

## ORIGINAL RESEARCH

### Satisfaction and usability of the recombinant chorionic gonadotropin prefilled pen: a survey in Italy

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#### Abstract

**Background:** Due to high purity, recombinant human chorionic gonadotropin (hCG) is suitable for subcutaneous injection, and hence for self-administration, in assisted reproduction. To increase usability and reduce the risk of dosing errors, a prefilled pen was produced. We investigated the ease of administration and satisfaction with the product amongst patients and healthcare professionals.

**Methods:** A survey was conducted amongst women with infertility who underwent in vitro fertilization treatments with recombinant hCG to trigger ovulation in various clinics in Italy.

**Results:** A total of 276 Italian women were interviewed. The median score of preference for the prefilled pen in comparison with hCG powder to be reconstituted in the solvent was rated as 9 (range 8–10), and 125 women answered that the prefilled pen had major advantages. Reasons for preference of the prefilled pen were linked to ease of use and safety: avoidance of

dosage mistakes and of concern of such, ease of administration, certainty that the drug is correctly taken, safe administration and no anxiety. The procedure for recombinant hCG administration through the prefilled pen was judged as easy by 80% of respondents, with a median score of 9 (range 8–10) for easiness on a 1–10 scale. Out of 276 respondents, 249 (90%) had no problem with the injection.

**Conclusion:** Overall, the respondents reported a favourable perception of the prefilled pen with hCG, which was reported to be easy to use and perceived to prevent dosage mistakes.

**Keywords:** assisted reproduction, human chorionic gonadotropin, prefilled pen, survey.

#### Citation

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## Introduction

In assisted reproduction techniques, human chorionic gonadotropin (hCG) purified from the urine of pregnant women has been used to trigger the final stages of oocyte maturation, mimicking the luteinizing hormone surge. Indeed, the two hormones have considerable structural similarities and stimulate the same receptor.<sup>1,2</sup> It has long been known that urinary preparations of hCG (u-hCG) have considerable batch-to-batch variation and contain several contaminant proteins, mainly due to uncontrolled sources. These drawbacks result in variable clinical results, with unpredictable oocyte retrieval, and potentially contribute to the risk of ovarian hyperstimulation syndrome.<sup>2–4</sup> Recombinant hCG (r-hCG) is produced from genetically engineered Chinese hamster ovary cells through recombinant DNA technology. The hCG secreted into the culture medium is purified by chromatography

to yield a product with high specific activity. R-hCG has a pharmacokinetic profile comparable to that of u-hCG, within a dose range of 500–20,000 IU and has an elimination half-life of 30 hours.<sup>5</sup> The high purity of this product facilitates characterization and quantitation by physicochemical means and makes the drug suitable for subcutaneous injection and, hence, self-administration.<sup>1,2,6</sup>

An open-label, comparative, randomized, prospective clinical study of 297 women with infertility undergoing ovarian stimulation for assisted reproduction demonstrated that 250 mg of subcutaneous r-hCG was equivalent to 10,000 U of u-hCG in the induction of final follicular maturation. The two preparations were both well tolerated and had similar results with regards to number of retrieved oocytes, oocyte maturity, embryo development, luteal function and pregnancy outcome.<sup>6</sup>

Further studies were published confirming these results, and a meta-analysis published in 2016 found that there was no conclusive difference between r-hCG and u-hCG in terms of ongoing pregnancy/live birth rates (OR 1.15, 95% CI 0.89–1.49), in the incidence of ovarian hyperstimulation syndrome and in miscarriage rates (OR 0.72, 95% CI 0.41–1.25).<sup>7</sup>

Although r-hCG is safe and suitable for self-administration, many women may feel concerned by the fear of dosage or injection mistakes and may find it difficult to handle a syringe. To facilitate the procedure, a prefilled pen has been developed. Women with infertility trying to conceive and nurses attending these patients were questioned on the usability and risk of dosing errors comparing the existing r-hCG prefilled syringe with a prefilled pen. The overall risk of dosing errors was found to be similar with the pen than with the existing prefilled syringe, whereas the ease of use of the pen was rated favourably by patients and nurses.<sup>8</sup>

As a further insight into the clinical practice to optimize the use of the prefilled pen, a survey was conducted to investigate whether self-administration of r-hCG is correctly performed by Italian women and to evaluate patient satisfaction with the prefilled pen.

