Continuous wave Doppler ultrasound in evaluation of cerebral blood flow in neonates

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SUMMARY The cerebral circulation of 25 normal term infants was investigated using continuous wave Doppler ultrasound. Serial blood flow velocity signals were obtained from the common carotid and anterior cerebral arteries during the first week of life. The records were processed using a frequency spectrum analyser to provide cerebral blood velocity waveforms. The pulsatility index (PI), A/B ratio, and rise and fall slope of the waveforms were calculated. The results indicated that cerebrovascular resistance was raised appreciably on day 1 of life compared with later in the first week. In 18 of 25 infants (72%) there was no continuous carotid blood flow in the first hours of life. We suggest that the human cerebral circulation adapts to the process of birth in a similar fashion to that of animal models.

Intracranial haemorrhage and ischaemic hypoxic encephalopathy are major causes of mortality and morbidity in the newborn infant. The pathogenesis of these disorders is not, however, clearly understood and there is little information concerning cerebral blood flow.¹ Much of the data on cerebral circulation has been inferred from animal experiments,^{2,3} or has been obtained by venous occlusion plethysmography⁴ or by the use of isotopes.⁵ More recently Bada *et al.*⁶ used Doppler ultrasound to study the pulsatile flow in the anterior cerebral arteries of the newborn infant and this technique has since been employed to assess infants with hydrocephalus⁷ and patent ductus arteriosus.^{8,9} The pattern of cerebral blood flow in normal or distressed newborn infants has yet, however, to be fully elucidated. We used continuous wave Doppler ultrasound with frequency spectrum analysis to evaluate red blood cell velocity in the cerebral circulation of healthy newborn infants during the first week of life.

Patients and methods

Twenty five normal term infants with a mean birth-weight of 3380 g (range 2750-4420 g) and a mean gestational age of 40.0 weeks (range 37.6-41.9 weeks) were examined. In all these babies, who presented vertex and were delivered without assistance, labour started spontaneously and was not accelerated. The infants were studied twice on the first day of life and the first examination was within

6 hours of birth. Further assessments took place on days 2, 3, and 5. The examinations were carried out by the same person (P G) at least 1 hour after a feed apart from those performed on day 1. The following technique was used: the tip of a pencil probe of a bidirectional Doppler instrument (Medasonics Versatone D-9) operating at a frequency of 5 MHz was placed on the skin over each common carotid artery at the base of the neck using a water based gel as a coupling medium. The Doppler signals were monitored through headphones and the probe was manipulated to obtain the best quality signals which were then recorded on magnetic tape. The probe was then placed in a similar fashion over the anterior cerebral arteries as they course along the longitudinal fissure.

Audiofrequency analysis of the Doppler signals was performed with a frequency spectrum analyser (Medishields, Spectrascribe Mk II) that can provide sonagrams on light sensitive paper (Kodak-Linagraph, direct print paper). Chart recorder speed used in all recordings was 100 mm/s, and by measuring the distance between the waveforms the heart rate was calculated.

Sonagram

The velocities of red blood cells in an artery vary across its lumen and hence a wide spread of Doppler shifted frequencies is back scattered from these cells. The Doppler signals received thus contain a spectrum

of frequencies corresponding to the different velocities of blood cells within an artery. The sonogram displays this spectrum of frequencies on the Y axis with time on the X axis. The blackness of different parts on the sonogram reflects the number of cells at that particular velocity at that time. The outline of the sonogram represents the maximum velocity throughout the cardiac cycle and the shape of the waveform reflects the pulsatile nature of blood flow.

In adults the shape of the sonogram is characteristic of the arterial site. Thus sonograms of the peripheral arteries in the lower limbs where resistance to flow is high manifest a triphasic pattern with reverse flow in early diastole, whereas those of the carotid arteries that supply low resistance circulations exhibit forward flow throughout the cardiac cycle.¹⁰

In newborn infants sonograms of the common carotid artery (Fig. 1) are similar to those in adults and show 2 systolic peaks with continuous blood flow during diastole. The peaks in systole have been signified as A and B by Baskett *et al.*¹¹ Planiol and Pourcelot¹² referred to the systolic amplitude of the

Fig. 1 Sonogram recorded from the common carotid artery displaying frequency (velocity) on the Y axis and time on the X axis.

The maximum blood velocity waveform shows the parameters that were measured; AS, B, and D were measured as the height above the baseline. The tan of angles α and β were calculated to estimate the rise and fall slopes.

Fig. 2 Typical sonogram recorded from the anterior cerebral artery with the maximum blood velocity waveform.

waveform as S and the end diastolic amplitude D. The systolic amplitude S is thus equivalent to the peak height A of Baskett *et al.* In contrast, the sonogram of the anterior cerebral artery (Fig. 2) has a waveform with just 1 systolic peak.

