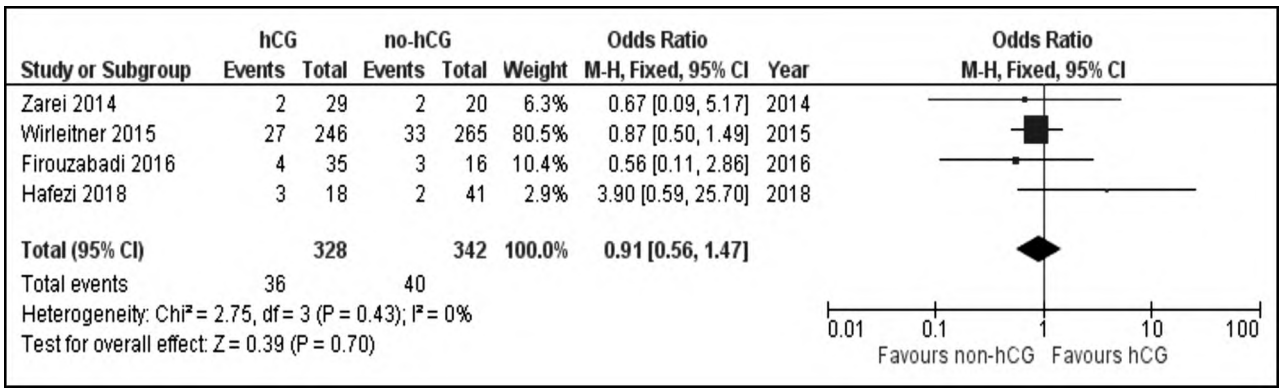

Fig. (7): Forest plot of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on Miscarriage rate.

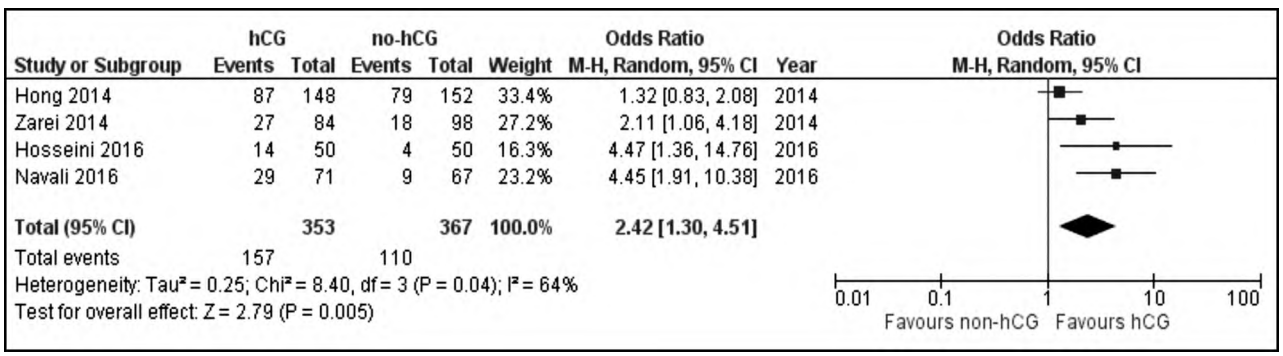

Fig. (8): Forest plot of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on Ongoing pregnancy rate.

