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Research Article

A COMPARATIVE STUDY ON THE EFFECTIVENESS OF SINGLE AND COMBINATION THERAPIES OF LETROZOLE AND GONADOTROPINS IN OVULATION INDUCTION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Background:Letrozole has been shown to be effective, in early trials, in inducing ovulation and pregnancy in women with anovulatory PCOS and inadequate clomiphene response and improving ovarian response to FSH in poor responders. Gonadotropins used for ovulation induction in women are either urinary or recombinant products.

Objective:The objectives of this study is to compare the effectiveness of single and combination therapies of Letrozole and Gonadotropins in ovulation induction in women with Polycystic Ovary Syndrome

Methods:A total of 85 subjects were included in the study; that underwent 115 stimulation cycles for ovulation induction. Group I comprising of 47 patients, had 69 cycles of the aromatase inhibitor Letrozole. Group II comprising of 27 patients, underwent 32 cycles of a combination of Letrozole and HMG while Group III included 11 patients who had 14 cycles of HMG alone.

Results:The study results showed that the pregnancy rate/cycle was highest in Group II (18.75%) while it was 10.14% and 7.14% in Groups I and III respectively. The miscarriage rate/cycle was 2.89% in Group I, 6.25% in Group II and 7.14% in Group III while the miscarriage rate/pregnancy was 28.57% in Group I, 33.33% in Group II and 100% in Group III. The ongoing pregnancy rate/cycle was 7.24% in Group I while it was 12.5% in Group II.

Conclusions:This study reveals that Letrozole may be a suitable first line therapy and a feasible alternative to the costlier gonadotropins for the induction of ovulation in the treatment of infertility associated with polycystic ovary syndrome.

Keywords: Letrozole, Gonadotropins, ovulation induction, Polycystic Ovary Syndrome.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a genetically complex endocrine disorder of women of uncertain aetiology and is a common cause of anovulatory infertility, menstrual dysfunction, and hirsutism.[1, 2] PCOS appears to be associated with an increased risk of metabolic aberrations, including insulin resistance and hyperinsulinaemia, type 2 diabetes mellitus, dyslipidaemia, cardiovascular disease, and endometrial carcinoma.[3-15] A uniform definition of PCOS does not exist, in large part because of its diverse and heterogeneous nature.[16, 17] It is typically defined as the association of hyperandrogenism with chronic anovulation in women without specific underlying disease of the adrenal or pituitary glands.[18] It is a true syndrome, being a heterogeneous collection of signs and symptoms that gathered together form a spectrum of disorder with a mild presentation in some, whilst in others there is a severe disturbance of reproductive, endocrine and metabolic function.[19] Letrozole, the most widely used aromatase inhibitor, has mainly been employed for the treatment of post-menopausal women with advanced breast cancer. [19, 20] It is given orally in a dose of 2.5–5 mg/day and is almost free of side effects.[21,22] Letrozole has been shown to be effective, in early trials, in inducing ovulation and pregnancy in women with anovulatory PCOS and inadequate clomiphene response[23] and improving ovarian response to FSH in poor responders.[24] Human Gonadotropins used for ovulation induction in women are either urinary or recombinant products. Urinary derivatives (HMG) contain 75 IU FSH and 75 IU LH per ampoule, a combination that is necessary for hypogonadotropic hypogonadic women, while the recombinant preparations contain either FSH or LH activity.[25] FSH is mandatory for follicular maturation and hence ovulation. Irregular cycles and anovulation in women with PCOS is characterized by arrested growth of antral follicles, and it has been thought that a relative lack of FSH contributes to the persistence of this problem. Although the use of letrozole and HMG is documented in ovulation induction, a comparative study of the three therapies has not been carried out, especially in Indian population. This present study aims to determine the ovarian response to the aromatase inhibitor letrozole, HMG and their combination , in terms of the growth, maturation and size of the follicles. The study which is focused on women undergoing treatment for anovulatory infertility associated with polycystic ovary syndrome thus has an ultimate objective to optimize the ovulation induction and aid in fertilization in these women. [26]

OBJECTIVE

The objective of this study is to compare the effectiveness of single and combination therapies of Letrozole and Gonadotropins in ovulation induction in women with Polycystic Ovary Syndrome.

