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COMPARATIVE STUDY BETWEEN DIFFERENT TYPES OF VAGINAL PROGESTERONE IN LUTEAL PHASE SUPPORT IN ICSI CYCLES

By

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ABSTRACT

Background: Assisted reproductive techniques (ART) include all fertility treatments in which the gametes (egg and sperm) are handled outside the human body with the aim of achieving a healthy conception. Common ART procedures include in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI), fresh or frozen embryo transfer, and IVF with donor oocytes. Luteal phase support through pharmaceutical drugs has been universally agreed.

Objective: To compare the effectiveness of different types of vaginal progesterone preparations for luteal support in patients undergoing Intracytoplasmic Sperm Injection.

Patients and Methods: The current randomized controlled clinical trial study was conducted on 300 patients who were following at the Assisted Reproductive Technology (ART) unit of the International Islamic Center for Population Studies and Research (IICPSR) of Al-Azhar University over the period from May 2016 to January 2018 after being approved by the ethical committee. The patients were divided into 3 equal groups received Prontogest vaginal suppositories 400 mg once per day, Group B received Crinone 8% (90 mg) vaginal gel once per day and Group C received Endometrin vaginal suppositories once per day.

Results: Comparison between studied group A (Prontogest), group B (Crinone) and group C (Endometrin) as regards demographic characteristics revealed no statistically significant differences. As regards the cause of infertility, a statistically significant increase in the number of patients with male and tubal factors in group B (Crinone) than group A (Prontogest). Concerning the laboratory hormonal profile of the studied groups before ICSI, there was a statistically significant increase in FSH and LH levels in group A (Prontogest) than group B (Crinone) and group C (Endometrin). On the other hand, there was a difference between the studied groups as regards prolactin and estrogen levels, but did not reach statistical significance. Comparison between studied groups, as regards Endometrial thickness, number of retrieved oocytes and number of transferred embryos revealed no statistically significant difference. Comparison between the studied groups, as regards pregnancy rates, revealed a statistically significant increase in pregnancy rates in group C than group A.

Conclusion: The use of Endometrin vaginal suppositories in patients undergoing ICSI had a statistically significant higher clinical pregnancy rates in comparison to Prontogest vaginal suppositories. On the other hand, Crinone vaginal gel had a higher clinical pregnancy rate than Prontogest.

Keywords: ICSI; Luteal phase; Vaginal Progesterone.

INTRODUCTION

Infertility is a disease defined by the failure to achieve a successful pregnancy after 12 months or more of appropriate, timed unprotected intercourse. Earlier evaluation and treatment may be justified based on medical history and physical findings and is warranted after 6 months for women over age 35 years *(Ray, 2012)*.

According to a study conducted by the Egyptian Fertility Care Society and sponsored by the World Health Organization (WHO), infertility affects 12 percent of Egyptian couples. Of these, 4.3 Percent suffer from primary infertility (have never conceived) and 7.7 percent suffer from secondary infertility (have conceived before, even if the pregnancy ended in a miscarriage or an ectopic pregnancy). The number of women aged 15 to 49 years in the reproductive age group exceeds 25 million, which means that at least 3 million women are infertile in Egypt *(Cozzolino et al., 2018)*.

World-wide, an estimated nine percent of couples meet the definition of infertility with 50-60% of them seeking care. Although there is some controversy about whether the proportion of the population with self-reported infertility is increasing, stable or decreasing, there has clearly been increasing utilization of assisted reproductive techniques (ART) *(Wiltshire et al., 2020)*.

Assisted reproductive techniques (ART) include all fertility treatments in which the gametes (egg and sperm) are handled outside the human body with the aim of achieving a healthy conception. Common ART procedures include in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI), fresh or frozen embryo transfer, and IVF with donor oocytes. Since the birth of the first IVF baby in 1978, the use of ART has increased tremendously and 1.7–4.0% of all children born today in developed countries are conceived through the use of ART. Advances in ART procedures, increased access to fertility services and delayed child bearing are all factors that contributing to the rise in the use of ART services *(Talaulikar and Arulkumaran, 2013)*.

