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COMPARATIVE STUDY BETWEEN EFFECT OF CLOMIPHENE CITRATE, TAMOXIFEN AND LETROZOLE ON ENDOMETRIAL THICKNESS IN INDUCTION OF OVULATION

By

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ABSTRACT

Background: Ovulation induction remains a milestone in the treatment of women with anovulatory infertility. For the last 40 years, the first line of treatment for anovulation in infertile women was clomiphene citrate (CC). It was appropriate because the drug was highly effective in inducing ovulation in selected patients with the advantages of being orally administered, relatively safe, and inexpensive. Letrozole (AI) has been introduced as a new treatment option that could challenge CC for ovulation induction. AIs are a new group of drugs join the fertility treatments. They are orally administered, easy to use and less expensive than other measurements like gonadotrophines, but more expensive than CC, and with minor side effects. Tamoxifen (TMX) has been also introduced as a simple oral alternative to CC in ovulation induction. It is similar in structure to CC, but with no peripheral anti-estrogenic actions, so, has no adverse effects on endometrial thickness and cervical mucus.

Objective: To compare the effect of clomiphene citrate, letrozole and tamoxifen on the endometrium in anovulatory patients using endometrial thickness and spiral artery Doppler as parameters for comparison during ovulation induction cycle.

Patients and methods: The study was carried out in Entag El-Harby Hospital. The patients were recruited from the outpatient infertility clinic between January 2021 and July 2021. This prospective study included 300 infertile women who were diagnosed as anovulatory infertility and meet the inclusion criteria. Patients were divided into three equal groups giving in Group 1: Clomiphene citrate, Group 2: Letrozole, and Group 3: Tamoxifen.

Results: There was no statistically significant difference in the patients' characteristics (age and BMI) between the three studied groups. There was a statistically significant difference as regards duration of infertility in the three studied groups. Enometrial thickness was better under letrozole and tamoxifen therapy. Spiral artery Doppler showed lower impedance with a lower resistance index (RI) and pulsatility index (PI) under letrozole and tamoxifen therapy. Ovulation rate was not significantly different between the three drugs. Pregnancy rate was not significantly different between the three drugs.

Conclusion: Letrozole and tamoxifen can induce similar or even better results than clomiphene citrate, and each of them can be used as a first line option for treatment of anovulatory infertility.

Keywords: Clomiphene Citrate, Tamoxifen, Letrozole, Endometrial Thickness, Induction of Ovulation.

INTRODUCTION

Infertility is the inability of a married couple to conceive within one year in spite of regular marital life. Globally 10-15% of the married couples are experiencing this problem. Anovulation accounts for about 20-25% of causes of infertility as ovulation is a core event for reproduction. Anovulation may be due to problems affecting the ovary, pituitary or hypothalamus. These causes have been organized by the world health organization (WHO) into three main categories based on the site of the lesion and as reflected by gonadotropin production: hypogonadotropic hypogonadism, normogonadotropic hypogonadism, and hypergonadotropic hypogonadism *(Propst and Bates, 2013)*.

Ovulation induction involves the use of medication to stimulate development of one or more mature follicles in the ovaries of women who have anovulation and infertility. These women don't regularly develop mature follicles without help from ovulation enhancing drugs as Selective Estrogen Receptor Modulator (clomiphene citrate and tamoxifen), Aromatase Inhibitors (letrozole), Gonadotropins, etc. Treatment with these drugs has the potential to result in pregnancy if the woman has good quality eggs in her ovaries and if other causes of infertility are absent *(Messinis, 2011* and *Propst and Bates, 2013).*

Clomiphene citrate (CC) is a non-steroidal selective estrogen receptor modulator (SERM), has both estrogen agonist and antagonist properties. It binds to estrogen receptors primarily in the hypothalamus, which interrupts the negative feedback of the increasing estrogen level and results in continued production of FSH, which stimulates follicular growth and maturation *(Roy et al., 2012)*.

