

# Recombinant Human Chorionic Gonadotropin versus Purified Human Chorionic Gonadotropin Trigger for *In vitro* Fertilization Intracytoplasmic Sperm Injection Cycle

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## Abstract

The recombinant human luteinizing hormone or human chorionic gonadotropin (hCG) has substantially taken over the product which was formulated from the urine of pregnant women. In addition to this, a number of randomized controlled trials have been conducted comparing the significance of recombinant hCG (rHCG) with urinary hCG in assisted reproduction. Nevertheless, the present study has collected secondary information based on the nature of the chosen research area. The acquired data and information have been analyzed using content analysis technique to review the methodology and findings of the selected research articles. With the use of rHCG as well as purified hCG, the serum level was equivalent at day 5 among women underwent intracytoplasmic sperm injection (ICSI) but this level abnormally increased among those injected with rHCG thus, minimizing the rate of pregnancy. It has been concluded that purified hCG trigger plays a more efficient role in inducing oocyte maturation and increasing the rate of pregnancy among women undergoing *in vitro* fertilization ICSI cycle in comparison to rHCG trigger.

**Keywords:** Assisted reproduction, hCG, trigger

## INTRODUCTION

For normal conception to occur, luteinizing hormone (LH) surge in the preovulatory phase induces maturation and ovulation. For decades, urinary human chorionic gonadotropin (hCG) has gained significant attention due to its structural similarity with endogenous LH thus achieving final oocyte maturation and an accurate timing to retrieve oocytes in association with protocols of ovarian hyperstimulation in assisted reproduction (*in vitro* fertilization [IVF] and intracytoplasmic sperm injection [ICSI] cycles).<sup>[1]</sup> Nevertheless, urinary hCG administration along with multiple follicular developments in cycles leads to the formation of several corpora lutea, as well as, supraphysiological levels of progesterone and estradiol along with sustained luteotrophic effect. Some studies have claimed certain negative effects of hCG on the quality of the embryo and endometrial receptivity despite its use to a greater level, internationally.<sup>[2]</sup> On the other side, the formation of ovarian hyperstimulation syndrome (OHSS) might be deteriorated and facilitated through the sustained luteotrophic

effect. A gonadotrophin-releasing hormone agonist as an alternative to hCG has found to be a role of a trigger in the release of LH, endogenously.<sup>[3]</sup> The purified gonadotropin has, however, found to be playing a more effective role than recombinant hCG (rHCG) to induce ovulation.

Notwithstanding the fact that purified urinary hCG is observed to be associated with several disadvantages such as constant variation in the activity, uncontrolled source, and lack of purity that could result in a range of different clinical outcomes.<sup>[4]</sup> In accordance with the World Health Organization, rHCG; as an alternative to the purified hCG, is used with ICSI and IVF

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for the final oocyte maturation in women. Correspondingly, it has been stated by several other studies that rHCG has substantially taken over the product which was formulated from the urine of pregnant women.<sup>[5]</sup> In addition to this, a number of randomized controlled trials have been conducted comparing the significance of rHCG with urinary hCG in assisted reproduction. However, equal numbers of oocytes were relatively acquired when women were triggered with either of these treatment groups.

The rhCG is derived through recombinant DNA technology from genetically engineered hamster ovary cells. In comparison to the purified trigger, the rHCG has gained significant attention because of its substantial purity, facilitating the quantitation as well as characterization by means of physicochemical, decreasing the need for bioassays of animals.<sup>[5]</sup> Nevertheless, little information has been reported to date in the preexisting literature on the cytoplasmic as well as nuclear maturation of women's oocytes acquiring rHCG. As stated by studies that both cytoplasmic and nuclear maturation must be completed in coordination to assure circumstances for consequent fertilization.<sup>[6]</sup> However, it has been observed that it is quite challenging in standard IVF to evaluate the cytoplasmic morphology of oocytes along with the appropriate phase of maturation due to the fact that cumulus always surrounds the oocytes.<sup>[7]</sup> The present research has been conducted to determine and assess the comparison between the efficacy of rHCG trigger and purified hCG trigger for IVF-ICSI cycle regarding the number of oocytes retrieved. The secondary objective of this study is to identify the pregnancy rate provided to either of the trigger in the maturation of oocytes.

## METHODS

Two important online databases have been accessed in this study, including PubMed and ScienceDirect. However, certain filters have been applied on these two databases while retrieving data and information on the efficiency of rHCG trigger and purified urinary hCG trigger for IVF-ICSI cycle. These filters include, the date i.e., the data published since 2010 was accessed, free full-text and both randomized control trials and original research studies were accessed.