The success of in vitro fertilization/ intracytoplasmic sperm injection (IVF/ICSI) treatments depends upon many known and unknown factors; the most important being the implantation window. The implantation rates have not yet reached the desired level despite the advancements observed in that field.

Oocyte quality and endometrial receptivity factors have important roles in the implantation process *(Nastri et al., 2014)*.

The luteal phase is defined as the period between ovulation and either the establishment of pregnancy or the onset of menstruation two weeks later. Following ovulation, the luteal phase of a natural cycle is characterized by the formation of a corpus luteum, which secretes steroid hormones including progesterone and estradiol (E2). If conception and implantation occur, the developing blastocyst secretes human chorionic gonadotrophin (HCG) *(Practice Committee of the American Society for Reproductive Medicine, 2017)*.

During assisted reproductive technology (ART) treatment, the use of

gonadotropin-releasing hormone (GnRH) agonists and the aspiration of follicular fluid can lead to a relative progesterone deficit and inappropriate preparation of the endometrium for embryo implantation *(Roque et al., 2013).*

The use of pharmaceutical luteal support to reach the physiological ratio of estrogen to progesterone could only be beneficial as defective production of progesterone may impair implantation and pregnancy rates, hence the important role of this hormone supplementation in early pregnancy. Methods of luteal phase support include corpus luteum stimulation to secrete endogenous estrogen and progesterone by serial injections of human chorionic gonadotrophin (HCG) or with exogenous replacement of progesterone *(Tokgoz et al., 2019).*

The use of HCG for luteal phase is associated with a marked increase in the risk of ovarian hyperstimulation syndrome (OHSS). Therefore, progesterone is the preferred choice *(de Ziegler et al., 2018).*

Nowadays the need for luteal support in ART treatment has been universally agreed. Progesterone can be administered by oral, intramuscular or vaginal routes. However, the optimal route has not yet been established. There is increasing evidence that vaginal and intramuscular progesterone are at least equally effective, considering the rate of biochemical and clinical pregnancies as well as their outcomes. However, through the use of vaginal progesterone, reiterated painful application of intramuscular injections and their complications, such as local soreness, abscesses, and inflammatory reactions, were avoided *(Lawrenz et al., 2019).*

The current work aimed to compare the effectiveness of different products of vaginal progesterone preparations for luteal phase support in patients undergoing Intracytoplasmic Sperm Injection.

PATIENTS AND METHODS

The current study was a randomized controlled clinical trial study, was conducted on 300 patients who were following at the Assisted Reproductive Technology unit **(ART unit)** of International Islamic Center for Population Studies and Research **(IICPSR)** of Al-Azhar University over the period from May 2016 to January 2018 after being approved by the ethical committee.

The patients were divided into 3 equal groups: Group A received Prontogest vaginal suppositories 400 mg once per day, Group B received Crinone 8% (90 mg) vaginal gel once per day and Group C received Endometrin vaginal suppositories once per day.

The patients were selected to be included in the study according to the following criteria: Age 20-35 years, presence of regular menstrual cycle with a length of 21- 35 days, no relevant systemic disease e.g hypertension and diabetes mellitus, body mass index 18- 28 and Indication for ICSI are: Unexplained infertility, male factor, tubal factor after exclusion of the presence of the hydrosalpinex.

Patients were excluded from the study according to the following criteria: Patients with gross uterine pathology by U/S e.g liomyoma or endometrial polyp, body mass index > 28, poor responders

and Patients were not eligible for the study if progesteron therapy was contraindicated (presence of severe acute and chronic liver disease, Rotor or Dubin-Johnson syndrome, hepatocellular tumors, or known allergic reaction to one of the active constituents or inactive ingredients contained in the investigational medication).

