A Nutritional Supplement for Improving Fertility in Women

A Pilot Study

Lynn M. Westphal, M.D., Mary Lake Polan, M.D., Ph.D., M.P.H., Aileen Sontag Trant, Ph.D., and Stephen B. Mooney, M.D.

OBJECTIVE: To determine the impact of nutritional supplementation on optimization of reproductive health in women.

STUDY DESIGN: A double-blind, placebo-controlled pilot study was initiated to determine the effects of FertilityBlend™ (Daily Wellness Co., Sunnyvale, California), a proprietary nutritional supplement containing chasteberry and green tea extracts, L-arginine, vitamins (including folate) and minerals. Changes in progesterone level, basal body temperature, menstrual cycle, pregnancy rate and side effects were monitored.

RESULTS: Thirty women aged 24–46 years who had tried unsuccessfully to conceive for 6–36 months completed the study. After 3 months, the supplement group (n = 15) demonstrated a trend toward an increase in mean midluteal phase progesterone level (from 8.2 to 12.8 ng/mL, P = .08) and a significant increase in the average number of days in the cycle with basal temperatures > 37°C during the luteal phase (6.8–9.7 days, P = .04). The placebo group (n = 15) did not show any notable changes after treatment in any of the parameters studied. After 5 months, 5 of the 15 women in the supplement group were pregnant (33%), and none of the 15 women in the placebo group were (P < .01). No significant side effects were noted.

CONCLUSION: Nutritional supplementation may provide an attractive alternative or complement to conventional fertility therapy. (J Reprod Med 2004;49:289–293)

[This product] is a well-tolerated supplement that could be an attractive option for the optimization of reproductive health in some women.

Keywords: infertility, female; nutritional support; pregnancy rate; FertilityBlend™.

One of every 6 couples in the United States, and 1 of every 3 couples in their late 30s, have difficulty conceiving a child. In 30% of these couples, the man is infertile or subfertile; another 30% have difficulty conceiving due to female fertility issues. The remaining third is attributable to both male and fe-

From the Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, and Daily Wellness Co., Sunnyvale, California.

Supported in part by the Asian Cultural Teaching Foundation.

Address reprint requests to: Lynn M. Westphal, M.D., Department of Obstetrics and Gynecology, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305 (lynnw@stanford.edu).

Financial Disclosure: Dr. Trant is Director of Research and Development, Daily Wellness Co., manufacturer of FertilityBlend,™ the subject of this study. Dr. Polan is on the Scientific Advisory Board of Daily Wellness Co. and has options in the company. Daily Wellness Co. provided the authors with a grant to continue this study.

0024-7758/04/4904-0289/$15.00/0

male issues or has an unknown cause. In many of these cases, the infertility problems are treatable. If low fertility is due to a hormonal imbalance or nutritional deficiencies, nutritional supplementation may play an important role and should be considered a reasonable method of optimizing reproductive health.

Good nutrition and a healthful lifestyle can have a positive effect on fertility and childbearing. For example, an adequate intake of essential nutrients, such as folic acid, in the periconceptual period can lower the incidence of neural tube defects. Vitamins, minerals and specific cofactors play a major role in fertility function, although this is still an area that needs further investigation. William Keye, Jr., M.D., President of the American Society for Reproductive Medicine, commented, "The more we discover about the effects of nutrition on fertility, the better advice we can give our patients."[1]

Hormonal imbalance can be determined by blood tests of reproductive hormone levels. Measuring follicle-stimulating hormone, luteinizing hormone (LH) and estrogen on day 3 and progesterone on day 21 (luteal phase) of a normal cycle can indicate whether the hormonal state is compatible with pregnancy. Abnormal LH or progesterone production may result in an abnormal monthly basal body temperature chart. If progesterone is low, basal body temperature may not increase during the second half of the cycle after ovulation. Without sufficient progesterone, the endometrium is not adequately prepared for implantation of an embryo.

Vitex agnus-castus is an herb used to optimize luteal phase function. Clinical studies in Europe[2-4] used *Vitex* successfully to restore progesterone balance and improve fertility. In one study,[2,3] 39 of 45 women treated with *Vitex* tincture (40 drops) demonstrated increased progesterone levels, with 7 becoming pregnant within 3 months. In another study,[4] among 67 infertile women with oligomenorrhea or amenorrhea, those treated with a homeopathic *Vitex* preparation demonstrated increases in spontaneous menstruation, shorter cycles, earlier ovulation, improved progesterone levels during the luteal phase and more pregnancies. Loch et al[5] noted an increase in the pregnancy rate in women taking *Vitex* in a study of its effects on premenstrual syndrome (PMS) symptoms. No serious side effects were noted in that study of 1,634 women in Germany. One advantage of using *Vitex* rather than the commonly prescribed fertility medication, clomiphene citrate, is the decreased risk of multiple gestation. *Vitex* functions in a more natural and gentle fashion with the body to harmonize hormonal balance. *Vitex* has also been shown to reduce PMS symptoms and other menstrual cycle irregularities.[5-7]

