Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

## ORIGINAL RESEARCH

# CLOMIPHENE CITRATE VERSUS LETRAZOLE IN INTRAUTERINE INSEMINATION CYCLE

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**ABSTRACT:**

**Background:** Infertility is commonly defined as the failure of conception after at least twelve months of unprotected intercourse. The present study compared clomiphene citrate with letrazole and in intrauterine insemination cycle.

**Materials & Methods:** 90 women with unexplained infertility were randomized into 2 groups. Group I received 50 mg Clomiphene Citrate for 5 days and 75 IU of gonadotrophins (HMG) for 3–5 days and group II received 5 mg Letrozole and 75 IU of gonadotrophins (HMG) for 3–5 days. Parameters such as duration of infertility (years), day-2 FSH (mlU/ml), day-2 LH (mIU/ml), serum prolactin (mg/dl), multiple pregnancy (twins), no. of follicles >18 mm in diameter on the day of hCG, miscarriages, pregnancy rate and live births rate was recorded.

**Results:** Group I received CC+ HMG and group II received Letrozole + HMG. Each group comprised of 45 patients. day-2 FSH level was 8 mlU/ml in group I and 7 mlU/ml in group II, day-2 LH was 7 mlU/ml in group I and 8 mlU/ml in group II, serum prolactin level was 10.2 mg/dl in group I and 11.5 in group II. Duration of infertility was 4.0 years in group I and 4.3 years in group II. The difference was significant ($P< 0.05$). No. of follicles >18 mm in diameter on the day of hCG was 1.2 in group I and 2.5 in group II, multiple pregnancy (twins) in 3 group I and 2 group II, miscarriages was seen in 5 group I and 2 group II and live births rate was seen in 40 group I and 43 group II. The difference was non- significant ($P> 0.05$).

**Conclusion:** Letrozole along with gonadotrophins found to be effective as compared to Clomiphene Citrate decreasing gonadotrophins requirements and improving endometrial thickness.

**Key words:** Clomiphene citrate, Letrozole, Infertility

## Introduction

Infertility is commonly defined as the failure of conception after at least twelve months of unprotected intercourse. Superovulation and intrauterine insemination (IUI) are effective treatment for women with unexplained infertility.[1] IUI (Intrauterine Insemination) may be recommended as a first-line treatment in young couples with different etiologies of infertility such as male factor infertility, unexplained infertility and ovulatory disorders. Superovulation increases the probability of pregnancy by increasing the number of oocytes suitable for fertilization or by correcting any subtle defect in ovulation.[2]

Letrozole is a third-generation aromatase inhibitor which has been successfully used for ovulation induction in patients with polycystic ovary syndrome (PCOS).[3] Letrozole does not deplete estrogen receptor (ER) in target tissues, so it has no persistent anti-estrogenic effect.[4] It typically results in mono-ovulation and it may have no adverse effects on endometrium and cervical mucosa. It has a short half-life so it would be eliminated from the body rapidly. In euestrogenic anovulation, Clomiphene Citrate (CC) remains the primary therapy to induce

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

ovulation.[5] Clomiphene Citrate is an antiestrogen that leads to a 60%–85% ovulation rate and a 10%–20% pregnancy rate (PR) per cycle. This disparity in outcome is related to the antiestrogen effect of CC, which involves long lasting estrogen receptor (ER) depletion.[6] The present study compared letrazole and clomiphene citrate in intrauterine insemination cycle.

**Materials & methods**

The present study comprised of 90 women with unexplained infertility. All were informed regarding the study and their written consent was obtained.

Data of each patient was recorded followed by their randomization into 2 groups. Group I received 50 mg Clomiphene Citrate for 5 days and 75 IU of gonadotrophins (HMG) for 3–5 days and group II received 5 mg Letrozole and 75 IU of gonadotrophins (HMG) for 3–5 days. Parameters such as duration of infertility (years), day-2 FSH (mlU/ml), day-2 LH (mIU/ml), serum prolactin (mg/dl), multiple pregnancy (twins), no. of follicles >18 mm in diameter on the day of hCG, miscarriages, pregnancy rate and live births rate was recorded. Results thus obtained were subjected top statistical analysis. P value less than 0.05 was considered significant.

**Results**

**Table I: Distribution of patients**

| Groups | Group I | Group II |
|---|---|---|
| Method | CC+ HMG | Letrozole + HMG |
| Number | 45 | 45 |

Table I shows that group I received CC+ HMG and group II received Letrozole + HMG. Each group comprised of 45 patients.