## Methods

A survey was developed with the assistance of an independent third party with broad experience in market research in the pharmaceutical setting (Doxa Pharma, Milan, Italy). The survey was proposed on the day of prefilled pen pick-up to all consecutive women who underwent in vitro fertilization treatments and were treated with r-hCG for ovulation trigger. At the time of triggering, the choice of medication (r-hCG *versus* u-hCG) was solely up to the physician and the patients had no choice. The questionnaire was delivered online via a computer-assisted personal interview, between February and April 2020. Closed multiple-choice questions, with either single or multiple answers, were included. Preferences were expressed on a 1–10 score scale. Interviews were anonymous. According to Italian law, when anonymous surveys are conducted without the use of clinical data, no ethical approval is required. The questionnaire contained semistructured questions. Data were analysed by descriptive statistics and were presented as absolute numbers or percentages or median (interquartile range). Due to the descriptive nature of the study, statistical analysis was not expected.

## Results

Overall, 276 Italian women were interviewed. They were based in different regions (108 in Lombardia, 25 in Veneto, 52 in Lazio, 33 in Campania and 58 in Puglia). The median age was 38 (35–41) years, with only 6% younger than 30 years or older than 45 years.

Ovarian stimulation had been previously performed in 70% of respondents. Preference for the preparation style of the r-hCG

was investigated: on a 1–10 scale, where 10 corresponds to maximum satisfaction, the median score of preference for the prefilled pen in comparison with hCG in powder form to be reconstituted in the solvent was rated as 9 (range 8–10), and 125 women answered that there was a considerable advantage in the use of the prefilled pen.

Reasons for the preference of the prefilled pen were linked to ease of use and safety: avoidance of dosage mistakes (score 9, range 8–10) and of concern of such (score 9, range 8–10), easy administration (score 9, range 7–10), certainty that the drug is correctly taken (score 9, range 7–10), safe administration (score 9, range 7–10) and no anxiety (score 9, range 7–10). Perception of increased efficacy due to the preparation received a lower score (8, range 6–10).

The procedure of administration of the r-hCG prefilled pen was judged as easy by 80% of respondents, with a median score of 9 (range 8–10). Out of 276 respondents, 249 (90%) had no problem with the injection and 204 (74%) did not ask for advice. An online tutorial video was viewed by 80 (29%) women. The prefilled pen would be recommended to other women by 247 (90%) respondents.

## Discussion

This is a descriptive study aiming to define the satisfaction of the population using the r-hCG prefilled pen. The article presents the information obtained from a survey on women undergoing ovarian stimulation with a prefilled pen preparation of r-hCG, to investigate the perception and satisfaction with the product. Overall, the respondents reported a favourable perception of the prefilled pen, reporting that it is easy to use and was perceived to prevent dosage mistakes. Most of the respondents expressed a high preference for the prefilled pen in comparison with a reconstituted powder with the same hormonal product.

These results are in agreement with the study by Saunders et al. in Germany, investigating patient and nurse perceptions of the usability of the r-hCG prefilled pen in comparison with a prefilled syringe.<sup>8</sup> A higher cumulative usability test score was found for the prefilled pen; the overall risk of dosing errors was not higher with the pen. The ease of use of the pen was rated favourably by both patients and nurses. Both user groups were confident that they could inject the correct dose using the pen.<sup>8</sup>

The r-hCG was demonstrated to be intact, free from contaminant proteins and to contain very low levels of oxidized gonadotropin hCG.<sup>9</sup> These characteristics make the recombinant product more reliable in comparison with u-hCG, which contains a number of urine-derived protein contaminants as well as hCG-related metabolites, mainly oxidized molecules.<sup>9</sup>

As reported earlier, a clinical trial demonstrated r-hCG to be well tolerated and effective in the induction of final follicular maturation and to be not inferior to u-hCG for several clinical

parameters.<sup>6</sup> Furthermore, a first meta-analysis reported significantly less frequent local injection site effects with r-hCG than with u-hCG and no differences in clinical and embryological parameters.<sup>10</sup> Another meta-analysis on 18 randomized studies including almost 3000 women, concluded that there were no differences between r-hCG and u-hCG in live birth or ongoing pregnancy rates or rates of ovarian hyperstimulation syndrome, which is one of the most feared side effect of the procedure.<sup>7</sup>

The findings reported by the present article should be interpreted according to the following limitations. First, the survey had a merely descriptive nature, and therefore no statistical analyses were conducted. Moreover, only those patients who used r-hCG were invited to answer

the questionnaire. Thus, it was not possible to perform a real comparison of the use of r-hCG in the prefilled pen or reconstituted powder form.

## Conclusion

In summary, the prefilled pen preparation of r-hCG has many advantages for both patients and healthcare professionals. The purity of the compound prevents batch-to-batch variation, facilitates subcutaneous use and provides a lower risk of side effects. The prefilled pen, on the other hand, helps women to self-administer the compound without concerns regarding dosage or injection mistakes and makes them more comfortable with the treatment.

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