Intraovarian blood flow during spontaneous and stimulated cycles

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This study was undertaken to investigate intraovarian blood flow during the early follicular, periovulatory and mid-luteal phases, during spontaneous and stimulated ovarian cycles. Transvaginal ultrasonography with colour flow imaging was used to measure the pulsatility index in eight patients with spontaneous cycles, 20 patients undergoing induction of ovulation with clomiphene citrate and 11 patients undergoing controlled ovarian hyperstimulation using gonadotrophin-releasing hormone analogues. All patients were studied during the early follicular, periovulatory and mid-luteal phase. Intraovarian blood flow velocity waveforms were found in 20% of cases at the early follicular phase, in 56% during the periovulatory phase and in 85% during the mid-luteal phase (P < 0.001). Pulsatility index at the early follicular phase was found to be 1.05 ± 0.02, during the periovulatory phase 0.99 ± 0.22 and during the mid-luteal phase 0.85 ± 0.22. The appearance of intraovarian flow velocity waveforms may suggest either ovarian neovascularization or final follicular maturation or luteinization, which can be detected or measured by Doppler technology.

Key words: Doppler ultrasound/intraovarian blood flow/normal cycle/ovarian stimulation

Introduction

The recent introduction of transvaginal sonography with colour Doppler imaging has facilitated the detection of small calibre vessels in the ovarian parenchyme. Relatively little is known concerning the pattern of intraovarian velocity waveforms in the normal menstrual cycle or in patients stimulated for in-vitro fertilization (IVF). Collins et al. (1991), investigating a single patient, suggested that intraovarian vascularization may be a predictor of ovulation. Campbell et al. (1993) observed a marked increase in blood flow within the leading follicle during the periovulatory phase in spontaneous cycles. Furthermore, Kupesic and Kurjak (1993) reported that ovarian blood velocity tended to increase during the day of ovulation and found no differences between spontaneous and stimulated cycles. Weiner et al. (1993), looking at patients undergoing ovarian stimulation for IVF, found a negative correlation between the intraovarian pulsatility index and the number of preovulatory follicles. Recently Strigini et al. (1995) reported a significant reduction in the intraovarian pulsatility index in patients undergoing ovarian stimulation with follicle stimulating hormone (FSH) on the day of oestradiol peak. The aims of the present study were: (1) to evaluate the intraovarian blood flow during different phases of the menstrual cycle under different treatment regimens; (2) to assess whether there may be an association between 17β-oestradiol and progesterone concentrations, number and size of follicles and intraovarian blood flow

Material and methods

Transvaginal ultrasonography using a 5 MHz curvilinear, transvaginal probe with colour flow mapping (Aloka 680 SSD: Aloka Co., Japan) was used. The high pass filter was set on 100 Hz, and pulse repetition frequency was 2–12 kHz, for all Doppler spectral analyses. The angle-independent pulsatility index (PI) was calculated electronically according to the formula: PI = S – D/A, where S is the maximum, D the minimum and A the mean Doppler shift frequency throughout the cycle. The pulsatility index was measured in eight spontaneous cycles, 20 clomiphene citrate (CC)-induced cycles (Ikaclomin, Teva Pharmaceutical Industries Israel, 50 mg b.i.d. for 5 days), and in 11 patients undergoing controlled ovarian hyperstimulation (COH) using gonadotrophin-releasing hormone analogue (GnRHα) (Decapeptyl 3.75 mg: CR, Ferring Sweden), FSH, human menopausal gonadotrophin (HMG), human chorionic gonadotrophin (HCG) (Metrodin, Pergonal, Chorigon respectively; Teva Pharmaceutical Industries, Israel) for IVF (Shechter et al., 1994).

In the spontaneous and CC-induced cycles the patients were studied in the early follicular phase between days 4–5, in the periovulatory phase between days 12–13 and during the mid-luteal phase between days 20–23. In the IVF group patients were studied during the hypo-oestrogenic phase, on the day of HCG administration and 7–8 days after embryo transfer. At each point transvaginal ultrasonography was performed and the following parameters were determined: ovarian appearance, endometrial thickness and pulsatility index (PI) in uterine, ovarian and intraovarian arterial vessels. At each point oestradiol and progesterone values were measured using specific solid phase radioimmunoassay techniques (Coat-a-count: Diagnostic Products Corporation, Los Angeles, CA).

Statistical analysis comprised of appropriate Student's t-test on the parametric variables and chi square or Fisher's exact test on the non-parametric variables

Results

Table I describes plasma values of oestradiol and progesterone during the different phases of the cycle in the different
signals in the different treatment regimes. Intraovarian velocity concentrations in the mid-luteal phase in the COH group were statistically significantly lower than during this phase in the spontaneous, CC and spontaneous groups.

