CEOG Clinical and Experimental Obstetrics & Gynecology

Original Articles

Reproductive Biology Section

Efficacy of a single injection of human chorionic gonadotropin at peak follicular maturation in natural cycles on pregnancy rate and mid-luteal hormonal and sonographic parameters

J.H. Check[1,2], J.R. Liss[2], G. DiAntonio[2], D. Summers[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 discover if infertile women with presumed luteal phase deficiency would improve pregnancy rates, mid-luteal sera estradiol (E2) and progesterone (P), and increase the percentage of women achieving a mid-luteal sonographic homogeneous hyperechogenic endometrial texture by the addition of a single injection of human chorionic gonadotropin (hCG). *Materials and Methods:* Women with over one year of infertility with regular menses and with no other known infertility factor were presumed to have the need for extra P in the luteal phase based on previous studies. Women aged ≥ 30 years were selected along with women < 30 years who had pelvic pain or dysmenorrhea. Women aged 40-45 were evaluated separately. They were treated with either vaginal micronized P 8% twice daily alone or 10,000 units of hCG at the time of peak follicular maturation was also given. Women were eliminated if they did not achieve an 18-24 average diameter follicle with a serum E2 of > 200 pg/ml. Seven days after ovulation, sera E2 and P were measured along with endometrial thickness and echo patterns. *Results:* The only significant difference between groups was an increased mid-luteal serum E2 in the group receiving additional hCG. However, this did not result in an increased pregnancy rate. *Conclusions:* In general, adding a single injection of hCG to P luteal support does not improve pregnancy rates in natural cycles where women were treated with supplemental P.

Key words: Human choronic gonadotropin; Progesterone; Luteal phase defect; Homogeneous hyperechogenic endometrial echo pattern; Endometrial thickness; Serum estradiol.

Introduction

There are studies suggesting that merely achieving a relatively low peak mid-luteal phase serum progesterone (P) level of five ng/ml not only allows the development of normal secretory classical histological changes but also allows apparently normal molecular markers of endometrial receptivity [1]. Nevertheless there is evidence that P supplementation alone in the luteal phase can improve pregnancy rates especially in women over age 30 or even younger women with pelvic pain possibly associated with endometriosis [2-6].

In the luteal phase, the endometrial texture changes, possibly related, in part, to the effects of P, so that the typical triple-line pattern seen at peak follicular maturation changes to a homogeneous hyperechogenic (HH) pattern. There is evidence that there is a lower pregnancy rate in both in vitro fertilization (IVF) cycles or non-IVF cycles including completely natural ones if an HH pattern is not achieved by mid-luteal phase [7,8].

Human chorionic gonadotropin (hCG) has a long half- life, and it is not only able to advance meiosis and aid in oocyte release, but it may stimulate the corpus luteum and, theoretically, could increase certain other hormones, e.g., estradiol (E2) and cytokines made by the corpus luteum, which could aid in a successful implantation.

The objective of the present study was to determine if adding hCG to P supplementation could improve pregnancy rates and/or allow a higher percentage of women achieving an HH mid-luteal endometrial echo pattern.

Materials and Methods

Since the efficacy of P supplementation for infertility was only demonstrated in those allowing a mature follicle of ≥ 18

Revised manuscript accepted for publication August 3, 2015

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLIII, n. 3, 2016
doi: 10.12891/ceog3231.2016

7847050 Canada Inc.
www.irog.net

mm average diameter with a serum E2 exceeding 2,00 pg/ml, those women not achieving a mature follicle were excluded [3, 4]. Only women with at least one year of infertility, bilateral patent fallopian tubes, and a male partner with normal semen parameters were included.

Intrauterine insemination was not allowed so women failing to demonstrate any live sperm in the cervical mucus 8-24 hours after intercourse at the time of peak follicular maturation were excluded. The women were divided into two age groups: ≤ 39 years and 40-45 years. The only women < age 30 years that were included were those with pelvic pain and/or dysmenorrhea and presumed or known to have endometriosis.

Clinical pregnancy rates (defined as a live baby eight weeks from conception) up to the first three treatment cycles were obtained for each group according to whether they received exclusive P supplementation or had in addition to P supplementation a single injection of 10,000 IU hCG, which was given at the time of peak follicular maturation.