Vitamin B_6 (pyridoxine) has been shown to improve conception rates as well as to treat PMS symptoms, but whether this is due to primary insufficiency is unclear.[8] Vitamin B_{12},[9] folic acid,[10] vitamin E,[11] multivitamins,[12] magnesium,[13] selenium[13], iron[14] and zinc[15] have been shown to improve female fertility.[16]

Antioxidants may be helpful in reducing oxidative stress to ova, sperm and reproductive organs. Vitamins C and E are usually used for this purpose, but green tea may work equally as well. In studying the effects of caffeine on conception (usually considered a negative effect), Caan et al[17] found that drinking tea (as opposed to other caffeinated beverages) approximately doubled the odds of conception per cycle.

L-arginine, an amino acid, helps improve circulation to the reproductive organs; that may enhance oocyte development and implantation of the embryo. Battaglia et al[18] monitored uterine and follicular Doppler flow in response to L-arginine treatment during *in vitro* fertilization treatment cycles in poor responders. The L-arginine–treated group demonstrated improved Doppler flow rates, a lower cancellation rate and an increased number of oocytes collected and embryos transferred. Of the 17 women in the L-arginine supplementation group, 3 became pregnant as compared to zero of the 17 in the nonsupplemented group.

As a result of both the documented and proposed mechanisms of various natural products, it was postulated that a combination regimen (FertilityBlend™, Daily Wellness Co., Sunnyvale, California), as a systematically designed blend of natural products, might provide a synergistic impact in support of human reproductive health.

Materials and Methods

Thirty women, aged 24–46 years, who had tried unsuccessfully to conceive for 6–36 months, were enrolled in the study, and completed the 3-month trial. Written, informed consent was obtained from each participant before entry into the study. Institutional review board approval was obtained. None of the participants received any pharmacologic treatments for infertility during the course of the study or for at least 1 month prior to enrolling. Of

the 30, 15 received placebo, and 15 received FertilityBlend™, administered in a randomized, double-blind, placebo-controlled fashion. Supplements were taken daily, 3 capsules per day (could be taken at one time), for 3 menstrual cycles after initial baseline measurements. All subjects received an additional 3 months of supplement after successful completion of the study. FertilityBlend™ is a proprietary, natural nutritional supplement containing chasteberry and green tea extracts; the amino acid L-arginine; vitamins E, B_6, B_{12} and folate; iron; magnesium; zinc and selenium. Changes in midluteal phase progesterone level and basal body temperature, as well as length of menstrual cycle, pregnancy rate and incidence of side effects, were monitored. Progesterone levels were evaluated via immunoassay. Luteal measurements were made at baseline and after 3 months of nutritional supplementation.

Results

Mean age, weight and number of months attempting to conceive were similar ($P > .10$) for the women in the supplement and placebo groups (Table I). Mean ages for the supplement and placebo groups were 34.3 and 35.3 years of age, respectively; average weights for both groups were 64.5 kg, and lengths of time attempting to conceive (before the study) were 16.8 and 14.2 months, respectively. There were no significant differences between the 2 groups in regard to previous evaluation and the cause of infertility (Table I). More women had previously been pregnant in the placebo group; that could be considered a positive bias for that group, although no one conceived in that group during the study period.

Table I *Patient Characteristics and Pregnancy Rates in the Placebo and Supplement Groups*

Characteristic	Supplement mean (n = 15)	Placebo mean (n = 15)
Mean age (yr)	34.3	35.3
Weight (kg)	64.5	64.5
Months of trying*	16.8	14.2
No. of nulligravidas (%)	10[a] (67)	4 (27)
No. with no prior assessment (%)	6 (40)	6 (40)
No. with endometriosis (%)	2 (13)	0
No. with ovulatory dysfunction (%)	2 (13)	3 (20)
No. with unexplained/other infertility (%)	5 (33)	6 (40)
No. conceiving after 3 mo (%)	4 (27)[b]	0
No. conceiving after 5 mo (%)	5 (33)[c]	0

*Months of actively trying to conceive.
[a]Statistically higher number than in placebo group at $P = .02$, Bayesian binomial analysis.
[b,c]Significantly higher number than in placebo group at $P = .02$ and $P < .01$, respectively, Bayesian binomial analysis.

