



USE OF LETRAZOLE FOR OVULATION INDUCTION WITH GOOD SUCCESS RESULTS: STUDY DONE IN A SMALL PRIVATE SETUP

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ABSTRACT

Clomiphene citrate and letrazole are two commonly used drugs for ovulation induction. Clomiphene citrate binds to the estrogen receptor at hypothalamus, blocking negative feedback effect of estrogen leading to increase GnRH and gonadotropic release thus causing ovulation. Letrazole is an aromatase inhibitor. Aromatase inhibitor act by blocking the conversion of androgens to estrogens in the ovarian follicles, peripheral tissues, and in the brain. This result in, fall in circulating and local estrogens. Thus, negative feedback effect of estrogens to hypothalamic pituitary axis is blocked causing release of FSH and thus ovulation. We studied letrazole for ovulation induction in a small private setup and found success rate of 37.17%.

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INTRODUCTION

Drugs commonly used for ovulation induction is Clomiphene citrate and Letrazole, both differ in mechanism of action. Letrazole is an aromatase inhibitor. Aromatase inhibitor act by blocking the conversion of androgens to estrogens in the ovarian follicles, peripheral tissues, and in the brain. This result in, fall in circulating and local estrogens and rise in intraovarian androgens. The negative feedback of estrogens to hypothalamic pituitary axis is blocked by fall in circulating estrogen levels. Thus, there is a surge in follicle stimulating hormone (FSH) release, which results in follicular growth. Since, the feedback mechanism is intact; normal follicular growth, selection of dominant follicle, and atresia of smaller growing follicle occurs; and thereby facilitating monofollicular growth¹⁻⁵. Another likely mechanism of action of the aromatase inhibitors is by increasing intraovarian androgens. This leads to increases the follicular sensitivity to FSH.

Clomiphene citrate binds to the estrogen receptor. Its effectiveness in ovulation induction can be attributed to actions at the hypothalamic level. Reduced levels of estrogen negative feedback trigger normal compensatory mechanisms that alter the pattern of pulsatile hypothalamic gonadotropin-releasing hormone (GnRH) secretion to stimulate increased secretion of pituitary gonadotropins that, in turn, stimulate the growth of ovarian follicle and initiate ovulation⁶.

Thus, to summarize aromatase inhibitor has certain advantages over clomiphene citrate like, it doesn't deplete ER throughout

the body, it is short acting (half-life 45 mins), hypothalamic pituitary axis is intact.

MATERIAL AND METHODS

Retrospective data of 6 months, from January 2018 to June 2018 was collected from a private hospital of Gwalior, Madhya Pradesh. Patients recruited has following criteria,

1. Age < 35 years
2. Primary and secondary infertility
3. Atleast one patent fallopian tube in HSG
4. Husband with normal semen analysis according to WHO criteria

Letrazole 2.5 mg BD beginning from day 2 of menstruation for 5 days was prescribed. The starting dose was one tablet/day (letrozole 2.5 mg) and if ovulation was not achieved, the dose would be doubled in the second cycle. Maximum daily dose is 5 mg (two tablets). Patient was called for ultrasonography on day 11, follicular number, size and endometrial thickness was noted. Follicular size was noted in two perpendicular dimension and mean value is calculated. Endometrial thickness was measured at the point of greatest dimension. When follicle diameter ≥ 18 mm reached patient counselled to have regular intercourse and asked to follow up after 2 days. Ovulation was checked in ultrasonography by regression in follicular size and presence of free fluid in pouch of Douglas. Patient was advised to take micronized progesterone after ovulation for 14 days and advised to notice the overdue of period and to do urine pregnancy test to check for conception. Patients who

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conceived, was followed, both continuation of pregnancy and abortion is noted.

RESULTS

Among induced patients, 58 patients were conceived making success rate of letrozole in this private setup of 37.17 %. On following, 9 patients underwent abortion while rest continued their pregnancy.

Total no of patients induced with letrozole		156
Total no of patients conceived	58	37.17%
No. of patients continued with pregnancy	49	31.4%

DISCUSSION

From many years, clomiphene citrate was used for ovulation induction for anovulatory infertility. Clomiphene citrate has many side effects because of its antiestrogenic effect on endometrium, cervical mucus. Clomiphene citrate get deposited in tissues, leading to prolonged depletion of estrogen receptors causing side effects like hot flushes, perimenopausal symptoms. Another complication associated with clomiphene citrate is multiple follicle development and multiple pregnancy. Many studies suggested that despite high rate of ovulation with clomiphene citrate it is associated with low pregnancy rate and early pregnancy loss⁷. Thin endometrium and non trilaminar endometrium at mid cycle contributed to it. Many studies had done comparing clomiphene citrate with letrozole for ovulation induction. Few studies reported similar ovulation rate of both drugs⁸⁻¹⁰. Another study suggested higher rate of ovulation with letrozole as compared to clomiphene citrate¹¹. Mitwally *et al* suggested that patient with thin endometrium with clomiphene citrate showed an increase in endometrium thickness with letrozole with good results⁷. In our study, 4 multiple pregnancy noted among 156 pregnant patients who was induced with letrozole.

Our study showed good success rate of ovulation with letrozole, so it can be used alternatively to clomiphene citrate for ovulation induction in an anovulatory infertility cases.

Even with limited facilities and adequate selection of patients for ovulation induction letrozole has shown good results.

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