Clomiphene citrate anti-estrogenic effect causes long standing estrogen receptor depletion due to its long half-life (2 weeks), so it has adverse effects on the quality and quantity of cervical mucus and negative impact on endometrial development causing its significant thinning, implantation failure and decreased blood flow during the peri-implantation stage *(Ray et al., 2012* and *Hussain et al., 2013)*. It can induce ovulation in 60-80% of anovulatory women but only 20-40% becomes pregnant *(Richard et al., 2010)*.

Tamoxifen (TMX) is a non-steroidal selective estrogen receptor modulator (SERM). Commonly used today as an adjuvant therapy in treatment of breast cancer. It acts primarily by binding to estrogen receptors at hypothalamus, this competitive inhibition results in a perceived drop in endogenous estrogen levels, eventually leading to increased gonadotropins secretion and subsequent induction of ovulation *(Steiner et al., 2011)*. It may also improve folliculogenesis by involving a direct action on the ovary without intervention of hypothalamo-pitutary system. It acts as an agonist on estrogen receptors of endometrium and vaginal mucosa, its half life is short (5-7 days) leading to favorable cervical mucus, better endometrial thickness and may be better endometrial blood flow *(Dhaliwal et al., 2011* and *Steiner et al., 2011)*.

Tamoxifen can induce ovulation in about 50-90% of anovulatory women with

pregnancy rate 30-50%. This better results due to high score in endometrium, cervical mucus and better functioning corpus luteum *(Dhaliwal et al., 2011* and *Pant, 2013)*.

Letrozole (AI) is highly selective Aromatase Inhibitor, prevents conversion of androgen to estrogen, thus releasing the hypothalamo-pitutary axis from the negative feedback, resulting in an increase of FSH secretion from the anterior pituitary. The accumulated androgens in the ovary further increase the follicular sensitivity to FSH *(Kamath and George, 2011)*.

Letrozole is devoid of any anti-estrogenic peripheral actions so doesn't deplete estrogen receptors *(Kamath and George, 2011)*. It has short half-life (48 hours) thus has no adverse effects on the quality and quantity of cervical mucus and has positive impact on endometrial development causing its significant thickening, better implantation and increase blood flow during the peri-implantation stage. It can induce ovulation in about 80% of anovulatory women with high pregnancy rate *(Roy et al., 2012* and *Hussain et al., 2013)*.

In our study, we tried to compare the effect of CC, letrozole and TMX on the endometrium in anovulatory patients using endometrial thickness and spiral artery Doppler as parameters for comparison during ovulation induction cycle.

PATIENTS AND METHODS

The study was carried out at Entag El-Harby Hospital. The patients were recruited from the outpatient infertility clinic between January 2021 and July 2021.

Sample size calculation:

The required sample size has been calculated using the G*Power© software version 3.1.0 (Institut für Experimentelle Psychologie, Heinrich Heine Universität, Düsseldorf, Germany).

This prospective study included 300 infertile women who were diagnosed as anovulatory infertility and met the inclusion criteria.

This study followed the ethical committee rules of Obstetrics and Gynecology, Al-Azhar University.

For all women with anovulatory infertility in this study; explanation of the study procedures were done to all women sharing in the study and informed written consents were obtained.

Inclusion Criteria:

1. Age: 18 - 35 years.
2. Body mass index (BMI): 18 - 30 kg/m2.
3. Patients with normogonadotropic hypogonadism (WHO type 2).
4. Normal uterus and patent fallopian tubes proved by hystrosalpingography (HSG).
5. Normal semen analysis of the husband.
6. Normal serum Prolactin.
7. Women with documented anovulation by measuring progesterone on day 21 or by performing ultrasound during ovulation phase.

Exclusion Criteria:

1. Hyperprolactinemia, thyroid dysfunction, active liver diseases, etc.
2. Local diseases as endometriosis, ovarian tumors, hydro- or pyosalpinx etc.
3. Patients with previous history of ovarian drilling.