After 3 months, an increase in mean midluteal phase progesterone levels was noted in the supplement group (8.2–12.8 ng/mL, $P = .08$), whereas the levels in the placebo group remained relatively constant (11.4–12.3 ng/mL, $P = .38$ [Figure 1]). The supplement group also demonstrated an increase in the average number of days in the cycle with basal temperatures >37°C during the luteal phase (6.8–9.7 days, $P = .04$ [Figure 2]). The placebo group remained relatively constant in luteal temperatures >37°C, with an average of 6.7 days >37°C at month 1 and 6.5 at month 3 ($P = .44$). Neither group exhibited any consistent patterns in cycle length changes (Table II), although 4 of the 15 women in the supplement group moved toward a more normal, 28–30-day cycle from shorter or longer cycle lengths.

By the end of the 3-month study, 4 of the 15 women in the FertilityBlend™ group were pregnant (27%) as compared to none in the placebo group ($P = .02$ [Table I]). An additional subject became pregnant during her fifth month on the supplement (33%, $P < .01$). (All subjects were given a 3-month supply of free supplement after completing the study.) The 5 women who became pregnant ranged in age from 24 to 38 years (mean, 32.4) and had been attempting to conceive for 6–30 months (mean, 15.6). Two had abnormally low progesterone levels initially. The 4 who were pregnant in the first 3 months all demonstrated an increase in the number of days with temperatures >37°C on their basal temperature charts. The subject who was pregnant after 5 months on the supplement did not show this temperature rise until later. Two noted distinct signs of ovulation on their temperature charts that they had not observed before. Ovulation was confirmed by home ovulation kit.

The pregnancies resulted in 4 healthy, live births. One pregnancy resulted in a miscarriage; implantation on a leiomyoma appeared to contribute to this loss. After the study was completed, 1 of the patients in the placebo group switched to the supplement and conceived 2 months later. This pregnancy also resulted in a healthy, live birth.

No significant side effects were noted in the study. Three women in the active group (none in the placebo group) complained of slight nausea

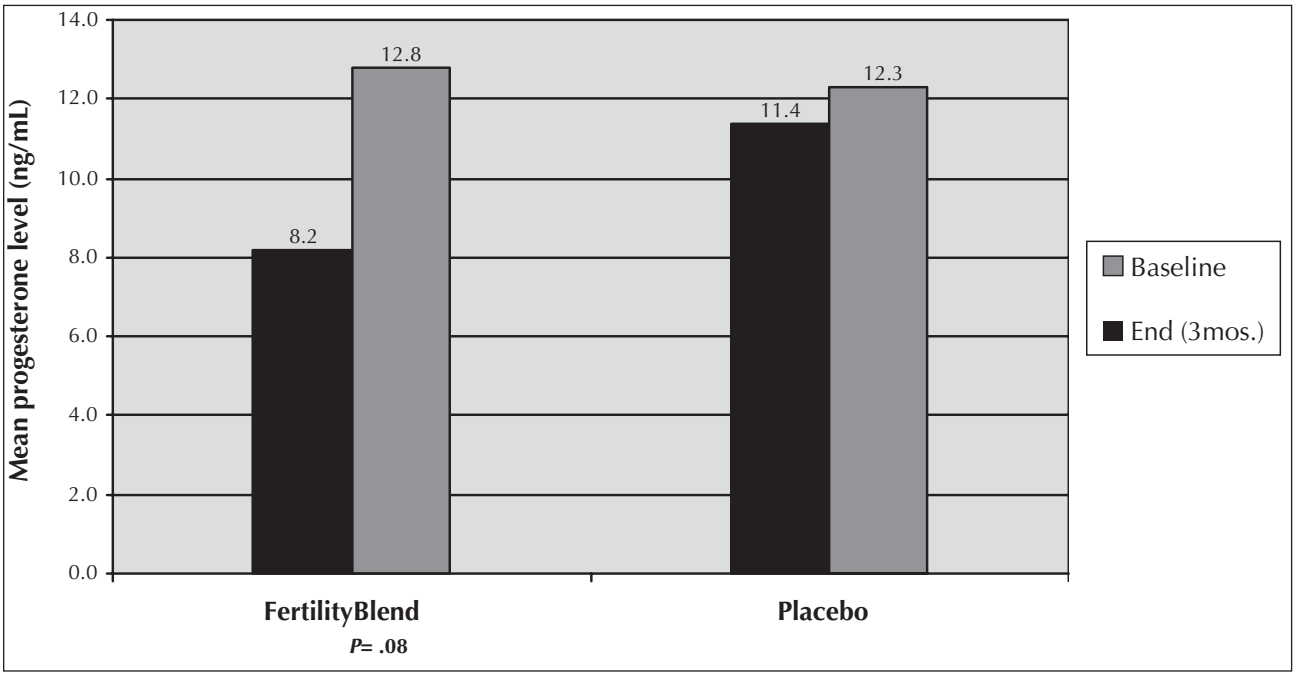

Figure 1 Mean progesterone levels at baseline and after 3 months of FertilityBlend™ Supplement (N = 30).

when taking the supplement on an empty stomach, but that was corrected by taking it with food. Two women in the supplement group noted that their menstrual cycles were more regular, 2 noted shortened cycles, and 1 noted more erratic cycles. Of the 14 women on the supplement, 1 noted less spotting and improved PMS symptoms. Two women on placebo noted increased PMS symptoms, and 4 noted irregular cycles. Since this was the first time many of these women had charted their basal body temperature, they may have become more aware of irregularities in their cycles.

