

## RESEARCH ARTICLE

# Outcome of Intrauterine Injection of Human Chorionic Gonadotropin before Embryo Transfer in Patients with Previous IVF/ICSI Failure: A Randomized Study

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## ABSTRACT

**Aim:** To evaluate the effect of intrauterine injection of 500 IU hCG before embryo transfer in patients with previous ICSI failure.

**Background:** The implantation process is the most important part of pregnancy, a lot of factors are responsible for implantation, it is well known that majority of pregnancies are lost during the implantation phase and often is undetected. It is known that hCG has an important function in angiogenesis and reduces the inflammatory response which in turn favor the implantation process. hCG is secreted early during the pregnancy, hence plays an important role.

**Methods:** A prospective randomized study was conducted in Radhakrishna Multispecialty Hospital and IVF Centre, Bengaluru, India. Total patients for ICSI cycle was 83(n). Out of which 32 patients were recruited in this study. The study group (n = 16) received intrauterine administration of 500 IU hCG before ET. The control group (n = 16) underwent ET without hCG.

**Results:** In both the groups, the mean age of the patients was around 29, the estradiol level mean was around 2569 ± 895 and in control group around 2467 ± 906. It was noted that fertilization rate in test group was around 88% and in control group around 75% hence showing that injection hCG proved its beneficial. It was noted that maximum embryos was from nondonor in test group, donor fresh embryos were around 3.

**Conclusion:** The intrauterine injection of 500 IU hCG before embryo transfer statistically improved the implantation rates and pregnancy rates with good outcome.

**Keywords:** Intrauterine hCG, Embryo transfer, Pregnancy rate.

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**Conflict of interest:** None

## INTRODUCTION

Every pregnancy is precious, and in today's fast world infertility of late has become a disease of rich than poor. Usually occurs in the working affluent class as seen in day to day practice. Infertility is defined as failure to conceive even after trying by regular mode of intercourse for more than a year of unprotected intercourse. IVF<sup>1</sup> of late has been an important modality in treatment of infertility. Standard protocols which includes controlled ovarian stimulation, follicular monitoring, oocyte retrieval under TVS ultrasonographic techniques, embryo culture and embryo transfer techniques<sup>2</sup> are followed. Asepsis also plays an important role contributing in success. As we know that the implantation process is the most important part of pregnancy, a lot of factors are responsible for implantation, it is well known that majority of pregnancies are lost during the implantation phase and often is undetected.<sup>3</sup> hCG helps in maintenance of corpus luteum after interacting with LHCG receptor of the blastocyst, thus allowing corpus luteum to secrete progesterone<sup>4-6</sup> which is essential in 1st trimester of pregnancy, hCG plays an important role in angiogenesis also. It is also understood that hCG may repel the immune cells of mother in turn protecting the fetus. In spite of all these the clinical pregnancy rates are around 30% only.<sup>7</sup> One of the most important of studies were done by Licht et al in 1998 which showed the direct effect of hCG on the endometrium.<sup>8</sup> hCG is also known to have an important role in placental development.<sup>9</sup>

It was reported that in several studies about the increase in C3 protein mRNA levels stromal cells in the endometrial biopsy culture of an infertile women during implantation window.<sup>10</sup> There is a definite positive correlation between beta-hCG concentration and implantation rates.<sup>11</sup> Studies are still being conducted in this field of interest. Hence, our study focuses on role of intrauterine hCG before embryo transfer and their effect on pregnancy rates and to confirm its benefits.

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## METHODS

This was a prospective study done in Radhakrishna Multi-specialty hospital and IVF Centre in Bengaluru in Southern India. All patients for IVF cycle were enrolled. A simple randomization was done following computerized program. Consent was taken from the patient. The patients were followed up to delivery. The ovulation induction techniques were given depending on individual characteristics. Prospective randomized study from April 2013-March 2014. Total patients for ICSI cycle (Fig. 1) was 83(n). Out of which 32 patients were recruited in this study. The study group (n = 16) received intrauterine administration of 500 IU hCG before ET. The control group (n = 16) underwent ET without hCG.

Ovarian stimulation was chosen as per patient characteristics. The embryo transfers were performed on day 3 (Fig. 2). ASRM guidelines were followed regarding the number of embryos to be transferred. During the procedure, the patient is put in lithotomy position. Perineum cleaned with NS, the cervix was visualized with Cusco's speculum. All the excess mucus was removed which may interfere with successful embryo transfer. 0.1 ml of hCG was diluted with fertilization media. "For injection, (Fig. 3) diluted hCG was taken in a IUI catheter and syringe, which was instilled 7 minutes before the embryo transfer under USG guidance about 0.5 cm near the Fundus. The soft catheter was introduced and preloaded embryos were transferred to the cavity under abdominal ultrasound guidance. After successful procedure, speculum withdrawn and catheter removed after a few minutes. In the control group, same technique was used but without the injection hCG in the beginning. The pregnancy test was performed two weeks after the transfer. If test was positive then was followed by transvaginal ultrasound technique to search for gestational sac and later heart rate. After the confirmation, patient is followed up until delivery.

The biochemical pregnancy was confirmed after quantitative values of a serum test of  $\beta$ -human chorionic gonadotropin was positive. The clinical pregnancy rate was considered as a viable pregnancy when there is evidence of a gestational sac, embryo and fetal heart rate at the time of ultrasound evaluation.

Both clinical and biochemical pregnancies are important to show the benefits of adding hCG to an altered embryo. According to guidelines and various studies, it was estimated that 30 to 40% of total IVF cycles actually became successful. Statistical analysis was done to compare the outcomes.

