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

SADAF ZAHRA SYED, FARIHA AKRAM, S M AFTAB HASSAN

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). The mechanism by which metformin results ovulation induction is not clear but seems to act on the liver, increasing glucose usage and decreasing insulin resistance. It is also thought that metformin results in reduction in ovarian androgenic production and improves srecretion of luteinizing hormone, leading to ovulation.

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

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.

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).

First, discuss the effects of Pioglitazone for infertile women, with the involvement of Metaphorin in patients such as Ota H, et al polycystic ovarian 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 pioglitazogene pacing.

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 according to the importance of methodology to conduct another study to describe the correct PCO 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 termination of oral drugs. Scan was done on 12th day 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.
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 age 30years and age 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 ≤30 years 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

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>n</td>
<td>51</td>
</tr>
<tr>
<td>Mean</td>
<td>28.18</td>
</tr>
<tr>
<td>SD</td>
<td>4.55</td>
</tr>
</tbody>
</table>

### Table 2: Comparison of egg size with study group

<table>
<thead>
<tr>
<th>Egg size (mm)</th>
<th>Study group</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>n</td>
<td>51</td>
</tr>
<tr>
<td>Mean</td>
<td>19.49</td>
</tr>
<tr>
<td>SD</td>
<td>3.47</td>
</tr>
</tbody>
</table>

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

### Table 3: Frequency distribution of ovulation

<table>
<thead>
<tr>
<th>Ovulation</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>Yes</td>
<td>73</td>
</tr>
<tr>
<td>No</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
</tr>
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</table>

### Table 4: Comparison of ovulation with study groups

<table>
<thead>
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<th>Ovulation</th>
<th>Study group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pioglitazone</td>
<td>Metformin</td>
</tr>
<tr>
<td>Yes</td>
<td>43</td>
<td>30</td>
</tr>
<tr>
<td>No</td>
<td>8</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>51</td>
</tr>
</tbody>
</table>

Chi value=8.14 p-value=0.004*  

### Table 5: Comparison of conception with study groups

<table>
<thead>
<tr>
<th>Conception</th>
<th>Study group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pioglitazone</td>
<td>Metformin</td>
</tr>
<tr>
<td>Yes</td>
<td>32</td>
<td>9</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>51</td>
</tr>
</tbody>
</table>

Chi value=21.57 p-value=0.000  

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

<table>
<thead>
<tr>
<th>Ovulation</th>
<th>Study group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pioglitazone</td>
<td>Metformin</td>
</tr>
<tr>
<td>Age ≤30 years</td>
<td>32</td>
<td>25</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Age &gt;30 years</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Study group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pioglitazone</td>
<td>Metformin</td>
</tr>
<tr>
<td>Age ≤30 years</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>No</td>
<td>15</td>
<td>32</td>
</tr>
<tr>
<td>Age &gt;30 years</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>4</td>
<td>10</td>
</tr>
</tbody>
</table>

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 androgenes7–9.

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\(^9\) 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
to beter to thiazolidinedione’s for the treatment of PCOS or vice
versa. Another study by Sangeeta\(^4\) 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 pioglitazone/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 Glueck et al\(^11\) combined 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
Bretenthaler 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-sensitzing 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 clophimene, or when compared with clophimene. 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.

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