In this study the waveforms were analysed by measuring the following parameters.

(1) The pulsatility index (PI) defined as the difference between the systolic and diastolic amplitudes divided by the systolic amplitude $(S-D)/S$.¹² This is an index of resistance to blood flow with a high value representing a high cerebrovascular resistance.

Fig. 3 Pulsatility index (PI) (mean (SD)) of the common carotid arteries on days 1, 2, 3, and 5.

PI day 1 (examinations (a) and (b)) v days 2, 3, and 5, $P < 0.001$.

PI day 1 examination (a) v day 1 examination (b), $P < 0.001$.

(2) The A/B ratio, namely the ratio of the primary peak in systole (A) to the secondary peak (B) in the waveform of the common carotid artery.¹¹ This has been found to correlate with health and disease in adults.

(3) The rise and fall slopes estimated by calculating the tan of the angle of the rise (α) and the fall (β) of the waveform.^{13,14} The rise slope depends on cardiac contractility, the density of the blood, and the elasticity of the vessel wall whereas the fall slope reflects the cerebrovascular resistance.

Results

The 25 infants were examined on a total of 112 occasions. Eleven infants had only 1 study performed on day 1 while 1 baby left hospital before the day 5 examination. Two hundred and twenty six common carotid arteries and a similar number of anterior cerebral arteries were insonated. Satisfactory Doppler signals were obtained from all but 12 observations when excessive movements prevented adequate recordings. Waveforms of the left and right sides did not differ appreciably so the data obtained each day from the 2 sides were analysed together.

Fig. 3 shows the PI (mean (SD)) from the common carotid arteries on each day they were studied. The PI of both examinations on day 1 was significantly higher ($P<0.001$) than on day 2 and subsequent days. Furthermore the PI of the first examination on day 1(a) was significantly higher ($P<0.001$) than that of the second examination 1(b). In 18 of the 25 babies the cerebrovascular resistance was so high on the first examination on day 1 that continuous blood flow did not occur throughout diastole (Fig. 4). On the second examination, however, 2 infants only showed this type of waveform.

The PI (mean (SD)) from the anterior cerebral arteries (Fig. 5) was also significantly higher in both

Fig. 4 Typical sonagram from the common carotid artery on day 1. There is absence of continuous blood flow during diastole.

Fig. 5 Pulsatility index (mean (SD)) of the anterior cerebral arteries on days 1, 2, 3, and 5.

Day 1(a) v days 2, 3, and 5, $P<0.001$.

Day 1(b) v days 2, 3, and 5, $P<0.05$.

Day 1(a) v day 1(b), $P<0.01$.

examinations on day 1 compared with subsequent days (day 1(a) v days 2, 3, and 5 $P<0.001$; day 1(b) v days 2, 3, and 5 $P<0.05$). The PI of day 1(a) was significantly higher ($P<0.01$) than that of day 1(b).

Calculation of the A/B ratio of the common carotid artery showed a progressive fall in the value from day 1 to day 5 (Fig. 6) but there was only a significant difference ($P<0.01$) between the values on day 1 and day 5.

The rise slope of the common carotid arteries varied widely (Table). The mean on the day 1(a) examination was significantly higher ($P<0.01$) than

Fig. 6 Ratio of the primary peak in systole (A) to the secondary peak (B) in the waveform of the common carotid artery (mean (SD)) on days 1, 2, 3, and 5.

Day 1(a) and (b) v day 5, $P<0.01$.

Table Rise slope common carotid arteries

Day	No	Mean	(SD)
1(a)	50	25.5	(11.7)
1(b)	26	21.6	(7.5)
2	50	19.1	(8.3)
3	49	19.4	(6.5)
5	42	23.0	(12.0)

Day 1(a) v days 2 and 3, $P < 0.01$.

that on days 2 and 3. There was no significant day to day variation in the rise slope of the anterior cerebral artery or the fall slope of either the common carotid or anterior cerebral arteries. The mean heart rate calculated from the sonagrams of the common carotid arteries was 130/m on the day 1(a) examination, 113/m on day 1(b), 116/m on day 2, and 112/m on day 3. On day 5 some babies were more active during the examinations and the mean heart rate was 124/m.