SUBJECTS AND METHODS

The study was conducted at the Fertility center Out-patient department of Kovai Medical Center and Hospital, Coimbatore, a multi-disciplinary, super specialty corporate hospital. The study included all the polycystic ovary patients who met the study criteria and required ovulation induction. A total of 85 subjects were included in the study; that underwent 115 stimulation cycles for ovulation induction. Group I comprising of 47 patients, had 69 cycles of the aromatase inhibitor Letrozole. Group II comprising of 27 patients, underwent 32 cycles of a combination of Letrozole and HMG while Group III included 11 patients who had 14 cycles of HMG alone.

***Inclusion criteria*:**

- Gender: Females
- Age : 20- 35 years
- PCOS: at least two diagnostic criteria
- Infertility due to anovulation
- Patients desiring to conceive and require fertility medications

***Exclusion criteria*:.**

- Absence of any of the inclusion criteria
- Patients receiving therapy outside the study period.

The Kovai Medical Center and Hospital Ethics Committee reviewed and approved the study proposal and granted consent to carry out the study at Kovai Medical Center and Hospital.

Study Protocol

PCOS patients with infertility who fulfilled the study criteria, and were given Letrozole or HMG or a combination of both for ovulation induction as part of fertility treatment were evaluated and their clinical records were reviewed and documented.

Depending on the therapy given to them, the subjects were categorized into three groups.

Group I : Received Aromatase inhibitor Letrozole 2.5 mg bd on cycle days 2 to 6.

Group II : Received Letrozole 5 mg per day from days 2 to 6 and HMG starting on day 5 of the cycle.

Group III : Received HMG 75 IU, IM starting day 3 of cycle.

All patients were monitored in the early and late parts of the follicular phase. The ultrasound data taken from the day 7 of the menstrual cycle was collected and monitored to determine the ovarian response and follicular growth. Subsequent monitoring was done based on patient's response on day 7. Ovulation was triggered by the administration of 5000 IU of Human Chorionic Gonadotropin (hCG) IM when the lead follicle reached 15-20 mm in size. Endometrial thickness was monitored and recorded. IUI was performed 36-40 hours after the hCG administration. Pregnancy was diagnosed qualitatively using urine pregnancy test cards. Clinical pregnancy was confirmed by ultrasound on observing fetal cardiac pulsation four weeks after a positive pregnancy test.

Statistical analysis

The various measures were expressed as mean ± SD. Analysis of variance was performed for comparison of parameters between the three groups using Graphpad Prism software. Z test (Two-proportion test) was done to compare the proportions between two groups using online Z test at www.dimensionresearch.com.

RESULTS

Demographic Variations

An analysis of the age distribution among the subjects showed that in the Group I, 24 (51.06%) patients fell in the '20-25' age group while 17 (36.17%) belonged to the '26-30' age group. The remainder, 6 (12.76 %) patients were aged '30-35'. In Group II the majority, 17 (62.96%) patients belonged to the '26-30' age group while there were 5 (18.51%) patients each in the '20-25' and '30-35' age group. In Group III, out of the total 11 patients, 5 (45.45%) fell in the '20-25' age group, 4 (36.36%) in the '26-30' and 2 (18.18%) in the '30-35' age group. It has been reported in other studies that 40% to 50% of women with PCOS are obese; weight gain has also been associated with this syndrome.