Random sequence was generated by the supervisor using MS Excel. The random sequence was placed in sequentially numbered, opaque and sealed envelopes to be opened at time of enrollment by an investigator who prepared the study drug and had no further involvement with the care of the patient.

After obtaining consents from the patients for participating in this study, they were subjected to **history taking**, **clinical examination** and **investigations** (baseline transvaginal ultrasound, hormonal profile, hysterosalpingogram, diagnostic laparoscope and semen analysis for the husband).

Long protocol for ovarian stimulation (daily subcutaneous injections of Triptorelin or leuprolide acetate or depot injection on day 21 of the cycle, adequacy of down regulation will be confirmed on the second day of bleeding following GnRH agonist administration by fall in the serum level of E2 (< 50 pg/ml), followed by gonadotrophin stimulation).

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. Also qualitative variables were presented as number and percentages. The comparison between groups with qualitative data was done by using **Chi-square test**. The comparison between two groups with quantitative data and parametric distribution were done by using **Independent t-test**, while data with non-parametric distribution were done by using **Mann-Whitney test**. The comparison between more than two groups with quantitative data and parametric distribution were done by using **One Way ANOVA test**, while data with non-parametric distribution were done by using **Kruskall Wallis test**. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

RESULTS

Table (1) shows the demographic distribution of the patients included in the study as regarding the age, BMI, the duration of marriage in years, the type of infertility (1ry or 2ry) and the previous ART trials.

Table (1): Demographic characteristics of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin) with positive and negative pregnancy test

Pregnancy / Parameters		Negative	Positive	P-value
		No. = 182	No. = 118	
Age (years)	Mean±SD Range	28.16 ± 4.34 19 – 37	27.41 ± 4.27 19 – 35	0.138
BMI (Kg/m2)	Mean±SD Range	25.07 ± 3.07 20 – 30	24.92 ± 2.54 20.12 – 30	0.660
Married for (years)	Median(IQR) Range	6 (3 – 8) 1 – 17	5 (3 – 7) 1 – 34	0.064
Infertility	1ry 2ry	130 (71.4%) 52 (28.6%)	86 (72.9%) 32 (27.1%)	0.784
Previous ART trials	No Yes	116 (63.7%) 66 (36.3%)	88 (74.6%) 30 (25.4%)	0.049

*:Chi-square test; •: Independent t-test; ǂ: Mann Whitney test

Table (2) shows the causes of infertility in the different groups, where the male factor was the most common cause in the three groups followed by the tubal factor and the unexplained infertility.

Table (2): Causes of infertility in the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin)

Groups / Causes	Group A (Prontogest)		Group B (Crinone)		Group C (Endometrin)		P-value
	No.	%	No.	%	No.	%	
Male factor	54	54.0%	60	60.0%	46	46.0%	0.011
Tubal factor	22	22.0%	32	32.0%	36	36.0%	
Unexplained	24	24.0%	8	8.0%	18	18.0%	

*: Chi-square test

Table (3) shows the baseline hormonal profile (FSH, LH, Prolactin and E2) of the patients in the three groups before undergoing the ICSI.

Table (3): Laboratory hormonal profile of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin) before ICSI

Groups / Parameters		Group A (Prontogest)	Group B (Crinone)	Group C (Endometrin)	P-value
		No. = 50	No. = 50	No. = 50	
FSH	Median(IQR) Range	6 (5.2 – 7.3) 2.1 – 17.6	6 (4.8 – 6.5) 2.7 – 9.9	5.6 (4.6 – 6.5) 1.8 – 12.7	0.079
LH	Median(IQR) Range	4.1 (2. 9 -6.2) 1.4 – 9.9	3.2 (2. 3 – 4.3) 0.61 – 7	3.4 (2.7 – 4.1) 1.7 – 11	0.000
Prolactin	Median(IQR) Range	16.2 (11 – 24) 1.4 – 47.9	16 (13 – 24) 2.9 – 99	14 (10 – 21) 0.9 – 40	0.052
E2	Median(IQR) Range	50.5 (40 – 67) 2.7 – 118	46 (38 – 56) 2.9 – 86	43 (31 – 59) 13 – 214	0.149

Kruskall Wallis test

Table (4) shows the comparison between the different groups of the study as regarding the endometrial thickness, the number of the retrieved oocytes and the number of the transferred embryos in the ICSI process.

