Cetrorelix Acetate: A Novel Approach to Ovulation Induction in India

Module 2

Tailoring Cetrorelix Acetate for Indian Patients

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Infertility in India: Cultural and Social Implications

Only after giving birth to a child is a woman's life considered worth or complete in a patriarchal society like India. She does not receive respect from her family or society until she becomes a mother. In India becoming a parent is regarded as one of the most significant life achievements. Because of the value of fertility and the lack of understanding regarding infertility, it is not uncommon to discover a male with multiple wives merely because he was unable to have a progeny from his first marriage (Gupta, 2002; Manimekalai, Poulpunitha & Veeramani, 2020). Inhorn (1995) studied about the impact of infertility among Egyptian women and found that infertility's social repercussions place poor Egyptian urban women at the centre of a network of stormy relationships with spouses, in-laws, and neighbours. In Egyptian society women are often blamed for infertility and face threats of divorce or polygyny, harassment, and communal ostracism. Infertility and Patriarchy delves at the lives of infertile women, whose personal tales depict their everyday fight to avoid marginalization and shame. A study by Guntupalli & Chenchelgudem (2004) on infertility among Chenchu tribe of the Nallamalai forest area of Andhra Pradesh, India and came up with some startling findings such as Chenchus associate infertility with spirits and dietary habits, and their treatment-seeking behaviour is based on traditional herbal knowledge and spiritual beliefs. Consumption of umbilical cord is also thought to be a fertility treatment. In this investigation, it was discovered that medical assistance was sought entirely from traditional healers rather than qualified medical practitioners. Most women who infertility at some point in their lives had reported being treated with herbal tea or paste derived from medicinal roots, leaves, or seeds. Most women think that animal sacrifice and prayer to the Goddess Pinnamma can heal infertility. In India infertility is often considered as a curse of God. In non-Western societies including India, supernatural beliefs and alternative sources of treatment are preferred. Though biomedicine has made tremendous progress in the field of infertility, it is not available and accessible for poor and rural couples. Another study on tribal society of Khairwars belonging to Sidhi district of Madhya Pradesh by Kumar (2007) had similar findings. It confirmed that tribal people are heavily dependent on traditional medicinal practices to heal infertility. The study also revealed that infertile tribal women suffer most profoundly in their relationship with their in-laws and

other community members. Rouchou (2013) conducted a study on consequences of infertility in developing countries and opined that every culture holds different reasons and beliefs as to why infertility is stigmatized however, discriminatory practices adopted are universal. In developing countries, social stigmas attached to infertility include, loss of social status, social isolation, women are not allowed to join auspicious occasions, sometimes gifts and financial benefits received by women during marriage are taken away when she is diagnosed with infertility leaving a long-lasting psychological impact on women. The subsequent section sheds light on the profound impact of infertility on women.

Sociocultural Stigma associated with infertility

In patriarchal families the gender of a child is directly related to the extent of respect and freedom a mother will enjoy. This is the reason why women with girl child are often subjected to discrimination compared to those in the family with a male child. In such a scenario, not having any offspring itself becomes a stigma questioning the femininity of a woman and putting a question mark on her entire existence. Bornstein (2021) in her study among the couples with infertility in rural Malawi considers infertility-related stigma a public health issue. She contends that infertility is related with a number of negative health effects, including societal stigma, relationship instability/divorce, depression, and intimate partner violence in some cases. In societies where gender roles and social status are intrinsically tied to parenthood, such consequences are intensified. Infertility can strain relationships with extended family members, who may put pressure on couples to have children or make offensive comments. It can also cause problems with property inheritance and social expectations about having children to carry on the family lineage.