Menstrual History

Menstrual dysfunction usually oligomenorrhoea, amenorrhoea, irregular menstruation or dysmenorrhoea is a common symptom of PCOS. The menstrual history collected showed that there was no clear majority among the study groups as far as regularity of menstruation is concerned. There were 20 (42.55%), 14 (51.85%), and 6 (54.54%) from Group I, Group II, Group III respectively whose menstruation was irregular and 27 (57.44%), 13 (48.14%) and 5 (45.45%) patients from Group I, Group II and Group III respectively who were having regular menstruation. The majority of the study subjects, 25 (53.19%) from Group I, 16 (59.25%) from Group II and 4 (36.36%) from Group III did not have dysmenorrhoea during menstruation. In the Group I, 11 (23.40%) patients had mild, 4 (8.51%) had moderate while 7 (14.89%) had severe dysmenorrhoea. In Group II, dysmenorrhoea was present as mild in 6 (22.22%) patients, moderate in 1 (3.70%) and severe in 4 (14.81%) patients. In Group III, only 1 (9.09%) had moderate dysmenorrhoea while an equal number of patients, 3 (27.27%) had mild and severe dysmenorrhoea each.

Hormonal Implications

Suppressed FSH values (<3.5 MIU/mL) were found in 3 (6.38%) patients from Group I, 1 (3.70%) patient from Group II and 1 (9.09%) from Group III. In the remaining patients the FSH values fell between the normal range of 3.5-12.5 MIU/mL. Prolactin levels were elevated (>30 ng/mL) in 6 (12.76%) patients from Group I, 3 (11.11%) patients from Group II and 1 (9.09%) patient from Group III; and were normal (upto 30 ng/mL) in the remaining patients. 9 (19.14%) patients from Group I, 5 from (18.51%) Group II and 2 from (18.18%) Group III showed elevated LH values (>12.6 MIU/mL). Hyperandrogenism is a key feature of PCOS often manifesting as acne or hirsutism. [26, 27] However in this study population the prevalence of acne as well as hirsutism was lesser than normally reported. Only 6 (12.76%), 4 (14.81%) and 3 (27.27%) patients from Group I, Group II and Group III respectively presented with acne while the remaining 41 (87.23%), 23 (85.18%) and 8 (72.72%) patients from Groups I, II and III respectively did not report acne. Mild form of hirsutism, particularly over arms, legs, face and breast was seen in 4 (8.51%), 2 (7.40%) and 1 (9.09%) patients from the Groups I, II and III respectively. 1 (2.12%) patient from Group I and 4 (14.81%) patients from group II reported moderate hirsutism while there was a single case (9.09%) of severe hirsutism in Group III. This deviation from the normal prevalence could be due to an increased awareness among the women on the pharmacological as well as non-pharmacological management of these features.

Ovulation Details

The majority of ovulation induction cycles resulted in ovulation. There were in total 115 ovulation induction cycles of which 66 cycles of Group I, 29 cycles of Group II and 13 cycles of Group III resulted in ovulation. The number of stimulation cycles that were anovulatory, was very few in each group; it being only 3 (4.34%) cycles of Group I, 3 (9.37%) cycles of Group II and 1(7.14%) cycle of Group III. 42 (60.86%), 14 (43.75%) and 8 (57.14%) cycles from Group I, Group II and Group III respectively resulted in the development of a single follicle; i.e. were uniovulatory.

Follicular dynamics

Nature of follicular genesis as a primary outcome was based on the duration of follicular genesis. It was classified as normal, early/short and delayed. 3 (4.34%) cycles of Group I, 3 (9.30%) cycles of Group II and 1 (7.14%) cycle from Group III were anovulatory and thus follicular genesis was absent in those cycles. Follicular genesis of 3 (4.34%) ovulatory cycles from Group I went unmonitored due to the failure of patients to report for the scan. Group I comprised of 49 (71.01%) cycles in which the follicular development was normal. 3 (4.34%) cycles were classified as early/short in which the follicles matured in less than 9 days. There was delayed follicular genesis (> 15days) in 11 (15.94%) cycles. In Group II, 24 (75%) of the cycles were normal with regard to the development of follicles while the remaining 5 (15.62%) were early/short. There were no cases of delayed follicular genesis. In Group III, 10 (71.42%) cycles had normal follicular genesis while in the remaining 3 (21.42%) cycles, the development of follicles were delayed.

