ORIGINAL ARTICLE

Comparison of efficacy of Metformin versus Pioglitazone on Ovulation in patients of polycystic ovarian syndrome

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ABSTRACT

Aim: To compare the efficacy of Metformin with Pioglitazone for ovulation induction in patients presenting with polycystic ovarian syndrome.
Study Design: The study was randomized control trial.
Setting: Department of Obstetrics and Gynaecology, Lady Willingdon Hospital Lahore
Duration: from 28-11-2016 to 27-05-2017 (6 months).
Methods: The patients number 102 were enrolled in the study after fulfilling he inclusion criteria. Informed consent and demographic information was taken. The patients were divided into two groups. Efficacy was observed after 06 months of administration of therapies. Data collected was entered and analyzed on SPSS version 20.
Result: In womanwith mean age of Pioglitazone group was 28.18±4.55 years and in metformin group was 28.16±4.78 years. The ovulation was noted in 43 patients with Pioglitazone and 30 patients with metformin. Conception occurred in 32 patients with Pioglitazone and 9 patients with metformin. Significant difference has been observed in both groups regarding ($p<0.05$).
Conclusion: It has been proved in our study that effectiveness of Pioglitazone is statistically more significant than metformin in ovulation induction.
Key words: Efficacy, Pioglitazone, Metformin, Polycystic ovarian syndrome, Ovulation

INTRODUCTION

Polycystic ovary syndrome is a disease of odd syndrome and collection, when put together, as a series of light disease presentation, some of them seriously interfere with reproduction, endocrine and metabolic functions. It is characteristic of polycystic ovarian syndrome (irregular menstrual period): hyperandrogenism, insulin resistance, inappropriate secretion of obesity and gonadotropins (LH ratio / FSH)[1].

Polycystic Ovary syndrome (PCO) Reproduction age in one of the most common endocrine diseases, 6.6 prevalence of – 6.8% .2 PCO is a syndrome of unknown etiology, main observation is fertility disorders. However, in the last 15 years, a significant contribution to the pathogenesis of syndrome in the role of insulin resistance (IR) .3 assumes, the most common endocrine disorder can now be considered to have concentrated[2, 3].

Similarly, one of the common causes of infertility and ovulatory dysfunction is often considered ovulatory disease present in 70% of women[4].

Weight loss, ovarian androgens and suppression of progestin oral contraceptives: the treatment methods of this syndrome have been proposed various treatment methods, GnRH Agonist, anti-Androgen, stimulation ovulation and insulin sensitive drugs such as metformin and Pioglitazone is the most common treatment[5].

The mechanism by which metformin results ovulation induction in women with polycystic ovarian syndrome is understanding. Pregnancy rate analysis has shown that metformin and clomiphene significant therapeutic effect (odds ratio of 4.40.95% confidence interval to 1.96 9.85)[6].
First, discuss the effects of Pioglitazone for infertile women, with the involvement of Metaphorin in patients such as Ota H, et al polycystic ovary syndrome, ovulation clomiphene or metformin in multiple ovarian syndrome, in nine cases (77.77%) Confirming the seven women are doing an average 11.3 week piogliatogen pacing[4].

PioGlitazone reduces fat, muscle and insulin sensitivity, action on the liver, increasing glucose usage and decreasing PCOS patients with androgen hyperlipidemia. On the other hand, another study is Sangeeta[1].

Motivation of ovulation was found that 32% of metformin, pheologitazone group was 56%. Research is reason that this important change is to us to conduct another study to describe the correct PCO efficiency of drug management in our population. Therefore, to find a well-designed random tests can provide ovulation induction treatment, and future methods of successful pregnancy can provide patients.

PATIENTS AND METHODS

A total of 102 patients (51 in each group) fulfilling inclusion / exclusion criteria from gynaecology outpatient department was engaged by lottery method. Participants were divided into two groups with informed consent approved by the ethical committee of the hospital. Group A was selected to Pioglitazone and Group B to Metformin.

History and physical examination was done contacting hormonal profile including day 2 serum FSH, LH Prolactin, testosterone and mid luteal phase progesterone and ultrasound examination of Pelvis was also completed in all patients. Group a obtained oral 30mg of Pioglitazone once daily for three months. Group B took oral 850mg of metformin twice daily for three months. After 3 months, patients were evaluate on ultrasound for ovulation and conception. Then patients were further followed for further three cycles by mature follicle seen on ovum tracking on transvaginal scan with continuation of trial drugs. Scan was done on 12thday of menstrual cycle. If follicular size <18mm, then females were further followed-up on alternate days till 16th day for assessment of ovulation. The females who achieved ovulation or conception, drugs were stopped. But females failed to achieve ovulation, drugs were continued for 6 months. Effectiveness was observed after 06 months of administration

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of drugs and all results were documented by the researcher on the Performa.

