Severe intrauterine growth retardation; assessment of its origin from fetal arterial flow velocity waveforms

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Accepted for publication 15 October 1985

Summary

Doppler blood flow velocity waveforms in the umbilical artery and fetal internal carotid artery were recorded in a total of 10 patients with severe intrauterine growth retardation (IUGR) and marked oligohydramnios to establish a fetal or utero-placental origin of IUGR. Gestational age varied between 28 and 37 wk. Negative maternal serology ruled out fetal infections. In six patients, IUGR was associated with abnormal flow velocity waveforms, indicating utero-placental insufficiency. Following delivery, these infants showed no structural defects; moderate to marked placental infarction was documented in 4 out of 6 cases. In the remaining four patients, IUGR was associated with normal flow velocity waveforms, suggesting a fetal origin of the IUGR. Following delivery, all four infants revealed structural defects, only one of which was diagnosed prenatally. Twice an abnormal karyotype was the underlying cause. There was no placental infarction. These preliminary data suggest that combined recording of the flow velocity waveform in the above-mentioned vessels may provide valuable additional information as to the cause of IUGR and as such be helpful in determining obstetric management.

fetal blood flow velocity waveforms; Doppler ultrasound; intrauterine growth retardation; oligohydramnios

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Introduction

Severe intrauterine growth retardation (IUGR) associated with marked oligohydramnios constitutes a considerable problem with respect to establishing the cause of IUGR and subsequent obstetric management. Particularly in the presence of structural defects, IUGR is associated with a poor fetal outcome. Whereas prenatal ultrasound has been shown to be of considerable value in the detection of fetal structural anomalies, the presence of marked oligohydramnios may greatly restrict the quality of fetal imaging even with present high-resolution real-time scanners. Calculation of the head-to-abdomen circumference (H/A) ratio [1] has been helpful in differentiating between asymmetrical and symmetrical growth retardation. Whereas the former usually is a result of diminished uteroplacental function, the latter mostly suggests a fetal origin of the growth restriction. However, in the presence of severe IUGR, particularly associated with marked oligohydramnios, it may be difficult to obtain a reliable measurement of the head and/or upper-abdominal circumference.

With the introduction of combined real-time and Doppler ultrasound systems, a simple non-invasive method of measuring human fetal blood flow velocities has become available [2]. End-diastolic blood flow velocities values have been shown to be reduced at the lower thoracic level of the fetal descending aorta [3,4] and umbilical artery [5,6] and raised in the fetal internal carotid artery [7] in the presence of IUGR, secondary to reduced placental function.

The aim of the present study was to establish to what extent blood flow velocity measurements in the umbilical artery and fetal internal carotid artery allow differentiation between fetal and uteroplacental pathology in the presence of severe IUGR and oligohydramnios.

Material and methods

A total of 10 patients with severe IUGR and marked oligohydramnios were referred to our centre in order to try and establish a fetal or uteroplacental cause of the IUGR. Gestational age was certain, as determined by early crown–rump length or BPD measurement, and varied between 28 and 37 wk. IUGR was defined as:

(a) a clinical discrepancy of more than 2 wk in fundal height on two successive antenatal appointments combined with ultrasonic findings of upper abdominal and head circumference measurements below the 5th percentile according to the nomograms established by Campbell and Wilkin [8] and Campbell [9]. Head to abdominal (H/A) ratio values were subsequently calculated according to the method of Campbell and Thoms [1].

(b) postnatal confirmation by birthweight below the 5th percentile for gestational age according to Kloosterman’s Tables [10], corrected for maternal parity and fetal sex. Marked oligohydramnios was defined as being present if no pocket of amniotic fluid more than 1 cm across at its broadest point was revealed on real-time scanning [11].

Following maternal blood screening for infections, for example toxoplasmosis, cytomegaly virus, herpes, rubella and syphilis, a detailed two-dimensional real-time
search for the presence of fetal structural anomalies was carried out in each subject using a mechanical sector scanner (Diasonics, CardioVue 100, 5 MHz transducer). This was followed by the recording of the blood flow velocity waveform in the umbilical artery and internal carotid artery over at least five consecutive cycles using a combined mechanical sector and pulsed Doppler system (Diasonics CardioVue 400, 3 MHz Doppler transducer) for calculation of the Pulsatility Index as first described by Gosling and King [12]. Amniocentesis for fetal karyotyping was considered in each case.

