Embryonic and Fetal Circulation Studied by Transvaginal Color Doppler

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Ultrasound is already an essential component of obstetric evaluation, but is gaining even more attention as Doppler techniques open new avenues into the diagnosis of blood flow disturbances in the fetus. Some investigators claim that Doppler is the biggest advance in fetal medicine in years (1). The role of fetal and uteroplacental blood flow studies is now well established in obstetric management, but until now there has been no reliable way to measure blood flow in the embryonic period non-invasively. Transvaginal color Doppler is a recently developed diagnostic tool that allows us to look closely at early embryonic development and to make blood flow studies in embryonic and fetal vessels.

PATIENTS AND METHODS

The study included 114 pregnant women volunteers whose gestational age ranged between 5 and 14 weeks. They were recruited from patients scheduled for termination of pregnancy on request. An additional 31 patients with pathologic early pregnancies were examined. Seventeen of these had an ultrasonically diagnosed blighted ovum, 11 had missed abortion, and in three cases a molar pregnancy was diagnosed.

All patients were examined with a 5 MHz transvaginal probe and the equipment employed was an Aloka Color Doppler, models SSD-350 and SSD-680 (Aloka Co., Japan). A condom and gel were placed over the head of the transducer, and the probe was then introduced gently into the vagina with the patient placed in the lithotomy position. After visualization of the pelvic anatomy by B-mode sonography, superimposed color Doppler was used to detect blood flow. The red or blue color indicated the vascular region to be examined by the pulsed Doppler technique for flow velocity waveform analysis. Peak systolic and end-diastolic Doppler shifts were recorded and the Pourcelot resistance index (RI) was calculated (2). This angle-independent index is believed to be a good assessor of downstream vascular
transvaginal color doppler

TABLE 1. Resistance index of the uterine artery in the first trimester of pregnancy (n = 145)

<table>
<thead>
<tr>
<th>Patients</th>
<th>n</th>
<th>mean Rl</th>
<th>2 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pregnancy</td>
<td>114</td>
<td>0.81</td>
<td>0.11</td>
</tr>
<tr>
<td>Blighted ovum</td>
<td>17</td>
<td>0.77</td>
<td>0.13</td>
</tr>
<tr>
<td>Missed abortion</td>
<td>11</td>
<td>0.69</td>
<td>0.09</td>
</tr>
<tr>
<td>Mola hydatidosa</td>
<td>3</td>
<td>0.76</td>
<td>0.07</td>
</tr>
</tbody>
</table>

RI, Pourcelot resistance index.

Resistance. On each record five separate cardiac cycles were examined and the mean value was calculated. The mean duration of the procedure was 10 min. The spatial-peak temporal average intensity was about 80 mW/cm², which is well within the highest limit recommended by the United States Food and Drug Administration for use in fetal medicine.

In all patients we tried to obtain signals from both the uterine arteries and the intervillous space. In 114 patients with normal pregnancies, additional analysis of signals from the umbilical artery and fetal aorta were performed. Fetal brain circulation was also investigated.

RESULTS

Uterine Arteries

Color Doppler signal from both uterine arteries could easily be seen in all patients just lateral to the cervix at the level of the cervicocorporeal junction of the uterus. The calculated resistance indices for the two groups of patients (normal and pathologic intrauterine pregnancy) are given (Table 1). RI values ranged from 0.64 to 0.95, but statistical comparison of mean RI values for the various subgroups studied (normal pregnancy—mean RI 0.81 ± 0.11; blighted ovum—mean RI 0.77 ± 0.13; missed abortion—mean RI 0.69 ± 0.09; molar pregnancy—mean RI 0.76 ± 0.07) did not reveal any significant difference between the values obtained.

