ORIGINAL RESEARCH PAPER

Gynecology

COMPARISON OF EFFICACY OF TAMOXIFEN CITRATE AND CLOMIFENE CITRATE IN OVULATION INDUCTION- PRIMARY INFERTILITY

KEY WORDS: ovulation induction, clomifene citrate ,tamoxifen citrate.

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ABSTRACT

BACKGROUND – Ovulation Induction refers to the therapeutic restoration of the release of eggs per cycle in women.The aim of the study is to compare the effectiveness of Tamoxifen citrate and Clomifene citrate in ovulation induction and to compare the age wise efficacy of the drug. **METHODS**: A total of 90 infertility patients were included in the study, and 45 were allocated to group A and 45 in group B.Group A was given Clomifene citrate 50 mg and group B was given Tamoxifine 40 mg from day 5 to 9.**RESULTS:** The number of patients who ovulated in first cycle is 26.6%, second cycle 40% and third cycle is 26.6% in group A. In group B the number of patients who ovulated in first cycle is 24.4%. second cycle 48.8%, third cycle 20% respectively. The mean pregnancy rate in clomifene group is 22.22% ans tamoxifen is 24.4% with P value of >0.05 showed no significant difference in both group.**CONCLUSION:** Tamoxifen was better drug for ovulation induction when compared with clomifene citrate which is standard drug usually used for ovulation induction. This is because of the endometrial thickness which is needed for implantation is better with tamoxifen..

INTRODUCTION

Infertility is defined as the failure to achieve clinical pregnancy after 12 months of regular unprotected sexual intercourse.

Infertility is the serious health issue worldwide, affecting approximately 8 - 10 % of couples worldwide. (1)according to a report by WHO , one in every four couples in developing countries is affected by infertility.

Primary infertility is infertility in couple who have never conceived.

A variety of treatment options are now available to treat infertility.

Ovulation induction remains the mainstay in this treatment, especially in anovulatory infertility.

Ovulation induction refers to the therapeutic restoration of the release of one or two eggs per cycle in the woman who either has not been ovulating regularly or has not been ovulating at all.

Oral agents like clomiphene citrate and tamoxifine citrate are the drugs of choice Both the drugs are nonsteroidal triphenylethylene derivative The infertility physician should have through knowledge of the differenttreatment options available and about patient selection.

This study was conducted in the Gynaecology department, Vinayaka Mission Medical College and hospital, Karaikal In our study the efficacy of the clomiphene citrate and tamoxifen citrate are compared with ovulation induction, endometrial thickness, monofollicular development and pregnancy outcome.

MATERIALS AND METHODS

This is a Comparative prospective study done in the Gynaecology department, Vinayaka Mission Medical College and hospital, Karaikal, after getting approval from the Ethical Committee. This is done in patients with failure of ovulation who were divided in to group A and group B of 45 patients each. Group A was given Clomifene citrate 50 mg and group B was given Tamoxifine 40 mg from day 5 to 9. The efficacy of drug is assessed by measuring serum progesterone Estrogen, FSH. Serial follicular study and endometrial thickness measurement done by transvaginal ultrasound.

INCLUSION CRITERIA:
All reproductive age women with primary infertility with anovulatorycause: 20-35 years.

EXCLUSION CRITERIA:
Women with secondary infertility.Failed artificial reproductive techniques.Male factor infertility and women with other factors of in fertility were excluded.

After explaining about the study, informed written consent was taken from all the study individuals, which was explained in their vernacular language which was approved by ethical committee of the institution.

Graphical representation of data: Data collected were entered in Excel Spread sheet and P Value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical Software:data was analysed using STATA statistical software package release 1.

RESULTS :

	CC No of patients =45	TX No of patients = 45	P value
Age of patients	28.7 (±4.7)	30.2(±4.9)	>0. 05
Duration of infertility	53(±42.1)	63(±48.4)	>0.05
No of cycles : Nil	6.6%	6.67%	>0. 05
1	26.67%	24.44%	
2	40%	48.89%	
3	26.67%	20%	

Table 1 : Shows the age distribution , duration of infertility ,No of follicles . (mean +/- SD)

The mean age group in clomiphene is 28.7yrs and with tamoxifen is 30.2yrs , and p value is more than 0.05, which shows there is no significant difference in two groups .

The mean duration of infertility in clomiphene i s 53 % and

with tamoxifen is 63%, and p value is more than 0.05 ,which shows there is no significant difference in two groups .