Table (4): Endometrial thickness, number of retrieved oocytes and number of transferred embryos of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin)

Parameters \ Groups		Group A (Prontogest) No. = 50	Group B (Crinone) No. = 50	Group C (Endometrin) No. = 50	P-value
Endometrial thickness before embryo transfer (mm)	Median(IQR) Range	10 (9 – 12) 1 – 14	10 (9 – 11) 5 – 13	10 (9 – 11) 8 – 13	0.615
No. of oocytes	Median(IQR) Range	6 (4 – 8) 2 – 18	6 (4 – 8) 1 – 18	5 (4 – 7) 1 – 14	0.358
No. of transferred embryos	Median(IQR) Range	2 (2 – 3) 1 – 3	2 (2 – 3) 1 – 3	2 (2 – 3) 1 – 3	0.749

Kruskall Wallis test

Table (5) shows the comparison between the different groups of the study as regarding the number and the embryonic stage of the transferred embryos (compact, 8A, 8B, blastocysts, and morula). The table also shows the difference in the range and mean value of the quantitative B-HCG, which shows that group C (Endometrin group) has the highest values followed by group B (Crinone group) and the lowest is the group A (Prontogest group).

Table (5): The embryonic stages of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin)

Parameters \ Groups		Group A (Prontogest) No. = 100	Group B (Crinone) No. = 100	Group C (Endometrin) No. = 100	P-value
Compact	1	18 (18.0%)	10 (10.0%)	4 (4.0%)	0.001*
	2	8 (8.0%)	18 (18.0%)	6 (6.0%)	
	3	8 (8.0%)	6 (6.0%)	2 (2.0%)	
8A	1	36 (36.0%)	26 (26.0%)	20 (20.0%)	0.143*
	2	12 (12.0%)	12 (12.0%)	20 (20.0%)	
	3	10 (10.0%)	16 (16.0%)	16 (16.0%)	
8B	1	28 (28.0%)	18 (18.0%)	14 (14.0%)	0.002*
	2	0 (0.0%)	6 (6.0%)	0 (0.0%)	
	3	2 (2.0%)	2 (2.0%)	0 (0.0%)	
Blastocysts	1	4 (4.0%)	2 (2.0%)	6 (6.0%)	0.047*
	2	4 (4.0%)	8 (8.0%)	10 (10.0%)	
	3	4 (4.0%)	0 (0.0%)	0 (0.0%)	
Morula	1	14 (14.0%)	0 (0.0%)	10 (10.0%)	0.000*
	2	2 (2.0%)	0 (0.0%)	6 (6.0%)	
	3	0 (0.0%)	2 (2.0%)	8 (8.0%)	
Quantitative BHCG	Mean ± SD Range	743.56 ± 247.36 423 – 1423	769.26 ± 372.71 442 – 1769	807.00 ± 407.15 321 – 1710	0.730•

*: Chi-square test; •: One Way ANOVA test.

Table (6) shows that the pregnancy rate was highest in the Endometrin group followed by Crinone group and the least pregnancy rate was seen in the Prontogest group. On the other hand, the abortion rate was highest in the Prontogest group followed by the Crinone group and the least abortion rate was in the Endometrin group. The living birth rate was highest in the Prontogest group followed by the Crinone group and the least living birth rate was in the endometrin group; however, the Endometrin group has the highest living twin birth rate.