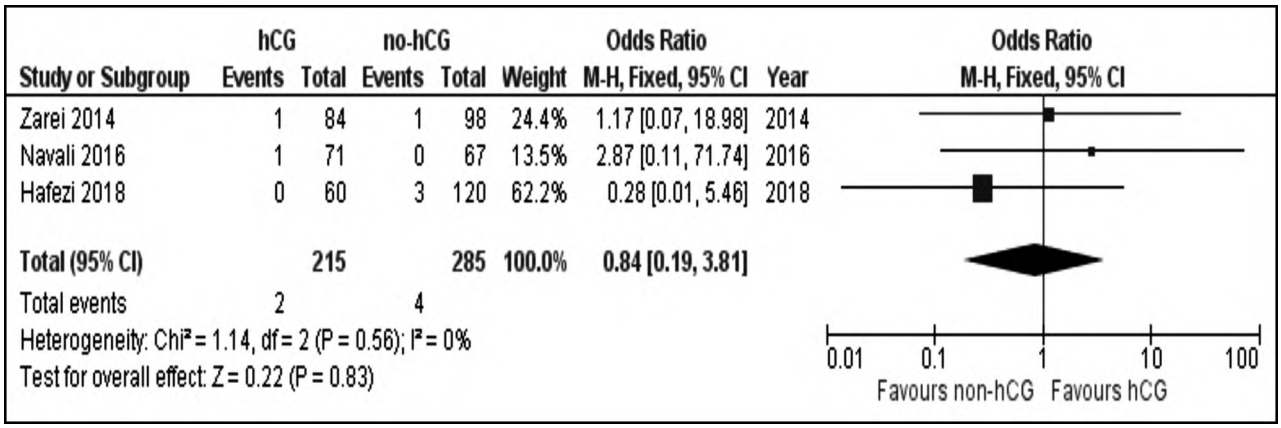

Fig. (9): Forest plot of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on Ectopic Pregnancy rate.

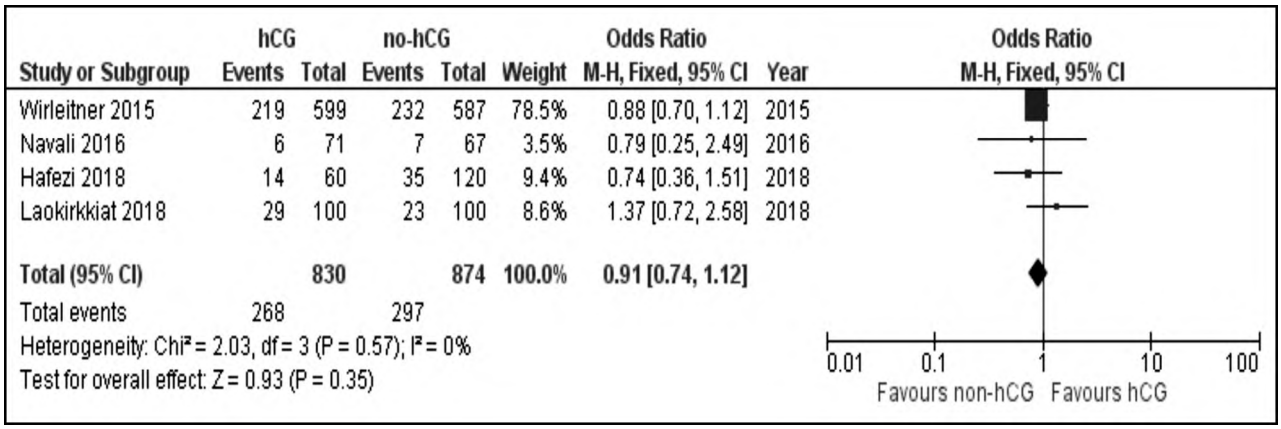

Fig. (10): Forest plot of the quantitative synthesis of the effect of intrauterine infusion of hCG prior to embryo transfer on Live birth rate.

Discussion

The benefit of intrauterine injection of hCG before transferring the embryos into the uterine cavity was based on the results of many studies showing that hCG is produced by the blastocyst before its implantation and is increasingly produced after implantation. hCG is the first known human embryo-derived signal through which the embryo influences the immunologic tolerance and angiogenesis at the maternal-fetal interface **[3]**.

It has also been demonstrated that hCG plays an important role in the proliferation of myometrial smooth muscle cells as well as the reduction of cell contractility via the regulation of the gap junctions between smooth muscle cells and intracellular calcium **[13]**. Moreover, hCG increases progesterone receptors.

No standard dose was agreed in the studies included. In our opinion, the different doses evaluated in these clinical trials may be a good point in favor of use of this regimen even in small doses. However, the results of this meta-analysis showed that there was no statistically significant difference in the implantation rate between the hCG group and control group.

In addition to that, there were no statistically significant differences in the live birth rate, biochemical pregnancy rate, miscarriage rate and ectopic pregnancy rate between both groups.

On the other side, the results indicated that there were statistically significant differences in the clinical and ongoing pregnancy rates between groups.

Comparison with other studies:

Conflicting results were postulated by many studies regarding the benefit of intra uterine perfusion of hCG before embryo transfer. Recently it has been reported that intrauterine injection of hCG in a dose of 500IU prevents the alteration of endometrial protein expression **[14]**.