Endometrial Dynamics

An excellent endometrium characterized by thickness of 1.0-1.2 cm was observed in 54 (78.26%) patients from Group I, 19 (59.37%) patients from Group II and 5 (35.71%) patients from Group III on the day of hCG. The proportion of cycles in which the endometrium attained a thickness of greater than 1.0 cm was significantly greater in the Group I than the other groups (p 0.042, 0.002). 9 (13.04%) patients from Group I, 9 (28.12%) from Group II and 7 (50%) from Group III had endometrial thickness of 0.7- 1.0 cm. This was good enough for successful implantation to occur. A 'just satisfactory' endometrium (0.5-0.7 cm) was observed in one patient (1.44%) from Group I.

Details of IUI

In 12 (17.39%) of the induction cycles IUI procedure was cancelled. The major cause of cancellation of IUI cycles in Group I was anovulation and non-monitoring. Early rupture of follicles and poor follicular response resulted in cancellation of 2 cycles each (16.67%). Other reasons for cancellation included thin/early endometrium [1 (8.33%)] and male factor [1 (8.33%)]. In Group II, there were 4 (12.5%) cancelled IUI cycles due to anovulation (3.75%) and thin endometrium (1, 25%). In Group III, 3 (21.43%) of the cycles had to be cancelled for IUI due to anovulation (1, 33.33%) and poor follicular response (2, 66.67%).

Pregnancy rates and outcomes

7 (14.89%) patients from Group I conceived during the course of the study; however 2 (4.25%) were aborted by miscarriages. In Group II, 6 (22.22%) patients conceived but two of them (7.40%) had miscarriages. In Group III, one patient conceived (9.09%) but later had a miscarriage. Thus there were 5 (71.42%) ongoing pregnancies in Group I, 4 (66.66%) in Group II and none in Group III. However, the study results showed that the pregnancy rate/cycle was highest in Group II (18.75%) while it was 10.14% and 7.14% in Groups I and III respectively. The miscarriage rate/cycle was 2.89% in Group I, 6.25% in Group II and 7.14% in Group III while the miscarriage rate/pregnancy was 28.57% in Group I, 33.33% in Group II and 100% in Group III. The ongoing pregnancy rate/cycle was 7.24% in Group I while it was 12.5% in Group II.