The no of patients ovulated with clomiphene is 26.67% in first cycle, 40% in second cycle and 26.67% in third cycle. and no of patients ovulated with tamoxifen is 24.4% in first cycle, 48.89% in second cycle and 20% in third cycle. p value is more than 0.05, which shows there is no significant difference in two groups

	CC	TX	P value
Endomet rial	6.7(±1.8)	8.7(±1.3)	<0.01
No of dominan t follicle : NIL	6.67%	17. 78	<0.01
1	24.44	53. 33	
2	55.56	17.78	
3	11.11	11.11	
4	2.22%	0.00%	
Size of Dominant	15.6(+2.6)	15.1(+2.7)	>0.05
Mean progeste rone	11.2(±5.5)	12.3(±5.1)	>0.05
Mean oestroge n level	195.7(±78.3)	269.7(±84.8)	<0.01

Table 2: Shows endometrial thickness ,no of dominant follicle, mean oestrogen level , mean progesterone level.

The endometrial thickness in clomiphene is 6.7mm and with tamoxifen is 8.7mm , and p value is less than 0.01 ,showing clomifene group had significant difference compared to tamoxifen groups .

The most common side effect of tamoxifen citrate is endometrial hyperplasia which is not seen in our study.

In this study in tamoxifen group 53% had single follicular development,17% had two follicular development,11% had three follicular development . Clomiphene had 24 % had single follicular development,55% had two follicular development and 11% had three follicular development.

The multiple follicular growth was seen among clomiphene citrate group as compared to tamoxifen citrate.

Size of dominant follicle growth showed no significant difference with p value less than 0.05%.

The mean oestrogen in clomiphene group is 195.7 pg/ml and tamoxifen group was 259.7 pg/ml . P value was less than 0.01 showing oestrogen levels are well maintained in tamoxifen group than in clomiphene group.

The mean progesterone level in clomiphene is 11.2 ng/ml and in tamoxifen is 12.3 ng/ml. P value was more than 0.05 which shows no significant difference in both the groups .

	CC	TX	
pregnancy	22.22	24.44	>0.05
Pregnancy			
Aborti	4.4 %	2.22%	<0.05
Twi	2.2	0.0	<0.

Table 3: Shows Pregnancy by ovulation induction.

Steiner et al.2005, in a meta analysis concluded that CC and tamoxifen are equally effective in includingovulation ,Pregnancy outcome.

Out of 45 patients who were treated with clomiphene citrate 11 patients became pregnant in different ovulation cycles.

Out of 45 patients who were treated with tamoxifen citrate 13 patients became pregnant in different ovulation cycles.

Among the patients who became pregnant in clomiphene group two patients had spontaneous abortion, and whereas patient who became pregnant in tamoxifen group one patient had spontaneous abortion .p value was less than 0.05 showing significant difference among two groups.

DISCUSSION :

In our study the efficacy of the drug are compared with endometrial ovulation.

Williamson et al.1993, in 45 patients reported an ovulation rate of 81% and percentage ovulatory cycles of 63.1 higher to the results of our study with ovulatory rate of 80% and ovulation cycle 55%

In the study of 110 by **Boostanfar et al.2001,**the quoted ovulation rate was 44.2% in tamoxifen group and 45.5% in clomiphene group,are lesser to our study of ovulation which is 78% in tamoxifen group and 80 % in clomiphene group.

Gulekli et al reported an ovulation rate of 70% in cases of folicystic ovarian disease which is less than our study.In our study, we did not study the pregnancy rate with 80mg which could be done as the next step,

Pregnancy outcome

The pregnancy rate was 24.41% which was much higher than reported by **Sugimani et al,1993** which was only 4.8%

The pregnancy rate in present study at the dose of 40 mg was 24.4% which was lower than that reported by **Williamson et al.1997** and **Gulekli et al** which was 35%

A study by **Mohammad Hasan et al.2011** the pregnancy outcome was 18.7% in tamoxifen group which is lesser than our study where it is 24.4%

Endometrial thickness

In the study by **Reynolds et al** between clomiphene and tamoxifen was P <0.01 as was the case in our study which was also P<0.01.

The endometrial thickness in tamoxifen group in the study by **Ahmedbad way et al,2011** 10.1 which is higher than in our study where it was 8.1mm .

Adverse effect

In our study there was no incidence of adverse effect while in the study by **Williamson et al.** and **Klopper et al .** Did report mild side effects in the form of headache and mild ovarian enlargement.

The present study has shown that tamoxifen and clomiphene citrate is a good ovulation-inducing agent and is devoid of side - effects and complication in women with anovulation.

CONCLUSION :

Tamoxifen was better drug for ovulation induction when compared with clomifene citrate which is standard drug usually used for ovulation induction.

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