that when concentrations of luteinising hormone are high throughout the follicular phase, as in some women with polycystic ovaries, the hormone penetrates the follicle and allows the oocyte to mature prematurely, resulting in ovulation of an oocyte that is physiologically aged. Such oocytes are unlikely to be fertilised or will tend to produce embryos that implant poorly and therefore abort. Data that support this model were reported in studies of pigs in which premature ovulation (and presumably maturation of oocytes) was induced with human chorionic gonadotrophin and in studies of rats in which insemination was delayed. In both studies the interval between maturation of the oocytes and fertilisation was extended and rates of fertilisation and embryo survival were impaired. In women extension of the interval between ovulation and insemination was associated with a striking increase in the rate of miscarriage. Moreover, Stanger and Yovich, Howles et al, and Punnonen et al have reported that high concentrations of luteinising hormone in the few days before oocytes were collected from women for in vitro fertilisation were associated with impaired rates of fertilisation and conception. 

Our results show that high concentrations of luteinising hormone during the follicular phase, found in many women with the polycystic ovary syndrome, have a deleterious effect on the success of induction of ovulation and conception and may be a causal factor in early pregnancy loss. As recent studies suggest that the polycystic ovary syndrome is common, both in patients attending infertility clinics and in the general population, many patients may perhaps experience early miscarriage because of an endocrine disturbance. A potential treatment for these patients is to induce ovulation with exogenous gonadotrophins after desensitisation of the pituitary with a superactive analogue of luteinising hormone releasing hormone.

Absence of end diastolic frequencies in umbilical artery: a sign of fetal hypoxia and acidosis

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One of the main challenges of antenatal management is distinguishing between normal small fetuses and growth retarded fetuses, which are at increased risk of intrapartum death or asphyxia at birth. Cordocentesis and analysis of fetal blood gases have shown that some fetuses that are small for gestational age are chronically hypoxic and acidic. Cordocentesis, however, is an invasive procedure and not widely available. In hypoxic fetuses the blood velocity in the aorta is decreased. Doppler measurement of blood velocity is non-invasive but requires expensive pulsed Doppler equipment and an experienced operator. The presence or absence of end diastolic frequencies in the umbilical artery can be ascertained with continuous wave Doppler equipment, which is much cheaper and requires less training of the operator. We examined the relation of the oxygen tension and pH in fetal blood with the absence of end diastolic frequencies in flow velocity waveforms of the umbilical artery.

Methods and results

We studied the fetuses of 59 healthy pregnant women who had been referred from other units for investigation of fetal growth retardation. The fetuses were of 21-36 weeks' gestation and had an abdominal circumference below the fifth centile of our normal range. Blood flow velocity waveforms for the umbilical artery were obtained with continuous wave Doppler ultrasound and analysed by a spectrum analyser (Doptek Spectrascan analyser 9000, Doptek, Chichester). A 100 Hz filter was used to eliminate the low frequencies obtained from movements of the arterial wall. With the mother semirecumbent and the fetus apnoeic, the Doppler probe was moved over the uterus until the umbilical cord waveform was identified.

tile luteinising hormone releasing hormone therapy in women with polycystic ovary syndrome. Fertil Steril 1988;49:956-60.

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by its characteristic pattern of pulsatile arterial flow and constant venous flow. The waveforms were defined as abnormal if shifts in frequency at the end of diastole were absent in recordings obtained from three different points on the maternal abdomen. A sample of fetal blood was taken from the umbilical vein by cordocentesis, and the oxygen tension and pH were determined (figure).

The degree of fetal smallness was expressed as the number of standard deviations by which the observed abdominal circumference differed from the normal mean for gestational age, and the severity of hyponxia was expressed as the difference between the oxygen tension observed and the normal mean for gestational age. The correlation between the degree of fetal smallness and the pH of blood from the umbilical vein (r = -0.059) or the severity of fetal hypoxia (r = -0.02) was not significant. Seven fetuses had normal oxygen tensions and pH, 25 were hypoxic, five were acidic, and 22 were both acidic and hypoxic.

Comment

Increased impedance to blood flow in the umbilical artery, as shown by the absence of frequencies at the end of diastole, seems to be a good marker of fetal asphyxia. As all the patients in this study had been referred, and therefore preselected, we cannot comment on the prevalence of this marker in fetuses that are small for gestational age.

The absence of significant correlation between the degree of smallness of the fetus and hypoxia or acidosis shows that uteroplacental insufficiency is not the only cause of small fetal size. Moreover, many babies that are growth retarded because of uteroplacental insufficiency have birth weights that are within the normal range for gestational age. If waveforms of flow velocity in the umbilical artery prove to be as useful a marker of prenatal asphyxia in well grown fetuses as they are in small fetuses they may replace measurement of fetal size for the antenatal prediction of fetal asphyxia. Missed diagnoses of fetal hypoxia might account for some "unexplained" stillbirths.


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Recurrence early miscarriage and polycystic ovaries

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The aetiology of recurrent miscarriages (three or more consecutive spontaneous abortions) is poorly understood. A recent trial suggested that the cause may be immunological, but the polycystic ovary syndrome may also have a role. Spontaneous abortions occur in about 30% of pregnancies after induction of ovulation in women with the syndrome regardless of the treatment used. Because polycystic ovaries are also found in women who ovulate, we investigated a possible association between polycystic ovaries and recurrent miscarriages in women with spontaneous ovulatory cycles. As defects in the luteal phase, which may occur in women with polycystic ovaries, may be related to miscarriage we also assessed progesterone secretion.

Subjects, methods, and results

We studied 56 consecutive patients presenting to the recurrent miscarriage clinic; all ovulated spontaneously. We recorded their menstrual histories, their heights and weights, and whether they had acne or hirsutism. Ultrasonography of the pelvis was performed, and polycystic ovaries were identified. Blood was taken for measurement of luteinising hormone concentration. A control group of 11 parous volunteers with no history of disturbance of their ovulatory cycles or recurrent miscarriages were examined similarly. Early morning urine specimens were collected daily throughout an ovulatory cycle from 30 women who had had recurrent miscarriages, and the concentration of pregnanediol-3a-glucuronide, the major urinary metabolite of progesterone, was measured. Values were compared with those obtained in five controls and in 20 cycles in nine normal, non-parous women (table).

Forty six (82%) of the 56 women who had had recurrent miscarriages, had polycystic ovaries compared with two (18%) of the 11 parous women (χ² = 15.5, p < 0.001). Age, body mass index, and length of the ovulatory cycle were not significantly different among all the groups of women. Six of the 46 patients with recurrent miscarriages and polycystic ovaries had mild or moderate hirsutism and 13 had acne, whereas only one of the 10 women with recurrent miscarriages and normal ovaries had hirsutism (and acne). None of the parous control women was hirsute or had acne. The serum luteinising hormone and mid-luteal pregnanediol-3a-glucuronide concentrations were normal in all of the women with recurrent miscarriages.