Discussion

Nutritional supplementation may play an important role in optimizing fertility health, leading to

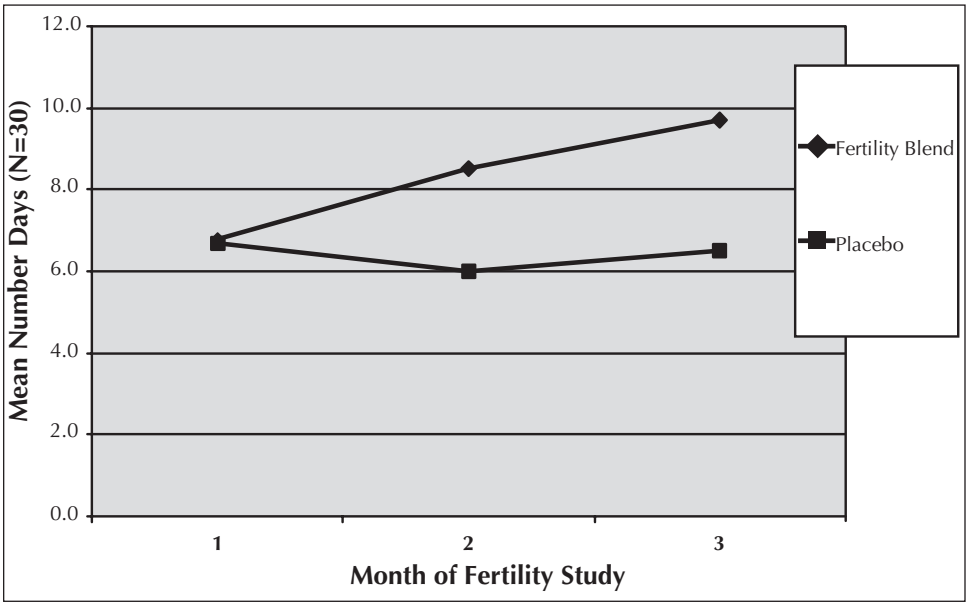

Figure 2 Mean number of days >37°C in the luteal phase on the basal temperature chart.

Table II *Comparison of Progesterone Levels, Days >37°C on Basal Temperature Chart (Luteal Phase) and Menstrual Cycle Length Between the Supplement and Placebo Groups*

Variable	Supplement mean (n=15)	Placebo mean (n=15)
Initial progesterone (ng/mL)	8.2	11.4
End progesterone (ng/mL)	12.8[a]	12.3
Days >37°C		
Mo 1	6.8	6.7
Mo 2	8.5	6.0
Mo 3	9.7[b]	6.5
Cycle length		
Mo 1	30.5	29.5
Mo 2	28.8	30.6
Mo 3	29.7	29.9

**Number of days in cycle with basal temperature readings >37°C during the luteal phase.
[a]Significantly higher than initial time value at $P = .08$, 1-tailed t test.
[b]Significantly higher than initial value at $P = .04$ and higher than placebo group value at $P = .06$, 1-tailed t test.

improved conception rates and providing an alternative or complement to conventional fertility therapy. FertilityBlend™ is a well-tolerated supplement that could be an attractive option for the optimization of reproductive health in some women. Good nutrition is a prerequisite of fertility and childbearing and may be particularly important for those deciding to become pregnant at an advanced age. In the current pilot study, nutritional supplementation increased mean midluteal phase progesterone levels, increased the average number of days in the cycle with basal temperatures >37°C during the luteal phase and resulted in a pregnancy rate of 33% as compared to 0% in the placebo group.

The role of nutritional supplementation in fertility is an extremely important area of research. This pilot study is being expanded to a larger, multicenter study with the goal of evaluating at least 100 women, including those with low luteal phase progesterone or menstrual irregularities. In this way, we may be able to define the women most likely to benefit from nutritional supplements. Similarly, evaluation of a FertilityBlend™ formulated for men is in progress to determine its effect on sperm concentration and motility in men initially low in these levels.

Acknowledgments

Many thanks for help with the study from Bhagyashree Kelshikar and the REI Laboratory, Stanford Hospital, which performed the progesterone analyses.

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