Area of lateral ventricles measured on cranial ultrasonography in preterm infants: association with outcome

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Abstract
The association between measurements of lateral ventricle area (determined by serial ultrasound scans) and outcome was studied in 70 preterm neonates of 33 weeks’ gestation or less. The study group was subdivided into four groups according to cranial ultrasonographic findings at 2 weeks postnatal age: group A (n=15) had isolated periventricular/intraventricular haemorrhage and dilated ventricles; group B (n=20) had periventricular/intraventricular haemorrhage and dilated ventricles; group C (n=24) had periventricular/intraventricular haemorrhage and periventricular leucomalacia with or without dilated ventricles; and group D (n=11) had isolated periventricular leucomalacia. Eighty seven preterm infants with no evidence of intracranial disease and good neurodevelopmental outcomes at 2 years formed the control group. A poor outcome was observed in infants in group B, C, and D, particularly in those who had persistent dilated ventricles at 6 weeks postnatal age and extensive periventricular leucomalacia. There was no difference in outcome between group A and controls. During the first six weeks of life ventricular area growth velocities were significantly higher in groups B, C, D, compared with normal controls and group A. We suggest that persistent ventricular dilatation at this early stage carries a bad prognosis, which is the result of atrophy of the brain.

Periventricular/intraventricular haemorrhage and periventricular leucomalacia are relatively common complications in small preterm infants, and the most common neonatal complication of these cerebral lesions is ventricular dilatation. Palmer et al., and more recently Shankaran et al., have shown that infants with both periventricular/intraventricular haemorrhage and ventricular dilatation do not progress as well in their later development as infants with haemorrhage alone. Little is known about the natural history of ventricular dilatation after periventricular/intraventricular haemorrhage in infants who do not develop clinical posthaemorrhagic hydrocephalus, and its association with neurodevelopmental outcome.

In a previous prospective study, we reported a reference range for ventricular area size and growth velocity in preterm infants. The present longitudinal cranial ultrasonographic and clinical study was designed to assess (i) the growth velocity of the lateral ventricle areas during the first year of life in preterm infants who had periventricular/intraventricular haemorrhage with or without periventricular leucomalacia; (ii) the growth velocities of their head circumferences compared with the data obtained from normal controls; and (iii) whether successive measurements of ventricular area and early recognition of an increase in ventricular growth velocity are helpful in predicting neurodevelopmental outcome.

Patients and methods
Between October 1984 and July 1986, a total of 94 preterm infants of 33 weeks’ gestation or less with ultrasonographic evidence of periventricular/intraventricular haemorrhage with or without periventricular leucomalacia during the neonatal period, were enrolled in a longitudinal cranial ultrasonographic and clinical study. Fifteen died in the neonatal period (haemorrhage grade IV: n=6, haemorrhage grade III: n=4, and leucomalacia: n=5). Four were lost to follow up (leucomalacia: n=1, haemorrhage grade II: n=1 and haemorrhage grade I: n=2). Five infants, with cerebral malformation (n=1), congenital anomalies (n=2), and meningitis (n=2) were excluded from the study.

The remaining 70 patients who survived for the duration of the study, were grouped according to ultrasonographic diagnosis at two weeks postnatally. Group A comprised infants with isolated periventricular/intraventricular haemorrhage alone; group B infants with periventricular/intraventricular haemorrhage and dilated ventricle but without periventricular leucomalacia; group C infants with periventricular/intraventricular haemorrhage and leucomalacia with or without dilated ventricles; group D infants with isolated periventricular leucomalacia.

Eighty seven normal preterm infants, with no intracranial abnormalities formed the control group. The reference range for their ventricular area size and growth velocity and their neurodevelopmental outcome have been previously reported.

ULTRASOUND MEASUREMENTS
Infants were prospectively scanned with an Advanced Technology Laboratory (Bellevue) mechanical sector scanner and 7.5 MHz transducer. Scanning was carried out through the anterior fontanelle in the coronal and parasagittal planes, initially within 48 hours of birth, then serially at three to four day intervals until the age of 2 weeks, and thereafter once a week or more if necessary until discharge from
hospital. Further scans were then performed serially at 2, 4, 6, and 9 months and, if the anterior fontanelle was still open, at 12 months.