Table (6): Pregnancy and abortion rates of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin)

Parameters \ Groups		Group A (Prontogest)		Group B (Crinone)		Group C (Endometrin)		P-value
		No.	%	No.	%	No.	%	
Pregnancy	Negative	68	68.0%	62	62.0%	52	52.0%	0.065
	Positive	32	32.0%	38	38.0%	48	48.0%	
Abortion	Negative	26 6	81.2%	26	68.4%	28	63.6%	0.243
	Positive		18.8%	12	31.6%	16	36.4%	
Living birth	Negative	6	18.8%	12	31.6%	16	33.3%	0.499
	Single	22	68.8%	22	57.9%	24	50.0%	
	Twin	4	12.5%	4	10.5%	8	16.7%	

*:Chi-square test

Table (7) shows numerical comparison between the different causes of infertility in the patients allocated in the study before the ICSI as well as the positive and negative pregnancy rates for them after performing the ICSI and it reveals that the highest success rate was in the patient with male factor cause of infertility followed by the tubal factor while the unexplained infertility had the least success rate.

Table (7): Causes of infertility of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin) with positive and negative pregnancy test

Causes \ Pregnancy	Negative (n = 182)		Positive (n = 118)		P-value
	No.	%	No.	%	
Male factor	90	49.5%	70	59.3%	0.235
Tubal factor	60	33.0%	30	25.4%	
Unexplained	32	17.6%	18	15.3%	

*:Chi-square test

Table (8) shows the comparison between P of the patients of the study as regarding the hormonal profile (FSH, LH, Prolactin and E2) before the ICSI as well as the positive and negative pregnancy rates after the ICSI.

Table (8): Laboratory hormonal profile of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin) with positive and negative pregnancy test before ICSI

Parameters \ Pregnancy		Negative	Positive	P-value
		No. = 182	No. = 118	
FSH	Median(IQR) Range	5 (5.2 – 7) 2.1 – 15.4	5.8 (4.1 – 6.5) 1.8 – 17.6	0.016
LH	Median(IQR) Range	3.4 (2.8 – 4.7) 0.61 – 9.2	3 (2.4 – 4.9) 1.2 – 11	0.095
Prolactin	Median(IQR) Range	15 (12 – 25) 0.9 – 99	16 (10 – 22) 4 – 38	0.620
E2	Median(IQR) Range	47 (37 – 64) 2.7 – 118	43 (36 – 59) 13 – 214	0.056

Mann Whitney test

Table (9) shows the comparison between the patients of the study as regarding the endometrial thickness, the number of the retrieved oocytes and the number of the transferred embryos before the ICSI as well as the positive and negative pregnancy rates after the ICSI.

Table (9): Endometrial thickness, number of retrieved oocytes and number of transferred embryos of the studied groups; Group A (Prontogest), Group B (Crinone) and Group C (Endometrin) with positive and negative pregnancy test

Parameters \ Pregnancy		Negative	Positive	P-value
		No. = 182	No. = 118	
Endometrial thickness before embryo transfer (mm)	Median(IQR) Range	10 (9 – 11) 5 – 14	10 (9 – 11) 1 – 13	0.429
No. of oocytes	Median(IQR) Range	6 (4 – 8) 1 – 18	6 (4 – 7) 1 – 18	0.387
No. of transferred embryos	Median(IQR) Range	2 (2 – 3) 1 – 3	2 (2 – 3) 1 – 3	0.627

ǂ: Mann Whitney test

DISCUSSION

The aim of the current study was to compare the effectiveness of different types of vaginal progesterone preparations for luteal support in patients undergoing Intracytoplasmic Sperm Injection. The main outcome measures in the three groups were evaluated in terms of: Biochemical pregnancy, clinical pregnancy, miscarriage, and ongoing pregnancy rates.

