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ORIGINAL ARTICLE

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Diagnosis of luteal phase defect by colour flow pulse doppler

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OBJECTIVE(S): To determine the efficacy of colour flow pulsed Doppler in diagnosing luteal phase defect (LPD) by comparing the flow velocity waveforms of ovarian and uterine artery in different phases of the same menstrual cycle in fertile women and in women with LPD.

METHOD(S): In a prospective study, 50 women at high risk for LPD were compared with 50 fertile women attending infertility clinic. A definite diagnosis of LPD was made by endometrial biopsy taken on day 25 of the menses using the criteria of Noyes et al[1]. The ovarian and uterine artery flow dynamics were studied in both the groups in all phases of menstrual cycle.

RESULTS: The mean pulsatility index (PI) was significantly higher in LPD group (n=15) compared to fertile group (n=44) in luteal phase of menstrual cycles ($p<0.001$) in the dominant side of the ovarian artery. The PI of ovarian artery in fertile group on dominant side was also significantly lower ($p<0.001$) in early, mid and late luteal phases as compared to that on nondominant side. The uterine artery also showed a statistically significant ($p<0.001$) lower end-diastolic velocities in LPD group as compared to the end diastolic velocities in the control group in all phases of luteal cycle.

CONCLUSION(S): Colour flow Doppler is an effective noninvasive method for diagnosing luteal phase defect.

Key words: color doppler, luteal phase defect

Introduction

Luteal phase deficiency (LPD) has been implicated as a cause of infertility and early abortion in 3.4 to 34% of infertile women[2]. The confirmation of LPD can be obtained by endometrial biopsy, serial progesterone estimations and basal body temperature[3]. Introduction of color flow imaging and pulsed Doppler analysis has provided a noninvasive method of assessing the vascular and morphological changes in the ovary and the endometrium. We hypothesize that LPD is due to decreased vascularization of corpus luteum which may result in reduced delivery of steroid precursors to the ovary or inadequate progesterone production thereby resulting in LPD. Therefore, this study was done with the following objectives in mind (a) To determine whether colour flow pulsed Doppler analysis of the corpus luteal blood flow in normal cycle differs from cycle with a LPD and (b) To find out the role of colour Doppler flow imaging in the diagnosis of LPD.

Patients and Methods

Fifty women, with regular menstrual cycles and at risk for luteal phase defect i.e. age >35 years with history of infertility and recurrent abortions, were examined by transvaginal colour Doppler for uterine and ovarian artery flow dynamics in various phases of a single menstrual cycle [(Early follicular (cycle days 6-8), late follicular (cycle days 9-12), early luteal (day of ovulation plus 2-4 days), midluteal (day of ovulation plus 5-6 days), late luteal (day of ovulation plus 9-11 days)]. Endometrial biopsy was taken on day 25 of the cycle. Biopsy was considered out of phase if it was dyssynchronous by >2 days in relation to the day of ovulation as determined by transvaginal sonography in the same cycle using the criteria of Noyes et al[1] for definitive diagnosis of LPD[3]. Another group of 50 fertile women with regular cycles were taken as control.

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Results

Out of 50 study cases, 4 did not show any sonographically visible dominant follicle and remained anovulatory. They were excluded from the study. Out of 46 ovulatory women 15 (32.6%) were diagnosed as LPD on endometrial biopsy. Out of 50 control cases, 6 women (12%) showed features of LPD on endometrial biopsy.

Table 1 shows comparison between various flow dynamics (Resistance Index (RI), Pulsatility index (PI), Peak systolic velocity (Vmax) and End diastolic velocity (Vmin) of ovarina artery between fertile and LPD groups of women. The PI in normal fertile women started decreasing in early luteal phase (0.570 ± 0.017) and reached nadir in midluteal phase (0.4180 ± 0.016), with slight increase again in late luteal phase (0.647 ± 0.021) but still lower than the PI in early and late follicular phase. The PI for LPD groups of women was found to be significantly higher in early luteal (0.922 ± 0.077, p<0.001), midluteal (0.644 ± 0.055 p<0.001), and late luteal (0.890 ± 0.043 p <0.001) phase in comparison to fertile women. Similarly the RI was also significantly higher in LPD patients in comparison to control in early and late luteal phase (p <0.001 and <0.01 respectively). No significant change could be demonstrated in Vmax and Vmin except for Vmin in early luteal phase (5.986 ± 0.393 in fertile women vs 4.273 ± 0.211 in the LPD group, p <0.001). Table 2 demonstrates significantly higher end diastolic velocities in the uterine artery in the fertile group as compared to those in the LPD group with p <0.001 in early, mid, and late luteal phases. Pulsatility Index was significantly higher only in the miduteal phase (p<0.5) and in late luteal phase (p<0.001). Table 3 shows an obvious difference in the value of different flow indices of ovarian artery between dominant (containing active corpus luteum) and nondominant side in the fertile group.