The coronal sonographic plane was used to measure the area of the lateral ventricles at the mid-body level as previously described. Ultra-
sonographic definitions and classifications, as well as diagnostic methods, remained uniform throughout the study. The severity of the haemorrhage was defined according to the four
grade system of Papile et al.7 Periventricular
leucomalacia was defined according to the
criteria established by Fawer et al,7 and the sites
of the changes were described separately and
defined as frontal leucomalacia, occipital leuco-
malacia, frontoparietal leucomalacia, and
frontoparieto-occipital leucomalacia in cases of
extensive lesions affecting the entire peri-
ventricular white matter.

Early ventricular dilatation at two weeks
postnatally was defined as the ventricular ratio
of one or both lateral ventricles of greater than
0-37:1 (upper limit of normal for preterm
infants) in at least two successive studies.9

Initial measurement of ventricular dilatation
during the first two weeks of life was defined
according to the ventricular ratio and not
ventricular area, as the entire outline of
the lateral ventricle is often not seen during
the early stage of a periventricular/intraventricular
haemorrhage particularly when a large amount
of blood has filled the ventricle.

For follow up purposes the criteria we used to
subdivide the babies into four groups were the
maximum grade of haemorrhage or leuco-
malacia, and the presence or absence of ventri-
cular dilatation at two weeks postnatally. Tran-
sient ventricular dilatation was defined as a
temporary (less than six weeks) increase in size
of lateral ventricles. Persistent dilatation was
defined when still observed at six weeks.

NEURODEVELOPMENTAL ASSESSMENT AND
FOLLOW UP

Gestational age was determined from maternal
dates and the score developed by Dubowitz et al.10 The babies were then examined by medical
staff not concerned in the neonatal care, at the
ages of 4, 6, 9, 12, 18, and 24 months. The
follow up examination consisted of detailed
neurological examination and an assessment of
development using the Brunet-Lezine psycho-

motor development scale corrected for gesta-
tional age. This test is a French adaptation of
the Gesell and Amatruda scale.11 12 The items
of the Brunet-Lezine test include the assess-
ment of posture, oculomotor coordination,
language, and sociability. Evaluations of vision
and hearing were also made. Neurodevelop-
mental outcome was classified as: normal;
moderate neurological abnormalities (transient
abnormality of tone); developmental delay
(developmental quotient of less than 80); cere-
bral palsy (spastic diplegia, quadriplegia, or
hemiplegia); and neurosensory impairment
(auditory or visual impairment). The results of
the repeated neurological examinations between
18 and 24 months postnatal age were the criteria
for the presence or absence of neurodevelop-
mental abnormalities.

DATA ANALYSIS

Postnatal growth velocity (rate of growth) of
occipitofrontal circumference and ventricular
area, which is the slope of growth as a linear
function of time of examination for each infant,
was calculated. Regressions of occipitofrontal
circumference on postnatal age, and of ventri-
cular area on postnatal age, were calculated by
considering the slope for each subject and then
by averaging the slopes. Linear regression
analysis (y=ax+b) by pooling all the data in the
whole sample (n=70) and in each group (A, B,
C, and D), was used to evaluate the relation of
ventricular area to postnatal age, of occipito-
frontal circumference to postnatal age, and of
ventricle area to occipitofrontal circumference.

The score on the Brunet-Lezine scale corrected
for gestational age and obtained at the latest
examination between 24 and 30 months
postnatal age was used for analysis. One way
analysis of variance was performed on the
clinical characteristics and the Brunet-Lezine
scale score to test the differences between each
group. Analysis of variance for repeated
measurement of ventricular area and head
circumference growth velocities was performed
to test the differences between each group.