Mid-luteal phase pelvic sonography was performed to evaluate endometrial thickness and endometrial echo patterns and compared according to age and whether the women were taking hCG or not. Mid-luteal sera P and E2 levels were obtained and compared according to age group and according to taking hCG or not. Chi-square analysis, Fisher's exact test or standard *t*-test were used where appropriate.

Results

For women aged ≤ 39.9 years, the three-month clinical pregnancy rate in women taking P exclusively was 23.5% (4/17) and for those taking P plus hCG the pregnancy rate was 17.6% (3/17) (Fisher's exact test, p = NS). For those taking P exclusively 62.5% (10/16) achieved the appropriate HH pattern in mid-luteal phase *vs.* 68.7% (11/16) for those taking P plus hCG (Chi-square analysis, p = NS). The mean endometrial thickness in the mid-luteal phase for those taking P only was 13.0 mm *vs.* 16.2 mm for P plus hCG (Student *t*-test, p = NS).

In women aged 40-45, only one of 24 women conceived (one of the 12 taking hCG plus P) but she had a miscarriage so the clinical pregnancy rate was 0% for both during the three months of the study.

For those taking P exclusively 41.6% (5/12) achieved the appropriate HH pattern *vs.* 50.0% (6/12) for those taking P plus hCG (p = NS, Fisher's exact test). The mean endometrial thickness for those taking P only was 9.9 mm *vs.* 9.3 mm for P plus hCG (p = NS, Student *t*-test).

The mid-luteal serum E2 and P for those taking P exclusively were 118 pg/ml and 22.3ng/ml, respectively, *vs.* 144 pg/ml and 22.4ng/ml, respectively, for those taking P plus hCG (p = NS, Student *t*-test for P, $p < 0.05$, Student *t*-test for E2, $p < 0.05$).

Discussion

Despite increasing the mid-luteal phase E2 and P levels in women ≤ 39 years, the addition of hCG to P support for the luteal phase does not seem to improve pregnancy rates. For women ≤ age 39, the power of the study with 34 randomized patients was small and possibly a larger study could show some benefit related to improved fecundity of adding hCG. However, even with this small series, there was not even a trend for improving pregnancy rates.

References

[1] Usadi R.S., Groll J.M., Lessey B.A., Lininger R.A., Zaino R.J., Fritz M.A., Young S.L.: "Endometrial development and function in experimentally induced luteal phase deficiency". *J. Clin. Endocrinol. Metab.*, 2008, *93*, 4058.

[2] Check J.H., Adelson H.G.: "The efficacy of progesterone in achieving successful pregnancy: II, in women with pure luteal phase defects". *Int. J. Fertil.*, 1987, *32*, 139.

[3] Check J.H., Nowroozi K., Wu C.H., Adelson H.G., Lauer C.: "Ovulation-inducing drugs versus progesterone therapy for infertility in patients with luteal phase defects". *Int. J. Fertil.*, 1988, *33*, 252.

[4] Check J.H.: "Progesterone therapy versus follicle maturing drugs - possible opposite effects on embryo implantation". *Clin. Exp. Obstet. Gynecol.*, 2002, *29*, 5.

[5] Check J.H., Liss J., Check D.: "The beneficial effect of luteal phase support on pregnancy rates in women with unexplained infertility". *Fertil. Steril.*, 2013, *99*, S23.

[6] Check J.H., Cohen R.: "The role of progesterone and the progesterone receptor in human reproduction and cancer". *Expert Rev. Endocrinol. Metab.*, 2013, *8*, 469.

[7] Check J.H., Dietterich C., Lurie D.: "Non-homogeneous hyperechogenic pattern 3 days after embryo transfer is associated with lower pregnancy rates". *Hum Reprod.*, 2000, *15*, 1069.

[8] Check J.H., Gandica R., Dietterich C., Lurie D.: "Evaluation of a nonhomogeneous endometrial echo pattern in the midluteal phase as a potential factor associated with unexplained infertility". *Fertil. Steril.*, 2003, *79*, 590.

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