Table 1.Comparison of pulsed Doppler results of ovarian artery blood flow in luteal phase deficient (LPD) and fertile group

Sampling Time	Pulsatility index (PI)		Resistance index (RI)		Peak systolic velocity (Vmax)		End diastolic velocity (Vmin)	
	LPD Mean ± SE	Fertile Mean ± SE	LPD Mean ± SE	Fertile Mean ± SE	LPD Mean ± SE	Fertile Mean ± SE	LPD Mean ± SE	Fertile Mean ± SE
Early follicular	n=10 0.983±0.072	n=37 0.816±0.021[a]	n=10 0.589±0.020	n=37 0.536±0.007[a]	n=10 12.172±1.312	n=37 11.384±0.644	n=10 4.971±0.631	n=37 5.409±0.268
Late follicular	n=11 1.029±0.076	n=41 0.931±0.066	n=11 0.601±0.020	n=41 0.559±0.014	n=11 19.719±3.07	n=41 12.701±0.670	n=11 7.003±1.326	n=41 5.475±0.318
Early luteal	n=12 0.922±0.077	n=44 0.570±0.017[b]	n=12 0.548±0.026	n=44 0.427±0.008[b]	n=12 9.78±0.519	n=44 10.583±0.731	n=12 4.273±0.211	n=44 5.986±0.393[b]
Mid luteal	n=7 0.644±0.055	n=44 0.418±0.016***	n=7 0.469±0.024	n=44 0.350±0.011	n=7 8.015±1.055	n=44 7.499±0.250	n=7 4.363±0.538	n=44 4.81±0.125
Late luteal	n=7 0.890±0.043	n=44 0.647±0.021***	n=7 0.619±0.043	n=44 0.473±0.008[c]	n=7 17.742±1.135	n=44 16.759±1.444	n=7 5.165±1.069	n=44 8.398±0.636[c]

P < 0.05*, P<0.01**, P < 0.001***, Rest of the differences are nonsignificant [a] P=0.03, [b] p=0.0025 [c] P=0.0001

Table 2. Comparison of pulsed Doppler results of uterine artery blood flow in luteal phase deficient (LPD) and fertile women

Sampling me	Pulsatility index (PI)		Resistance index (RI)		Peak systolic velocity (Vmax)		End diastolic velocity (Vmin)	
	LPD Mean±SE	Fertile Mean±SE	LPD Mean±SE	Fertile Mean±SE	LPD Mean±SE	Fertile Mean±SE	LPD Mean±SE	Fertile Mean±SE
Early follicular	n=15 2.395±0.135	n=44 2.186±0.055	n=15 0.837±0.015	n=44 0.838±0.006	n=15 30.113±1.539	n=44 28.214 ± 1.430	n=15 5.448±0.597	n=44 4.548±0.247
Late follicular	n=15 2.553±0.153	n=44 2.342±0.066	n=15 0.857±0.014	n=44 0.844±0.006	n=15 33.586±2.744	n=44 31.609±1.575	n=15 4.756±0.766	n=44 4.841±0.170
Early luteal	n=11 2.669±0.345	n=41 2.236±0.086	n=11 0.849±0.030	n=41 0.818±0.012	n=11 20.91±2.758	n=41 26.532±1.583	n=11 2.701±0.428	n=41 4.717±0.286***
Mid luteal	n=15 2.836±0.285	n=44 2.144±0.029*	n=15 0.990±1.31	n=44 0.843±0.005	n=15 21.593±1.586	n=44 35.264±1.662***	n=15 2.736±0.389	n=44 5.425±0.249***
Late luteal	n=14 2.878±0.152	n=44 2.030±0.051***	n=14 1.018±0.136	n=44 0.801±0.005	n=14 22.750±1.333	n=44 22.168±0.694	n=14 2.922±0.267	n=44 4.421±0.194***

P < .05 = .025 P < .001 = .0001, Rest of the differences are nonsignificant

Table 3. Comparison of pulsed Doppler results of ovarian artery blood flow on dominant and nondominant side in the fertile group women