DISCUSSION

An analysis of distribution of weight among this study population showed that the maximum number of Group I patients, 18 (38.29%) weighed between '60-69' kg, which is a slightly heavier range for women of 20-35 years. 14 (29.78%) patients weighed between '50-59' kg while 13 (27.65%) fell in the 40-49 kg group. There was only 1 (2.12%) patient each in the heavier '70-79' and '80-89' kg group. In Group II patients, 11 (40.47%) weighed between '50-59' kg while 5 (18.51%) belonged to the '40-49' kg weight group. The 9 (33.33%) patients weighing between '60-69' and the 2 (7.40%) patients weighing between '70-79' fell in the heavier range. There were no patients weighing more than 79 kg. In Group III, 2 patients (18.18%) weighed between 40-49 kg while the remaining patients distributed evenly [3 (27.27%) patients each] between the weight ranges, '50-59', '60-69' and '70-79' kg. In the group III too there was no one weighing more than 79 kg. The majority of the study subjects were housewives; 39 (82.97%) of Group I patients, 23 (85.18%) of Group II and 10 (90.90%) of Group III patients. Only 8 (17.02%) patients from Group I, 4(14.81%) from Group II and 1(9.09%) from Group III were employees. In Group I, 18 (38.29%) patients were suffering from infertility for '1-3' years, 13 (27.65%) for '3-5' years, 8 (17.02%) patients for '5-7' years while another 8 (17.02%) were infertile for more than 7 years. In Group II while 6 (22.22%) patients were infertile for '1-3' years, there were 8 (29.62%) patients with infertility for '3-5' and '5-7' years each and 5 (18.51%) patients with duration of infertility for more than 7 years. In the Group III, the majority of patients, 4 (36.36%) were infertile for 3-5 years while 3 (27.27%) patients had infertility for 5-7 years. There were 2 (18.18%) patients with infertility for 1-3 years while an equal number were infertile for more than 7 years. The amount of menstruation was moderate in majority of the subjects as seen in 45 (95.74%) patients from Group I, 22 (81.48%) from Group II and 11(100%) from Group III. There were 2 (4.25%) patients in Group I who had scanty menstruation while Group III had 3 (11.11%) patients with scanty menstruation as well as 2 (7.40%) with profuse menstruation. The elevated LH/FSH-ratio with disproportionate increase in LH values and low FSH secretion is a common clinical feature of PCOS. The hormonal profile of the patients showed that there was altered ratio of LH/FSH in 41 (87.23%) patients in Group I, 19 (70.37%) patients from Group II and 7 (63.63%) patients from the Group III. is present in majority of the patients in each study group. [Table: 1] The proportion of total induction cycles which were ovulatory, anovulatory and uniovulatory showed no significant difference regardless of the therapy followed. [Table: 2] as the therapy given to the patients in each group differed, there was significant difference ($p < 0.0001$) in the average number of days of stimulation required to produce the desired ovulation in each group. Patients on Letrozole alone (Group I) required on an average, 5 days of stimulation while those on combination of Letrozole and HMG (Group II) needed an average of 9.13 ± 1.07 days. Group III patients i.e. those on HMG alone required 8.36 ± 2.10 days of stimulation [Table: 2]. The average day of hCG trigger varied significantly between the three groups ($p = 0.004$). hCG was administered for the Group I patients on the day 13.56 ± 1.81 of menstrual cycle. Letrozole treatment seems to alter the day of hCG trigger with the co-treatment Group II getting hCG administered as early as on day 11.72 ± 2.23 while for the Group III patients it was administered a little later on the day 13.82 ± 2.71. This might be due to the fact that these patients received treatment from day 7 onwards while for the other groups, the administration of Letrozole began earlier on day 2. [Table: 2] The cotreatment of letrozole and HMG produced significantly fewer proportion of delayed cycles than HMG alone therapy.(p 0.02) [Table: 3]. There was no significant difference in the average number of follicles developed in each group on the day of hCG as the result of the ovulation induction. An average of 1.48 ± 1.02 follicles of all sizes developed with Letrozole therapy (Group I), 1.75 ± 1.34 follicles developed with the combination therapy of Letrozole and HMG (Group II) while 1.79 ± 1.25 follicles developed with HMG therapy (Group III). [Table: 3]

Table1: Hormonal Parameters.

SL NO	Basal hormonal Values		GROUP I	GROUP II	GROUP III
1	**FSH**	<3.5	3 (6.38%)	1 (3.70%)	1 (9.09%)
	(MIU/ml)	3.5-12.5	44 (93.61%)	26 (96.29%)	10 (90.90%)
2	**PROLACTIN**	Upto 30	41 (87.23%)	24 (88.88%)	10 (90.90%)
	(ng/ml)	>30	6 (12.76%)	3 (11.11%)	1 (9.09%)
3	**LH**	2.4-12.6	38 (80.85%)	22 (81.48%)	9 (81.81%)
	(MIU/ml)	>12.6	9 (19.14%)	5 (18.51%)	2 (18.18%)
4	**Presence Of Altered Ratio**		41 (87.23%)	19(70.37%)	7(63.63%)

Table: 2 Features Of Ovulation Induction Cycles.