Results

Seventy preterm infants were studied. Their
clinical details and the distribution in centiles
of their weight are shown in table 1. There were no
significant differences among the four groups in

Table 1 Clinical details of the four groups studied. Values are expressed as mean (SD)

| Group | Birth weight (g)* | Gestational age (weeks) | Appear score at:
|-------|------------------|------------------------|-----------------------|
| A     | (periventricular/ | n=15)                  | 1 minute:
|       | intraventricular |                        | 5 minutes:
|       | haemorrhage)     |                        | No of days ventilated | 11:87 (24-94)
| B     | (periventricular/ | n=20)                  | (2)                   | (2)                   | (2)                   | 15-71 (20-14)
|       | intraventricular |                        | 7 (2)                 | 11 (2)                | 11 (2)                | 21-8 (27-3)  
|       | haemorrhage and |                        | 6 (3)                 | 6 (2)                 | 6 (2)                 | 14 (21-2)    
|       | dilated         |                        | 7 (3)                 | 7 (3)                 | 7 (3)                 |             
|       | ventricles)      |                        | 8 (2)                 | 6 (2)                 | 6 (2)                 |             
| C     | (periventricular/ | n=24)                  |                        |                      |                      |             
|       | intraventricular |                        |                        |                      |                      |             
|       | haemorrhage and |                        |                        |                      |                      |             
|       | periventricular  |                        |                        |                      |                      |             
|       | leucomalacia)   |                        |                        |                      |                      |             
| D     | (periventricular | n=11)                  |                        |                      |                      |             
|       | leucomalacia)   |                        |                        |                      |                      |             

*Centiles of the weight: 5° (900), 10° (1000), 15° (1050), 20° (1200), 50° (1400), 75° (1660), 85° (1740), 90° (1800), 95° (1850).
birth weight, gestational age, Apgar score at 1 and 5 minutes, or duration of ventilator use.

The main ultrasonographic appearances in the four groups are shown in table 2. None of the 70 infants underwent repeat drainage of cerebrospinal fluid; in none was a shunt procedure carried out.

### OCCIPITOFRONTAL CIRCUMFERENCE IN RELATION TO POSTNATAL AGE

The relation of occipitofrontal circumference to postnatal age was significant in the total group (n=70, r=0.79; p<0.0001; occipitofrontal circumference=0.47, postnatal age=26 weeks). There was no significant difference between the occipitofrontal circumference and postnatal age among groups A (r=0.76; occipitofrontal circumference=0.48, postnatal age=26 weeks), group B (r=0.82; occipitofrontal circumference=0.46, postnatal age=27 weeks) and normal controls (n=87, r=0.80; occipitofrontal circumference=0.44, postnatal age=28 weeks). Analysis of covariance showed that the regression lines of the occipitofrontal circumference/postnatal age association between controls and group C (r=0.45; occipitofrontal circumference=0.47, postnatal age=25 weeks) and group D (r=0.75; occipitofrontal circumference=0.42, postnatal age=25 weeks) were parallel; there was, however, a significant difference between controls and group C (p<0.0001) and between controls and group D (p<0.0001).

The average of the slopes of occipitofrontal circumference for the four groups was 0.44 (0.07) cm/week. During the first six postnatal weeks there was no significant difference in the mean (SD) occipitofrontal circumference growth velocity (cm/week) among the four groups and normal controls: controls=0.53 (0.13); group A=0.56 (0.13); group B=0.56 (0.21); group C=0.53 (0.10); and group D=0.50 (0.11).

### VENTRICULAR AREA IN RELATION TO POSTNATAL AGE

The relation of ventricular area to postnatal age was highly significant among the four groups (n=70, r=0.45; p<0.0001; ventricular area=0.95, postnatal age=6.6 weeks). When group A and normal controls were compared (analysis of covariance), there was no significant difference in the ventricular area and postnatal age association. There was, however, a significant increase in ventricle size in relation to postnatal age in groups B, C, and D compared with both normal controls and group A (p<0.0001, analysis of covariance between groups B, C, D, and controls). Except for group A and controls, the regression lines of the ventricular area and postnatal age association were not parallel (fig 1).

The average of the slopes of ventricular area for the four groups during the first six postnatal weeks was 0.85 (1.02) mm²/week.