All patients were divided by the computer allocation method into 3 equal groups:

Group A was under ovulation induction with clomiphene citrate. Patient took 100 mg of the drug daily for 5 days, starting from day 3 to day 7 of the cycle. Each tablet of the drug was 50 mg. So, the patient took the dose in the form of 2 tablets all together after breakfast for one cycle.

Group B was under ovulation induction with letrozole. Patient took 5 mg of the drug daily for 5 days, starting from day 3 to day 7 of the cycle. Each tablet of the drug was 2.5 mg. So, the patient took the dose in form of 2 tablets all together after breakfast for one cycle.

Group C were under ovulation induction with tamoxifen. Patient took 60 mg of the drug daily for 5 days, starting from day 3 to day 7 of the cycle. Each tablet of the drug was 20 mg. So, the patient took the dose in form of 3 tablets all together after breakfast for one cycle.

All patients were subjected to the following:

History: Detailed history was taken. It included age, duration of infertility, menstrual history, symptoms and signs suggestive of endocrine disorders, history of chronic diseases including diabetes mellitus and hypertension, surgical history including laparoscopy and laparotomy.

Physical examination: General examination for determination of acne, obesity, scar of previous pelvi-abdominal operations, abdominal examination for determination of enlarged uterus, enlarged ovaries, and vaginal examination for determination of congenital anomalies.

Investigations:

1. Hormonal profile on day 2-5 of the cycle: FSH, LH, E2, Prolactin, TSH, free T3 and T4.
2. Hysterosalpingography (HSG) to confirm tubal patency.
3. Semen analysis to rule out male factor.
4. Transvaginal ultrasound was done on day 3 of the cycle then day 10 then, followed up every other day until the mean diameter of the largest follicle reaches 18 mm, then the endometrial thickness in mm was measured in the sagittal view as the maximum thickness between the highly reflective interfaces of the endometrial–myometrial junction. If no dominant follicle appeared at day 14 or 15 of the cycle, transvaginal ultrasound will be continued till day 20, if no follicle appeared also, it considered as failure of the cycle.
5. Doppler ultrasound to measure the endometrial blood flow in form of pulsatility index (PI) and resistance index (RI) at the time of maximum follicle growth (18 mm or more) or on day 20 of the cycle in absence of dominant follicle. On day of ovulation normal PI (0.84± 0.14) and RI (0.48±0.06).

- **Resistance index (RI):** It is the difference between the peak systolic flow velocity and the end-diastolic flow velocity divided by the peak systolic flow velocity was measured from the flow velocity waveform.
- **Pulsatility index (PI):** It is the difference between the peak systolic flow velocity and the end diastolic flow velocity divided by the mean.

6. Pregnancy test was done after 2 weeks of ovulation, to detect biochemical pregnancy.

Statistical methods:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data with parametric distribution were expressed as mean ± SD (Standard deviation) and compared using One Way ANOVA test followed by post hoc analysis using LSD test when significant while quantitative data with non-parametric distribution were expressed as median and interquartile range (IQR) and compared using Kruskall-Wallis test followed by post hoc analysis using Wilcoxon Rank test when significant. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. P value < 0.05 was considered significant.

RESULTS

There was no statistically significant difference in the patients' characteristics (age and BMI) between the three studied groups, P value > 0.05. There was a statistically significant difference as regards duration of infertility in the three studied groups (P <0.01) **(Table 1)**.

Table (1): Patients' characteristics and duration of infertility in the three study groups

Variables \ Groups	Clomiphene (N=100)	Letrozole (N=100)	Tamoxifen (N=100)	p-value●
	Mean ±SD	Mean ±SD	Mean ±SD	
Age (yr)	27.5 ± 4.1	27.2 ± 3.9	27.5 ± 4.1	0.832
BMI (kg/m^2)	26.9 ± 1.7	26.8 ± 1.7	26.7 ± 1.5	0.689
Duration of infertility (yr)	1.9 ± 0.7	1.9 ± 0.7	*2.2 ± 0.7	0.002

●: One Way ANOVA; *: Post hoc analysis by LSD test; Significant difference between tamoxifen and the two other groups at p-value = 0.002

There were no statistically significant difference as regards type of infertility (Primary or Secondary), Ovulation and follicle diameter in the three studied groups (P > 0.05) **(Table 2)**.

