



SUBFERTILE PATIENTS; EFFICACY OF LETROZOLE AS A FIRST LINE DRUG IN IN TERM OF PREGNANCY RATE

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Article received on:

12/08/2015

Accepted for publication:

14/12/2015

Received after proof reading:

09/02/2016

INTRODUCTION

Sub fertility is defined as “Inability to conceive after 12 months of regular unprotected intercourse.”¹ Sub fertility is classified as primary and secondary. Those who never conceived said to have primary sub fertility, while those who have become pregnant at least once but unable to conceive again said to have secondary subfertility.² Infertility is estimated to affect 8 to 12 percent of couple’s worldwide.³

Sub fertility causes great stress to many couples causing increasing number of them to seek specialist sub fertility care. Worldwide it is estimated that 1 in 7 couples have problem in conception while the incidence similar in most countries independent of level of country development.⁴ The incidence of infertility in any community varies between 5% and 15%.⁵ Both partners in relationship contribute to potential fertility and both may be sub fertile

In general population, conception is expected to occur in 84% of women within 12 months and 92%

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ABSTRACT... Objective: To determine the efficacy of Letrozole as a first line drug in sub fertile patients in term of pregnancy rate. **Study Design:** Case series study. **Setting:** Outpatient Department of Gynecology, Nishtar Hospital Multan. **Period:** May 2012 to December 2012. **Material and methods:** A total of 246 females with primary subfertility were enrolled in study from gynecological outpatient department. **Results:** Mean age of the patients was 25.92 ±3.93 years. 132 patients (54.0 %) had BMI of 2-25 kg/m² and 101 patients (41%) had increased of BMI 26-30 kg/m² and 13patients (5%) were obese and had BMI of >30 kg/m². 42 patients (17%) were illiterate. 54 patients (22%) were primary to middle and 62(25%) were matric and 88(36%) were FSC and > than FSC. 39(16%) patients had monthly income 10,000 and 120(49%) patients had monthly income 10,000 -30,000 and 87(35%) patients had monthly income >30,000. Pregnancy was seen in 34% (83 patients). **Conclusion:** Aromatase inhibitors, Letrozole significantly increases pregnancy rate as a primary treatment in subfertility patients.

Key words: Primary subfertility. Letrozole. An ovulatory subfertility. Ovulation induction.

Article Citation: Abbass S, Ahmed E, Shabbir I. Subfertile patients; efficacy of letrozole as a first line drug in in term of pregnancy rate. Professional Med J 2016;23(2):152-155. DOI: 10.17957/TPMJ/16.3052

within 24 months.⁶ Between 8 to 12% of couples in the world have difficulty in conceiving a child at some point in their lives thus affecting 60 to 80 million people.⁷

Hence most of the clinicians defer investigations and treatment for 1 year if no apparent problem is observed in the couple. Following an understandable reassurance and counselling⁸ all that needed is “wait and see” policy. Sub fertility is a complex disorder resulting from one or more factors in either partner i.e. male factor infertility accounts for 25% of infertile couples, while 25% remain unexplained. 50% are female causes with 25% being due to an ovulation and 25% tubal problems⁹, endometriosis 10%⁶, pelvic inflammatory disease 5.5%¹⁰, polycystic ovary syndrome (PCOS) 20–33%¹¹, while

Other factors may be general factor, hypothalamic pituitary, ovarian, cervical, and vaginal and genetic.¹²

Hormonal profile, like serum FSH, LH, prolactin,

serum androgen levels are done where clinically indicated. Following a normal semen analysis report detailed evaluation of female partner is done. In a female with regular menstrual cycle normal ovulation can be expected in up to 80% of cases. Various tests to assess ovulation include rise in basal body temperature chart by 0.5 °C in mid cycle, positive Spinbarkeit and ferning test on examination of cervical mucus in second half of menstrual cycle, day 21 serum progesterone more than 30 n mol/L and pelvic ultrasonography.¹³

Ovulatory dysfunction is one of the most common causes of female subfertility when other fertility factors are normal. Almost 20% infertility is caused by anovulation. Ovulation induction is the method for treating an ovulatory subfertility. Once ovulation is achieved, pregnancy can be achieved.¹⁴

This study was designed to determine the effectiveness of letrozole as a first line drug in subfertility patients leading to focus treatment of an ovulatory infertility to increase chance of conception.

MATERIAL AND METHODS

This Case series study was carried out in the Outpatient Department of Gynecology, Nishtar Hospital Multan from May 2012 to December 2012. A total of 246 females with primary subfertility were enrolled in study from gynecological outpatient department.

RESULTS

For age wise distribution of patients with primary subfertility, 98 (40%) patients were of 18-25 years of age, 123 (50%) patients belonged to 26-30 years of age, and 25 (10%) patients belonged to 31-35 years of age. Most frequent age group was 26-30 years of age with 123 patients. The mean age of the patients was 25.92 ± 3.93 years. Age of the patients ranged from 18-35 years. Regarding body mass index (BMI), 132 patients (54%) had BMI between 20-25 kg/m² and 101 patients (41%) had BMI between 26-30 kg/m² and 13 patients (5%) had BMI between 31-35. Results are shown in the form of tables.