Cultural and Religious Beliefs and Infertility

Perceptions and attitudes about infertility are also influenced by cultural and religious beliefs. Some people may use alternative or traditional cures, rituals, or religious practices that may or may not be successful. Individuals may be discouraged from obtaining evidence-based medical interventions as a result of these beliefs. A study by Sewpaul (1999) on culture religion and infertility in South Africa among the African and Indian communities confirms that cultural

beliefs provide significance to the infertile experience of a couple. Couples with infertility approach treatment based on their cultural backgrounds and life experiences. For instance, the couples from Hindu religion linked infertility to the Karmic life cycle. They attached infertility to their past misdeeds and sins overburdening themselves with regret and guilt. As mentioned earlier in the paper, tribal societies too have a cultural lens to see infertility and the treatment adopted is driven by nature cure based on traditional medicinal practices guided by a traditional healer

Socio-Economic Impact of Infertility

According to Patel (2016), children are a reliable source of manpower in many rural and developing countries and provide economic security in old age; infertility frequently leads to marital instability and the possibility of divorce or abandonment, resulting in financial insecurity. Certain customary laws and cultural customs encourage discrimination against infertile women and may exacerbate the scourge of gender inequality. Women with infertility are often mistreated and ostracized resulting into the loss of their property and material wealth. In many cases, a husband remarries and disowns his first wife owing to infertility. As per Nahar (2012), infertility may lead to abandonment and more economic hardship if women have to pay back their bride wealth or pay bride wealth for husbands to enter into new unions. The major financial crisis arises when a couple wishes to go for Assisted Reproductive Technology (ART) such as In-vitro Fertilization (IVF) or Surrogacy. The cost of treatment is too expensive for a couple from meek financial background. A study by Dyer & Patel (2012) on the economic impact of infertility on women in developing countries suggests that infertility can result in impoverishing health costs as well as economic instability or hardship as a result of societal implications. The health systems of the developing countries too fail to meet the expectations of couples with infertility from lower social strata. Infertility has a significant impact on women’s mental well-being, social positioning, social relationships and financial stability. In developing countries like India, the socio-cultural stigma surrounding infertility exacerbates women's difficulties, leading to blame, shame, and social marginalization. Inability to conceive can create severe psychological pain damaging marital harmony and disagreements with extended family members leading to isolation and discrimination.

Infertility in India: Prevalence and Risk Factors

Infertility, particularly primary infertility, is a significant public health issue in India, with studies showing its prevalence varies across different regions and demographic groups. A study aimed at estimating the prevalence of primary infertility among women of reproductive age in urban Central India and investigating associated risk factors revealed that, of the 570 women surveyed, 51 women (8.9%) experienced primary infertility. The prevalence rate found in this study was lower than the trends typically reported in developing countries. This lower rate may be attributed to the better availability of healthcare facilities in the region where the study was conducted.

On a global level, the World Health Organization (WHO) reported the prevalence of primary infertility in India to be between 3.9% (age-standardized for women aged 25–49 years) and 16.8% (age-standardized for women aged 15–49 years) based on the “age but no birth” definition. Another large population-based study by Boivin et al. found that the prevalence of primary infertility ranged from 3.5% to 16.7% in more developed countries and from 6.9% to 9.3% in less-developed countries, with an estimated median prevalence of 9%. This study included women aged between 20 and 44 years who were married or in a consensual union. Similarly, another study conducted by Adamson et al. in South India reported a prevalence of 12.6% for primary infertility. The women in this study were between 15 and 30 years of age. Similar prevalence rates have been observed in studies from the Kashmir region. Another significant study by Kumar explored infertility problems among women aged 15–49 years in both Khairwar and non-Khairwar tribes in rural Central India. The overall prevalence of primary infertility in this population was found to be 14.2%, with the Khairwar tribe showing a higher rate (17.2%) compared to the non-Khairwar population (10%). The author attributed this higher rate to the limited access Khairwar tribes have to the Indian healthcare system and their reliance on local traditional healers (referred to as "gunias"). These findings highlight that the prevalence of primary infertility not only varies between different countries but also within regions of a single country. Another challenge in comparing these studies is the variation in inclusion criteria, which makes direct comparisons difficult.