The molecular properties of hCG were studied extensively as hCG was postulated to have a role in trophoblastic differentiation **[15]**. In studies using

intra uterine micro dialysis found that intrauterine hcg injection decreases insulin like growth factor binding protien1 (IGFBP1) and macrophage colony stimulating factor (MCSF) but increases leukemia inhibitory factor (LIF) and vascular endothelial growth factor (VEGF) [9]. Endometrial decidualization and vascularization [16]. Extra villous cytotrophoblast (EVT) cell proliferation, ETV invasion [17].

It is shown that there is a key role for hCG in regulating the inflammatory response and angiogenesis during embryo implantation, and an altered damaged endometrial receptivity by the IVF treatments can be overcame by injecting hCG before the embryo transfers [18].

The link between the embryo and its near environment is the core in the process of implantation. The pharmacokinetics of hCG could be known as the underlying mechanism of effect of intrauterine injection of hCG to improvement implantation and pregnancy outcome.

IL-8 is the mediator that enhances implantation and it is significantly increasing after administration of hCG [19].

It was proved that there is a positive correlation between the serum level of hCG with the level of trophoblast tolerance as well as the number of uterine natural killer cells [20].

hCG release of angiogenic factors, and angiogenic effects of hCG through receptor activation of transforming growth factor beta in endothelial cells are the possible mechanisms of hCG to improve implantation [12].

The different doses injected in different studies may be a prove to the biological effects of intra uterine infusion of hCG. In the study by Mansour et al., [4], the intrauterine injection of 100, 200, and 500IU of hCG before embryo transfer was compared to control group. However, the significant difference regarding pregnancy rate was detected with 500IU dose.

In a randomized controlled trial by Mostajeran et al., [12] they assessed the effects of intrauterine hCG injection before transferring the embryos on the outcome of the IVF or ICSI cycles and the results showed that the pregnancy rate was higher than in control group (28.6% vs.12.5%, respectively), but the difference between groups was not significantly different.

In the study of Mostajeran et al., [12], higher dose of hCG in comparison with Mansour et al., [4] study has been assessed, but they did not find a significant difference between intrauterine injection of 700IU of hCG in comparison with control group, which was in contrast to the findings in Mansour et al.'s study.

The cause of difference in the results between Mansoure and Modtajeran is the different inclusion and exclusion criteria [21].

In Zarei et al.'s study [22] pregnancy rate in patients who received 250 g g intrauterine rhCG before embryo transfer was 32.1% which was significantly higher than 18.4% in those who received placebo.

In a randomized trial by Santibañez et al., [21], patients with a history of recurrent miscarriage and implantation failure and received an intrauterine injection of 500IU of hCG before the embryo transfer, and pregnancy rate in this intervention group was compared with pregnancy rate in another control group who did not receive hCG. The pregnancy rate in hCG group was 50.4% and was significantly higher than in control group (33%).

This difference was not significantly different in a dose of 700IU of HCG [21]. Despite the higher pregnancy rate in hCG group if compared to control group in Mostajeran et al., [12] study (28.6% vs. 12.5%, respectively).

The differences between these results and may be explained by differences in sample size and time of injection. In addition, use of thawed embryo transfers in some studies is another possible cause of difference between findings [21].

However, this method has some advantages being not expensive and is a cost-effective method in infertile women. Other advantage is that it does not consume additional time for the embryologist and clinical staff and does not require complex training.

Limitations of this study:

Firstly, this meta-analysis lacked evaluation of the rate of OHSS in studies. That may be due to the dose of hCG given to patients was ranged from (100 to 700IU) and this considered low dose to produce OHSS. Secondly, although the random-effects model was used to minimize the heterogeneity, it cannot be abolished. The heterogeneity may relate to the size of studies that ranged from 94 to 1186 patients. Additionally, the quality of reported studies was uneven, which may also lead to heterogeneity. The methods of randomization, concealment, and blinding were unclear in some

included studies, some of which also had incomplete and selective outcome data. Thirdly, although comprehensive searches were undertaken to ensure that all eligible studies were included, there is still the possibility that some potentially eligible studies were left out. All these factors may lead to bias.