Intervillous Space

A color signal seen within a hyperechoic area in close proximity to the gestational sac was considered to be due to intervillous blood flow. When a consistent color signal was obtained in that region, a clear flow velocity waveform of high velocity and low resistance was always easily obtained (Fig. 1). Color flow signals were visualized in 40% of cases at 5 weeks gestation and in 100% of cases from the 7th
FIG. 1. Intervillous blood flow detected by transvaginal color Doppler at 5 weeks of gestation. Waveform analysis showed increased diastolic flow and low resistance (right). f, intervillous color flow.

week of gestation onward (Table 2). Mean RI values were 0.37±0.08 in normal pregnancies, 0.34±0.05 in blighted ovum pregnancies, 0.41±0.07 in the cases of missed abortion, and 0.39±0.11 in molar pregnancies. It should be stressed that in seven cases of missed abortion and five cases of blighted ovum we were unable to detect any intervillous flow.

| TABLE 2. Visualization rate by color Doppler signal of uterine artery, intervillous space, umbilical artery, fetal aorta, and intracranial circulation (n = 114) |
|---|---|---|---|---|---|
| Weeks | n | A. uterina | Intervillous space | A. umbilicalis | Aorta | Brain |
| 5 | 10 | 100% | 4 (40%) | 0 | 0 | 0 |
| 6 | 17 | 100% | 9 (53%) | 5 (29%) | 6 (24%) | 0 |
| 7 | 25 | 100% | 100% | 100% | 13 (93%) | 0 |
| 8 | 14 | 100% | 100% | 100% | 100% | 0 |
| 9 | 5 | 100% | 100% | 100% | 100% | 0 |
| 10 | 7 | 100% | 100% | 100% | 100% | 0 |
| 11 | 3 | 100% | 100% | 100% | 100% | 0 |
| 12 | 14 | 100% | 100% | 100% | 100% | 7 (41%) |
| 13 | 12 | 100% | 100% | 100% | 100% | 10 (83%) |
| 14 | 4 | 100% | 100% | 100% | 100% | 4 (100%) |
FIG. 2. Aortic blood flow detected at 8 weeks of gestation. Waveform analysis showed prominent systolic flow and no diastolic flow (right). e, embryo.

Umbilical Artery

Doppler color signals from the umbilical artery can only occasionally be seen at the 6th gestational week (29%), but are consistently obtained from the 7th gestational week onward (Table 2). During the period under investigation neither diastolic flow in umbilical arteries nor signals from the umbilical vein could be identified. This finding can be explained on the basis of slow, low volume umbilical cord flow at that gestational age which is below detectability with the present color Doppler sensitivity and 100 Hz high-pass filter pulse-wave Doppler.

Fetal Aorta

The fetal aorta can be visualized using transvaginal color Doppler from the 7th week of gestation in 24% of cases, and from 9 weeks onward in 100% of cases (Table 2). Waveform analysis showed no diastolic flow and a high regular systolic Doppler shift (Fig. 2).

Intracranial Circulation

It was possible to obtain clear and persistent intracranial color flow signals from 12 weeks of gestation onward. Small velocity flow with a notable diastolic component was seen (Table 2).
DISCUSSION

Two-dimensional ultrasonography allows direct assessment of the biometric, morphologic, and dynamic status of the fetus. The use of the recently developed Doppler techniques allows access to another type of information, the measurement of circulatory flows in the fetal as well as the maternal blood vessels. Although investigators have focused mainly on late second and third trimester pregnancy, Doppler studies have recently expanded to the first trimester as well (3–11). Its overall value in early pregnancy has yet to be established. It has been found that Doppler waveform patterns in the first trimester differ markedly from those found later in pregnancy (6). For example, the umbilical artery waveform has no diastolic component early in the first trimester under physiological conditions. This contrasts with the third trimester, when absent diastolic flow is associated with poor fetal outcome (7). Diastolic flow begins to increase around the 12th to 17th week, indicating the decrease in placental resistance.

