



Randomised Trial of Letrozole and Clomiphene combination Vs Letrozole monotherapy for Infertility

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Objectives

- In India 10-15% of couples experience infertility, out of all 30% percent couples have unexplained infertility.
- Unexplained infertility often treated with superovulation using clomiphene, letrozole or gonadotropins, combined with IUI.
- Letrozole - benefit over CC for ovulation induction , does not block estrogen receptors in both central and peripheral target tissues, and normal central feedback mechanisms intact.
- Since letrozole and clomiphene have different mechanisms of action, it was postulated that combination of these medication may result in an improved ovulation over letrozole alone.
- This study was done to compare the efficacy of clomiphene citrate and letrozole combination Vs letrozole alone for ovarian stimulation in women with unexplained infertility in terms of developing and ruptured follicles, endometrial thickness and pregnancy and to compare side effect profile of both the regimens.**

Design

- Open label randomized control study
- Conducted in the Department of Obstetrics & Gynaecology of King George's Medical University, Lucknow, India.
- Over the period of 1 year on 180 infertile women.

Methodology

Inclusion Criteria

- Women who gave written informed consent were taken.
- Healthy female subjects with unexplained infertility.
- Age: 18 to 40 years

Exclusion Criteria

- Not giving consent
- Bilateral tubal blockade
- Uncorrected thyroid disease
- Untreated hyperprolactinemia
- Medical conditions (i.e., uncontrolled type 1 or 2 diabetes mellitus, hypertension)

Total no of Women with unexplained infertility = 180 (90 cases and 90 controls)

Women evaluated on the basis of history, general physical examination ,clinical examination and investigations

Group 1
Received combination of letrozole 5 mg OD and clomiphene citrate 50 mg OD

GROUP 2
Received letrozole 5 mg OD alone.

Follicular Monitoring was done as per protocol, Inj HCG 10,000IU IM given for trigger to all the women, IUI done according to feasibility. All the women were followed till next menses / pregnancy

Results

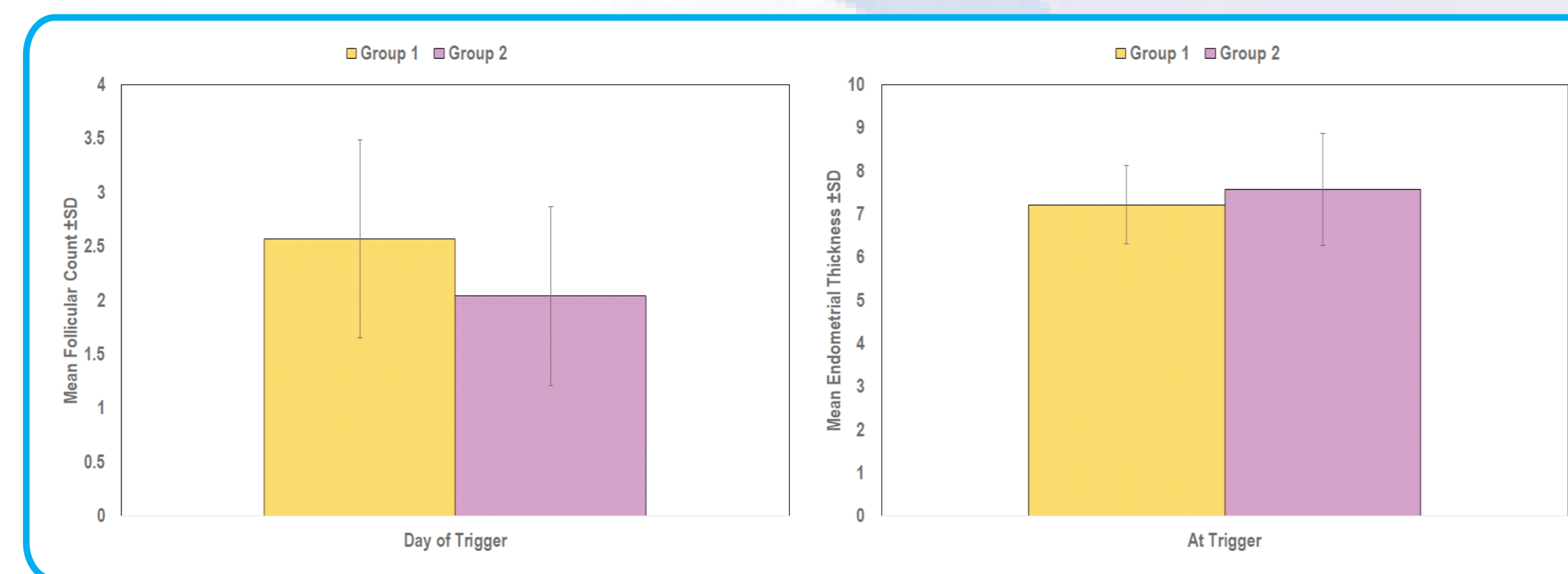
Demographic Profile- Both the groups receiving Clomiphene plus Letrozole and Letrozole alone were found to be comparable in terms of demographic profile like age, occupation, BMI, type and duration of infertility.