Demographic and Socioeconomic Risk Factors

Several demographic factors have been found to be significantly associated with primary infertility. These include higher levels of education, employment, living in nuclear family settings, and a higher socioeconomic status. In recent years, rapid urbanization, an improved standard of living, and increased education levels have empowered women to become more independent and adopt modern lifestyle trends. This shift in lifestyle, particularly changes in dietary habits and physical inactivity, is considered to contribute to the development of primary infertility. Socioeconomic status is also a recognized risk factor for infertility, with women from higher socioeconomic backgrounds often exhibiting risk factors associated with infertility.

In addition to socioeconomic factors, the study revealed that the prevalence of primary infertility increases with advancing age, higher body mass index (BMI), irregular menstrual patterns, and a family history of infertility. As societal norms evolve, women are prioritizing education and career advancement, leading to delayed marriages and childbearing. This shift in societal expectations has been identified as a risk factor for primary infertility in multiple studies. Obesity is another major risk factor, as it directly contributes to hormonal imbalances and menstrual dysfunction, both of which negatively affect reproductive health. Furthermore, a family history of infertility—such as cases in mothers or sisters—places women at higher risk of developing infertility problems, largely due to hereditary genetic conditions. The study also emphasized the importance of menstrual hygiene in influencing fertility. Unhygienic menstrual practices, such as reusing cotton clothes, washing them without proper soap, and drying them indoors without exposure to sunlight, increase the risk of lower reproductive tract infections, irregular menstrual cycles, and, ultimately, infertility.

Psychological Impact of Infertility

Infertility has a profound psychological impact, particularly in countries like India, where having children is seen as a critical milestone for a successful marriage. Women with long-standing infertility issues are more likely to suffer from mental health problems such as anxiety, panic attacks, and agitation. As the duration of infertility increases, so does the level of anxiety, creating a vicious cycle that exacerbates infertility. In this study, stress and depression were found to be significantly associated with infertility, a trend consistent with findings from other studies. Infertile women experience heightened stress, frustration, and emotional distress,

which can contribute to marital problems and an overall decline in psychological well-being. These women also face negative social consequences, including marital instability, stigmatization, and abuse. Various studies suggest that the longer infertility persists, the more severe the psychological stress becomes. This stress further impacts fertility by creating additional emotional and marital tensions, leading to a further decline in reproductive health.

Common Causes of Infertility in Indian Women

The causes of primary infertility in Indian women are varied and complex, and it is important to recognize that infertility can result from factors affecting both the male and female reproductive systems. Some of the most common causes of primary infertility in women include:

- **Polycystic Ovary Syndrome (PCOS):** PCOS is one of the leading causes of infertility in women. It is a hormonal disorder characterized by multiple cysts on the ovaries, which can interfere with regular ovulation. Women with PCOS may take longer to conceive and have a lower fertility rate compared to women without this condition. PCOS is one of the most prevalent endocrine and metabolic disorders in women of reproductive age and can cause significant delays in achieving childbirth.
- **Fallopian Tube Blockage:** Blocked or damaged fallopian tubes can prevent sperm from reaching the egg or hinder the fertilized egg from reaching the uterus, thereby causing infertility. Conditions such as pelvic inflammatory disease (PID), endometriosis, or previous surgeries are common causes of fallopian tube damage. Tubal factors account for approximately 14% of cases of subfertility.
- **Uterine Abnormalities:** Structural abnormalities of the uterus, such as fibroids, polyps, or congenital malformations, can impair fertility by interfering with implantation or increasing the risk of miscarriage. Congenital uterine abnormalities represent a wide range of uterine shapes that may negatively affect reproductive potential.
- **Endometriosis:** Endometriosis is a condition where the tissue that lines the uterus (endometrium) grows outside of the uterus. This leads to a chronic inflammatory response, causing scar tissue and adhesions that can damage a woman's pelvic anatomy. These complications interfere with the functioning of the fallopian tubes and ovaries, thereby leading to infertility.

