Reproductive Biology Insights

ORIGINAL RESEARCH

Do Hormonal Characteristics of the Luteal Phase Affect the Conception Rate of Women Undergoing IUI Treatment in the Following Menstrual Cycle?

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Abstract

Objective: The present study was performed to evaluate whether the hormone profiles of the mid-luteal phase impact on the chances of conceiving during the following menstrual cycle in connection with intrauterine insemination (IUI) treatment.

Design: Observational clinical study.

Setting: Infertility clinic.

Patient(s): 92 women underwent a total of 288 IUI treatment cycles, without use of exogenous hormones.

Intervention(s): The mid-luteal hormone profiles including levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, oestradiol, progesterone, androstenedione and testosterone, were measured in the preceding cycle of IUI treatment.

Main outcome measure(s): The mid-luteal hormone profiles were correlated to whether the women conceived in the following natural menstrual cycle in which IUI treatment was performed and to whether ovulation occurred on the same ovary in two consecutive cycles (ipsilateral ovulation) or jumped from one ovary to the other (contralateral ovulation).

Result(s): When ovulation occurred from the same ovary in two consecutive cycles mid-luteal levels of progesterone of the preceeding cycle were significantly lower in conceptional than non-conceptional cycles. No significant differences of LH, FSH, estradiol, androstendione and testosterone were observed when correlating the different parameters.

Conclusion(s): Lower mid-luteal progesterone levels seem to enhance chances of conception when ovulation occurs in the same ovary for two consecutive cycles.

Keywords: conceptional cycle, mid-luteal hormone profile, natural menstrual cycle, ovulation pattern, progesterone

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Introduction

In natural menstrual cycles conditions in one cycle may affect conditions of the following cycle. When ovulations alternate between the two ovaries the follicular phase length is shorter compared to when ovulation occur from the same ovary.[1–3] Moreover, ovulation jumping between the ovaries in two consecutive menstrual cycles seemed to be accompanied by increased chances of conception in the latter of the two cycles as compared to two ovulations originating in the same ovary.[3–8] There is also some evidence to suggest that oocytes released from the right ovary possess a higher pregnancy potential than oocytes released from the left ovary.[9]

Previously we found that hormonal characteristics on cycle day 3 in the normal menstrual cycle correlated to the likelihood of achieving conception in connection with IUI treatment, expressed by increased levels of oestradiol and an increased oestradiol/androgen and oestradiol/FSH ratios.[10] These observations have in the present study been extended to include measurements of hormonal profiles of the midluteal phase of the preceding cycle and have been related to whether the ovulation occurred in the same ovary or jumped between the ovaries.

The aim of the present study was to understand further how hormones of the luteal phase affect the conception rate of women undergoing IUI treatment in the following menstrual cycle.

Materials and Methods

Data for this study was collected between August 1997 and November 2002. This is an observational study. A total of 92 women receiving treatment with IUI were included. All women showed regular menstrual cycles (29.4 ± 2.4 days, range 25–35) with an intercycle variation of less than 7 days. They all had two intact ovaries without ovarian cysts and none had ovulation disorders. All these 92 women underwent sonohysterosalpingography and they showed bilateral tubal patency and no endometrial cavity abnormalities.[11] The IUI treatment resulted in 44 women conceived (age: 29.8 ± 3.8, mean ± SD, range 22–38). In total these 44 women had undergone a total of 117 treatment cycles (ie, 44 conceptional and 73 non-conceptional). The remaining 48 women who did not conceive underwent a total of 171 treatment cycles (age 30.3 ± 3.8 years, range 23–38). The causes of infertility among the 44 women who conceived were male factor, 34 and unknown, 10. Those among the 48 women who did not conceive were male factor, 37 and unknown, 11. We compared women's age, body mass index (BMI), husband's age and semen analysis between pregnant women and non-pregnant women. In the present study we used 'pregnant woman' who had conceptional cycle and 'non-pregnant woman' who did not show any conceptional cycle but showed only non-conceptional cycles during IUI treatment. None of the women received any exogenous medication. Following informed consent blood samples were drawn for assessing the hormone profiles 7 days after ovulation (defined by follicle disappearance as observed with transvaginal ultrasound) in the first of the two consecutive cycles and treatment was performed in connection with the second cycle. Monitoring included assessment of concentrations of serum luteinizing hormone (LH: mIU/ml), follicle-stimulating hormone (FSH: mIU/ml), prolactin (ng/ml), oestradiol (E2: pg/ml), progesterone (P: ng/ml), androstenedione (A: ng/ml) and testosterone (T: ng/dl) 7 days after ovulation. Hormone concentrations were measured using automated chemiluminescence system (Bayer-Medical Ltd, Tokyo, Japan) for LH, FSH, prolactin, E2, P and T and radioimmunoassay for A. Intraassay variance was within 5% and interassay variance was within 6%. IUI was performed on a next day following a positive urinary LH test or on the same day when the LH test was strongly positive. Clinical pregnancy was confirmed by the presence of a gestational sac with transvaginal ultrasound. The study protocol was approved by the Institutional Review Board of M&K Health Institute.