Table 1 : Intergroup comparison of Endometrial Thickness at and Antral Follicular Count at Day 2

	Interval	Group 1 (n=90)		Group 2 (n=90)		Statistical tests	
		Mean	SD	Mean	SD	't'	'p'
ET thickness	Day 2	5.31	1.11	5.38	0.78	-0.530	0.597
Antral follicular count	Day 2	5.33	1.71	5.10	2.37	0.758	0.449

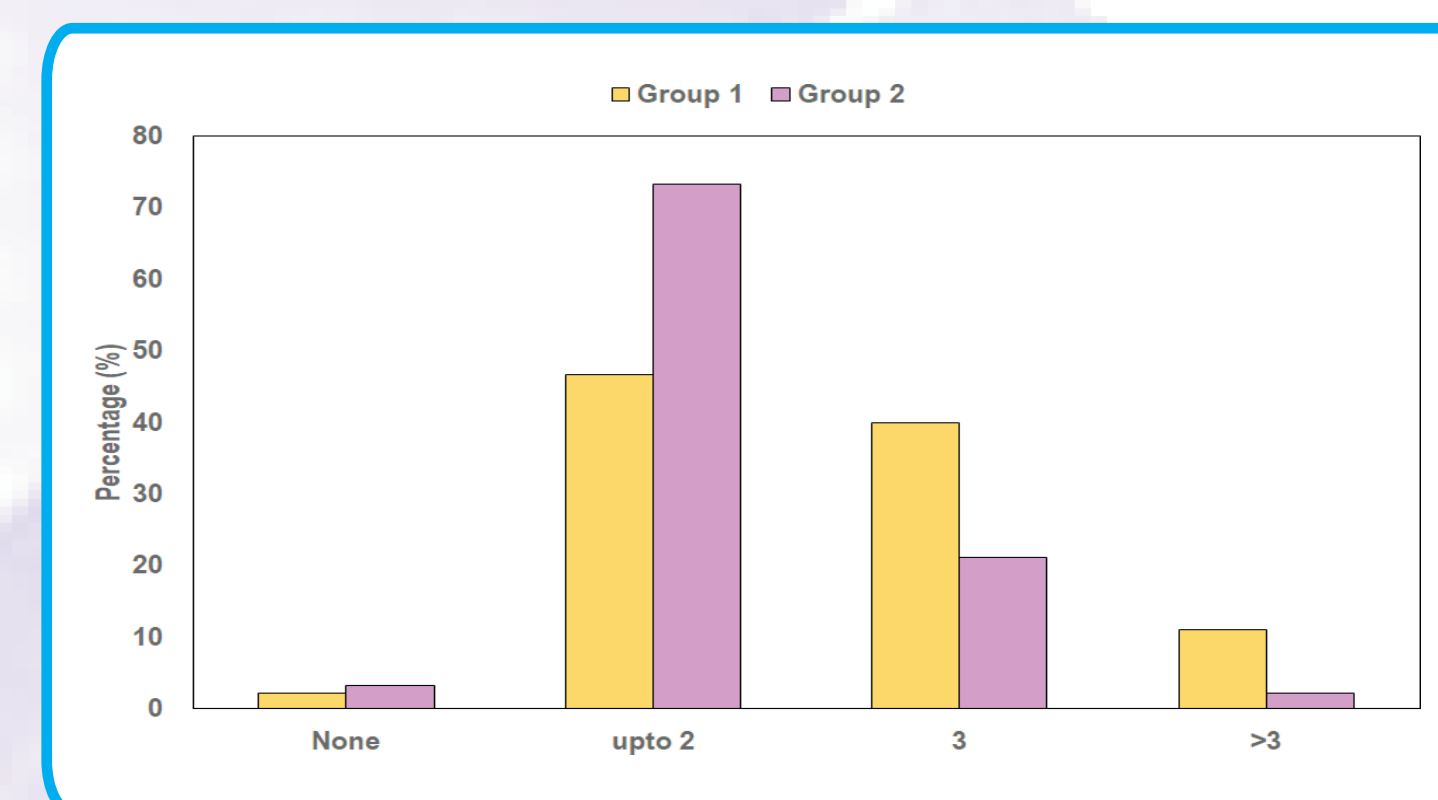
On Day 2 of menses both groups had comparable endometrial thickness and antral follicular count.