- **Ovulation Disorders:** Irregular or absent ovulation is another common cause of infertility. Conditions like hypothalamic dysfunction, polycystic ovary syndrome (PCOS), and premature ovarian failure (POF) can disrupt ovulation, making conception difficult.
- **Hormonal Imbalances:** Imbalances in hormones such as follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid hormones, or prolactin can disrupt ovulation and fertility. Hormones play a crucial role in the development and regulation of reproductive function and the menstrual cycle.
- **Age-related Factors:** As women age, their fertility naturally declines. In India, societal norms often lead to delayed marriages and childbearing, increasing the risk of infertility due to age-related factors. The woman's age is the most important determinant of a couple's fertility. As age increases, so does the rate of infertility, and the success rates of infertility treatments decrease. Studies have shown that women over 35 years of age experience significantly lower pregnancy rates compared to younger women.
- **Emotional and Psychological Factors:** Stress, anxiety, and other emotional challenges can disrupt hormonal balance and negatively impact the reproductive system. In a patriarchal society like India, the psychological stress related to infertility is often exacerbated by social pressures, leading to conditions such as depression and anxiety, which can further complicate the ability to conceive.

Psychological Stress and Coping Mechanisms in Infertility

Infertility, while not life-threatening, can be an overwhelming experience for many couples. It brings with it a complex mix of emotional, psychological, and financial challenges, which can be difficult to manage without proper support. This article explores the various psychological stressors linked to infertility, how they impact couples, and the different methods available for coping with these stressors, including counseling and therapy.

Emotional Impact of Infertility Diagnosis

The diagnosis of infertility can be an incredibly stressful and distressing event for couples. Though it does not threaten one's physical health, the emotional toll it takes is immense. Couples often experience a wide range of negative emotions, including anger, guilt, sadness, depression, anxiety, and loss of self-esteem. These feelings are further exacerbated by the financial strain that infertility treatments impose. For example, the cost of a single cycle of in vitro fertilization (IVF) in India ranges from INR 1,00,000 to 3,50,000, excluding additional expenses for medications and tests. The high cost often prevents some couples from pursuing treatment, leading to feelings of hopelessness.

In Indian society, having children is often seen as a key milestone in life, adding significant social pressure on infertile couples. This societal expectation can amplify the emotional stress and strain relationships—not only between partners but also with friends and family members. Many couples, feeling detached from their families and socially isolated, withdraw from their support networks, further compounding their psychological burden.

In addition, psychological stress is considered a potential clinical risk factor that may adversely affect male fertility. Research indicates that psychological stress can negatively impact semen parameters, and this stress, in turn, may affect the success rate of fertility treatments. The pressure and uncertainty associated with infertility treatments can lead to even higher levels of stress, potentially diminishing the chances of a successful outcome.

Stress from Failed Infertility Treatments

Fertility treatments, especially IVF, offer hope to infertile couples, but they do not guarantee success. Only about 50% of patients undergoing IVF become parents, and the likelihood of

achieving pregnancy decreases with age. Couples whose first IVF cycle fails may have to undergo multiple rounds of treatment, adding to both the financial burden and emotional strain. For couples who have experienced previous miscarriages, the degree of stress is particularly high. A lack of emotional and educational support during the treatment process only exacerbates these feelings of despair and frustration.

The emotional toll of failed treatments can be profound, especially for women. The constant cycles of hope and disappointment, coupled with financial and physical strain, can create a sense of helplessness, driving some couples to discontinue treatment altogether.

Psychological Support and Counseling for Infertility

Infertility Counseling:

Infertility counseling is an essential tool for helping couples manage the emotional and psychological challenges of infertility. A qualified mental health professional (MHP) offers fertility counseling to individuals or couples considering or undergoing reproductive treatments. Counseling can be conducted in individual, couple, or group formats and is designed to meet the unique needs of patients. Counseling is particularly important during times of high distress, such as after a failed treatment cycle, during pregnancy after infertility, in cases of multiple pregnancies, or when facing the end of medical treatments. Counseling sessions focus on the emotional crisis linked to an unfulfilled desire for children and the stress of repeated medical interventions with limited success.

