

TAMOXIFEN: AN ALTERNATIVE APPROACH IN CLOMIPHENE RESISTANT POLYCYSTIC OVARIAN SYNDROME PATIENTS

Pages with reference to book, From 89 To 90

B. Gulekli, G. Ozaksit, N.O. Turhan, S. Senoz, H. Oral, O. Gokmen (Department of Reproductive Endocrinology and Infertility, Zekal Tahir Burak Women's Hospital, Ankara, Turkey.)

ABSTRACT

Twenty patients with ultrasound diagnosed polycystic ovaries and high luteinizing hormone levels who failed to respond to clomiphene citrate were given tamoxifen to induce ovulation. Tamoxifen 20 mg daily (group 1, n=10) and 40 mg daily (group 2, n=10) was given for 5 consecutive days from the third to seventh day of the cycle. Treatment was monitored by serial ultrasound scans and assessment of serum estradiol. Human chorionic gonadotrophin (hCG) was administered when at least one follicle was >16mm and serum estradiol level was >300pg/ml per follicle. Ovulation was confirmed with detection of the follicular rupture ultrasonographically 2 days after hCG and midluteal progesterone levels. The ovulation rate achieved in group 2 patients was significantly higher ($p=0.01$) than group 1. Three pregnancies were achieved in group 2 patients while there was no pregnancy in group 1. The only side effect was ovarian cyst formation in one patient in group 1. As a result, tamoxifen might be a good choice for clomiphene resistant patients prior to treatment with surgery or hMG (JPMA 43: 89, 1993).

INTRODUCTION

Multiple methods can be used to induce ovulation in patients with polycystic ovaries (PCO). Clomiphene Citrate (CC) is the first choice of treatment in many infertility clinics with an ovulation rate of about 80% and pregnancy rate is 40%¹⁻³. When this agent fails to correct the situation one can choose one of the other methods which are available. The results of surgical treatments (ovarian wedge resection and laparoscopic electrodiathermy) are variable and any beneficial effect is short lived. On the other hand the medical methods for inducing the ovulation in clomiphene resistant polycystic ovarian syndrome (PCOS) patients will be human menopausal gonadotrophins (hMG or pure FSH) with or without gonadotrophin releasing hormone analogs. Before this relatively expensive choice we tried tamoxifen in patients who failed to respond CC. Tamoxifen is a potent, non-steroidal anti-estrogen. Its mechanism of action in clomiphene resistant patients is not clear.

PATIENTS AND METHODS

The study group comprised of 20 women with ultrasound diagnosed PCO as defined by Adams et al⁴ and elevated LH/FSH ratio, who failed to ovulate with CC 200 mg/daily at least in their 3 subsequent cycles. Tamoxifen 20 mg daily (group 1, n= 10) and 40 mg daily (group 2, n= 10) was given for 5 consecutive days from the third to the seventh cycle day. All these women were non-prolactinaemic and they had no other endocrine disorder. Before beginning the treatment venous blood samples were obtained on day 3 of their cycles for determination of estradiol (E2), progesterone (P), gonadotrophins and prolactin (PRL) and a preliminary ultrasound scan was performed. Treatment was monitored by serial ultrasound scans and assessment of serum E2 levels. Ultrasound was performed on alternate days from day 10 until ovulation was occurred or it became apparent that the cycle was anovulatory. Serum

E2 and P levels were also measured on the days of ultrasound scanning. Human chorionic gonadotrophin (hCG) was administered in a dosage of 10,000 IU when at least one follicle was ≥ 16 mm and serum E2 level was ≥ 300 pg/ml per follicle. Ovulation was detected with follicular rupture ultrasonographically confirmed by serum B-hCG levels 20 days after proposed ovulation. Data were analyzed on a desk top computer using a statistical package (SPSS-PC). Fisher's exact probability test and paired t-tests were used to determine statistical significance, the results were expressed as the mean \pm the standard error of mean (SEM).

RESULTS

After the first tamoxifen trial the results were analyzed. There was no significant difference between the groups regarding their age and baseline hormone levels (Table I).

TABLE I. Clinical and hormonal data in tamoxifen treated clomiphene resistant PCOS patients.

	Group 1	Group 2
Age	26.2 \pm 1.1	26.7 \pm 1.2
Baseline E2 (pg/ml)	69.0 \pm 16.7	70.7 \pm 13.9
Baseline P (ng/ml)	1.08 \pm 0.02	0.94 \pm 0.06
Baseline FSH (IU/L)	7.2 \pm 1.5	7.5 \pm 1.1
Baseline LH (IU/L)	13.8 \pm 0.3	14.3 \pm 0.7

Values are mean \pm SEM.

Interval between the commencement of treatment and ovulation was a mean of 10.2 \pm 1.0 days in group 1 and 11.1 \pm 1.2 days in group 2, which did not reach statistical significance. The results of treatment are shown in Table II.

TABLE II. Outcome of therapy.

	Group 1	Group 2
Ovulation rate	1/10 (10%)	7/10 (70%)*
Pregnancy rate	-	3/10 (30%)
Abortion rate	-	1/3 (33%)

Values are mean \pm SEM.

*P < 0.05

Three singleton pregnancies were achieved in the study period. One of the three pregnant women in the study had abortion during an early period of pregnancy, the other two pregnancies are currently at an advanced stage. In one of the group 1 patients a 49x40 mm ovarian cyst was detected in her right ovary during follicular phase. This patient failed to ovulate. This was the only side effect that was recorded during the study.

DISCUSSION

This preliminary study suggests that tamoxifen may be an alternative to the treatment of clomiphene resistant patients. Furthermore, in the patients who were not clomiphene resistant Weseley et al⁵ report more successful results regarding ovulation and pregnancies achieved. Ovulation and pregnancy achieving efficiency of tamoxifen was also evaluated in comparison with dosage in this study. The patients who are anovulatory previously with CC responded to 40mg daily tamoxifen with a rate of 70% while women who were treated with 20 mg daily did not respond favourably. Treatment with 40mg was considered necessary in order to induce satisfactory rates of ovulation in clomiphene resistant PCOS patients. However, we were not able to show similar results with pregnancy rates but we believe that larger number of treatment cycles could possibly produce a higher pregnancy rate. On the other hand while Borenstein et al⁶ described their successful results without any side effect, we detected an ovarian cyst which caused anovulation in that cycle. Further investigations will be necessary in the future concerning this matter. Finally, we conclude that tamoxifen 40 mg daily might be a good choice for clomiphene resistant PCOS patients prior to treatment with surgery or hMG.

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