## RESULTS

Total patients for ICSI/IVF cycle was 83(n). Out of which 32 patients were recruited in this study. The study group (n = 16) received intrauterine administration of 500 IU hCG before ET. The control group (n = 16) underwent ET without hCG.

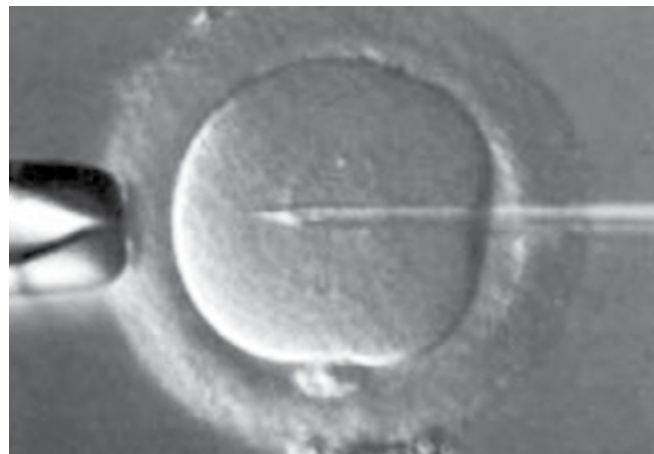


Fig. 1: ICSI

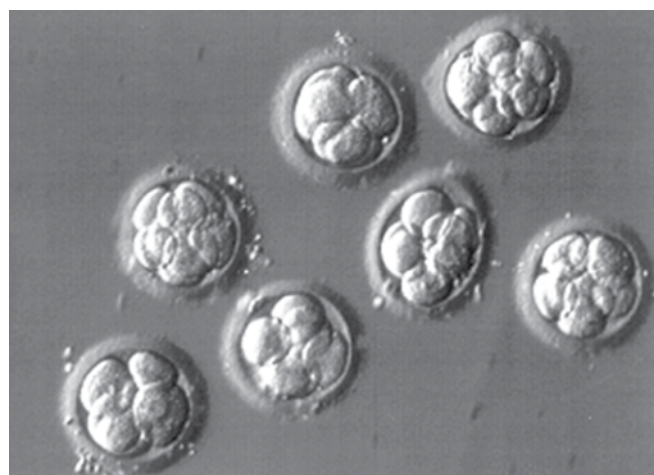


Fig. 2: Embryos



Fig. 3: hCG injection technique

It is noted from Table 1 that, in both the groups, the mean age of the patients was around 29, the estradiol level mean was around  $2569 \pm 895$  and, in control group, around  $2467 \pm 906$ .

It was noted from Table 2 that fertilization rate in test group was around 88% and in control group, around 75% hence showing that injection hCG proved its beneficial.

From Table 3, it was noted that maximum embryos were from nondonor in test group, donor fresh embryos were around 3.

## DISCUSSION

Hence from this study, we can elicit that there is a clear cut benefit of intrauterine 500 IU hCG before embryo transfer. It is a comparative study between two randomized groups to prove the outcome. These sort of procedures can definitely benefit various cases of failures in IVF/ICSI. As we know various studies have<sup>4</sup> definitely proved the important role of hCG in these conditions for implantation, etc. It is well known that majority of pregnancies are lost during the implantation phase and often is undetected.<sup>3</sup> It is known that hCG has an important function in angiogenesis and the inflammatory response which in turn favors the implantation process. hCG is secreted early during the pregnancy,<sup>3-5</sup> hence plays an important role. Various advances have occurred in the recent phases, however, pregnancy rates remain around 30% of the total.

This study included various patients including patients with history of repeat pregnancy losses. Selection biases were removed with computer based programs. Various standard protocols have been followed during the procedure of embryo transfer. Clear aseptic methods and ultrasound guidance to confirm the transfer was done. Our study clearly correlated with other various studies done all over the world.<sup>4-11</sup> The intrauterine injection of hCG before the

embryo transfer is a simple procedure. Adequate training is not required for the procedure. Once the procedure is finished then the patients are again followed up by confirming the pregnancy. Once confirmed then the patients are advised a TVS ultrasound to confirm gestational sac as well as heart beat. Then the patients are followed upto term until delivery in our setup.

## CONCLUSION

It was noted that intrauterine injection of 500 IU hCG before embryo transfer statistically improved the implantation rates and pregnancy rates with good outcome and can be performed easily by any infertility trained personnel without any special expertise.

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**Table 1:** General evaluation

	<i>hCG group</i>	<i>Control group</i>
No. of oocytes retrieved cycles (n)	16	16
Women's age	29.68 $\pm$ 4.63 (23-39)	29.62 $\pm$ 4.91 (21-37)
Infertility period	7.43 $\pm$ 1.89 (5-11)	6.87 $\pm$ 2.57 (4-13)
Estradiol level	2569 $\pm$ 895	2467 $\pm$ 906

**Table 2:** Postretrieval rates

	<i>hCG group</i>	<i>Control group</i>
No. of oocytes retrieved	11.43 $\pm$ 4.83 (3-21)	11.18 $\pm$ 3.60 (5-18)
No. of MII oocytes	10.43 $\pm$ 4.44 (2-17)	9.87 $\pm$ 3.03 (5-16)
Fertilization rate per retrieved oocyte	88%	75%
No. of embryo per transfer	2.9 $\pm$ 0.4	2.9 $\pm$ 0.5

**Table 3:** Embryo details

<i>Types of embryos</i>	<i>hCG group (N = 16)</i>	<i>Control group (N = 16)</i>
Fresh embryos from nondonor	8	7
Thawed embryos from nondonor	4	4
Donor fresh embryos	3	4
Donor thawed embryos	—	1
Thawed oocytes from nondonor	1	—
Fertilization rate per retrieved oocytes	88%	75%