J. of Obst. & Gyn. of India Vol. 51, No. 1: Jan Feb 2001 Pg 89-91

Studies by Doppler Ultrasound for comparison of uterine blood flow parameters in normo-ovulatory and dysovulatory (PCO) subjects

Kakoli Ghosh Dastidar

Dept. of Diagnostic Ultra Sound, Infertility Clinic & IVF Centre, 208, Rash Behari Avenue, Calcutta – 29.

Summary

Polycystic ovarian disease is one of the commonest endocrinopathies in women of reproductive age group. A number of clinical and endocrinological features have long been attributed to this entity. In recent years ultrasound criteria, also form a backbone of diagnosis. Treatment modalities have evolved; many of which have successfully induced ovulation in the anovulatory varieties of PCOD. Inspite of these, pregnancy rate has been dismally low in these patients. The thickening with hardening of blood vessels in vascular diseases has been thought to be partly androgen mediated. Such processes reduce vascular supply. Could similar androgen excess-mediated flow reduction be found in arteries supplying the uterus in PCO patients?

Introduction & Objective

Polycystic ovarian disease is one of the commonest endocrinopathies (Van Der, et al 1996) in women of reproductive age group. Though amongst women with suggestive clinical features, the incidence of ovarian enlargement with enhanced stromal echodensity and subcapsular cysts may be quite high on transvaginal ultrasound study they may be present in women with no endocrinological disturbance also. (Jacobs, 1994). In a series of suspected cases, incidence of PCO was reported to be 92% in hirsutes and 87% in women with oligomennorrhoea (Adams et al, 1986). The etiology of this pathology remains largely unknown (Balen, 1994). Normal enhancement of ovarian volume takes place at two stages of development. One around the age of 7-8 years due to increased circulating androgens and again at puberty due to rising gonadotropin level and action of growth hormone, insulin-like growth factor –1 (IGF-1) and insulin (Bridges et al, 1993). Low levels of follicle stimulating hormone (FSH) at puberty-onset causes partial folliculogenesis resulting in development of multifollicular ovaries (MFO) (Stanhope et al, 1985) with multicystic structures having transverse diameter greater than 8mm in contrast to PCO where they are between 2-8mm in diameter. Multifollicular appearance is also seen with stimulation of ovary with pulsatile gonadotropin releasing hormone treatment in hypogonadotropi hypogonadism. But their echocharacter in this situation is distinctly different from polycystic ovaries.

On initiation of treatment with various agents 50% to 96% of PCO cases will ovulate but the pregnancy rate has been dismally low. Even in patients exposed to technically advanced Assisted Reproductive Procedures (ART) like In Vitro Fertilization and Embryo Transfer (IVF-ET), the rate of success at each stage has been poorer in PCO subjects. The cause has remained a mystery.

In trying to evaluate the milieu at implantation

we wanted to find out the vascular parameters of arteries supplying the uterus in general and endometrium in particular in the peri-implantation phase of the menstrual cycle and to compare the findings with normal subjects to identify parameter deviation if any.

Material & Methods

To study the uterine perfusion in PCO patients we undertook a study on 52 patients suffering from PCOD (Gr-A) and studied them by colour and pulsed Doppler in the peri-implantation period of stimulated cycles on days, 3, 6 and 7 after ovulation was detected by ultrasound. The data was compared to equal number 52 (Gr-B) of normo-ovulatory subjects undergoing treatment with us for male factor infertility. However 4 patients from Group-A and 6 patients from Group-B did not complete the study. So data of 46 patients from each group was eventually studied.

Results

Table I
Mean Spiral Artery Velocimetry

Cases	S/D	P.I	R.I
Normo Ovulatory	37.6/18.0	1.45	0.68
PCO Patients	29.2/10.4	1.74	0.88

Table II
Mean Uterine Artery Velocimetry

Cases	S/D	P.I	R.I
Normo Ovulatory	7.3/6.4	0.63	0.50
PCO Patients	9.8/2.6	1.65	0.84

The flow parameters like Peak Systolic flow, End-diastolic flow in cms/sec and flow indices like Pulsatility Index and Resistance Index of uterine arteries of both sides and sub-endometrial spiral arteries were studied in three consecutive cardiac cycles and their mean recorded. High pass filter was adjusted between 50-100 Hz to eliminate low amplitude echos from slow moving structures like vessel wall. An Ultramark ATL9 HDI commercially available equipment with 5 Mhz transvaginal probe was used for the study. After vessel identification by colour, pulsed Doppler studies were undertaken for all arteries studied.