The mean ventricular growth velocity (mm²/week) during the first six postnatal weeks in each group is shown in table 3. There was no

### Table 2 Main ultrasonographic diagnoses

<table>
<thead>
<tr>
<th>Group</th>
<th>A (periventricular/ intraventricular haemorrhage) (n=15)</th>
<th>B (periventricular/ intraventricular haemorrhage and dilated ventricles) (n=20)</th>
<th>C (periventricular/ intraventricular haemorrhage and periventricular leukomalacia) (n=24)</th>
<th>D (periventricular leukomalacia) (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grades of periventricular/intraventricular haemorrhage:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8</td>
<td>7</td>
<td>10</td>
<td>NA</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td>NA</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td>NA</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>Periventricular leukomalacia:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal</td>
<td>NA</td>
<td>NA</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Occipital</td>
<td>NA</td>
<td>NA</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Frontal-parietal</td>
<td>NA</td>
<td>NA</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Fronto-parieto-occipital</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Dilated ventricles: Early (two weeks)</td>
<td>NA</td>
<td>20</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Transient (&lt;six weeks)</td>
<td>NA</td>
<td>12</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Persistent (&lt;six weeks or more)</td>
<td>NA</td>
<td>8</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

NA, not applicable.

![Figure 1](http://adc.bmj.com/)

*Figure 1* Regression lines of the area of the lateral ventricles during the postnatal period in the four groups compared with normal controls. N=normal controls (n=87, r=0.52, p<0.0001, ventricular area=0.38 mm², postnatal age=7 weeks); A=periventricular/intraventricular haemorrhage (n=15, r=0.32, p<0.0001, ventricular area=0.38 mm², postnatal age=10 weeks); B=periventricular/intraventricular haemorrhage and dilated ventricles (n=20, r=0.58, p<0.0001, ventricular area=1.33 mm², postnatal age=5 weeks); C=periventricular/intraventricular haemorrhage and periventricular leukomalacia (n=24, r=0.43, p<0.0001, ventricular area=0.96 mm², postnatal age=7 weeks); and D=periventricular leukomalacia (n=11, r=0.26, p<0.01, ventricular area=0.66 mm², postnatal age=8 weeks).
Table 3 Ventricular area growth velocity (mm²/week) during the first six postnatal weeks. Values are expressed as mean (SD).

<table>
<thead>
<tr>
<th>Group</th>
<th>Controls (n=87)</th>
<th>A (periventricular/intraventricular haemorrhage) (n=15)</th>
<th>B (periventricular/intraventricular haemorrhage and dilated ventricles) (n=20)</th>
<th>C (periventricular/intraventricular haemorrhage and intraventricular leucomalacia) (n=24)</th>
<th>D (periventricular leucomalacia) (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.39 (0.19)</td>
<td>1.85 (1.07)</td>
<td>0.90 (0.45)</td>
<td>0.78 (0.64)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NS</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0004</td>
<td>p&lt;0.0005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NS, not significant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2 Regression lines of the area of the ventricles and head circumference in the four groups compared with normal controls. N = normal controls (n=87, r=0.54, p<0.0001, ventricular area=0.72 mm², occipitofrontal circumference = 11 cm); A = periventricular/intraventricular haemorrhage (n=15, r=0.45, p<0.0001, ventricular area=0.85 mm², occipitofrontal circumference=12 cm); B = periventricular/intraventricular haemorrhage and dilated ventricles (n=20, r=0.61, p<0.0001, ventricular area=2.8 mm², occipitofrontal circumference=66 cm); C = periventricular/intraventricular haemorrhage and intraventricular leucomalacia (n=24, r=0.45, p<0.0001, ventricular area=1.67 mm², occipitofrontal circumference=31 cm); and D = periventricular leucomalacia (n=11, r=0.36, p<0.0001, ventricular area=1.54 mm², occipitofrontal circumference=21 cm).

Figure 3 Ventricular area growth velocity in relation to the neurological and developmental outcome. Abnormal outcome (n=34) = developmental quotient <80, and normal outcome (n=36) = developmental quotient 80 or more.

