



Effectiveness and safety of gonadotropins used in female infertility: a population-based study in the Lazio region, Italy

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Abstract

Purpose Infertility is a topic of growing interest, and female infertility is often treated with gonadotropins. Evidence regarding comparative safety and efficacy of different gonadotropin formulations is available from clinical studies, while real-world data are missing. The present study aims to investigate effectiveness and safety of treatment with different gonadotropin formulations in women undergoing medically assisted procreation treatments in Latium, a region in central Italy, through a real-world data approach.

Methods A retrospective population-based cohort study in women between the ages of 18 and 45 years who were prescribed with at least one gonadotropin between 2007 and 2019 was conducted. Women were enrolled from the regional drug dispense registry, and data on their clinical history, exposure to therapeutic cycles (based on recombinant “REC” or extractives “EXT” gonadotropin, or combined protocol “CMD” (REC + EXT)), and maternal/infantile outcomes were linked from the regional healthcare administrative databases. Multivariate logistic regression models were applied to estimate the association between exposure and outcomes.

Results Overall, 90,292 therapeutic cycles prescribed to 35,899 women were linked to pregnancies. Overall, 15.8% of cycles successfully led to pregnancy. Compared to extractives, recombinant and combined treatments showed a stronger association with conception rate ($RR_{REC} \text{ adj} = 1.06$, 95% CI: 1.01–1.12; $RR_{CBD} \text{ adj} = 1.17$, 95% CI: 1.11–1.24). Maternal outcomes occurred in less than 5% of deliveries, and no significant differences between treatments were observed (REC vs EXT, pre-eclampsia: $RR \text{ adj} = 1.24$, 95% CI: 0.86–1.79, ovarian hyperstimulation syndrome: $RR \text{ adj} = 1.25$, 95% CI: 0.59–2.65, gestational diabetes: $RR \text{ adj} = 1.06$, 95% CI: 0.84–1.35). Regarding infantile outcomes, similar results were obtained for different gonadotropin formulations (REC vs EXT: low birth weight: $RR \text{ adj} = 0.98$, 95% CI: 0.83–1.26, multiple births: $RR \text{ adj} = 1.06$, 95% CI: 0.92–1.23, preterm birth: $RR \text{ adj} = 1.03$, 95% CI: 0.92–1.26).

Conclusions Efficacy and safety profiles of REC proved to be similar to those of EXT. Regarding the efficacy in terms of conception rate and birth rate, protocols using the combined approach performed slightly better. Outcomes related to maternal and infantile safety were generally very rare, and safety features were overlapping between gonadotropin formulations.

Keywords Gonadotropins · Infertility · Administrative health data · Real-world evidence · Cohort · Effectiveness · Safety

Background

According to the World Health Organisation, infertility affects up to 15% of reproductive-aged couples worldwide [1], and the same percentage has been estimated also in Italy [2]. Among couples hit by infertility, in most cases, causes can be attributable to either males (qualitative and quantitative alterations of semen parameters) or females (tubal disease, ovulatory disorders, endometriosis), while in approximately 15% of couples' infertility remains unexplained Carson and Kallen [3].

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