To access relevant information on the aforementioned online databases, some key terms have been devised to narrow down the hit of search. These include, "hCG," "recombinant hCG," "purified hCG," "recombinant hCG trigger," "purified hCG trigger," "ICSI cycle," and "IVF."

Research studies were retrieved, and based on their title and abstract, only five of them have been included in the present research to be reviewed and used for the formulation of the research outcomes. The acquired data and information have been analyzed using content analysis technique to review the methodology and findings of the selected research articles.<sup>[8,9]</sup> Types of patient participant were those couples with infertility undergoing IVF-ICSI, who had triggering of ovulation with either purified urinary hCG 10000 IU or rHCG 250 µg. The

primary outcome was total number of oocytes retrieved, the secondary outcome was live birth rate or pregnancy rate if available.

## Inclusion criteria

Eligible studies include those underwent IVF-ICSI with either protocol antagonist or long agonist down regulation, where the age ranges between 20 and 40, and regular menstruation. Studies excluded those who used triggering by gonadotrophin agonist or recombinant LH injections, age more than 40, and cycles of intrauterine insemination or timed intercourse with superovulation.

## RESULTS AND DISCUSSION

A randomized controlled trial was conducted by Madani *et al.* reviewed and compared the efficacy of rHCG trigger and purified or urinary hCG trigger in inducing the number of oocytes in ovulation among women who underwent ICSI cycles.<sup>[10]</sup> Their findings showed evidence that the average number of oocytes retrieved per follicles includes  $77.16 \pm 17.61$ ,  $69.84 \pm 17.44$ , and  $71.82 \pm 15.09$  in 500 µg rHCG, 250 µg rHCG, and 10,000 IU urinary hCG, respectively. They conclude that equivalent number of oocytes was retrieved in both groups.<sup>[10]</sup>

Similarly, Papanikolaou *et al.* conducted a randomized control trial of 119 patients with antagonist protocol who claimed that there found to be high number of oocytes retrieved, higher pregnancy rate, and higher live birth rate by rHCG group but similar blastulation rate in both groups, higher first-trimester abortion with the urinary group and higher OHSS with the recombinant group.<sup>[11]</sup> On the contrary, Srinivas *et al.* showed evidence that women who were treated with rHCG trigger depicted an equivalent number of oocytes retrieved in both groups but a higher pregnancy rate within the urinary purified group although it is not significant statistically, in addition to similar side effects as OHSS.<sup>[12]</sup> Berger *et al.* reviewed the impact of rHCG trigger on the rate of ovulation in the IVF-ICSI cycle, he confirmed similar outcomes of urinary hCG and rHCG.<sup>[13]</sup>

However, Mosaad *et al.* showed that the number of oocytes retrieved is similar in both groups but the pregnancy rate was higher in the urinary group. Moreover, rHCG group had higher rate of progesterone elevation<sup>[14]</sup> and this elevation can have a detrimental effect on implantation and thus on pregnancy rate.<sup>[15,16]</sup>

It is evident from these research findings that the effectiveness of purified hCG is significantly higher than rhCG.

Considering the acquired research outcomes, this review highlights increasing the rate of pregnancy among women who undergone an IVF ICSI cycle, purified urinary hCG trigger plays a more efficient role in comparison to recombinant-hCG that reduces the probability of pregnancy in females as a result of its disadvantage in producing abnormal levels of serum progesterone.<sup>[17]</sup> From the aforementioned results that despite

recombinant-hCG trigger being clearer and purer than purified hCG trigger, the number of oocytes produced by both of these treatment groups was equivalent.<sup>[10]</sup> This finding is against Youssef *et al.* were they found that the clinical pregnancy rate was similar in both group urinary hCG and rHCG.<sup>[18]</sup> Another point regarding the number of oocytes retrieved that the number of oocytes was equal in both groups; in line with Eftekhar *et al.*<sup>[1,18]</sup>

This review article has some limitations; it has not provided an in-depth information on the efficiency of other comparative triggers including agonist trigger and recombinant LH, in the context of some other aspects using these two triggers that could play role in enhancing the rate of pregnancy and oocyte maturation in a more effective and pure manner. The strength of this review is that it has significantly determined that the purified hCG trigger is more effective than rHCG trigger. As the number of oocytes retrieved was similar in both groups, but pregnancy rate is higher with the purified could be due to the similarity with the normal physiology of ovulation.

## CONCLUSION

Purified hCG trigger has an equivalent efficacy in inducing oocyte maturation, safety profile, and positive pregnancy rates among women undergoing IVF-ICSI cycle in comparison to rHCG trigger. Since the cost is less with the urinary purified hCG; it should be a recommended first choice for triggering ovulation.

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## Conflicts of interest

There are no conflicts of interest.

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