Sl no	Ovulation induction	Group i	Group ii	Group iii
1	total no of stimulation cycles	69	32	14
2	no of anovulatory cycles	3(4.34%)	3(9.37%)	1(7.14%)
3	no of ovulatory cycles	66 (95.65%)	9 (90.62%)	13(92.85%)
4	no of uniovulatory cycles	42 (60.86%)	14 (43.75%)	8(57.14%)
5	average no of days of stimulation/cycle	5	9.13±1.07	8.36±2.10
6	average day of hcg administration	13.56±1.81	11.72± 2.23	13.82±2.71

Table: 3 Follicular Parameters.

Sl no	Follicular Parameters	Group i	Group ii	Group iii
1	nature of follicular genesis			
	normal	49(71.01%)	24(75%)	10(71.42%)
	early/ short	3(4.34%)	5(15.62%)	-
	delayed	11(15.94%)	-	3(21.42%)
	anovulatory	3(4.34%)	3(9.30%)	1(7.14%)
2	no of follicles on the day of hcg	102	56	25
3	avg no of follicles on the day of hcg	1.48±1.02	1.75±1.34	1.79±1.25
4	no of mature follicles on the day of hcg	82	52	15
5	avg no of mature follicles on the day of hcg	1.19±0.86	1.63±1.18	1.07±0.83
6	size distribution of follicles on the day of hcg			
	< 1.5 cm	20(19.60%)	4(7.14%)	10(40%)
	1.5-2.3 cm	78(76.47%)	51(91.07%)	15(60%)
	>2.3 cm	4(7.14%)	1(1.78%)	-
7	avg size of follicles on the day of hcg	1.736± 0.384	1.823± 0.254	1.4340± 0.4337

Similarly, there was no significant difference in the number of mature follicles (>1.5 cm) on the day of hCG. An average of 1.19 ± 0.86 mature follicles were observed in Group I while there were observed, 1.63 ± 1.18 follicles and 1.07 ± 0.83 follicles in Groups II and III respectively. In addition, there was significant difference between the three groups in the proportion of follicles that attained a size greater than 1.5 cm; with the Group II follicles showing the largest proportion [92.86%, (p 0.032, 0] while it was 80.39% and 60% in Group I and Group III respectively (p 0.032). This implies that while the maximum number of follicles developed with HMG alone therapy, the proportion of follicles that attained maturity is lower than in other groups. [Table: 3]

However, the sizes of follicles were significantly more in the Letrozole treated Groups I and II. The follicles had an average size of 1.736 ± 0.384 cm in Group I, 1.823 ± 0.254 cm in Group II while the follicles achieved and average size of only 1.434 ± 0.4337 cm in HMG alone treated Group III. There were 20 (19.60%) follicles smaller than 1.5 cm in Group I while there were 4 (7.14%) follicles smaller than 1.5 cm in Group II. In Group III, there were 10 (40%) follicles less than 1.5 cm; which was considerably more than in the other groups. There were 78 (76.47%) follicles in Group I sized between 1.5 and 2.3 cm while the number was 51 (91.07%) in Group II and 15 (60%) in Group III. 4 (7.14%) follicles from Group I, 1 (1.78%) had a size greater than 2.3 cm. There were no follicles larger than 2.3 cm in Group III. [Table: 3] The endometrium was too thin or early (<0.5 cm) on the day of hCG in 2 (2.89%) patients from group I, 4 (12.5%) from Group II and 2 (14.28%) from Group III. It is seen that majority of the Group I and II patients developed thickness of 1.0-1.2 cm; while in Group III the endometrial thickness in majority of the patients was 0.7-1.0 cm the proportion of which was significantly different between the groups III and II (p 0.002). [Table: 4] A need for cancellation of the IUI cycles due to over response did not arise in any of the groups. There was no significant difference in the proportion of cancelled IUI cycles among the groups. [Table: 5] Co-treatment of Letrozole with gonadotropins was reported to result in pregnancy rates similar to and miscarriage rates higher than gonadotropin alone therapy. [28] Multiple pregnancies are a major problem associated with gonadotropin therapy. [29] However, in this study there were no cases of multiple pregnancies in any of the three groups. All the pregnant cases showed a single gestational sac in the ultrasound scan. The pregnancy rates and the proportion of outcomes between the three groups showed no significant difference regardless of the various therapies followed.Thus, the patients who were treated with letrozole, alone and in combination with HMG showed results comparable to HMG alone group.[Table:6]