Table (1): Type of infertility and rate of ovulation and follicle diameter in the three study groups

Variables \ Groups	Clomiphene (n=100)	Letrozole (n=100)	Tamoxifen (n=100)	p-value*
	N (%)	N (%)	N (%)	
Type of infertility				
Primary	76 (76.0%)	72(72.0%)	74 (74.0%)	0.812
Secondary	24 (24.0%)	28 (28.0%)	26 (26.0%)	
Ovulation				
Not ovulated	34 (34.0%)	28 (28.0%)	32 (32.0%)	0.648
Ovulated	66 (66.0%)	72 (72.0%)	68 (68.0%)	
Follicle diameter				
<18 mm	34 (34.0%)	28 (28.0%)	32 (32.0%)	0.648
≥18 mm	66 (66.0%)	72 (72.0%)	68 (68.0%)	

*: Chi-square test

There was a statistically significant difference as regards number of follicles in the three studied groups (P < 0.001). CC group showed development of more number of follicles during ovulation induction than the Letrozole and tamoxifen groups **(Table 3)**.

Table (3): Number of follicles in the three study groups

Variables \ Groups	Clomiphene (n=100)		Letrozole (n=100)		Tamoxifen (n=100)		p-value
	Median (IOR)	Mean ±SD	Median (IOR)	Mean ±SD	Median (IOR)	Mean ±SD	
Number of follicles	*2 (0 to 4)	2.0*±0.9	1 (0 to 2)	1.2 ±0.4	1 (0 to 2)	1.2 ±0.4	**<0.001**#

#: Kruskall Wallis test; *Post hoc analysis using Wilcoxon Rank test; significant difference between clomiphene and the two other groups at p-value < 0.001
IQR: Interquartile range

There was a statistically significant difference as regards endometrial thickness and Doppler indices (PI and RI) as measured by trans-vaginal U/S in the three studied groups (P <0.001). CC group showed a significant lower endometrial thickness, and significant higher Doppler (PI and RI) indices than letrozole and tamoxifen groups **(Table 4)**.

Table (4): Endometrial thickness and Doppler indices of endometrial vessels (spiral artery) in the three study groups.

Variables \ Groups	Clomiphene (N=100)	Letrozole (N=100)	Tamoxifen (N=100)	P-value●
	Mean ±SD	Mean ±SD	Mean ±SD	
Endometrial thickness (mm)	6.9* ± 1.2	9.6 ± 1.6	9.8 ± 1.7	**<0.001**
Endometrial PI	1.67* ± 0.21	1.39 ± 0.16	1.41 ± 0.14	**<0.001**
Endometrial RI	0.72* ± 0.03	0.63 ± 0.03	0.62 ± 0.03	**<0.001**

●: One Way ANOVA test; *: Post hoc analysis using LSD test; Significant difference between clomiphene and the two other studied groups

There was a significant negative correlation coefficient between endometrial thickness and Doppler indices (PI and RI) in the three studied groups. So, the relation was an inversely proportional, as endometrial thickness increased, the Doppler indices (PI and RI) decreased and vice versa **(Table 5)**.

Table (5): Correlation between endometrial thickness and endometrial PI and RI

Parameters / Endometrial Thickness (mm)	Endometrial PI		Endometrial RI	
	Correlation coefficient (r)	p-value	Correlation coefficient (r)	P-value
All study population (n=150)	-0.850	<0.0001	-0.837	<0.0001
Clomiphene group (n=50)	-0.695	<0.0001	-0.58	<0.0001
Letrozole group (n=50)	-0.776	<0.0001	-0.716	<0.0001
Tamoxifen group (n=50)	-0.927	<0.0001	-0.818	<0.0001

Spearman correlation coefficients

There was no statistically significant difference as regards the pregnancy rate in the three studied groups (P > 0.05). But clinically, there was a significant difference as regards the pregnancy rate. Pregnancy rate with letrozole was higher than clomiphene and tamoxifen **(Table 6)**.