Conslusion:

In conclusion, intrauterine injection of 500IU hCG at ET increases implantation and pregnancy rates. These findings suggest that intrauterine injection of hCG could be considered an adjuvant to traditional ET protocols. However, others showed no beneficial effect before blastocyst transfer.

This study supports with goog evidence the positive association of intrauterine injection of HCG before embryo transfer with increase in clinical and ongoing pregnancy rate, but no changes neither in biochemical pregnancy nor in implantation rate. However more controlled trials are recommended to determine the precise role of intrauterine injection of Hcg on clinical, ongoing and biochemical pregnancy rates.

Recommendations:

1- Use of intrauterine injection of hCG prior to embryo transfer in ICSI/IVF cycles is not associated with increased risk of ectopic pregnancy or miscarriage.

2- Do not use intrauterine injection of hCG prior to embryo transfer to increase implantation rate or live birth rate, as there is no strong evidence to support a beneficial outcome from it.

3- Conduct more controlled trials to determine the precise role of intrauterine injection of hCG on clinical, ongoing, and biochemical pregnancy rates.

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تأثير حقن هرمون الجو نادوتروفين المشيمى داخل الرحم قبل نقل الأجنة على معدل الانغماس فى دورات الحقن المجهرى : دراسة تحليلية تلوية

خلفية البحث: يعُتبر فشل الانغراس عاملاً مقيداً رئيسياً فى تقنيات الإنجاب المساعد. ولذلك، فإن الفهم الأفضل للآليات الجزيئية المسؤولة عن الزرع قد يساعد الأطباء على علاج العقم وفقدان الحمل المبكر.

أهداف البحث: كان الهدف من هذا العمل إجراء مراجعة منهجية وتحليل تلوى لتقييم آثار الحقن داخل الرحم لهرمون الغدد التناسلية المشيمية البشرية وتقييم أهميته قبل نقل الأجنة. تأثير الجرعات المختلفة من موجهة الغدد التناسلية المشيمية البشرية المراد حقنها وآثارها المفيدة على بيئة بطانة الرحم ومعدل الانغراس ومعدل الحمل فى نتائج التلقيح الصناعى.

نتائج البحث: استراتيجية البحث (موجهة الغدد التناسلية المشيمية البشرية أو موجهة الغدد التناسلية المشيمية البشرية PubMed أو موجهة الغدد التناسلية المشيمية البشرية المؤتلفة أو موجهة الغدد التناسلية المشيمية البشرية المؤتلفة) و (تقنيات الحقن التناسلى أو الحقن التناسلى داخل الرحم) أو التخصيب فى المختبر أو الحقن المجهرى أو الإخصاب فى المختبر أو حقن الحيوانات المنوية داخل الهيولى أو نقل الأجنة.

استراتيجية البحث: موجهة الغدد التناسلية المشيمية البشرية أو موجهة الغدد Science Direct EMBASE التناسلية المشيمية البشرية و الحقن داخل الرحم أو تسريب بطانة الرحم و(تقنيات الإنجاب المساعدة أو الإخصاب فى المختبر أو حقن الحيوانات المنوية داخل الهيولى أو نقل الأجنة). المرشحات: المجلات الطبية فقط، الوصول المفتوح، الكلمة الرئيسية فى العنوان (داخل الرحم).

استراتيجية البحث: (موجهة الغدد التناسلية المشيمية البشرية أو موجهة الغدد التناسلية المشيمية CENTRAL البشرية أو الغدد التناسلية المشيمية البشرية المؤتلفة أو موجهة الغدد التناسلية المشيمية البشرية المؤتلفة) و (تقنيات الحقن التناسلى أو الحقن التناسلى داخل الرحم) أو التخصيب فى المختبر أو الحقن المجهرى أو الاخصاب فى المختبر أو حقن الحيوانات المنوية داخل الهيولى أو نقل الأجنة.

الخلاصة: الحقن داخل الرحم لـ ٥٠٠ وحدة دولية من موجهة الغدد التناسلية المشيمية البشرية عند نقل الأجنة يزيد من معدلات الانغراس والحمل. تشير هذه النتائج إلى أن الحقن داخل الرحم لموجهة الغدد التناسلية المشيمية البشرية يمكن اعتباره مساعداً لبروتوكولات نقل الأجنة التقليدية.