Role of Psychotherapy:

Psychotherapy is another important resource for couples coping with infertility. Often, couples do not openly discuss their feelings with each other, and psychotherapy provides a safe space for them to express their emotions. Men, in particular, may have difficulty articulating their feelings due to societal norms. Therapy helps individuals and couples navigate the stages of denial, anger, blame, shame, and despair that often accompany infertility. For those hesitant to share their infertility struggles with others, therapy offers a confidential environment to process their emotions.

Therapists play a vital role in guiding couples through the psychological challenges of infertility and help them develop healthy coping mechanisms. Therapy is especially useful

before patients begin fertility treatments, as it helps couples address the emotional and psychological impact of infertility early in the process. Psychotherapy has also been shown to reduce symptoms of depression, anxiety, and stress, potentially improving the likelihood of conception.

Relaxation Techniques to Reduce Stress

Various relaxation techniques can significantly reduce the emotional stress associated with infertility treatments. Techniques such as meditation, deep breathing, guided imagery, and yoga have been found to alleviate anxiety and improve the overall quality of life for women undergoing fertility treatments. For instance, yoga has been shown to reduce negative emotions and enhance well-being in women struggling with infertility. Incorporating these techniques can help couples better manage the stress and emotional rollercoaster that often accompanies fertility treatments.

Self-Administered Interventions

In addition to professional counseling, there are self-administered psychological interventions that can help individuals cope with the stress of infertility. One such intervention is the Cognitive Coping and Relaxation Intervention (CCRI), which encourages positive reappraisal and helps patients manage their stress independently. Studies have shown that CCRI improves coping mechanisms, reduces anxiety, and enhances the quality of life for couples undergoing IVF.

Another self-help tool is the Positive Reappraisal Coping Intervention (PRCI), which teaches individuals to focus on the positive aspects of stressful situations. These self-administered options provide couples with accessible ways to manage their emotional health during the challenging fertility treatment process.

Addressing Patients' Needs Before, During, and After Treatment

Before Treatment:

Before starting fertility treatments, it is essential to address patients' beliefs, behaviors, and lifestyle choices that could impact reproductive health. The infertility team should encourage lifestyle modifications, such as adopting a healthy diet, exercising regularly, and reducing

caffeine intake, to improve fertility. It is also crucial for medical staff to approach patients with empathy and respect, avoiding negative or rushed communications that could discourage patients from continuing with treatment.

During Treatment:

During fertility treatments, psychological stress often peaks, particularly during critical moments such as ovum retrieval, embryo transfer, and waiting for pregnancy test results. For couples whose first IVF cycle fails, the combination of financial, physical, and emotional strain may lead them to discontinue treatment. Studies show that women experience higher levels of distress compared to men during the treatment process. Providing ongoing psychological support and encouraging active participation from both partners can help alleviate some of this stress.

After Treatment:

After fertility treatments, couples' needs vary depending on the outcome. For those whose treatments were unsuccessful, there is a heightened risk of depression, substance abuse, and even marital breakdown. Ongoing therapy and mental health support are critical for helping couples cope with the emotional fallout of failed treatments.

For those who successfully conceive through fertility treatments, anxiety often persists, especially regarding the viability of the pregnancy and the health of the baby. Medical staff should provide clear communication and emotional support to address these concerns and help couples navigate the uncertainties of pregnancy after infertility.

Role of the Infertility Team

The infertility team plays a critical role in managing both the physical and emotional aspects of infertility. Infertility is a life crisis for many patients, and its psychological impact can lead to a range of mental health issues, including anxiety, depression, and low self-esteem. Psychological interventions have been shown to reduce these symptoms and, in some cases, improve pregnancy outcomes.