**Table II: Assessment of variables**

| Parameters | Variables | Group I | Group II | P value |
|---|---|---|---|---|
| Day-2 | FSH (mlU/ml) | 8 | 9 | 0.98 |
| | LH (mIU/ml) | 9 | 8 | 0.97 |
| Serum Prolactin (mg/dl) | | 10.2 | 11.5 | 0.81 |
| Duration of infertility (years) | | 4.0 | 4.3 | 0.72 |

Table II, graph I shows that day-2 FSH level was 8 mlU/ml in group I and 7 mlU/ml in group II, day-2 LH was 7 mlU/ml in group I and 8 mlU/ml in group II, serum prolactin level was 10.2 mg/dl in group I and 11.5 in group II. Duration of infertility was 4.0 years in group I and 4.3 years in group II. The difference was significant (P< 0.05).

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

**Graph I: Assessment of variables**

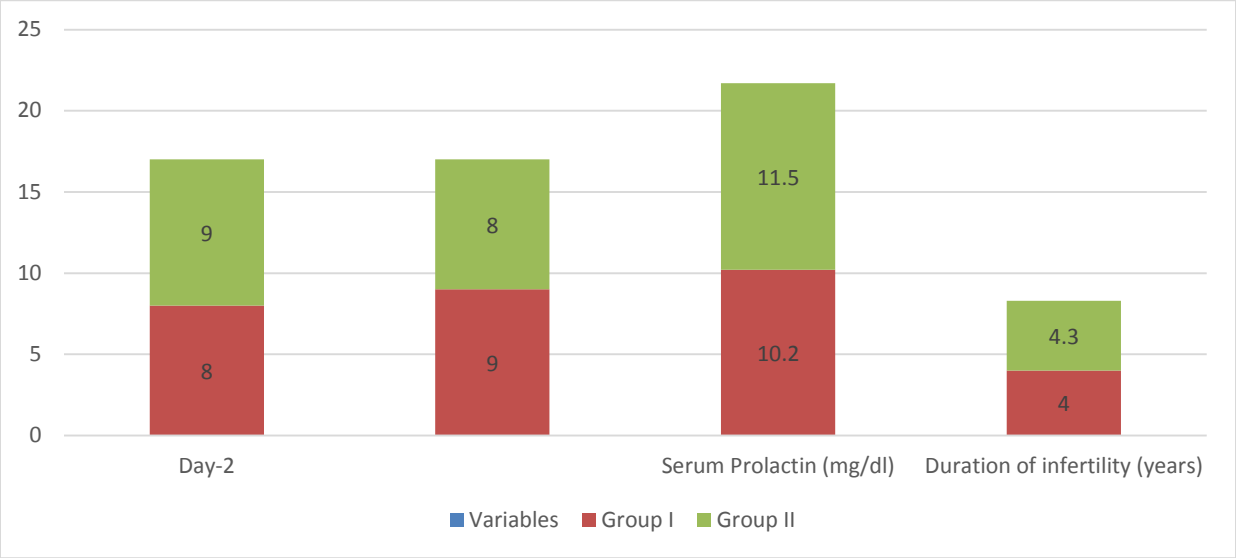
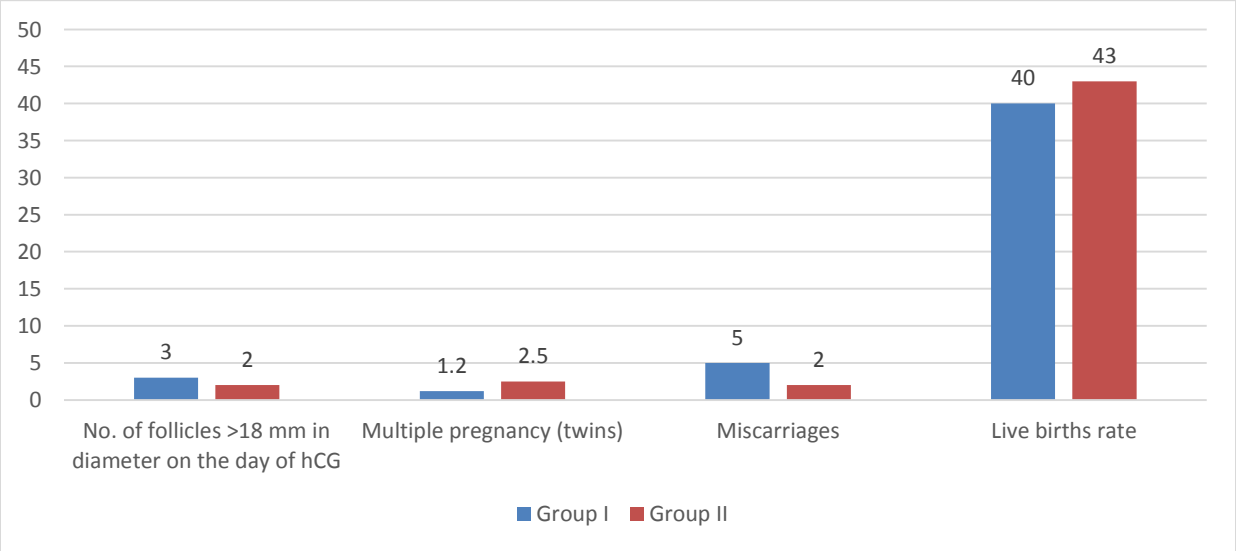