Table (6): Pregnancy rate in the three study groups in one cycle

Groups / Variables	Clomiphene (n=100)	Letrozole (n=100)	Tamoxifen (n=100)	P-value
Pregnancy	N (%)	N (%)	N (%)	
Negative	84 (84.0%)	72 (72.0%)	80 (80.0%)	0.108
Positive	16 (16.0%)	28 (28.0%)	20 (20.0%)	

*: Chi-square test

DISCUSSION

The groups in our study were matched as regard to age, BMI, type and duration of infertility.

The current study showed a statistically significant difference between the three groups regarding the endometrial thickness, which was significantly thinner in group 1 (CC) than the other two groups; group 2 (letrozole) and group 3 (TMX).

Our results were in agreement with *Pant (2013),* who showed that the results were ovulation rate (65% and 63% respectively), pregnancy rate (13.6 % and 17.4% respectively). These results showed no significant difference between the two groups. Endometrial thickness showed significant difference, which was thicker in TMX group > 8 mm and CC <8 mm.

Also *Hussain et al. (2013)* showed that numbers of follicles were higher in CC than letrozole, ovulation rate was significantly higher in letrozole group (78.7%) than CC group (53.3%). Pregnancy rate was higher in letrozole group (25.3%) than CC group (16%). Mean endometrial thickness was higher in letrozole group (9.2mm) than CC group (8.4mm).

Roy et al. (2012) showed that the number of follicles were higher in CC group than letrozole group. Ovulation rate

was almost of no difference in CC group (67.9%) and letrozole group (66.6%), pregnancy rate was significantly higher in letrozole group (43.8%) than CC (26.4%), mean endometrial thickness was significantly higher in letrozole group (9.1mm) than CC group (6.3mm).

Selim and Borg (2012) showed that ovulation rate was slightly higher in letrozole group (70.6%) than CC group (64.6%), pregnancy rate was slightly higher in letrozole group (28.4%) than CC group (20.2%). Mean endometrial thickness was higher in letrozole group (9.9mm) than CC group (7.7mm). Mean endometrial blood flow (PI and RI) was significantly lower in letrozole group (1.27, 0.75) than CC group (1.67, 0.87).

Elsedeek and Elmaghraby (2011) showed that the number of follicles were higher in CC group than letrozole group, ovulation rate which was higher in letrozole group (69.5%) than CC (61.4%). Pregnancy rate was higher in letrozole group (33%) than in CC group (28%), mean endometrial thickness was higher in letrozole group (8.3mm) than CC group (7.2mm).

On the other hand, our results disagreed with *Badawy et al. (2010)* showed that the number of follicles were significantly higher in CC than letrozole group. Ovulation rate was higher in CC group (70.9%) than letrozole group (67.5%). Pregnancy rate was higher in CC group (17.9%) than letrozole group (15.1%). Endometrial thickness was also higher in CC group (8.5- 10mm) than letrozole group (8- 8.2mm). Due to different in sample size, duration and method.

Also, disagreed with *Kar (2012)*, who showed that the number of follicles were higher in CC group (multi-follicular) than letrozole group (monofollicular), ovulation rate was higher in letrozole group (73.08%) than CC group (60.78%). Pregnancy rate was significantly higher in letrozole group (21.56%) than CC group (8%). Mean endometrial thickness was almost the same between the two groups (letrozole 7.65mm and CC 7.61mm). Due to different in sample size, duration and method.

Reynolds et al. (2013) showed that ovulation induction by CC, occurred but with thin endometrium (4.8- 6.3mm), then retreated with TMX, endometrial thickness improved (7.5- 11mm).