SPSS-20 was used for Data entry. Variables like age was presented as mean±S.D and qualitative variables gender were presented as frequency and percentages. Comparison of two groups Metformin and Pioglitazone apply independent sample t-test. P-value≤ 0.05 was taken as significant.

RESULTS

In these study total 102 females patients were enrolled. The mean age of the patients in Pioglitazone group was 028..18±4.55 year and its mean value in metformin group patients was 28..16±4.78 years (Table 1). In our study the mean value of egg size of the patients in Pioglitazone group was 19.49±3.47 mm and its mean value in metformin group patients was 17.73±4.98 mm (Table 2).

The study results showed that the ovulation was noted in 73(71.6%) patients and it was not found in 29(28/4%) patient (Table 3).

The ovulation was noted in 73 cases in which 43 were from Pioglitazone group and 30 were from metformin group. Hence, it was statistically significant difference was found between the study groups with ovulation i.e. p-value=0.004 (Table 4).

Our study the conception done in 41(40.20%) patient and it was not done in 61(59.80) patients. In this study the conception done in 41 cases in which 32 were from Pioglitazone group and 9 were from metformin group. Statistically significant difference was found between the study group with conception i.e. p-value=0.000 (Table 5).

In Pioglitazone group ovulation was noted in 57 cases and metformin group in 25 cases. In this study with patients of ≤ 30years age. In the other group ≥ 30 years ovulation occur in 11 cases with pioglitazone and 5 cases with metformin. In group stratified by age difference was significantly high that is P-value 0.037 and 0.029 (Table 6)

Similarly the conception rate with patient ≤ 30years age was high with pioglitazone that is 33 cases and 24 cases with metformin. Patient of 30 years of age conception occur on only 08 cases with pioglitazone. Stratified by age P-value 0.000 and 0.002 respectively shows difference significantly higher (Table 7).

Table 1: Comparison of age with study group

Age (years)	Study group	
	Pioglitazone	Metformin
n	51	51
Mean	28.18	28.16
SD	4.55	4.78

Table 2: Comparison of egg size with study group

Egg size (mm)	Study group	
	Pioglitazone	Metformin
n	51	51
Mean	19.49	17.73
SD	3.47	4.98

Ind. T test=2.076 p-value=0.041*

Table 3: Frequency distribution of ovulation

Ovulation	Study group	
	Pioglitazone	Metformin
Yes	73	71.6
No	29	28.4
Total	102	100.0

Table 4: Comparison of ovulation with studygroups

Ovulation	Study group		Total
	Pioglitazone	Metformin	
Yes	43	30	73
No	8	21	29
Total	51	51	102

Chi value=8.14 p-value=0.004*

Table 5: Comparison of conception with study groups

Conception	Study group		Total
	Pioglitazone	Metformin	
Yes	32	9	41
No	19	42	61
Total	51	51	102

Chi value=21.57 p-value=0.000

Table 6: Comparison of ovulation with study groups stratified by age (years)

Ovulation	Study group		Total
	Pioglitazone	Metformin	
Age ≤ 30 years			
Yes	32	25	57
No	7	16	23
Age >30 years			
Yes	11	5	16
No	1	5	6

Table 7: Comparison of conception with study groups stratified by age (years)

Pregnancy	Study group		Total
	Pioglitazone	Metformin	
Age ≤ 30 years			
Yes	24	9	33
No	15	32	47
Age >30 years			
Yes	8	0	8
No	4	10	14

DISCUSSION

This compares to join the ovulation with Pioglitazone efficacy in patients with randomized controlled trial was conducted in obstetrics and gynaecology, hospital Lahore metformin and polycystic ovarian syndrome.

In the current practices Metformin with the drug of choice for the treatment of type 2 diabetes increases insulin with the menstrual cycle diabetes US Food and Drug Administration (used by the FDA) as an oral anti-hyperglycemic drugs is a biguanide ovulation to reduce the level of 0.71 73 about improving and circulation androgens[7-9].

In our study, 73 cases of Pioglitazone, 30 cases of metformin group, 32 cases of Pioglitazone group, 43 cases in 29 cases of metformin compared to metformin, the group, Pioglitazone group, shows a significantly better statistically significant result in ovulation and pregnancy cases. I know. P-value of E= 0.004 and 0.000 Discusses some of the following conclusion.

In another study by Razzaq as a Moona a group (metformin) showed the effect, while Group B (Pioglitazone Group) 29 (82.86%) 19 (54.29%), p-value=0.010. in comparison with metformin, pyoglytogen is more effective in inducing ovulation in women with polycystic ovary syndrome.