Statistical evaluation of multiple groups was performed using ANOVA first and when a statistical difference was detected Tukey-Kramer procedure was used to perform one by one comparison among four groups. Differences were considered significant at $P < 0.05$. Results are presented as mean ± SD.

Results

As shown in Table 1 there were no significant differences of women's age, BMI, husband's age and semen analysis between pregnant women and non-pregnant women.

Table 1. Comparison of women's age, BMI, husband's age and semen analysis between pregnant women and non-pregnant women.

	Pregnant women (n = 44)	Non-pregnant women (n = 48)	*P*-value
Women's age (years)	29.8 ± 3.8 (22–38)	30.3 ± 3.8 (23–38)	*P* = 0.6041
BMI (kg/m^2)	20.5 ± 2.7 (17.1–30.3)	20.7 ± 2.6 (17.3–30.0)	*P* = 0.7371
Husband's age (years)	33.5 ± 4.5 (25–43)	33.4 ± 5.1 (24–42)	*P* = 0.8663
Sperm count (10^6/ml)	13.1 ± 9.7 (3–50)	13.4 ± 10.0 (2–60)	*P* = 0.8924
% motility (%)	25.9 ± 19.6 (4–70)	26.3 ± 18.5 (5–75)	*P* = 0.9322

Note: Mean ± SD.

The mid-luteal serum concentrations of LH, FSH, prolactin, E2, P, A and T of the preceding cycle prior to the IUI treatment cycle in which ovulation was either occurring contralateral (C) or ipsilateral (I) side in relation to previous ovulation irrespective of conception are shown in Table 2. There were no significant differences of different hormone levels between (C) and (I).

The mid-luteal serum concentrations of the preceding cycle in relation to the (C) and (I) ovulation pattern of conceptional and non-conceptional cycles in the group of women who became pregnant and in those who did not conceive are shown in Table 3. With regard to (C) and (I) ovulation patterns there were no significant differences in levels of LH, FSH, prolactin, E2, A and T between conceptional and non-conceptional cycles. *P* levels of ipsilateral ovulation in conceptional cycles were significantly lower than that of non-conceptional cycles among both pregnant and non-pregnant women (AC vs. AI, $P = 0.0454$; AI vs. BI, $P = 0.0335$).

Discussion

The present study shows that conditions created by the corpus luteum is likely to affect the following menstrual cycle and have an impact of whether or not conception will occur, at least in connection with IUI treatment. When ovulation occurs on the same ovary in two consecutive menstrual cycles lower mid-luteal progesterone levels of the preceding cycle seem to augment chances of pregnancy during the subsequent cycle, although concentrations of a number of other hormones remain similar. This may express a local inhibitory effect of progesterone on follicular development, which is then manifested in the following cycle as a reduced chance of conception.

Serum progesterone levels have been used to measure luteal function. The peak of progesterone level is seen 7 to 8 days after ovulation and therefore we measured the hormone profiles 7 days after follicle disappearance by transvaginal ultrasound. Because the progesterone secretion from corpus luteum is pulsatile in nature three measurements between 5 to 9 days after ovulation is recommended.[12] However, in order to reduce patients' pain we measured one sample of progesterone levels during the morning hours which are generally the highest in nature.[13]

There is ample evidence to suggest that progesterone may have a local inhibitory effect on follicular growth in animal studies[14,15] and in humans.[16,17] The effect of progesterone is expressed through a progesterone-binding protein with receptor like features located on the surface of rat granulosa cells.[18,19] Progesterone suppressed the binding of ^{125}I-FSH to porcine granulosa cells in vitro.[20] In addition, progesterone caused atresia of oocytes and follicles using mouse ovarian fragments in vitro.[21] Progesterone inhibited FSH-stimulated oestrogen production through inhibition of aromatase activity

Table 2. Mid-luteal hormone profiles of the former cycle of contralateral (C) and ipsilateral (I) ovulations of all cycles.