Results

Tables I and II represent the pertinent details relative to the 10 patients. All patients had severe IUGR and marked oligohydramnios according to the criteria established at the onset of the study, rendering it impossible to carry out amniocentesis for fetal karyotyping. There was no serological evidence of maternal infections.

TABLE I

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Gest. age (wk)</th>
<th>H/A ratio</th>
<th>Ultrasound findings</th>
<th>Mode of delivery; fetal outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Structural defects</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H/A ratio</td>
<td>PI UA</td>
<td>PI ITA</td>
</tr>
<tr>
<td>1</td>
<td>28</td>
<td>?</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>↑</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>?</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>↑</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>↑</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>6</td>
<td>37</td>
<td>↑</td>
<td>-</td>
<td>↑</td>
</tr>
</tbody>
</table>

TABLE II

Gestational age, head-to-abdomen (H/A) ratio, prenatal diagnosis of structural defects, mode of delivery and fetal outcome in six patients with abnormal Pulsatility Index (PI) values in the umbilical artery (UA) and fetal internal carotid artery (ICA).

<table>
<thead>
<tr>
<th>H/A ratio = head-to-abdomen circumference ratio; ↑ = raised ( &gt; +2 S.D.), ? = measurement failed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI UA = Pulsatility Index umbilical artery; ↑ = raised ( &gt; +2 S.D.).</td>
</tr>
<tr>
<td>PI ICA = Pulsatility Index fetal internal carotid artery; ↓ = reduced ( &lt; -2 S.D.).</td>
</tr>
<tr>
<td>LSCS = caesarean section.</td>
</tr>
</tbody>
</table>
TABLE II

Gestational age, head-to-abdomen (H/A) ratio, prenatal diagnosis of structural defects, mode of delivery and fetal outcome in four patients with normal Pulsatility index (PI) values in the umbilical artery (UA) and fetal internal carotid artery (ICA).

H/A ratio = head-to-abdomen circumference ratio; N = normal, t = raised (> +2 S.D.).

PI_{UA} = Pulsatility Index umbilical artery; N = normal.

PI_{ICA} = Pulsatility Index fetal internal carotid artery; N = normal.

LSCS = caesarean section.

MCA = multiple congenital abnormalities: slight hydrocephaly, spina bifida occulta, syndactyly, pulmonal atresia, scalp defect.

<table>
<thead>
<tr>
<th>Pat No.</th>
<th>Gest. age (wk)</th>
<th>Ultrasonic findings</th>
<th>Mode of delivery; fetal outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H/A ratio</td>
<td>Structural defects</td>
<td>PI_{UA}</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>N absent kidneys; N no bladder filling</td>
<td>N</td>
</tr>
<tr>
<td>8</td>
<td>29</td>
<td>N -</td>
<td>N</td>
</tr>
<tr>
<td>9</td>
<td>31</td>
<td>N -</td>
<td>N</td>
</tr>
<tr>
<td>10</td>
<td>32</td>
<td>N -</td>
<td>N</td>
</tr>
</tbody>
</table>

In patients 1–6 (Table I), no fetal structural defects were observed, the Pulsatility Index in the umbilical artery (PI_{UA}) was significantly raised (> +2 S.D.) and the Pulsatility Index in the internal carotid artery (PI_{ICA}) significantly reduced (< -2 S.D.) according to the normal values reported by Wladimiroff et al [7]. The fetal H/A ratio was significantly raised (> +2 S.D.) in four out of six cases according to the nomogram by Campbell and Thoms [1]; no upper-abdominal circumference could be obtained in the remaining two cases. Caesarian section was carried out in patients 1, 3, 4 and 5 because of pathological fetal heart rate tracings, which were characterized by loss of beat-to-beat variability and appearance of recurrent decelerations. Fetal birthweight was always below the 5th percentile. Placental infarction was moderate (approx. 20%) in patients 5 and 6 and marked (≥ 50%) in patients 2 and 3. The overall mortality was 33%.