Three kinds of Doppler equipment are presently used in obstetrics: continuous-wave Doppler (CWD), pulsed-wave Doppler (PWD), and color Doppler-coded imaging (CD). The CWD can use a simple and relatively cheap hand probe or it can be coupled with an imaging sonographic transducer or built into sonographic equipment. The PWD is commonly built into imaging sonographic equipment, where the Doppler beam is coaxial or at a variable angle with the sonographic image. The CD has until now been of limited use due to the cost of the equipment. However, it seems that color Doppler could increase the reproducibility of measurements, especially in the maternal circulation. With this modality it is possible to visualize even small vessels clearly, thus enabling accurate placing of pulsed Doppler sample volume. Furthermore, the visualization of flow direction yields information on flow profile. Color Doppler could reaffirm the value of volume flow measurement. Since there is no difference between the vessel diameter measured on B-mode and flow width, the vessel diameter can be accurately measured even in situations when the investigated vessel lies parallel to the ultrasound beam. Such cases are optimal for flow measurement. With good quality of Doppler signal and accurate diameter measurement the accuracy of volume flow measurement could be significantly improved (3).

We have combined color and pulsed-wave Doppler transvaginal sonography. The combination has given us the possibility of screening the vascularization of the entire pelvis rapidly. Only in cases when a color signal is detected away from major pelvic vessels has the time-consuming off-line pulse wave Doppler measurement been undertaken. The trophoblast invades the maternal tissues, and it is possible to get very high blood flow from the maternal arteries into the spaces around them. It is thus worth using this vascular signature of intervillous blood flow as a way confirming early pregnancy development. In this study the signals from the intervillous space umbilical artery and uterine arteries were easily obtained, but we were unable to detect any statistically significant difference in blood flow between normal and pathologic intrauterine pregnancies. This finding does not corroborate observations of
Schaaps and Soyeur (6), whose scanning technique was obviously different (they were unable to detect flow in the normal trophoblast). Thus much more standardized, probably multicenter, work is required before final conclusions can be drawn.

To sum up, embryonic and fetal vessels can easily be visualized by transvaginal color Doppler, and the pulsed Doppler beam can thus easily be directed at the vessel of interest. Color Doppler has been found to be particularly useful in demonstrating intervillous blood flow, flow in the fetal aorta and the intracranial circulation, as well as the uterine artery blood flow. If pulsed Doppler alone is used, the localization of blood flow is a time-consuming and relatively difficult procedure. The guidance of a pulsed Doppler beam by transvaginal color Doppler helps to locate areas of the most abundant flow and makes examination much faster and more accurate.

REFERENCES

DISCUSSION

Dr. Pollak: Could you expand your remarks on the reduced cerebral blood flow in growth retardation?

Dr. Kurjak: This was outside the scope of my presentation. However, we are studying various vessels with conventional color Doppler in our high-risk patients, including the uterine artery, the umbilical artery, the descending part of the fetal aorta, and the fetal cerebral arteries, to see if we can identify a brain-sparing effect. If there is abnormal blood flow in the fetomaternal vessels, the vessels of immediate interest are the cerebral or carotid arteries. The earliest sign of a dangerous situation in the fetus, whatever maternal complication is present, is reduced or absent diastolic flow, and there is an obvious difference between normal diastolic flow in the middle cerebral artery in normally oxygenated fetuses and reduced blood flow in growth-retarded fetuses.
Dr. Dawes: Does color Doppler improve the quantitative measurement of blood flow? And does it make the measurement quicker?

Dr. Kurjak: It certainly improves quantitative measurement but there are still many sources of error in trying to calculate volume of blood flow per kg fetal weight. However I believe that color Doppler will make such measurements more accurate and reproducible. The measurements can also be made much more quickly since the color can guide us to the structure of interest, after which we can superimpose pulsed Doppler for a brief period to get the required information.

Dr. Dawes: I noticed that on one or two occasions you had flows in opposite directions, presumably concurrent artery and vein.

Dr. Kurjak: Iliac arteries produce various blood flow patterns as part of their normal Doppler signature. This is a well-known phenomenon and I believe it results from the high peripheral resistance in the leg vessels producing a reversed signal in the pelvic vessels.

Dr. Hope: I am worried that abnormal middle cerebral artery waveforms could be caused by incomplete insonation of the vessel, and that management decisions are being made on the basis of these measurements.

Dr. Kurjak: Color Doppler always produces very typical signals and gives excellent orientation for the sample volume. So we visualize the vessel first and then put the sample volume inside the vessel. I am not worried that we are mistakenly identifying abnormal waveforms.