Table4: Endometrial Parameters

Sl no	Thickness of endometrium on day of hcg	Group i	Group ii	Group iii
1	≥1.0-1.2 cm	54 (78.26%)	19(59.37%)	5(35.71%)
2	≥0.7-<1.0 cm	9(13.04%)	9(28.12%)	7(50%)
3	>0.5-<0.7 cm	1(1.44%)	-	-
4	≤0.5 cm	2(2.89%)	4(12.5%)	2(14.28%)

Table: 5 Features of Iui Cycles

Sno	Iui cycles	Group i	Group ii	Group iii
1	number of iui cycles	57	28	11
2	number of cancelled iui cycles	12 17.39%)	4 (12.5%)	3 (21.43%)
	anovulation	3 (25%)	3 (75%)	1 (33.33%)
	non-monitoring	3 (25%)	-	-
	early rupture	2 (16.67%)	-	-
	poor response	2 (16.67%)	-	2 (66.67%)
	thin/ early endometrium	1 (8.33%)	1 (25%)	-
	male factor	1 (8.33%)	-	-

Table 6: Results of Iui Cycles

Sl no	Category	Group i	Group ii	Group iii
1	no of patients conceived	7(14.89%)	6(22.22%)	1(9.09%)
2	pregnancy rate/ cycle	10.14%	18.75%	7.14%
3	no of miscarriages	2(4.25%)	2(7.40%)	1(9.09%)
4	miscarriage rate/ cycle	2.89%	6.25%	7.14%
5	miscarriage rate/ pregnancy	28.57%	33.33%	100%
6	no of ongoing pregnancies	5(71.42%)	4(66.66%)	-
7	ongoin pregnancy rate/cycle	7.24%	12.5%	-
8	no of gestational sac seen			
	1	5	4	-
	>1	-	-	-

CONCLUSIONS

In this study it was found that the aromatase inhibitor, letrozole when given alone or in combination with HMG results in ovulatory cycles which were comparable in number to the ovulatory cycles that results in an HMG alone treatment. The number of days of stimulation required was lesser for letrozole alone therapy, while the co-treatment with HMG required more number of days of stimulation when compared to the HMG alone therapy. However, despite the differences in the number of days of stimulation required, the average day of hCG administration was earlier in patients treated with either letrozole alone or in combination with HMG when compared to the patients on HMG therapy alone. Follicular genesis in the letrozole treated Groups I and II was normal in majority of the cycles which was comparable to the HMG therapy. Shorter cycles were found in the letrozole groups while the HMG therapy resulted in relatively more number of delayed follicular genesis. Ovulation induction with letrozole produced the same number of follicles as in HMG therapy while the proportion of follicles that attained maturity and their average size was significantly higher with letrozole therapy than HMG. The proportion of cycles which resulted in endometrial thickness greater than 1.0 cm was also higher in the Letrozole groups. In patients who received letrozole, the pregnancy rate/cycle was higher while the miscarriage rate/cycle was lower as compared to the patients on HMG alone. However, the proportion of outcomes of pregnancies was comparable in all the groups.

Thus, this study reveals that Letrozole may be a suitable first line therapy and a feasible alternative to the costlier gonadotropins for the induction of ovulation in the treatment of infertility associated with polycystic ovary syndrome. With the fertility related problems of PCOS and their awareness increasing at an alarming rate and since this study has the limitations of a non-randomized observational study, it is hoped that this will set a precedent for future studies in this field.

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