One of the challenges in addressing the psychological aspects of infertility is that couples often underreport their emotional distress. In the early stages of treatment, couples may be optimistic,

but as treatments progress and stress levels rise, the emotional toll becomes more evident. Encouraging couples to engage in regular therapy can help them manage the overwhelming emotions associated with infertility.

In the past, the prevalence of psychiatric disorders among infertile couples has been estimated to range from 25% to 60%. The psychological effects of infertility are further complicated by the medications used in treatment, which can have side effects that mimic symptoms of anxiety or depression. This makes it challenging to determine whether psychological symptoms are due to the medications or the infertility itself.

Some couples may find that lifestyle changes, such as improving their diet or increasing physical activity, can improve their fertility. However, for those who undergo multiple failed treatment cycles, the psychological burden can be immense. Therapy can help these couples explore other options, such as adoption, and develop new perspectives to cope with their situation.

Conclusion

Infertility can be an emotionally and psychologically taxing experience, with profound impacts on both individuals and couples. The financial burden of treatment, coupled with social pressures and emotional stress, often creates a complex web of challenges that requires both medical and psychological intervention. Counseling, psychotherapy, relaxation techniques, and self-administered coping interventions can all play a critical role in helping couples navigate the infertility journey. Addressing psychological stress not only improves emotional well-being but may also enhance the chances of treatment success. Through a combination of emotional support and medical care, couples can be better equipped to manage the challenges of infertility and its treatment.

Mechanism of Action and Clinical Applications of Cetrorelix

Cetrorelix is an important luteinizing hormone-releasing hormone (LH-RH) antagonist used in assisted reproductive technologies (ART), particularly for in vitro fertilization (IVF). Its primary role is to prevent premature ovulation during controlled ovarian stimulation, a key component of IVF procedures. The prevention of premature ovulation ensures that mature, intact follicles are produced, preventing cycle cancellation and improving the chances of successful fertilization.

Premature Ovulation in Controlled Ovarian Stimulation

Premature ovulation, driven by an early surge of luteinizing hormone (LH), can result in immature follicles, which are not ideal for successful IVF cycles. To prevent this, controlled induction of ovulation is needed. Cetrorelix, as a potent LH-RH antagonist, has proven effective in inhibiting the premature LH surge in women undergoing controlled ovarian stimulation. By delaying the LH surge, cetrorelix allows for proper follicular development, enhancing the chances of successful oocyte retrieval.

Several studies have demonstrated a dose-dependent relationship between cetrorelix administration and the delay in the LH surge. Additionally, the day of cetrorelix administration during the menstrual cycle has a significant impact on the timing of ovulation.

Role of Cetrorelix in Intrauterine Insemination (IUI)

The timing of intrauterine insemination (IUI) in relation to ovulation is critical for achieving optimal pregnancy rates. Supplementation with a GnRH antagonist like cetrorelix assists in accurately determining the appropriate time for administering human chorionic gonadotropin (hCG) to trigger ovulation. While some patients experience ovulation within 24-56 hours of the onset of the LH surge, others may ovulate between 8 and 40 hours after the peak LH levels. In patients with premature LH surges, an inconsistent ovulation schedule is observed, often requiring IUI to be performed twice over two consecutive days. However, this approach has

not shown a significant improvement in pregnancy rates, highlighting the complexities of managing premature LH surges in IUI cycles.

Clinical Applications in Indian Patients

Inhibition of Premature LH Surges in Assisted Reproduction

In women undergoing ART, such as IVF, ovulation is triggered by a surge in LH, which is in response to rising levels of estradiol produced by the maturing ovarian follicles. When gonadotropins are administered to induce the development of multiple follicles, supraphysiological estradiol levels can lead to a premature LH surge. This early surge may cause the luteinization of immature follicles, ultimately leading to developmental arrest and IVF cycle cancellation. The use of GnRH agonists has been effective approach for controlling premature LH surges by desensitizing the pituitary gland to GnRH. Although GnRH agonists initially stimulate the pituitary, prolonged use leads to receptor downregulation and suppression of LH release. This strategy has successfully increased pregnancy rates per IVF cycle.