Sampling time	Pulsatility index (PI)		Resistance index (RI)		Peak systolic velocity (Vmax)		End diastolic velocity (Vmin)	
	Dominant Mean±SE	Non-Dominant Mean±SE	Dominant Mean ±SE Mean±SE	Non-Dominant	Dominant Mean ± SE	Non-Dominant Mean ± SE Mean±SE	Dominant Mean ± SE	Non-Dominant
Early follicular	n=37 0.816±0.021	n=19 0.793±0.030	n=37 0.536±0.007	n=19 0.542±0.009	n=37 11.384±0.644	n=19 11.698±0.526	n=37 5.409±0.268	n=19 6.012±0.365
Late follicular	n=41 0.931±0.066	n=17 1.261±0.155	n=41 0.559±0.014	n=17 0.627±0.031*	n=41 12.701±0.670	n=17 12.461±1.179	n=41 5.475±0.318	n=17 4.105±0.233
Early luteal	n=44 0.570±0.017	n=10 1.254±0.120	n=44 0.427±0.008	n=10 0.671±0.036	n=44 10.583±0.731	n=10 13.39±0.738	n=44 5.986±0.393	n=10 4.534±0.717
Mid luteal	n=44 0.418±0.016	n=6 0.756±0.031	n=44 0.350±0.011	n=6 0.515±0.012	n=44 7.499±0.250	n=6 10.225±0.212	n=44 4.81±0.125	n=6 4.97±0.219
Late luteal	n=44 0.647±0.021	n=9 0.946±0.034	n=44 0.473±0.008	n=9 0.574±0.008	n=44 16.759±1.444	n=9 14.297±4.60	n=44 8.398±0.636	n=9 6.947±1.638

P < .05 = .025, P<.01 = .005, P <.001 = .0001 P < .05 = .025 P < .001 = .0001, Rest of the differences are nonsignificant

Discussion

Despite the relative infrequency of this entity, LPD was identified in 32.5% of the infertile and 12% of the fertile women in our population using the criteria of Noyes et al[1]. However, the prevalence of any abnormality is dependent upon the means of diagnosing the abnormality and definition of abnormality. Davis et al[4] using Noyes et al's[2] criteria of >2 days to define a lag reported the incidences of sporadic and sequentially paired out of phase endometrial biopsies, in normal fertile and infertile women to be 31.4% and 6.6% respectively. Similarly Nakajima and Gibson[5] on the basis of endometrial biopsy and Jordan et al[6] on the basis of integrated luteal progesterone <80ng/mL alone, reported its incidence in 7.1% and 21% respectively among infertile patients.

In fertile women, the lowest RI and PI in the midluteal phase as depicted in Table 1 is consistent with the fact of rapid neovascularisation within the wall of the corpus luteum and extremely high rate of blood flow in this tissue. This increased blood supply to the functional corpum luteum is very much necessary in the dominant ovary for delivery of precursors involved in steroidogenesis and for removal of progesterone. A slight increase in blood flow impedance in late luteal phase might be due to onset of corpus luteum regression and be related to tissue ischaemia[7]. Contrary to our results, Kurjak et al[8] demonstrated a decline in the impedance in the dominant ovarian artery much earlier, even 2-3 days before ovulation. Therefore, they concluded that all these changes in blood flow dynamics in corpus luteum were more complex and not purely related to action of progesterone.

The PI in ovarian artery was significantly higher in LPD patients when compared to normal fertile women in early luteal, midluteal, and late luteal phases of menstrual cycle (each with p<0.001, Table 1) with a significant decrease in end-diastolic velocity in early and late luteal phases (p<0.001). All these findings suggested towards the inadequate vascularization of the corpus luteum resulting in LPD. In consistence with our findings, Glock and Brumsted[2] also showed a significantly higher mean resistance index in LPD patients in midluteal phase (mean RI >0.5, range 0.51-0.64) in comparison to normal fertile women (mean RI <0.46, range 0.37 to 0.46). They also found lower, statistically non-significant, systolic and diastolic velocities in LPD group.

The blood supply to the uterus should be high in the late luteal phase for proper implantation[8]. Therefore, as demonstrated in Table 2, the statistically significant (p<0.001) lower end-diastolic velocities in uterine arteries in luteal phase in LPD group as compared to normal fertile women might cause poor endometrial receptivity and hence infertility or repeated abortions. A mean of PI >3 before embryo transfer could predict upto 35% of failures in achieving pregnancy[9]. Nargund et al[10] also demonstrated an inverse trend between endometrium laying and uterine artery impedance. Therefore, endometrial perfusion may be used to predict the implantation success rate and to reveal unexplained infertility problems.

Transvaginal Doppler ultrasound with colour flow imaging of uterine and ovarian artery can be used as a noninvasive modality to predict corpus luteal function, implantation success rate and can reveal unexplained infertility problems.

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