Monthly income	No. of Patients	Percentage
<10,000	39	16.0
10,000-30,000	120	49.0
>30,000	87	35.0

Table-I. Distribution of Patients according to socioeconomic status (n=246)

Educational status	No. of Patients	Percentage
Illiterate	42	17
Primary-middle	54	22
Matric	62	25
More or equal to Fsc/FA	88	36

Table-II. Distribution of Patients according to educational status (n=246)

Age (in years)	No. of Patients	%age	Pregnancy (Yes) (n=83)	%age
18 -25	98	40.0	30	31
26– 30	123	50.0	46	37
31 -35	25	10.0	7	28

Table-III. Pregnancy in relation to Age- Distribution of cases

MI	Patients (n=246)	%age	Pregnancy (yes)	%age
Normal (20-25kg/m ²)	132	54.0	49	37
Increased (26-30kg/m ²)	101	41.0	31	31
Obese (>30kg/m ²)	13	5.0	3	23
Total	246	100	83	

Table-IV. Outcome in relation to Body Mass Index

Monthly income	Patients (n=246)	%age	Pregnancy (yes)	%age
<10,000	39	16.0	9	23
10,000-30,000	120	49.0	43	36
>30,000	87	35.0	31	36
Total	246	100	83	

Table-V. Outcome in relation to socioeconomic status

Educational status	Patients	%age	Pregnancy (yes)N=83	%age
Illiterate	42	17	12	29
Primary-middle	54	22	18	33
Matric	62	25	21	34
>_Fsc/FA	88	36	32	36
Total	246	100	83	

Table-VI. Outcome in relation to educational status (n=246)

DISCUSSION

Infertility is a common clinical problem all over the world including our country. It forms a considerable amount of work load on gynecologists. This is a case series study carried out in gynecological outpatient department, Nishtar Hospital Multan. In present study, total number of patients visited gynecological OPD were 4000 out of which 540 were of infertility. 285 patients were of primary subfertility. So frequency of infertility patients in our area is 13% similar to results as described in one international study.⁵

Aromatase inhibitors are non-steroidal compounds that suppress oestrogen biosynthesis by blocking the action of the enzyme, aromatase, which converts androstenedione and testosterone to oestrogen. It is given in a dose of 2.5-5 mg/day and has been shown to achieve optimal suppression of serum oestrogen level and is almost free of side effects.¹⁴ The efficient oestrogen-lowering property of Letrozole induces an increased discharge of FSH from negative feedback effect of estrogen.¹⁵ With Letrozole, oestrogens production is eventually advanced by the induced FSH discharge.

In our study we gave Letrozole in dose of 5mg /day, same dose was given in study conducted in at KPC Medical college India and another study conducted at Department of Obstetrics and Gynecology, All India Institute of Medical Sciences (AIIMS), New Delhi, India.²¹ Pregnancy rate after taking 5 mg of Letrozole is 34% out of 246 patients. Results in our study were better

than the results observed at KPC Medical college Kolkata India in 2011 with conception rates of 27.3% after taking 5mg of letrozole.¹⁴ Our study results were slightly different from results of international study conducted At new Delhi India on July 2012 in which pregnancy rate was 43.8% after taking 2.5 – 5 mg of letrozole.¹⁶ Results were 26.3 in one study conducted at Department of Obstetrics and Gynecology, McGill University, Montreal, Quebec, Canada in which two doses of Letrozole were compared and pregnancy rates were higher in dose group of 5mg as compared to 2.5mg.¹⁷ Ganesh et al reported pregnancy rate of 23.39%.¹⁸ Casper RF. Has stated that Letrozole has potential role as first line agent in pts with PCOS.¹⁹

In our study most frequent age group was 26-30 years of age with 123 patients (50%) and 18-25 years of age with 98 patients (40%). In our study most of population was younger. Similar observation was made in an international study in kolkata India.

In our study 54% patients had normal BMI. 41% patients had increased BMI. 5% patients were obese. PCOS is most common cause of an ovulatory infertility and the frequency of PCOS among obese people is more. The incidence is high in Western Countries due to their dietary habits and life style. Obesity affects approximately one third of adults in United States. Among 280 patients in Pennsylvania diagnosed with PCOS based on clinical excess, the majority (87.5%) had a BMI of 26 kg/m² or greater.²⁰ In our study Letrozole were given in obese patients and normal BMI patients. Pregnancy rate were more in normal BMI patients as shown by results in study of new Delhi India 2012. Bayar.et al²¹ and Atay et al²² reported that Letrozole produces monofollicular ovulation in their studies therefore Siddiqui M, Mahmud N, Begum MR, Chowdhury TA proposes that follicular monitoring is not essential in all cases so, further reduces the cost of therapy.¹⁴

CONCLUSION

Aromatase inhibitors, Letrozole significantly



increases pregnancy rate as a primary treatment in subfertility patients.

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