Ota H, it is comparable with our study who studied Pioglitazone effectiveness in subfertile patients with PCOS, associated with clomiphene or metformin and regular ovulation induction, he concluded nine (77.77%), an average of seven to

Pioglitazone 11.3 weeks pregnant women had confirmed the beginning of pregnancy.

One study by X-J Li et al[10] resulted that thiazolidinedione were superior to metformin in reducing serum levels of free testosterone (P=0.03) and DHEA-S (P=0.002) after 3 months treatment. This meta-analysis do not indicate that metformin is better to thiazolidinedione's for the treatment of PCOS or vice versa. Another study by Sangeeta[1] found that ovulation induction rate with pioglitazone was 56% and 32 % with Metformin group. Ghada Abdel Fattah et al[10] concluded that the use of pipglitazone/metformin and CC is more effective than metformin and CC as regard ovulation and pregnancy rates in anovulatory women with CC-resistant PCOS. Ovulation rate was significantly higher in the Pioglitazone + metformin and CC group than the metformin and CC group (69.8% versus 48.8%) p: 0.002).

A study Conducted by Gluecketal[11]conbined effect of Pioglitazone with metformin in resistant polycystic ovarian syndrome cases shows reduce level of endrogen improved insulin sensitivity and induced ovulation.An other study by Brettenthaler et al[12] ovulation induction rate was raised from 5.06% to 41.2% with pioglitazone treatment as compared to placebo.

The Cochrane review updated by the Tang et al about insulin-sensitizing drugs (metformin, rosiglitazone, Pioglitazone, d-chiro-inositol) in women with PCOS, oligo/amenorrhea, and infertility and conclusion was that metformin is still superior for improving clinical pregnancy and ovulation rates. However, it is used alone or in combination with clomiphene, or when compared with clomiphene. Hence, the Metformin use is limited in improving reproductive outcomes in women with PCOS[13].

CONCLUSION

Our study proves that the results of ovulation induction are significantly better in patients with polycystic ovarian syndrome who took pioglitazone as compared to metformin.

REFERENCES

1. Sangeeta S. Metformin and Pioglitazone in polycystic ovarian syndrome: a comparative study. The Journal of Obstetrics and Gynaecology of India.2012;62(5):551-6.
2. Du Q wang Y-J, Yang S, Wu B, Han P, Zhao Y-Y. A systematic review
3. Wagan F. Polycystic ovarian syndrome: Response to metformin therapy.2011.
4. Ota H, Goto G, Yoshioka N. successful pregnancies with Pioglitazone in infertile patients with polycystic ovary syndrome. Fertlity and sterility.2008;90(3):709-13
5. Kjerulff LE, sanchez-Ramos L,DuffyD,Pregnancy outcomes in polycystic ovary syndrome: a metaanalysis. American journal of obstetrics and gynaecology.2011:204(6):558.e1-e6.
6. Kamalanathan S, Sahoo JP, SathyapalanT. Pregnancy in polycystic ovary syndrome. Indian journal of endocrinology and metabolism.2013;17(1):37.
7. Hull M. Epidemiology of infertility and polycystic ovarian disease: endocrinological and demographic studies. Gynaecological Endocrinology. 1987;1(3):235-45.
8. Knochenhauer E, Key T, Kahsar-Miller M, Waggoner W, Boots L, Azziz R. Prevalence of the polycystic ovary syndrome in unselected black and white women of the Southeastern United States: A prospective study 1. The Journal of Clinical Endocrinology & Metabolism. 1998;83(9):3078-82.
9. Sam S, Dunaif A. Polycystic ovary syndrome: syndrome XX? Trends in Endocrinology & Metabolism. 2003;14(8):365-70.
10. Li XJ, Yu YX, Liu CQ, Zhang W, Zhang HZ, Yan B, et al. Metformin vsthiazolidinediones for treatment of clinical, hormonal and metabolic characteristics of polycystic ovary syndrome: a meta-analysis. Clinical endocrinology. 2011;74(3):332-9.
11. Glueck CJ, Moreira A, Goldenberg N, Sieve L, Wang P. Pioglitazone and metformin in obese women with polycystic ovary syndrome not optimally responsive to metformin. Human reproduction.2003;18 (8):1618-25
12. Brettenthaler N, De geyter C, Huber PR, Keller U. Effects of the insulin sensitizer pioglitazone on insulin resistance, hyperandrogenism, and ovulatory dysfunction in women with polycystic ovary syndrome. The journal of Clinical and Endocrinogy& Metabolism. 2004;89(8):3835-40.
13. Tang T, Lord JM, Norman RJ, Yasmin E, Balen AH. Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, D-chiroinositol) for women with polycystic ovary syndrome, oligoamenorrhoea and subfertility. The Cochrane Library. 2012.