During the oocyte retrieval procedure for ART, granulosa cells are aspirated, the number depending on the aspiration technique. Aspiration of granulosa cells in this manner is associated with a disruption of the luteal phase, the extent of the disruption varying according to the vigor of the aspiration. Thus, the hormonal environment necessary for implantation may be altered, although this effect has not been observed consistently *(Garcia-Velasco et al., 2010).*

It is worth mentioning that the most common form of progesterone supplement has been used in Egypt was the daily intramuscular progesterone in oil administration which have led to severe inflammatory reactions, sterile abscesses and significant patient discomfort. Therefore; The vaginal route has now become the most favorable way to deliver progesterone for luteal phase support, although it is associated with some adverse effects e.g. vaginal discharge and perineal irritation can be influenced by the preparation and the dosage used perineal irritation was reported in 6%, 14%, 25-30% and 7-20% when tablets, capsules, suppositories and bio-adhesive gel were used respectively, this side effects will certainly affect patient comfort and compliance. However, the majority of published trials on luteal phase support focused on clinical efficacy of different forms, which should be evaluated with regards to side effects and patient convenience *(Panaino et al., 2016)*.

Our current study is a randomized controlled clinical study which was conducted on 300 patients who were following at the Assisted Reproductive Technology unit (ART unit) of International Islamic Center for Population Studies and Research (IICPSR) of Al-Azhar University over the period from May 2016 to January 2018 after being approved by the ethical committee.

Comparison between the studied groups; group A (Prontogest), group B (Crinone) and group C (Endometrin) as regards pregnancy rates which is the main outcome measure in our study, revealed statistically significant increase in pregnancy rates in group C than group A. Also, there was an increase in pregnancy rates in group C (Endometrin) than group B (Crinone) but didn't reach statistical significance.

Up to our knowledge our study was the first trial to compare the 3 types of progesterone, so these results are similar to a study by *Yanushpolsky (2015)* documented that Crinone vaginal gel has been shown to have an excellent coefficient of absorption into endometrial tissues with ability to induce appropriate secretory endometrial changes necessary for luteal phase support. A single daily dose (90 mg) was approved by FDA for progesterone supplementation in assisted reproductive technology (ART).

Also, a prospective randomized trial by *Ghanem and Al-Boghdady (2012)* comparing vaginal cream Crinone 8% investigated 126 patients undergoing cycles of IVF / ICSI. Patients received either Crinone 8% (n = 73) vaginally once daily or two Utrogest capsules (n=53) vaginally three times daily (600 mg). Clinical pregnancy rates were comparable (28.8 versus 18.9%), as were clinical abortion rates until 12 weeks of gestation (14.3 versus 10.0%) and clinical ongoing pregnancy rates (24.7 versus 17.0%) in the Crinone 8% and Utrogest groups, respectively.

This disagreed with *Polyzos et al. (2010)* who reported that no difference regarding the overall clinical and ongoing pregnancy rates between either vaginal gel or other vaginal preparations for LPS in IVF/ICSI cycles. Moreover, vaginal P gel at a dosage of 90 mg once daily results in equivalent clinical pregnancy rates compared with standard care treatment

with 600 mg (200 mg 3) of vaginal P capsules. The clinical implication of our findings is that women undergoing IVF/ICSI cycles and their physicians have the opportunity to use vaginal P gel for LPS and can anticipate the same success rate as with conventional treatment with the potential of adopting an easier and more convenient treatment modality.

There was no statistical significant difference in the number of living birth in the studied groups. This agreed with a meta-analysis by *Zarutskie and Philips (2009)* who demonstrated equal efficacy of all vaginal forms of progesterone as well as similar pregnancy and live birth rates.

CONCLUSION

The use of Endometrin vaginal suppositories in patients undergoing ICSI had a statistically significant higher clinical pregnancy rates in comparison to Prontogest vaginal suppositories. On the other hand, Crinone vaginal gel had a higher clinical pregnancy rate than Prontogest.