The current study showed a statistically significant difference between the three groups regarding the endometrial blood flow (spiral artery Doppler indices PI and RI), which was significantly higher in group (1) than the other two groups. So, groups (2 and 3) showed significant lower impedance than group (1).

Baruah et al. (2010) stated that the number of follicles were higher in CC group than letrozole group. Mean endometrial thickness was thicker in letrozole group (6.9mm) than CC group (5.9mm). Mean spiral artery RI and PI, letrozole and CC groups. The mean RI of spiral artery were 0.63 and 0.79 respectively, and the mean PI of spiral artery were 1.21 and 1.55 respectively. Both RI and PI in the letrozole group showed significant lower impedance compared to CC group. Pregnancy rate was 19% with letrozole and 12.5% with CC group. The effect of letrozole showed

a significantly better endometrial response compared to CC.

Our results were in agreement with *Elkattan (2012)* who showed that the mean spiral artery Doppler indices (PI and RI) which were significantly lower in letrozole (1.25, 0.62) than CC (1.45, 0.68).Also, *Selim and Borg (2012)* stated that the mean endometrial blood flow (PI and RI) was significantly lower in letrozole (1.27, 0.75) than CC (1.67, 0.87).

The current study showed a higher ovulation rate in group (2) than the other two groups, but these results were not statistically significant.

Elsedeek and Elmaghraby (2011) showed that letrozole (69.5%) and CC (61.4%), and *Dhaliwal et al. (2011)* showed that ovulation rate was 65.25% and pregnancy rate was 14.9%.

Our results were in agreement with *Kar (2012)* showed letrozole (73.08%) and CC (60.78%), *Selim and Borg (2012)* showed that letrozole (70.6%) and CC (64.6%), also *Hussain et al. (2013)* showed letrozole (78.7%) and CC (53.3%), Pant (2013) as CC was 65% and TMX was 63%.

Our results disagreed with, *Badawy and Gibreal (2011)* showed that CC 64% and TMX 51.6%, *Roy et al. (2012)* showed CC 67.9%, letrozole 66.6%, and *Badawy et al. (2010)*, CC 70.9% and letrozole 67.5%.

The current study showed higher Pregnancy rate in group (2) than the other two groups, but these results were not statistically significant.

Our results were in agreement with *Baruah et al. (2010)* showed that letrozole 19% and CC 12.5%, *Elsedeek and Elmaghraby (2011)* showed that letrozole 33% and CC 28%, *Dhaliwal et al. (2011)* showed that TMX 14.9%, and *Selim and Borg (2012)* showed that letrozole 28.4% and CC 20.2%, *Pant (2013)* showed that CC 13.6% and TMX 17.4%, *Hussain et al. (2013)* showed that letrozole 25.3% and CC 16%.

Due to different in sample size, duration and method Our results disagreed with *Badawy et al. (2010)* showed that letrozole 15.1% and CC 17.9%, *Badawy and Gibreal (2011)*, CC 18.7% and TMX 10.8%, *Elkattan (2012)* showed that letrozole 10% and CC 13.3%.

The current study showed a statistically significant difference between the three groups regarding the number of mature follicles. In group (1), the total number of mature follicles was higher than the other two groups (2 and 3). Group (1) has tendency to multi-follicular stimulation, while Groups (2 and 3) have tendency to mono-follicular stimulation. The follicular diameter wasn't significantly different between the three groups.

Our results were in agreement with *Badawy and Gibreal (2011)* with showed a higher number of follicles in CC than in TMX, *Elsedeek and Elmaghraby (2011)*, *Roy et al. (2012)*, *Hussain et al. (2013)*, All these show higher number of follicle in CC than letrozole.

Our study showed characteristic thicker endometrium and lower impedance (PI and RI) with letrozole and TMX therapy than CC, but ovulation rate and pregnancy rate showed no significant difference between any of the groups.

Dhaliwal et al. (2011), Selim and Borg (2012), Pant (2013), Hussain et al. (2013), support our study, as they show results close to our results.