**Table III: Assessment of pregnancy outcome**

| Parameters | Group I | Group II | P value |
|---|---|---|---|
| No. of follicles >18 mm in diameter on the day of hCG | 1.2 | 2.5 | 0.90 |
| Multiple pregnancy (twins) | 3 | 2 | 0.04 |
| Miscarriages | 5 | 2 | 0.02 |
| Live births rate | 40 | 43 | 0.93 |

Table III, graph I shows that no. of follicles >18 mm in diameter on the day of hCG was 1.2 in group I and 2.5 in group II, multiple pregnancy (twins) in 3 group I and 2 group II, miscarriages was seen in 5 group I and 2 group II and live births rate was seen in 40 group I and 43 group II. The difference was non- significant (P> 0.05).

**Graph I: Assessment of pregnancy outcome**



ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

**Discussion**

Unexplained infertility is one of the most frequent infertility diagnoses encountered by the gynaecologists. The two main oral agents for superovulation are clomiphene citrate (C. C.) and letrozole (LTZ).[7] Clomiphene citrate has been the most widely used first line drug for superovulation in infertile patients, both for timed intercourse as well as IUI since its introduction in 1960's.[8] The different indications for its use are polycystic ovarian syndrome (PCOS), unexplained infertility, IUI and mild stimulation protocols in in-vitro fertilization (IVF). It is a non-steroidal selective estrogen receptor modulator with predominant antiestrogenic action.[9] Clomiphene citrate has a long half-life around 2 weeks resulting in long lasting estrogen receptor depletion and antiestrogenic adverse effects on endometrium, and cervical mucus. The present study compared efficacy of clomiphene citrate and letrazole in intrauterine insemination cycle.[10] The present study compared letrazole and clomiphene citrate in intrauterine insemination cycle.

We found that group I received CC+ HMG and group II received Letrozole + HMG. Each group comprised of 45 patients. Chishty et al[11] included 160 patients and were divided into two groups of 80 each based on the drug given for ovulation induction. The drug was given for 5 days from D3 to D7 of menstrual cycle. IUI was done 38 - 40 hours after trigger and after confirmation of ovulation by sonography. The mean age, body mass index (BMI), duration of infertility, type and cause of infertility in both groups were similar. Ovulation rate was 85 % in letrozole group and 71.25 % in clomiphene citrate group, which was statistically significant (P0.035). There was no statistically significant difference between endometrial thickness and total days till ovulation between two groups. Monofolliculogenesis and clinical pregnancy rate were statistically significantly higher in letrozole group.

We observed that day-2 FSH level was 8 mlU/ml in group I and 7 mlU/ml in group II, day-2 LH was 7 mlU/ml in group I and 8 mlU/ml in group II, serum prolactin level was 10.2 mg/dl in group I and 11.5 in group II. Duration of infertility was 4.0 years in group I and 4.3 years in group II. Fouda et al[12] compared the efficacy of extended letrozole regimen with clomiphene citrate in women with unexplained infertility undergoing superovulation and intrauterine insemination (IUI) on 214 patients which were randomized into two equal groups who received either letrozole 2.5 mg/day from cycle day 1 to 9 or clomiphene citrate 100 mg/day from cycle day 3 to 7. Intrauterine insemination was performed 36 to 40 hours after HCG administration. Both groups were comparable with regard to number of mature follicles and the day of HCG administration. Serum estradiol was significantly greater in clomiphene citrate group and the endometrial thickness was significantly greater in extended letrozole group. The pregnancy rate per cycle and cumulative pregnancy rate were significantly greater in extended letrozole group.

We found that no. of follicles >18 mm in diameter on the day of hCG was 1.2 in group I and 2.5 in group II, multiple pregnancy (twins) in 3 group I and 2 group II, miscarriages was seen in 5 group I and 2 group II and live births rate was seen in 40 group I and 43 group II. Al-Fadhli et al[13] found that the pregnancy rate was significantly higher in patients with unexplained infertility treated with 5 mg/day compared with those treated with 2.5 mg/day. Mitwally et al[14] had reported acceptable pregnancy outcomes and lower rate of multiple gestation in letrozole group for ovarian stimulation.

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**Conclusion**

Letrozole along with gonadotrophins found to be effective as compared to Clomiphene Citrate decreasing gonadotrophins requirements and improving endometrial thickness.

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