Intraovarian velocity concentrations were also significantly higher in the periovulatory and early follicular phases. Progesterone concentrations in the mid-luteal phase were significant higher than in the periovulatory phase. In all groups of patients progesterone concentrations in the mid-luteal (ML) phase were statistically significantly lower than in the periovulatory phase (0.8 ± 0.4). In all cycles as compared to COH. In the COH group progesterone concentrations in the mid-luteal phase were statistically significantly lower than in the periovulatory phase.

No significant differences were found during the different phases of the cycle and between the different treatment regimes. In all groups statistically significant differences were found in the prevalence rate of detectable intraovarian blood flow signals in all the groups when early follicular phase waveforms were compared with the mid-luteal phase.

Figure 1 shows the detection rate of intraovarian blood flow signals in the different treatment regimes. Intraovarian velocity waveforms could be detected in the early follicular phase in 12, 30 and 9% of the spontaneous, CC and COH induced cycles respectively. In the periovulatory phase intravascular velocity waveforms were observed in 38, 55 and 73% of the spontaneous, CC and COH induced cycles respectively. In the mid-luteal phase intravascular velocity waveforms were observed in 75, 80 and 100% of the spontaneous, CC and COH induced cycles respectively.

While no statistically significant differences were found in the prevalence of detectable intraovarian blood flow signals between the different treatment regimes, a statistically significant difference was found in the prevalence rate of detecting blood flow velocity waveforms in all the groups when early follicular phase waveforms were compared with the mid-luteal phase waveforms. In the CC group the differences were also statistically significant when the periovulatory phase was compared with the mid-luteal phase.
Furthermore, in the COH group the differences were also statistically significant ($P < 0.001$) when the early follicular phase was compared with the periovulatory phase and the latter were compared with the mid-luteal phase.

Although not statistically significant, it appears from our study that the intraovarian PI decreases gradually from the early follicular through the periovulatory to the mid-luteal phase ($1.05 \pm 0.22$, $0.99 \pm 0.23$, $0.85 \pm 0.22$ (mean $\pm$ SEM) respectively) when all intraovarian measurements during the different ovarian phases are included. Statistically significant differences ($P < 0.01$) were also found in all groups between endometrial thickness in the early follicular phase when compared with the periovulatory and mid-luteal phases (Table II). Furthermore, statistically significant differences were found in the number of large follicles ($>14$ mm) in the COH group compared to the spontaneous and CC groups (Table II). No significant differences could be demonstrated in the PI in the uterine and ovarian arteries during the different phases of the cycle and in the different treatment groups of patients (Table III).

Discussion

Our data corroborate and extend results from previous work (Collins et al. 1991; Campbell et al. 1993; Tekay et al. 1995) related to intraovarian blood flow during the periovulatory period. Jauniaux et al. (1992) demonstrated that blood flow regulation to the corpus luteum in spontaneous pregnancies between 5 and 16 weeks of gestation is related to serum oestradiol and progesterone concentrations. In addition, it has been shown recently (Tekay et al., 1995) that intraovarian blood flow parameters are not related to the outcome of IVF. Furthermore, no significant Circadian fluctuations in mean intraovarian PI have been observed before and after the luteinizing hormone (LH) surge (Zaidi et al., 1995).

The results of the present study have demonstrated for the first time that intraovarian blood flow can be observed more frequently in patients undergoing ovarian stimulation compared to spontaneous cycles. These changes seem to reflect an increase in diastolic blood flow during the process of ovulation and luteinization similar to observations described by Weiner et al. (1993) and by Strigini et al. (1995). However, in contrast to their results, we did find a significant correlation between serum oestradiol values and intraovarian PI. Since in our study the COH group included only patients who were treated with GnRHa, we could clearly demonstrate that the appearance of detectable intraovarian blood flow rose from 9 to 73% prior to final follicular maturation induced by HCG and thus was LH independent.

Experimental studies in rabbits (Kranzfelder and Maurer-Schultz, 1989) showed a well developed perifollicular capillary network in the periovulatory period which is in concordance with our results. These capillary changes could be attributed to an increase in FSH, oestradiol, progesterone or other angiogenic factors. This may explain the relatively low occurrence rate of intraovarian blood flow in a hyperoestrogenic milieu and the relatively high occurrence rate in the periovulatory phase. The appearance of intraovarian blood flow may suggest ovarian neovascularization or final follicular maturation or luteinization.

Based on these results, it seems that intraovarian blood flow may be of value in prediction of the ovulation process and thus may increase the precision and efficacy of some of the assisted reproductive techniques.

References


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