	LH (iu/ml)	FSH (iu/ml)	Prolactin (ng/ml)	E2 (pg/ml)	P (ng/ml)	A (ng/ml)	T (ng/dl)
C	4.4 ± 2.6 (n = 155)	2.8 ± 1.2 (n = 155)	20 ± 11 (n = 155)	142 ± 44 (n = 157)	21.2 ± 7.3 (n = 157)	1.88 ± 0.66 (n = 126)	26.8 ± 13.6 (n = 123)
I	4.5 ± 2.6 (n = 131)	2.7 ± 1.0 (n = 131)	21 ± 10 (n = 131)	144 ± 53 (n = 131)	21.2 ± 8.1 (n = 131)	1.93 ± 0.64 (n = 113)	26.9 ± 12.5 (n = 109)
Total	4.4 ± 2.6 (n = 286)	2.8 ± 1.1 (n = 286)	20 ± 10 (n = 286)	143 ± 48 (n = 288)	21.2 ± 7.8 (n = 288)	1.90 ± 0.65 (n = 239)	26.9 ± 13.1 (n = 232)

Note: Mean ± SD.

Table 3. Mid-luteal hormone profiles of the former cycle of contralateral (C) and ipsilateral (I) ovulations of conceptional (**A**) and non-conceptional cycles (**B**).

	LH (iu/ml)	FSH (iu/ml)	Prolactin (ng/ml)	E2 (pg/ml)	P (ng/ml)	A (ng/ml)	T (ng/dl)
A							
C	4.3 ± 2.8 (n = 25)	3.0 ± 1.2 (n = 25)	17 ± 9 (n = 25)	132 ± 45 (n = 27)	22.8 ± 8.0# (n = 27)	1.81 ± 0.74 (n = 20)	26.9 ± 15.4 (n = 20)
I	4.7 ± 2.9 (n = 17)	2.8 ± 1.0 (n = 17)	22 ± 11 (n = 17)	154 ± 76 (n = 17)	16.5 ± 7.8# (n = 17)	1.72 ± 0.47 (n = 16)	21.6 ± 12.9 (n = 16)
B							
C	4.3 ± 2.6 (n = 130)	2.8 ± 1.2 (n = 130)	21 ± 11 (n = 130)	145 ± 44 (n = 130)	20.9 ± 7.3 (n = 130)	1.90 ± 0.63 (n = 106)	26.8 ± 12.6 (n = 103)
I	4.4 ± 2.6 (n = 114)	2.7 ± 1.1 (n = 114)	21 ± 10 (n = 114)	142 ± 50 (n = 114)	22.0 ± 7.9# (n = 114)	1.97 ± 0.66 (n = 97)	27.8 ± 12.2 (n = 93)

Notes: Mean ± SD. ANOVA: P(Progesterone), $P = 0.0364$; #AC vs. AI, $P = 0.0454$; AI vs. BI, $P = 0.0335$.

in cultured rat granulosa cells, suggesting a direct but reversible inhibitory action of progesterone on follicular development.[22–24] Also, progesterone administered before pregnant mares' serum (PMS) injection appears to inhibit early follicular growth and causes atresia, suppressing the proliferation of granulosa cells, and consequently suppresses superovulation induced by PMS and human chorionic gonadotropin (HCG) in hypophysectomized rats.[25] Taken together, results from the present study in combination with results from animal studies suggest that progesterone exerts a local paracrine effect on ovaries that reduces the optimal developmental capacity of subsequent follicles of that ovary during the following cycle.

A number of studies suggest a local antifolliculogenic effect of the corpus luteum.[26–31] Also, a negative effect of the corpus luteum on follicular growth is already present in the actual luteal phase, since the diameter of the largest follicle in the ipsilateral ovary containing the corpus luteum is smaller than that of the contralateral ovary without corpus luteum.[32] The present study corroborates these earlier findings and warrants further studies to elucidate the mechanisms by which progesterone and the corpus luteum in humans are capable of affecting follicular development prior to the gonadotrophin dependent stage.

In conclusion, lower mid-luteal progesterone levels are accompanied by a higher chance of becoming pregnant in the next cycle, especially in connection with ipsilateral ovulations. Corpus luteum, with progesterone as a likely mediator substance, may affect the health status of developing follicles locally and may subsequently affect the likelihood of releasing an oocyte with an optimal pregnancy potential. Thus, there seems to exist a link between mid-luteal hormone profiles (conditions of corpus luteum) and pregnancy potential of the oocyte of the dominant follicle of the next following cycle. The present study therefore suggests a renewed interest in the actions of progesterone exerted on small antal follicles that may further explain the present findings.

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Disclosures

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