In patients 7–10 (Table II), prenatal ultrasound examination once revealed renal agenesis (No. 7), whereas PI_{UA} and PI_{ICA} were within normal limits in all instances. H/A ratios were normal in all four patients. Following delivery, fetal congenital structural defects were present in all four patients, twice as a result of an abnormal karyotype (69XXX; trisomy 18). Caesarian section was performed in patients 9 and 10 following the appearance of pathological heart rate tracings. Fetal birthweight was always below the 5th percentile. The placentas demonstrated no infarctions. The overall mortality was 100%.
Discussion

In the present study, all patients revealed marked oligohydramnios associated with severe IUGR, constituting a high-risk group with a high perinatal mortality rate. The raised PI_{UA} values in patients 1–6 typically represent elevated umbilical placental flow resistance [5,6]. The severity of IUGR cannot be closely correlated with the percentage (macroscopic) placental infarction, and only in four out of these six patients could moderate to marked placental infarction be established as an indicator of uteroplacental insufficiency. Further evidence of a uteroplacental cause of IUGR in patients 1–6 is provided by the reduced PI_{ICA} values reflecting a brain-sparing effect in the presence of chronic fetal hypoxia [7]. High-resistance Doppler flow velocity waveforms have recently been reported in the arcuate artery [13] and in the internal iliac artery [14] in IUGR. The exact relationship between these maternal velocity waveforms and velocity waveforms in the umbilical artery has not been clarified yet. In patients 7–10 entirely normal PI_{UA} and PI_{ICA} values were obtained, suggesting a fetal origin of the IUGR. Fetal infection was unlikely, since maternal serology for toxoplasmosis, rubella, cytomegaly virus, herpes and syphilis was negative. Only in patient 7 was a fetal structural defect established (prenatally). The nature of the fetal structural defects in patients 8 and 9 was such that in the presence of marked oligohydramnios prenatal detection was impossible. Fetal microcephaly (patient 10) was missed as a result of normal H/A ratio values. IUGR may also be associated with chromosomal defects [15,16]. Indeed, structural defects were twice associated with an abnormal karyotype which was not diagnosed prenatally due to the lack of amniotic fluid, but was suspected in the presence of normal waveforms.

Trudinger and Cook [17] observed both normal and abnormal umbilical artery waveforms in IUGR associated with major fetal abnormalities. Normal umbilical artery waveforms were observed in fetuses with a low placental/fetal weight ratio reflecting a low fetal growth potential. Whereas in our study normal H/A ratios in patients 7–9 also indicate low fetal growth potential and are associated with normal PI_{UA} values, the findings by Trudinger and Cook [17] suggest that umbilical artery flow measurements alone may not always be helpful in differentiating between IUGR resulting from deprivation of oxygen or nutrient supply and IUGR associated with genetic abnormality or fetal infection. The same authors postulate that a process of obliteration of small arteries in the placenta may be triggered by the abnormal fetus.

Abnormal changes in H/A ratio are usually determined by the occurrence of the brain-sparing effect and as such the H/A ratio provides reliable information as to the cause of IUGR. However, in the presence of marked oligohydramnios it may be difficult to obtain reliable abdominal circumference measurements, as has been shown in our study.

As the PI_{ICA} is a more direct indicator of the brain-sparing effect, it is easier to obtain under these circumstances.

In conclusion, we feel that in the presence of severe IUGR and marked oligohydramnios combined calculation of the PI_{UA} and PI_{ICA} should provide valuable additional information as to the cause of the IUGR. Normal umbilical
artery and internal carotid artery PI values should alert the obstetrician to the possible presence of severe fetal structural abnormality with or without abnormal karyotype.

Acknowledgements

We would like to thank all colleagues for referring their patients to our Ultrasound Unit. We are particularly grateful to Diasonics/Sonotron for the use of the Diasonics CV 400 in this study.

References