Discussion

Doppler ultrasound has been used extensively in adults in the investigation of cerebrovascular disorders. In neonates the Doppler technique has been recently used to evaluate cerebral blood flow but there is controversy over its value in the determination of cerebral haemodynamics.^{15 16}

To date, neonatal studies using Doppler ultrasound in the determination of cerebral blood flow velocity have used zero cross detection in the processing of the Doppler shift signals. This simple system gives a trace of the average Doppler frequency but has several limitations that may produce unreliable results. Waveforms produced by zero cross detection may contain important errors or artefacts in up to 85% of instances.¹⁷ This problem may be overcome by the use of frequency spectral analysis to process the Doppler signals, as this technique meets all the requirements necessary for the analysis of peak velocity waveforms.¹⁸ In this study blood velocity waveforms from the common carotid and anterior cerebral arteries were investigated using continuous wave Doppler ultrasound with spectrum analysis, thus eliminating the inherent disadvantages of the zero cross frequency meter used by previous investigators.

Using continuous wave Doppler ultrasound it is not possible to calculate absolute values of red cell velocities without knowing the angle of the transducer to the insonated vessel. The values obtained from the PI, A/B ratio, and the rise and fall slopes of the waveform are independent of the incident angle, however, so these methods of evaluating red cell velocity may be used for serial determinations.

Hence information on cerebrovascular haemodynamics that cannot be calculated from volume flow determinations may be obtained.

The shape of the blood velocity waveform is a function of the forward compression wave caused by cardiac systole and the reflected waves from peripheral arterioles. After cardiac contraction a pressure gradient is created and forward blood flow occurs. This is opposed by the peripheral resistance with the result that blood velocity decreases. In the femoral artery where resistance is high, forward blood flow briefly ceases so that a period of reverse flow occurs during the cardiac cycle. The cerebral, renal, and fetoplacental circulations are of low resistance and forward flow continues throughout the cardiac cycle with the waveform remaining raised above the baseline. Examination of the blood velocity waveform can therefore be used to assess arterial haemodynamics. In the present investigation both the PI and the fall slope of the waveforms of the common carotid and anterior cerebral arteries were used to evaluate cerebrovascular resistance. The A/B ratio was used, in addition, to assess the resistance in the common carotid arteries.

The results of our investigation showed that the cerebrovascular resistance as reflected by the PI of both the common carotid and anterior cerebral arteries was appreciably higher on day 1 compared with subsequent days. Lucas *et al.*² showed that in lambs, clamping of the umbilical cord after birth resulted in a 30% decrease in carotid blood flow related to a marked increase in carotid vascular resistance. This alteration in vascular resistance has been ascribed to the sudden changes in blood gas tensions (principally the fall in P_{CO_2}) that follow the initiation of respiration and subsequent lung expansion.^{2 3} Our study suggests that the human cerebral circulation adapts to the process of birth in a similar fashion to animal models.

Doppler ultrasound studies on preterm babies have noted a sharp decrease in diastolic flow velocity in those with patent ductus arteriosus.^{8 9} It could be postulated that the high PI noted in our infants on day 1 was not caused by a raised cerebrovascular resistance but by a patent ductus arteriosus leading to abnormal haemodynamics. Gentile *et al.*¹⁹, however, using pulsed Doppler echocardiography, found the ductus arteriosus to be closed in 8% of newborn infants on day 1, in 50% on day 2, and in 100% by day 5. While we noted an appreciable drop in PI between days 1 and 2, the fact that no further change occurred by day 5 suggests that this alteration was not related to closure of the ductus arteriosus.

The cerebral circulation has been considered to be one of low resistance with blood flow present throughout diastole except in severe pathological

states. The striking feature of the present study, however, was the absence of continuous diastolic flow in the common carotid arteries in most infants studied during the first few hours of life. The importance of this finding will become evident when neonates in whom raised cerebrovascular resistance is expected are investigated. If these infants do not have continuous carotid blood flow on day 1, we will know that this is not a pathological feature.

Values of the A/B ratio of the common carotid artery showed a progressive decline from day 1 to day 5 but no abrupt change from day 1 to day 2 occurred as was seen for the PI. The fall slope of the waveform showed no notable day to day variation. These findings suggest that these methods of analysis are less sensitive indicators of cerebrovascular resistance in the neonate than the PI.

The rise slope of the waveform of the anterior cerebral arteries showed no appreciable change from day to day, whereas that of the common carotid artery was higher on day 1 compared with days 2 and 3. The rise slope is primarily a function of cardiac contractility, though it is also influenced by the density of the blood and the elasticity of the vessel wall. Because of important structural and functional differences between the fetal and adult myocardium, the fetus has a very limited ability to increase stroke volume, and cardiac output is almost completely dependent on heart rate. Despite the lack of experimentation on the human neonate it is assumed that the infant myocardium behaves like that of the fetus and thus the considerable variability in the heart rate of the newborn infant will be reflected as variability in cardiac contractility and the rise slope of the waveform. In the case of the carotid arteries the rise angle of the waveform was in general above 85°. Accordingly even a small variation in the angle will result in large change in the slope (the tan of the angle). Thus the change encountered in the rise slope of the waveform was likely to be caused by variation in the neonatal heart rate, as was seen when this was calculated from the sonagrams.

