Measurement of the transverse cerebellar diameter in preterm neonates and its use in assessment of gestational age

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SUMMARY

This study aims to confirm the relationship between gestational age (GA) and transverse cerebellar diameter (TCD), to define the prediction of GA by TCD, and assess the reliability of TCD measurements. Infants were included in the study if they had a routine cranial ultrasound scan by day 3, and the TCD was measured. Infants were excluded from the study if the GA was not known, if there was any cranio-spinal malformation or grade 3 or 4 intraventricular haemorrhage (IVH). The GA assessment was an early pregnancy scan or certain dates. Cranial ultrasound scans were done with a LOGIQ 500 scanner (GE Medical Systems, Waukesha, WI, USA) with a 7 MHz curvilinear sector probe (GE LOGIQ-C721; GE Medical Systems). The posterior fossa was scanned using the asterion as the acoustic window with the TCD measured in the coronal plane. Intra- and interobserver reliability were assessed. A total of 221 infants of known GA had their TCD measured. The linear regression for GA versus TCD is: $GA_{weeks} = (0.470 \times TCD_{millimetres}) + 13.162$ ($r = 0.89$, $r^2 = 0.79$, $P < 0.001$). The 95% confidence interval predicts GA to ± 2.33 weeks for a given TCD. Intra- and interobserver intraclass correlation coefficients are 0.98 and 0.99, respectively. Transverse cerebellar diameter correlates closely with GA and predicts GA to ± 2.33 weeks. Measurements of TCD have excellent reproducibility.

Key words: *cerebellum; gestational age; preterm infant; transverse cerebellar diameter; ultrasonography.*

INTRODUCTION

The transverse cerebellar diameter (TCD) serves as a reliable predictor of gestational age (GA) in the fetus and is a standard against which aberrations in other fetal parameters can be compared, especially when the GA cannot be determined by the date of the last menstrual period or an early pregnancy scan.[1–3] There are preliminary data available for preterm neonates from 23 to 32 weeks and 6 days (32[+6]) GA.[4] These data correlate TCD with GA assessed to completed whole weeks of gestation, and the TCD predicted GA to approximately ± 2.5 weeks.[4] The TCD may therefore be less helpful in determining GA in newborn infants. Refinement of the GA assessment to days of gestation may improve the degree of correlation and decrease the confidence intervals (CI) for the

prediction of GA. Standard measurements of TCD can also be used in the diagnosis of cerebellar hypoplasia when the GA is known[1] and TCD percentile charts can be used to assess cerebellar growth in preterm infants. There are no data available on the reproducibility of TCD measurements for single or multiple observers.

The aims of the present study are: (i) to confirm the relationship between GA and TCD and determine whether it improves with a larger sample size and the estimation of GA to the nearest day; (ii) to define the linear regression equation for prediction of GA by TCD with 95% CI for predicted values; (iii) to define percentile charts for cerebellar growth from 23 to 32[+6] weeks; and (iv) to assess intra- and interobserver reliability for TCD measurements.

METHODS

Subjects

We combined retrospective and prospective data from infants in the Intensive and Special Care Nurseries of the Royal Women's Hospital, Melbourne. Retrospective data were used from a previous study we conducted on infants from 1/1/97 to 30/11/97.[4] The neonatal and maternal notes were re-examined from each of the infants included in this study to determine the GA estimation to the nearest day. The prospective study involved infants born between 8/12/97 and 28/8/98.

In both studies, infants were included if they had a routine cranial ultrasound scan by day 3, and the TCD was measured. Routine cranial ultrasound scans are done on all infants < 1500 g birthweight and/or < 33 weeks GA on days 1, 3, 7 and 28. Infants were excluded if the GA was not known, if there was any cranio-spinal malformation or grade 3 or 4 intraventricular haemorrhage (IVH) according to the classification of Papile *et al*.[6] Measurements were taken from the first cranial scan done within the first three days of life. The GA assessment was based on an early pregnancy scan (< 18 weeks GA) or by certain dates (date of last menstrual period) if no antenatal scan was available. Dates were considered certain if it was recorded as such in the maternal notes.

Measurement

Cranial ultrasound scans were done with a LOGIQ 500 scanner (GE Medical Systems, Waukesha, WI, USA) with a 7 MHz curvilinear sector probe (GE LOGIQ-C721; GE Medical Systems). The posterior fossa was scanned using the asterion as the acoustic window. The asterion is the junction of the parieto-occipital and lambdoid sutures and is palpable just behind the pinna of the ear. The TCD measurement was taken in the coronal plane. The widest diameter of the cerebellum was measured (Fig. 1). The measurements were taken by one of three investigators (MS, MWD, FRB) and all measurements were validated by the senior neonatal ultrasonologist (FRB).

Data analysis

Data were initially entered into MICROSOFT EXCEL 97 and MINITAB (version 11.12) to determine the correlation coefficient, linear regression and 95% CI (of predicted values) for GA versus TCD. Smooth percentile curves for TCD versus GA were derived using the LMS method as described by Cole and Green,[6] assuming a normal distribution, a linear median curve and a coefficient of variation that increases linearly with the median.

