

Controlled Ovarian Stimulation with Urinary Gonadotrophins and Recombinant Gonadotrophins in Current Practice

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The main objective of the this study is to compare the effectiveness of ovarian stimulation with recombinant gonadotrophins (FSHr) versus urinary gonadotrophins (hMG) within the number of oocytes obtained and the number of embryos in the two patient groups, according to age groups and associated pathologies. The study design was retrospective, monocentric. All patients (71) who have addressed the In Vitro Fertilization Clinic of the Prof. Dr. Panait Sirbu Clinical Obstetrics and Gynecology Hospital during 01.01.2010 and 31.12.2010 were included in this research. The total number of oocytes (8.5 ± 3.9 vs 5.7 ± 3.9 , $p=0.045$), the number of fertilized oocytes (7.5 ± 3.6 versus 3.6 ± 2.8 $p=0.004$) and the number of embryos (6.6 ± 3.5 versus 3.7 ± 2.6 , $p=0.013$) were higher in women under 35 years of age treated with recombinant FSHr compared to women treated with urinary gonadotrophins hMG. Ovarian stimulation with recombinant gonadotrophins provides a greater number of oocytes and a greater number of embryos in all patients, regardless of age and associated pathology. There are many variables that can influence the success rate, but the first variable that can be controlled is the choice of FSHr in daily clinical practice.

Keywords: ovarian stimulation, gonadotrophins, embryos

Assisted Human Reproduction (ART) is a science that many practitioners compare with an art because the choice of stimulation protocols and drugs according to the particularity of each infertility case requires experience and a clinical sense, which are not found in standardized protocols. The therapeutic approach varies between clinics, and the choice of ovarian stimulation drugs often depends on the clinician's experience with a particular product, as well as the results previously obtained in similar cases. However, ovarian stimulation in IVF is extensively studied and improved, with the goal of obtaining standardized protocols to ease the work of clinicians and maximize the response to treatment in each population of patients.

Stimulation protocols differ through the initiation of stimulation and the drugs used for inhibition and stimulation. The main parameter that influences the clinician in choosing the ovarian stimulation protocol is patient's age. Age and ovarian reserve (assessed by AMH, serum anti Mullerian hormone or AFC - antral follicle count) cannot be changed [1-3] and are the only ones that provide an idea of the number of oocytes that could be harvested even before ovarian stimulation beginning. Starting from these two constants (age and ovarian reserve) that cannot be changed, each clinician chooses a stimulation protocol in favor of another, as well as the optimal dose of gonadotrophins for each patient [4-7].

Gonadotrophins have been used to treat infertility since the 1930's. The first preparations had animal origin, being followed by the appearance of human origin drugs (extracted from pituitary glands of human corpses). An important step forward was obtaining human menopausal gonadotrophins from the urine of postmenopausal women. Subsequently, highly purified urinary gonadotrophins produced by DNA technology appeared. Recombinant gonadotrophins are obtained by DNA technology using

culture on hamster ovarian tissue and are characterized by a high specificity and purity close to 100% [8,9].

Ovarian stimulation protocols and available medication

ART specialists may choose to use a gonadotropin releasing hormone (GnRH) agonist or a GnRH antagonist in order to suppress the LH (luteinizing hormone) peak. The treatment regimen may be started midway through the luteal phase, approximately one week after ovulation by administering a GnRH agonist, while gonadotropin stimulation may be started after confirmation of pituitary down regulation occurrence (long protocol) [10,11]. In case of short protocol, ovarian stimulation with gonadotrophins starts from day 2-3 of the menstrual cycle, and an agonist or GnRH antagonist can alternatively be used to prevent LH peak [12]. Substances used for stimulation are urinary or recombinant FSH, urinary or recombinant FSH and LH.

Until the appearance of GnRH antagonists, the long protocol was the most frequently used. Subsequently, because of the longer treatment duration, the higher doses of gonadotrophins required and the risk of hyperstimulation, the long protocol fell to second place in favor of the short GnRH antagonist protocol. Antagonist stimulation remains the first option for poor responders, primarily to avoid the suppressive effects that agonists have on follicular response and secondly to prevent premature LH peak, often seen in GnRH agonist alone stimulation [13].

Urinary hMG (human menopausal gonadotropin), derived from postmenopausal women's urine was for a long time the standard product used in controlled ovarian stimulation and ovulation induction. It contains both FSH (follicle stimulating hormone) and LH, but also other potentially biologically active urinary proteins. Some of the biological activity of LH in hMG is derived from hCG (human

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Table of Contents Gonadotrophins Current Research

1. Understanding the eBook Gonadotrophins Current Research
 - The Rise of Digital Reading Gonadotrophins Current Research
 - Advantages of eBooks Over Traditional Books
2. Identifying Gonadotrophins Current Research
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Gonadotrophins Current Research
 - User-Friendly Interface
4. Exploring eBook Recommendations from Gonadotrophins Current Research
 - Personalized Recommendations
 - Gonadotrophins Current Research User Reviews and Ratings
 - Gonadotrophins Current Research and Bestseller Lists
5. Accessing Gonadotrophins Current Research Free and Paid eBooks
 - Gonadotrophins Current Research Public Domain eBooks
 - Gonadotrophins Current Research eBook Subscription Services
 - Gonadotrophins Current Research Budget-Friendly Options
6. Navigating Gonadotrophins Current Research eBook Formats

- ePub, PDF, MOBI, and More
- Gonadotrophins Current Research Compatibility with Devices
- Gonadotrophins Current Research Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Gonadotrophins Current Research
 - Highlighting and Note-Taking Gonadotrophins Current Research
 - Interactive Elements Gonadotrophins Current Research
- 8. Staying Engaged with Gonadotrophins Current Research
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Gonadotrophins Current Research
- 9. Balancing eBooks and Physical Books Gonadotrophins Current Research
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Gonadotrophins Current Research
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Gonadotrophins Current Research
 - Setting Reading Goals Gonadotrophins Current Research
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Gonadotrophins Current Research
 - Fact-Checking eBook Content of Gonadotrophins Current Research
 - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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