Table 4 Neurological and developmental outcome of the four groups studied

<table>
<thead>
<tr>
<th>Group</th>
<th>A (periventricular/intraventricular haemorrhage) (n=15)</th>
<th>B (periventricular/intraventricular haemorrhage and dilated ventricles) (n=20)</th>
<th>C (periventricular/intraventricular haemorrhage and intraventricular leucomalacia) (n=24)</th>
<th>D (periventricular leucomalacia) (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No with developmental delay</td>
<td>4</td>
<td>9</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>(developmental quotient &lt;80)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No with moderate neurological</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>abnormalities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No with neurosensory impairment</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>No with cerebral palsy</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>
area growth velocities for the first six weeks in relation to the neurodevelopmental outcome.

Discussion

Infants in group A did not differ significantly from normal controls, though they kept slightly higher values of ventricular area throughout the study. In a cranial ultrasonographic study, Graziani et al. showed that the width of the lateral ventricles and brain hemispheres in a group of preterm infants with periventricular/intraventricular haemorrhage without early ventricular dilatation did not differ significantly from those of preterm infants without evidence of haemorrhage.13 D’Souza et al have shown that infants with haemorrhage alone had a similar ventricle width to biparietal diameter ratio compared with normal controls.14 The favourable outcome observed in this group is in agreement with similar results reported by others.7–13

Dilated ventricles usually occur in infants who have sustained moderate to severe haemorrhage, and may be related to posthaemorrhagic obstruction. Both Palmer et al and Stewart et al, however, have occasionally noted ventricular dilatation after small haemorrhages in the subependymal area and within the ventricles.4 5 7–15 Others have also described porencephalic atrophy resulting from haemorrhages in preterm infants.16

Dilated ventricles occurred even after small or moderate haemorrhage (group B). In infants with persistent dilatation, ventricular area remained significantly greater than in normal controls. There was no significant increase in cranial growth velocity despite the persistent increase of ventricular area. Although clinical signs and rapidly enlarging head circumference may be delayed or absent in small preterm babies with haemorrhage, the rate of growth of the occipitofrontal circumference in infants with posthaemorrhagic hydrocephalus in the absence of cerebral atrophy should be as great, if not greater, than that of infants without haemorrhage. Our results suggest therefore that posthaemorrhagic hydrocephalus alone is an insufficient explanation for dilated ventricles in some infants. Whether progressive brain atrophy is taking place or a decrease in early cranial growth related to the neonatal illness is occurring is not certain. Infants in group B with persistent dilated ventricles may have included those with brain atrophy as a result of diffuse hypoxic-ischaemic parenchymal damage not detected by ultrasonographic scanning, and subsequently associated with retarded development. Volpe et al have shown by positron emission tomography that periventricular infarction can be more extensive than the haemorrhage.16

In the 24 infants in group C and the 11 infants in group D, ventricular area growth velocity was significantly greater than that of normal controls; in addition, the rate of growth of occipitofrontal circumference remained significantly lower throughout the study, particularly in those with extensive lesions, suggesting diffuse cerebral atrophy with retarded development and cerebral palsy.

None of the infants with persistent dilated ventricles required shunts. In a recent study, Shankaran et al showed that the lack of ventricular decompression after ventriculoperitoneal shunt was strongly associated with poor outcome, suggesting that cerebral atrophy may have occurred before the insertion of the shunt in some infants with posthaemorrhagic ventricular dilatation.1

Early recognition of ventricular dilatation is important, as it seems to correlate with neurodevelopmental outcome. We chose to evaluate ventricular size quantitatively, because when ventricular dilatation occurs linear measurements do not reflect this change. Horbar et al, suggested that the lateral ventricular cross sectional area should be measured when dilatation occurred.17 This was done in one infant with posthaemorrhagic hydrocephalus by planimetry of multiple coronal sections.

In our study, although the overlap among the groups is important, early determination of ventricular area growth velocities seems to be discriminatory for assessing outcome. The relatively increased value of the SDs of the slopes of the ventricular area growth velocity, is explained by the fact that some infants (group B) had rapid posthaemorrhagic ventricular dilatation.

We conclude that longitudinal cranial ultrasonographic follow-up provides a useful assessment of brain in preterm infants. Comparison of direct ultrasound measurements (ventricular area) in the detection of changing ventricular size is helpful in planning treatment and in defining the relationship between neurodevelopmental outcome and cerebral lesions.

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