Intra- and interobserver reliability

To assess intraobserver reliability, the first 30 measurements done on infants in the study population were repeated by the same observer (MWD or MS). Usually the optimal 2-D image is frozen on the ultrasound screen and the measurement taken. For the repeat measurement the image was unfrozen, the
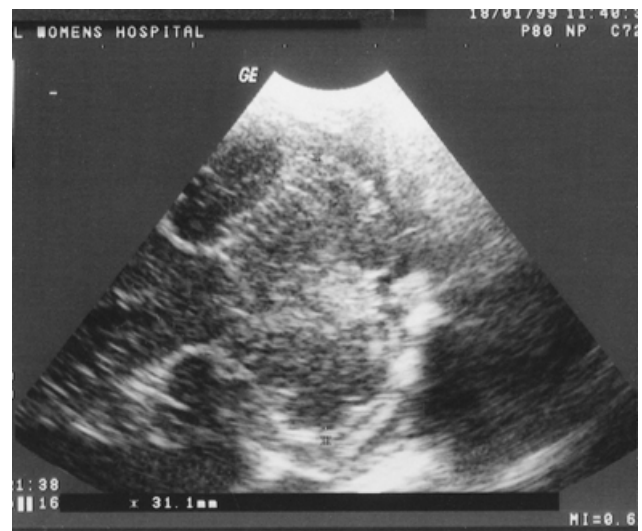

Fig. 1. Ultrasound scan of the posterior fossa demonstrating the measurement of the transverse cerebellar diameter.

ultrasound probe re-applied to the infant's head, the optimal image obtained again and another measurement taken.

Interobserver reliability was assessed in a separate population of infants (all < 33 weeks GA) not included in the study population. Thirty infants had measurements done by one observer and the measurements were then repeated by the second observer, who was blinded to the first observer's data. The measurements were done by MWD and MS.

The average difference between measurements should be close to zero and the variability between measurements is defined as the standard deviation of the differences between repeated measurements. The intraclass correlation coefficient as described by Jamart[7] was calculated for each variable and the strength of agreement scale of Brennan *et al*.[8] was used for interpretation. The strength of agreement or reliability was poor if the intraclass correlation coefficient was < 0.20, fair if between 0.21 and 0.40, moderate if between 0.41 and 0.60, good if between 0.61 and 0.80 and very good if ≥ 0.81.

RESULTS

The retrospective data-set consisted of 101 infants out of 302 admitted to the Unit who had their TCD measured at a GA (ranging from 23 to 32^{+6} weeks) that was estimated to the nearest day. Five infants were excluded from the original data-set because their GA estimate could not be determined to the nearest day. The mean ± SD GA was 28.9 ± 2.8 weeks and the mean ± SD birthweight was 1162 ± 397 g. The prospective data-set consisted of 120 infants out of 225 admitted to the Unit who had their TCD measured at a GA (ranging from 23 to 32^{+6} weeks) estimated to the nearest day. The mean ± SD GA was 29.2 ± 2.5 weeks and the mean ± SD birthweight was 1222 ± 405 g. There was no statistically significant difference between the mean GA values (unpaired *t*-test, $P = 0.40$) or mean birthweights (unpaired *t*-test, $P = 0.27$).

From the original retrospective data-set,[4] the regression equation for GA versus TCD was:

$$GA_{weeks} = (0.495 \times TCD_{mm}) + 12.147$$
$$r = 0.89, r^2 = 0.80, P < 0.001$$

with a residual variance (s^2) of 1.35 (s = 1.163). From the prospective data-set ($N = 120$), the regression equation for GA versus TCD was:

$$GA_{weeks} = (0.450 \times TCD_{mm}) + 13.727$$
$$r = 0.88, r^2 = 0.78, P < 0.001$$

with a residual variance (s^2) of 1.43 (s = 1.194). The regression coefficients are not significantly different between data-sets (*t*-test, $P = 0.17$), and the *s*-values are similar.

The combined data-set consisted of 221 infants with a mean ± SD GA of 29.0 ± 2.6 weeks and a mean ± SD birthweight of 1175 ± 403 g. The GA was determined by an early ultrasound scan in 191 of 221 (86%) infants and by certain dates in 30 of 221 (14%) infants. The regression equation with TCD in millimetres as the predictor (independent) variable and GA in weeks as the outcome (dependent) variable is:

$$GA_{weeks} = (0.470 \times TCD_{mm}) + 13.162$$
$$r = 0.89, r^2 = 0.79, P < 0.001$$

with a residual variance (s^2) of 1.39 (s = 1.178). The 95% CI (of predicted values) give a predicted GA to ± 2.33 weeks for a given TCD. Figure 2 shows percentile charts for TCD by GA from 23 to 32[+6] weeks GA.

The mean of the difference between two measurements by a single observer (intraobserver) was 0.05 mm, with a SD of 1.06 mm. The intraclass correlation coefficient was 0.98.