Figure 1 -Intergroup comparison of Endometrial Thickness and Follicular Count at Day of Trigger



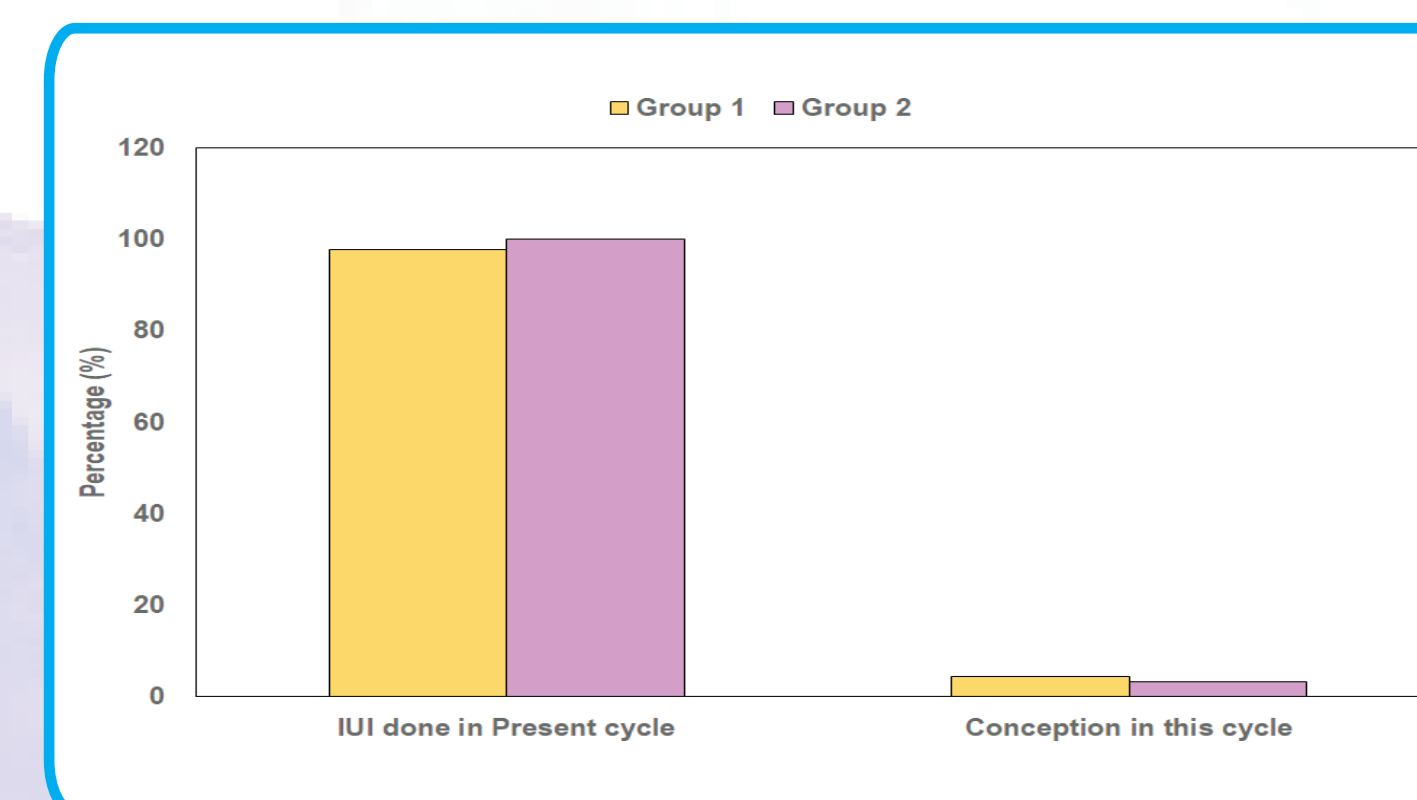
On the day of trigger, developed follicle count was more in group 1 as compared to group 2. Endometrial thickness was found to be more in group 2 as compared to group 1. Both differences were statistically significant.(p=0.034 and < .001 respectively)

Figure 2 Intergroup Comparison of Number of Ruptured Follicles



More follicles ruptured in group 1 as compared to groups 2 and the difference was statistically significant.(p=0.001)

Figure 3 Intergroup comparison of IUI and Conception in present cycle



In both groups most of the women underwent Intra uterine Insemination. Comparable conceptions occurred in both the groups(p=0.700)

Table 2 : Intergroup comparison of side effects

SN		Group 1 (n=90)		Group 2 (n=90)	
		No.	%	No.	%
1	Hot Flashes	7	7.8	4	4.4
2	Nausea	6	6.7	6	6.7
3	OHSS	1	1.1	0	0.0

$\chi^2=1.921$; $p=0.589$

Both the groups experienced comparable side effect profile.

Conclusion

- It was concluded that both the regimes i.e., combination of Clomiphene citrate plus Letrozole was found to be better in terms of number of developed follicles and number of ruptured follicles .
- Letrozole-alone regime being more effective in terms of endometrial thickness at trigger.
- Both regimens were equally efficacious in terms of pregnancy.
- Both regimens found to be comparable in terms of side effects profile.
- As the sample size was not very large, further studies may be done, to validate the result of this study.

References

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