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دراسة مقارنة بين انواع مختلفة من هرمون البروجستيرون في دعم مرحلة الاصفري في دورات الحقن المجهري

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خلفيـــة البحـــث: تشـمل تقنيـات الإنجـاب المسـاعدة جميـع علاجـات الخصـوبة التـي يـتم فيهـا التعامـل مـع الأمشـاج (البويضـة والحيوانـات المنويـة) خـارج جسـم الإنسـان بهـدف تحقيـق الحمـل الصـحي. تشـمل إجـراءات تقنيـات الإنجـاب المسـاعدة الإخصـاب فـي المختبـر مـع أو بـدون حقـن الحيوانـات المنويـة داخـل السـيتوبلازم، ونقـل الأجنـة الطازجـة أو المجمـدة، والتلقـيح الصـناعي مـع البويضـات المانحـة. تـم الاتفـاق عالميًـا على دعم المرحلة الأصفرية من خلال الأدوية الصيدلانية.

الهـدف مـن البحـث: مقارنـة فعاليـة أنـواع مختلفـة مـن مستحضـرات البروجسـترون المهبليـة للـدعم الأصـفري فـي المرضـى الـذين يخضـعون لحقـن الحيوانـات المنويـة داخل السيتوبلازم.

المريضـات و طـرق البحـث: أُجريـت الدراسـة التجريبيـة العشـوائية المضـبوطة الحاليـة علـى 300 مريضـة كـانوا يتـابعون فـي وحـدة تقنيـات الإنجـاب المسـاعدة بـالمركز الإسـلامي العـالمي للدراسـات والأبحـاث السـكانية بجامعـة الأزهـر خـلال الفتـرة مـن مـايو 2016 إلـى ينـاير 2018 بعـد الموافقـة عليهـا مـن قبـل لجنـة الأخلاقيـات. تـم تقسـيم المرضـى إلـى 3 مجموعـات متسـاوية، المجموعـة ا تلقـت تحاميـل مهبليـة برونتوجيسـت 400 مجـم مـرة واحـدة فـي اليـوم، المجموعـة ب تلقـت كرينـون جـل 8% (90مجـم) مـرة واحـدة فـي اليـوم والمجموعـة ج تلقـت تحاميـل اندومترين المهبلية مرة واحدة في اليوم.

نتـائج البحـث: أظهـرت المقارنـة بـين المجموعـة ا (برونتوجيسـت) والمجموعـة ب (كرينـون) والمجموعـة ج (انـدومترين) فيمـا يتعلـق بالخصـائص الديموغرافيـة عـدم وجـود فـروق ذات دلالـة إحصـائية. فيمـا يتعلـق بمسـبب العقـم، هنـاك زيـادة ذات دلالـة إحصـائية فـي عـدد المرضـى الـذين يعـانون مـن عوامـل الـذكورة فـي المجموعـة ب

(كرينون) من المجموعة أ (برونتوجيست). فيما يتعلق بتحاليل الهرمونات للمجموعات المدروسة قبل الحقن المجهري، كان هناك زيادة ذات دلالة إحصائية في مستويات هرمون اف اس اتش وال اتش في المجموعة ا من المجموعة ب والمجموعة ج.

من ناحية أخرى، كان هناك فرق بين المجموعات المدروسة فيما يتعلق بمستويات البرولاكتين والأستروجين، ولكن لم يصل إلى دلالة إحصائية. مقارنة بين المجموعات المدروسة فيما يتعلق بسماكة بطانة الرحم، فإن عدد البويضات المسترجعة وعدد الأجنة المنقولة لم يظهر أي فرق ذو دلالة إحصائية. مقارنة بين المجموعات المدروسة فيما يتعلق بمعدلات الحمل كشفت عن زيادة ذات دلالة إحصائية في معدلات الحمل في المجموعة ج من المجموعة أ.

الاستنتاج: كان لاستخدام التحاميل المهبلية الاندومترين في المرضى الذين يخضعون للحقن المجهري معدلات حمل إكلينيكية أعلى ذات دلالة إحصائية مقارنة بالتحاميل المهبلية برونتوجيست. من ناحية أخرى، كان للجل المهبلي كرينون معدل حمل سريري أعلى من برونتوجيست.