CEOG Clinical and Experimental Obstetrics & Gynecology

The effect of clomiphene citrate *vs.* letrozole on post-coital tests

J.H. Check[1,2], J.R. Liss[2], J. Vaniver[2]

[1] Cooper Medical School of Rowan University, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ
[2] Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ (USA)

Summary

Purpose: To determine if letrozole is less likely to create a hostile cervical mucus than clomiphene citrate. *Materials and Methods:* Post-coital testing compared at time of peak follicular maturation in women attaining mature follicles in first or second cycle of these two drugs. The study was randomized. Intercourse occurred at least 8-16 hours before. *Results:* Poor post-coital tests were found in twice the frequency in letrozole cycles than clomiphene citrate cycles. *Conclusions:* Despite its shorter half-life, letrozole seems to be as least as likely, if not more, to adversely affect cervical mucus.

Key words: Post-coital test; Cervical mucus; Clomiphene citate; Letrozole.

Introduction

Aromatase inhibitors, e.g., letrozole, because of a shorter half-life, have been considered to have less anti-estrogenic side effects resulting in less adverse effect on endometrial thickness, less vasomotor symptoms, and less premenstrual syndrome [1, 2]. Because of its anti-estrogen effect, clomiphene citrate frequently creates a hostile cervical mucus associated with poor post-coital tests [3]. A priori, if letrozole has less anti-estrogen effect than clomiphene, it seems logical that it should have less adverse on cervical mucus.

The objective of the study was to determine if a "good" post-coital test (defined as finding any sperm with progressive linear motion 8-12 hours after intercourse) is more likely to be found in letrozole *vs.* clomiphene stimulated cycles.

Materials and Methods

A randomized prospective pilot study was performed. Anovulatory women were randomly assigned to clomiphene citrate *vs.* letrozole. Starting dosages were 50 mg days 5-9 for clomiphene. Starting dosages were 2.5 mg days 5-9 for letrozole. If a serum estradiol of 200 pg/ml was not achieved, the dosage of clomiphene or letrozole would be doubled for cycle 2.

The post-coital test that was recorded was the one performed with the appropriate peak serum E2 and prior to the LH surge. Intercourse was 8-16 hours before the post-coital test. Only couples with male partners with normal semen parameters (including absence of antisperm antibodies) were selected for the study. If a mature follicle was not achieved in cycles 1 or 2, the patient was eliminated and a reserve was added to the study and given the same drug regimen.

All couples selected for the study did not want to have an intrauterine insemination performed if there was a poor post-coital test. Patients were given the option to try a second cycle with the same regimen and normal follicular maturation was achieved or they could switch to gonadotropin injections. If they switched, that cycle was not included in the data. Thus the number of second cycles could be unequal related to switching to gonadotropin therapy or pregnancy.

Results

The frequency of poor post-coital tests (no sperm with linear progressive motion in the mucus) is seen in Table 1 for cycles 1 and 2. Overall combining cycles 1 and 2 poor post-coital tests were found in three of 19 (15.7%) clomiphene cycles *vs.* five of 17 (29.4%) with letrozole.

Discussion

Though the frequency of poor post-coital tests was twice as high in the letrozole group *vs.* the clomiphene

Table 1. — *Relative effect of clomiphene citrate vs. letrozole on post-coital tests.*

	Clomiphene citrate	Letrozole
Cycle 1 – no. poor PCT	(n=12) 2 (16%)	(n=12) 4 (33%)
Cycle 2 – no. poor PCT	(n=7) 1 (14%)	(n=5) 1 (20%)

Revised manuscript accepted for publication July 15, 2015

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLIII, n. 2, 2016
doi: 10.12891/ceog3288.2016

7847050 Canada Inc.
www.irog.net

group, the study was not sufficiently powered to show a significant difference ($p > 0.05$, Chi-square analysis). However, because of the failure to demonstrate even a trend to support the initial hypothesis that the known less anti-estrogenic effects of letrozole could result in a lower frequency of poor post-coital tests, the study was discontinued. Possibly the shorter half-life of letrozole, and therefore less anti-estrogenic effects on endometrial thickness and vasomotor symptoms, was negated at the mucus level by a higher average peak serum E2 442.4 pg/ml for clomiphene *vs.* 372.3 pg/ml for letrozole.

References

[1] Mitwally M.F.M., Casper R.F.: "Aromatase inhibition improves ovarian response to follicle-stimulating hormone in poor responders". *Fertil. Steril.*, 2002, *774*, 776.

[2] Mitwally M.F.M., Casper R.F.: "Potential of aromatase inhibitors for ovulation and superovulation induction in infertile women". *Drugs*, 2006, *66*, 2149.

[3] Check J.H., Adelson H.G., Davies E.: "Effect of clomiphene citrate therapy on postcoital tests in successive treatment cycles including response to supplemental estrogen therapy". *Arch. Androl.*, 1994, *32*, 69.

Address reprint requests to:
J.H. CHECK, M.D., Ph.D.
7447 Old York Road
Melrose Park, PA 19027 (USA)
e-mail: laurie@ccivf.com