We have shown that Doppler ultrasound with spectrum analysis is a non-invasive and safe technique that may be used successfully in the evaluation of cerebral blood flow in the neonate. Its application may be useful in assessment of neonatal, pathological cerebral states. For term infants with birth asphyxia it is hoped that monitoring changes in cerebrovascular resistance will prove useful in the evaluation of the efficacy of ventilation and drugs. Studies of cerebral blood flow in preterm infants may contribute to our knowledge of the pathogenesis of intraventricular haemorrhage.

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References

- Volpe JJ. Cerebral blood flow in the newborn infant: relation to hypoxic-ischaemic brain injury and periventricular hemorrhage. *J Pediatr* 1979;**94**:170-3.
- Lucas W, Kirschbaum T, Assali NS. Cephalic circulation and oxygen consumption before and after birth. *Am J Physiol* 1966;**210**:287-92.
- Barker JN. Fetal and neonatal cerebral blood flow. *Am J Physiol* 1966;**210**:897-902.
- Cooke RWI, Rolfe P, Howat P. A technique for the non-invasive estimation of cerebral blood flow in the newborn infant. *J Med Eng Technol* 1977;**1**:263-6.
- Lou HC, Lassen NA, Friis-Hansen B. Impaired autoregulation of cerebral blood flow in the distressed newborn infant. *J Pediatr* 1979;**94**:118-21.
- Bada HS, Hajjar W, Chua C, Sumner DS. Noninvasive diagnosis of neonatal asphyxia and intraventricular hemorrhage by Doppler ultrasound. *J Pediatr* 1979;**95**:775-9.
- Hill A, Volpe JJ. Decrease in pulsatile flow in the anterior cerebral arteries in infantile hydrocephalus. *Pediatrics* 1982;**69**:4-7.
- Perlman JM, Hill A, Volpe JJ. The effect of patent ductus arteriosus on flow velocity in the anterior cerebral arteries: ductal steal in the premature newborn infant. *J Pediatr* 1981;**99**:767-71.
- Lipman B, Serwer GA, Brazy JE. Abnormal cerebral hemodynamics in preterm infants with patent ductus arteriosus. *Pediatrics* 1982;**69**:778-81.
- Nimura Y, Matsuo H, Hayashi T, et al. Studies on arterial flow patterns—instantaneous velocity spectrums and their phasic changes with directional ultrasonic Doppler technique. *Br Heart J* 1974;**36**:899-907.
- Baskett JJ, Beasley MG, Murphy GJ, Hymans DE, Gosling RG. Screening for carotid junction disease by spectral analysis of Doppler signals. *Cardiovasc Res* 1977;**11**:147-55.
- Planiol T, Pourcelot L. Doppler effect study on the carotid circulation. In: de Vlieger M, White DN, McCready VR, eds. *Ultrasonics in medicine*. New York: Elsevier, 1973:104-11.
- Fitzgerald DE. Doppler ultrasound arterial scanning. In: Verstraete M, ed. *Methods in angiology*. The Hague: Martinus Nijhoff, 1980:103-5.
- Fitzgerald DE. Carotid blood volume and velocity analysis in normal and diseased subjects. In: Black MM, Von Noort R, eds. *Proceedings of a workshop on the clinical and analytical evaluation of Doppler ultrasound blood flow measurements*. Sheffield:EEC Committee on Medical and Public Research, 1982:149-71.
- Bejar R, Merritt TA, Coen RW, Manning F, Gluck L. Pulsatility index, patent ductus arteriosus, and brain damage. *Pediatrics* 1982;**69**:818-22.
- Volpe JJ, Perlman JM, Hill A, McMenamin JB. Cerebral blood velocity in the human newborn: the value of its determination. *Pediatrics* 1982;**70**:147-52.
- Johnston KW, Maruzzo BC, Cobbold RSC. Errors and artifacts of Doppler flowmeters and their solution. *Arch Surg* 1977;**112**:1335-42.
- Coughlan BA, Taylor MG, King DH. On line display of Doppler shift spectra by a new time compression analyser. In: Reneman S, ed. *Cardiovascular applications of ultrasound*. Amsterdam: North Holland Publishing Co, 1974:55-65.
- Gentile R, Stevenson G, Dooley T, Franklin D, Kawabori I, Pearlman A. Pulsed Doppler echocardiographic determination of time of ductal closure in normal newborn infants. *J Pediatr* 1981;**98**:443-8.

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