Cetrorelix, a GnRH antagonist, achieves suppression of LH release without initial stimulation, making it an effective and faster alternative for controlling premature ovulation. It is typically administered for a shorter duration, with the average treatment lasting five days. The ability to begin treatment during the follicular phase of the menstrual cycle offers flexibility and control over the stimulation cycle.

Clinical trials have shown that cetrorelix is both safe and effective in preventing premature ovulation. The combination of GnRH antagonist treatment with oral contraceptive pill (OCP) programming has been widely used in ART, reducing the incidence of ovarian cyst formation associated with the traditional long luteal GnRH agonist protocol. Preliminary studies suggest that combining cetrorelix with OCPs is effective, well-tolerated, and convenient for patients.

Cetrorelix in Special Patient Populations

Certain groups of patients, including those who respond poorly to gonadotropin stimulation or those at high risk of ovarian hyperstimulation syndrome (OHSS), may benefit from pituitary suppression using cetrorelix. Studies comparing cetrorelix with GnRH agonists in poor responders indicate comparable pregnancy and implantation rates, with some studies reporting a higher number of embryos transferred in patients treated with cetrorelix.

In women with polycystic ovary syndrome (PCOS), research shows that while there are no significant differences in the number of oocytes retrieved or clinical pregnancy rates between cetrorelix and long GnRH agonist protocols, cetrorelix is associated with a shorter stimulation period. Furthermore, cetrorelix significantly reduces the incidence of OHSS, especially in high-risk patients. Studies have demonstrated a lower incidence of OHSS with cetrorelix compared to long GnRH agonist protocols.

Use of Cetrorelix in Healthy Premenopausal Women

In IVF procedures involving healthy premenopausal women, controlled ovarian stimulation aims to retrieve mature and intact oocytes. Premature LH surges, which occur in approximately 20% of cases, can result in premature ovulation and cycle cancellation. The primary goal is to delay the LH surge and allow for the retrieval of mature follicles. Cetrorelix, an LH-RH antagonist, has been successfully used in both short multiple-dose regimens and single-dose regimens to control ovulation.

Studies have demonstrated that the timing and dosage of cetrorelix administration play critical roles in controlling ovulation. Single doses of 1, 3, and 5 mg administered on day 8 of the menstrual cycle have been shown to delay the LH surge by an average of 4.1, 7.5, and 9.3 days, respectively. A pharmacokinetic and pharmacodynamic model has been developed to predict LH suppression and the subsequent delay in the LH surge, allowing for better planning and control of IVF cycles.

Analysis of LH Surge in Humans

Several methods have been used to analyze and characterize the LH surge in humans and non-human mammals. Various models, including deterministic and permissive models, have been proposed to explain the relationship between LH-RH and the LH surge. Techniques like cluster analysis and multiple-parameter convolution have been employed to model episodic bursts of LH and other hormones. Although many of these models rely on complex mathematical techniques, a simpler approach has been used to predict the LH surge shift based on the concentration-time profile of LH-RH antagonists. This approach has demonstrated accuracy in predicting the shift in LH surge following cetrorelix administration, offering valuable insights for optimizing IVF protocols.

Role of cetrorelix in the prevention and treatment of ovarian hyperstimulation syndrome: a prospective case control study

ABSTRACT

Background: Ovarian hyperstimulation syndrome (OHSS) has intrigued clinicians for many years because of its devastating consequences. As an iatrogenic condition resulting from elective ovarian stimulation in the quest for pregnancy, the need to completely prevent the syndrome is evident. Gonadotropin releasing hormone (GnRH) antagonist Cetrorelix has found to be effective in treatment of OHSS and some studies have found it to be helpful in prevention of this condition. Hence, we designed a hospital-based study to investigate the effect of Cetrorelix in preventing and treating OHSS in in-vitro fertilization – embryo transfer (IVF–ET) patients at risk of OHSS undergoing long and short protocol.