Result Analysis:

As shown in Tables I and II the vascularity of the uterine and endometrial arteries increases with recording of low resistance flow through all zones of the thickened endometrium throughout the cardiac cycle during peri implantation period, i.e, day 17-21 of normo-ovulatory subjects. While the vascular pattern of PCO subjects shows high pulsatility of both uterine and sub-endometrial arteries. The indices are markedly enhanced at spiral artery level presumably disturbing uterine perfusion. It is thought that whereas on the one hand the low resistance flow in normo-ovulatory subjects facilitates implantation by providing required nutrition to the implanting blastocyst high resistance flow of dysovulatory subjects hinders implantation.

Discussion

Various states of endocrinological disturbance have been reported in relation to PCO. Obesity leading to hyperinsulinism which causes both hyperandrogenemia (with increased conversion of androgens to estrone in peripheral fat) and raised IGF-1 augmenting ovarian response to gonadotropin has been blamed (Sampaolo et al, 1994). But since all PCO patients are not obese (in one study only 38.4% patients were overweight) it is uncertain whether PCO is the cause or effect of obesity. However, weight loss has been reported to have definite improvement on ovulatory status of these patients (Kiddy et al, 1989). Prevalence of diabetes mellitus in women with PCO has been reported to be quite high (Conway et al, 1992) and the calculated risk of development of cardiovascular disease in PCO cases is increased 7 times (Dahlgren et al, 1992). The main hypothesis for this is that the raised level of androgens promote atherogenesis (Stejanick et al, 1987) and favour hypertension. Thickening and hardening of blood vessels in vascular diseases are thought to be a fibrotic process which is in part mediated by androgen dependent collagen and elastin deposition within smooth muscle cells (Fischer and Swain, 1977) in general.

With respect to the uterine studies in both obese and lean PCO patients a positive correlation between androstenedione and uterine Pulsatility Index (PI) has been earlier confirmed, (Battaglia et al, 1995) and the increased flow resistance has also been seen in this present study. It prompts us to ask whether this reduced flow could then be the cause of the increased rate of early abortions, (Sagle et al, 1988) and poor implantation in PCO patients?

Conclusion

From this study, it appears appropriate to conclude th e

the raised vascular flow indices of uterine perfusion in PCO patients could be the cause for the poor rate of implantation and high early spontaneous abortions in PCO patients including those who ovulate in response to treatment. This has prompted us to supplement treatment cycles, in particular the peri-implantation phase, with vasodilator agents to see if they really did improve results. However detailed discussion of that study does not form part of this report.

Acknowledgement:

The author gratefully acknowledges the support and guidance of Dr. S. Ghosh Dastidar, during the research work on PCO patients whose data is presented here.

References

1. Adams J, Polson D. W and Franks S. Br. Med. J. 293: 355; 1986.
2. Balen A. Ultra. Obs. Gyn. 4; 4; 1994.
3. Battaglia C, Artini P. G, D'Ambrogio G, Genazzani A.D and Genazzani A.R. Am. J. Obst. Gyn, 172: 108; 1995.
4. Bridges N.A., Cooke A, Healy M.J.R, Hindmarsch P.C and Brook C.G.D. Fertil. Steril. 60: 456; 1993.
5. Conway G.S, Agarwal R, Betteridge D. J and Jacobs M. S. Clin. Endocrinol. 37: 119; 1992.
6. Dahlgren E, Jansen P.O, Johanssos S, Lapidus L and Oden A.. Acta. Obstet. Gynecol. Scand. 71: 599; 1992.
7. Fisher G.M and Swain M.L. Am. J. Physiol, 232: 617; 1977.
8. Jacobs H.S. Ultra. Obstet. Gynecol. 4: 3; 1994.
9. Kiddy D.S, Hamilton-Fairley D, Seppala M, Koistinen R, James V.H.T, Reed M.J and Franks S. 1994. Clin. Endocrinol. 31: 757; 1989.
10. Sagle M, Bishop A, Alexander F.M, Michel M. Bonnev R. C, Beard R. W and Franks. Br. Med. J 297: 1027. 1988
11. Sampaolo P, Livien C, Montonari I , Paganelli A, Salesi A and Lorini R. Ultra. Obstet. Gynecol. 4: 310; 1994.
12. Stanhope R, Adams J, Jacobs H. S and Brook C.G.D. Arch. Dis. Child. 60: 116; 1985.
13. Stejanick M. L, Williams P.T, Krauss R.M, Terry R.B, Vranizan K.M and Wood P.D. J. Clin. Endocrinol Metab. 64: 723; 1987.
14. Van Der S, West Huizen and Z M Van Der Spuy. Ultra. Obstet. Gynecol. 7: 335; 1996.