The mean of the difference between measurements by two observers (interobserver) was 0.01 mm, with a SD of 0.63 mm. The intraclass correlation coefficient was 0.99.
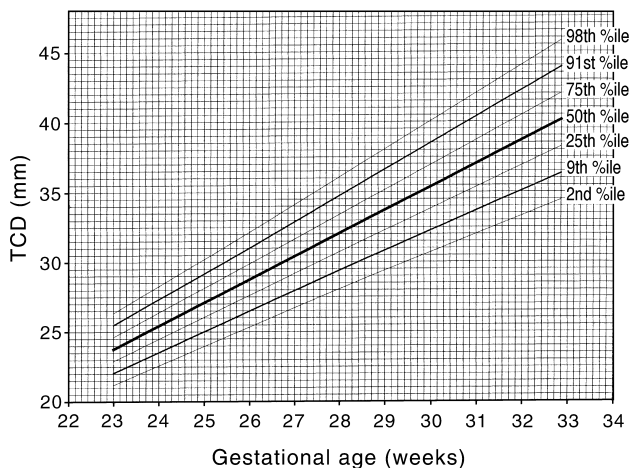

Fig. 2. Percentile charts for transverse cerebellar diameter (TCD) by gestational age from 23 to 32 weeks and 6 days (32[+6]).

DISCUSSION

Fetal studies have demonstrated the close relationship between the TCD and GA[1,9–11] with linear growth of the TCD during the second trimester. Data from the previous study confirmed that the TCD increases with GA in a linear fashion from 23 to 32[+6] weeks gestation when measurements are taken in the newborn infant.[4] In the present study we have shown that the TCD increases linearly from 23 to 32[+6] weeks and correlates closely with GA. The relationship between TCD and GA is not improved by refinement of GA estimation to the nearest day.

The measurement of TCD in the fetus continues to be a useful indicator for GA even in the presence of abnormal skull shapes,[1,12] fetal growth restriction,[3,13] multiple pregnancies[10,14] and large-for-dates fetuses.[11] Therefore, the TCD measurement of the fetus is resistant to these effects on other fetal measurements. Extrapolation to the newborn infant in the first few days of life is reasonable given the consistency of the TCD and GA correlation between fetal and neonatal studies.[4]

The present study predicts GA to within (95% CI) ± 2.33 weeks (16.3 days). In a recent study assessing the overall accuracy of assessing postnatal GA, Wariyar *et al.*[15] demonstrated that for infants < 32 weeks the most accurate clinical measure of GA in the newborn infant was the New Ballard Score (NBS).[16] The NBS overestimated the GA by 3 days with 95% CI of ± 2.57 weeks (24 days). This is similar to the original study by Ballard *et al.*,[16] which predicted GA (95% CI) to within ± 2.86 weeks (20 days) for infants from 20 to 44 weeks GA, and ± 3.10 weeks (22 days) for infants < 26 weeks. Others have also demonstrated the inaccuracy of the NBS in infants younger than 28 weeks GA.[17] Prediction of GA by postnatal ultrasound measurement of femur length (based on antenatal femur length data) has been shown to underestimate GA by approximately 1 week to within (95% CI) approximately ± 2.35 weeks (16.5 days).[18]

The NBS requires handling that an extremely preterm infant may not tolerate or may not be possible due to attached catheters, etc. It cannot be used if the infant is sedated or paralysed, and some physical characteristics cannot be assessed if there is generalized oedema. Postnatal ultrasound measurement of femur length requires extra handling, and may be inaccurate if there has been intrauterine growth restriction affecting long bone growth. Head ultrasounds are routinely performed in the first 3 days of life in preterm infants, even if critically ill, therefore measurement of the TCD can be done without extra handling.

No previous study in fetuses or neonates has examined the intra- or interobserver reliability of ultrasound measurement of TCD. We have shown that postnatal measurement of the TCD is readily reproducible with minimal intra- and interobserver differences. The intraclass correlation coefficient, which not only takes into account the difference between observations but also the variability between subjects,[7] is excellent for either one

or two different observers. The axial resolution of the ultrasound probe is approximately 0.2 mm, which is greater than the degree of difference seen within and between observers.

If the GA is known, then the TCD measurement can then be used as a tool to assist in the diagnosis of cerebellar hypoplasia and abnormalities of cerebellar growth (as a consequence of malformation, haemorrhage or ischaemic infarctions).[1,19,20] The percentile charts may also assist in monitoring cerebellar growth which can be abnormal after ischaemia and, possibly, phenobarb treatment.[21,22]

CONCLUSION

There is a close relationship between TCD and GA, with TCD increasing linearly from 23 to 32[+6] weeks. However, the relationship is not improved with a larger sample size and estimation of GA to the nearest day. The prediction of GA by measuring the TCD on neonatal cranial ultrasound scans is possible to ± 2.33 weeks. This degree of error is superior to any clinical assessment of GA in newborn infants. Measurement of the TCD on neonatal cranial ultrasound scans has excellent intra- and interobserver reliability.

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