CONCLUSION

Letrozole and TMX can induce similar or even better results than CC, and each of them can be used as a first line option for treatment of anovulatory infertility.

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دراسة مقارنة بين تأثير سيترات الكلومفين، التاموكسافين والليتروزول علي سمك بطانة الرحم أثناء تنشيط التبويض

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خلفية البحث: لا يزال تحريض الإباضة علامة فارقة في علاج النساء المصابات بالعقم الإباضي. وعلى مدار الأربعين عامًا الماضية، كان الخط الأول من علاج انقطاع الإباضة عند النساء المصابات بالعقم هو عقار سيترات الكلومفين، وكان مناسبًا، لأن الدواء كان فعالاً للغاية في إحداث التبويض لدى مرضى مختارين، مع مزايا تناوله عن طريق الفم، وآمن نسبيًا، وغير مكلف. وقد قدم الليتروزول كخيار علاجي جديد يمكن أن يتحدى سيترات الكلومفين لتحريض الإباضة. والذكاء الاصطناعي هو مجموعة جديدة من الأدوية تنضم إلى علاجات الخصوبة. يتم تناولها عن طريق الفم، وسهلة الاستخدام وأقل تكلفة من القياسات الأخرى مثل الغدد التناسلية، ولكنها أغلى من عقار سيترات الكلومفين، ولها آثار جانبية طفيفة. كما قدم عقار التاموكسافين أيضًا كبديل شفوي بسيط لسيترات الكلوميفين في تحريض الإباضة. وهو مشابه في تركيبه لسيترات الكلوميفين ولكن بدون إجراءات محيطية مضادة للإستروجين، لذلك ليس له أي آثار سلبية على سمك بطانة الرحم ومخاط عنق الرحم.

الهدف من البحث: مقارنة تأثير سيترات الكلومفين، والليتروزول والتاموكسافين على بطانة الرحم في مرضى عدم التبويض بإستخدام سماكة بطانة الرحم ودوبلر الشريان الحلزوني كمعلمات للمقارنة أثناء دورة تحريض الإباضة.

المريضات وطرق البحث: أجريت الدراسة بمستشفى الانتاج الحربي، وتم إختيار المريضات من عيادة العقم الخارجية بين يناير 2021 ويوليو 2021. وشملت هذه الدراسة 300 امرأة مصابات بالعقم تم تشخيصهن من حيث عقم عدم الإباضة ويستوفين معايير التضمين. وتم تقسيم المريضات إلى ثلاث مجموعات متساوية

أعطين في المجموعة 1: سيترات الكلومفين، والمجموعة 2: الليتروزول، والمجموعة 3: التاموكسافين.

نتائج البحث: لا توجد فروق ذات دلالة إحصائية في خصائص المرضى (العمر ومؤشر كتلة الجسم) بين المجموعات الثلاث المدروسة. وكان هناك فرقاً ذا دلالة إحصائية فيما يتعلق بمدة العقم في المجموعات الثلاث المدروسة. وكان سمك بطانة الرحم أفضل تحت العلاج ليتروزول وتاموكسيفين. وأظهر دوبلر الشريان الحلزوني مقاومة أقل مع إنخفاض مؤشر المقاومة و مؤشر النبض تحت علاج الليتروزول و التاموكسافين. ولم يكن معدل الإباضة مختلفًا بشكل كبير بين الأدوية الثلاثة، ولم يكن معدل الحمل مختلفًا بشكل كبير بين الأدوية الثلاثة.

الاستنتاج: يمكن أن يؤدي كل من الليتروزول و التاموكسافين إلى نتائج مماثلة أو حتى أفضل من عقار سيترات الكلومفين، ويمكن إستخدام كل منهما كخيار أول لعلاج عقم الإباضة.

الكلمات الدالة: سيترات الكلومفين، التاموكسافين، الليتروزول، سماك بطانة الرحم، تحريض الإباضة.