Methods: The study includes total 102 patients undergoing controlled ovarian stimulation COS for IVF/ICSI. All cases were stimulated using long and short protocol. Depending on whether a GnRH antagonist was given after ovum pick-up (OPU) the patients were divided in two groups: Cetrorelix (antagonist) group (n=51) and control group (n=51). The study group was treated with Cetrorelix 0.25 mg for 5 days commencing on the day of ovum pick up.

Results: Incidence of mild OHSS was significantly higher ($p=0.01$) whereas moderate to severe OHSS was significantly lower in the antagonist group ($p<0.05$). None of the patients had critical OHSS.

Conclusions: GnRH antagonist Cetrorelix administration in early luteal phase in patients undergoing long or short protocol is effective in prevention and treatment of OHSS.

GnRH Antagonist Cetrorelix Administration Before hCG for Protection of Ovarian Hyperstimulation Syndrome

Abstract

Objective: Studying the effect of GnRH antagonist administration on the day of hCG to cases of IVF/ICSI with estradiol level above 5000 ng/dl for protection of ovarian hyperstimulation syndrome.

Design: Prospective study.

Materials and Methods: Sixty patients undergoing controlled hyperstimulation COH, for IVF/ICSI using long agonist and E2 level on the day of hCG, are above 5000 ng/dl, 52 patients received single dose of cetrorelix 0.25 mg on the day of hCG, and 8 patients received two doses of 0.25 mg/day cetrorelix started one day before the day of hCG.

Results: There was no significant difference regarding patients BMI, number of stimulation days, recombinant FSH dose, and number of retrieved oocytes. Clinical pregnancy rate was 76.6% (46/60), in patients received single dose of antagonist PR were significantly higher 80.7% (42/52) versus 50% (4/8) in patients received two doses $p = 0.047$. Live birth rate was 50% (30/60), abortion rate was 20% (12/60), and preterm delivery was 20% (12/60). Mean E2 was 6853.2 ng/dl. Six patients developed moderate ovarian hyperstimulation OHSS (6/60) 10% and no cases of severe OHSS.

Conclusions: GnRH antagonist administration on the day of hCG in cases undergoing IVF/ICSI with long agonist protocol is effective in protection of OHSS and does not affect the clinical pregnancy rate nor live birth rate.

Prospective, randomized trial comparing cetrorelix acetate and ganirelix acetate in a programmed, flexible protocol for premature luteinizing hormone surge prevention in assisted reproductive technologies

Objective: To compare the safety and efficacy of single-dose cetrorelix acetate (3 mg) and daily ganirelix acetate (0.25 mg) in the inhibition of premature LH surge in women undergoing cycle-programmed ovarian stimulation before Assisted Reproductive Technology (ART).

Design: Prospective, open-label, randomized, comparative study.

Patient(s): One hundred eighty-five infertile patients undergoing ART.

Intervention(s): Single injection of cetrorelix (3 mg SC) or daily dose of ganirelix (0.25 mg SC) was administered when the lead follicle was ≥14 mm. Daily cetrorelix (0.25 mg) was administered if the criteria for hCG administration were not met 4 days after receiving 3 mg of cetrorelix.

Main Outcome Measure(s): Percentage of patients who did not have a premature LH surge, defined as LH <10 IU/L on the day of hCG administration. The IVF and embryo transfer (ET) outcomes were assessed.

Result(s): No patient in either treatment group had a premature LH surge. There were no statistically significant differences between treatments for any IVF/intracytoplasmic sperm injection (ICSI) or ET outcomes, including pregnancy rate (PR). However, cetrorelix required significantly fewer injections than ganirelix. Similar safety profiles were observed.

Conclusion(s): Cetrorelix and ganirelix effectively prevented LH surges in oral contraceptive (OC) pill-programmed, flexible protocols, with similar safety profiles and PRs; however, cetrorelix required significantly fewer injections, increasing patient convenience.

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