Dr. Hope: But I find the reproducibility of pulsed Doppler examinations of the neonatal head after birth worryingly poor.

Dr. Kurjak: Pulsed Doppler is completely different.

Dr. Hope: One can see the middle cerebral artery quite clearly in black and white and put the appropriate cursor in the appropriate place. What I am worried about is making management decisions based on reduced diastolic flow in the fetal brain. I don't think anyone has shown that intervention is necessary, or indeed has tested whether it is a reproducible finding. I don't know any data that confirm your assumptions that this finding means that the fetus should be delivered. You are presumably going to deliver many preterm babies on the basis of a finding that is incompletely understood at present.

Dr. Kurjak: I didn't say so. No single variable can be used to make the final decision. But if you have a growth-retarded fetus, already diagnosed by biometric measurements, if you have reduced pO\textsubscript{2} in fetal blood obtained from cordocentesis, and if you have noninvasive measurements of four fetal vessels all of which show abnormal size, then I don't think many of our colleagues would wait and see. There are several papers, (1,2), particularly from the Rotterdam center, showing that cerebral blood flow is a better index of fetal status than the others currently available.

Dr. Hope: I fully accept that it is a sign of fetal compromise. What I dispute is that the evidence exists for it to be used as a criterion for the timing of delivery, which is a different issue.

Dr. Dawes: What is the physiological basis for the changes you observe in the middle cerebral artery? Why do you think a reduction in diastolic flow occurs?

Dr. Kurjak: I believe that increased peripheral resistance is at least partly responsible.

Dr. Dawes: If you observe reduced flow in conjunction with hypoxemia and hypercapnia (which should cause cerebral vasodilatation) then there must be a reduction of arterial pressure. Is that a possible explanation? Or does anyone else have an explanation for this phenomenon? One of the difficulties in assessing intrauterine life is that you cannot measure pressure.
Dr. Kurjak: Your suggestion seems logical but we don’t know the answer. We are only capable of recognizing a reduced or absent diastolic flow, or even a reversed flow, which from clinical experience most of us find very dangerous.

Dr. Rosén: In our studies on sheep, carotid flow has always been maintained even with the most severe degrees of asphyxia. My suggestion is that the lack of diastolic flow in the middle cerebral artery may be a sign of a decrease in myocardial performance with lowered blood pressure, which would interfere with the circulation in a peripheral artery but would not be detectable in a central artery.

Dr. Jouppila: I should like to stress that up to now we have no clinical marker in Doppler studies that indicates with near 100% certainty that the time for active management has arrived. Some fetuses can tolerate very high peripheral vascular resistance in the umbilical artery and descending aorta, and large decreases in end-diastolic flow in the middle cerebral artery, but tolerance may vary from only a few days to 2 to 3 weeks. The only marker I have seen that is invariably ominous is retrograde flow in the descending aorta or umbilical artery. We have seen this in about 12 cases and most of them died during the few days following the observation.

Dr. Saling: In our evaluation of severely growth-retarded fetuses studied by black and white Doppler, we found that in the group of cases in which there was zero flow we had higher mortality if we waited until the cardiotocograph became abnormal. I think a step-by-step diagnostic program should be used. The first step is the diagnosis of growth retardation; the second is a change in the ratio between the carotid artery and the aorta; the third is the appearance of zero flow in the fetal vessels. When this happens we have a very dangerous situation with high mortality. From our own experience the demonstration of abnormal Doppler patterns detects severe danger better than cardiotocography alone, though perhaps computed cardiotocography will improve on what we have at present.

Dr. Saling: Is the energy emitted during color Doppler comparable with black and white Doppler or greater? How dangerous is it?

Dr. Kurjak: Color Doppler is no more risky than conventional Doppler. For example the machine I use produces 80 mW/cm², which is well within the Food and Drug Administration limits. With pulsed Doppler, the ultrasonic beam is focused and energy is concentrated on the region of interest, but identifying this region is often time-consuming. When color is used, all vessels can be visualized simultaneously and thus the region of interest can be identified promptly and the energy dose reduced.

REFERENCES