Renal artery blood flow velocity in very low birthweight infants with intrauterine growth retardation

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Abstract
Doppler ultrasound was used to measure left renal artery blood flow velocity and pulsatility index on the first, third, and seventh day of postnatal life in 18 very low birthweight small for gestational age (SGA) infants. The values were compared with those from 18 weight matched and 18 gestation matched controls. SGA infants had significantly lower blood flow velocity than their gestation matched controls throughout the first postnatal week (day 1: SGA 10 cm/s, controls 15 cm/s; day 7: SGA 17 cm/s, controls 28 cm/s). These data suggest that abnormalities of renal artery blood flow velocity persist after delivery in the SGA infant.

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Doppler ultrasound studies have demonstrated that in hypoxaemic small for gestational age (SGA) fetuses there is an increased pulsatility index, indicating an increased impedance to flow in the fetal descending thoracic aorta and renal arteries,[1] with a decreased pulsatility index in the middle cerebral artery. In such fetuses blood flow velocity is decreased in the aorta and increased in the middle cerebral artery.[2-4] It has been suggested that these findings are the consequence of a chemo-receptor mediated redistribution in the fetal circulation in favour of the brain and at the expense of the viscera. Postnatal Doppler studies have documented reduced blood flow velocity in the superior mesenteric artery and the coeliac axis of SGA infants,[5] suggesting that cardiovascular abnormalities that have been induced by fetal hypoxaemia may persist into postnatal life even when the infant is no longer hypoxaemic.

The aim of the present study was to determine whether similar abnormalities of renal artery blood flow velocity are present in SGA infants.

Patients and methods
Doppler ultrasound measurements of left renal artery blood flow velocity and pulsatility index were obtained on the first, third, and seventh postnatal days from 18 SGA infants with birth weights below 1500 g; in all cases the birth weights were below the 3rd centile for gestation. For each SGA infant, one gestation matched and one weight matched control was selected from a group of 100 appropriately

grown infants who had postnatal Doppler measurements performed. Serum creatinine values were available for index cases and controls.

Doppler ultrasound measurements were performed using a duplex ultrasound imaging and Doppler system (Sonos 100, Hewlett Packard). The aorta and left kidney were visualised in real time, and the precise location of the origin of the left renal artery was determined using Doppler ultrasound as the point of the maximum arterial Doppler signal. The longitudinal axis of the artery was then inferred as a line joining this point to the renal pelvis, so that the angle of insonation could be measured. A 3 mm range gate was used to sample signals arising from the renal artery only, and a 100 Hz filter excluded those signals arising from vessel wall movement. The time averaged mean of the peak velocity envelope (corrected for angle of insonation) and the pulsatility index of Gosling and King were measured from the flow velocity waveform.[6]

Student's unpaired *t* test was used to analyse the data. The pulsatility index data were significantly skewed and were analysed using log transformed data.

Results
The major characteristics of the three groups of infants are shown in the table. On the first day of postnatal life, the mean renal artery blood flow velocity of the SGA infants (10 cm/s) was significantly lower than in their gestation matched controls (15 cm/s, $t=2.4$, $p<0.05$; fig 1).
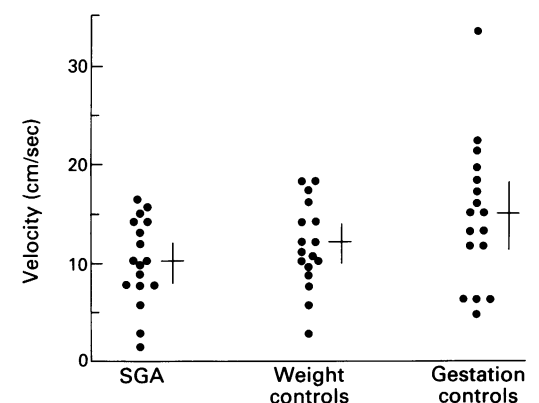

Figure 1   First day renal artery blood flow velocity measurements from SGA infants and their weight matched and gestation matched controls. Means and 95% confidence intervals are shown.

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Characteristics of the three groups. Arterial oxygen tension and blood pressure in the SGA infants were not significantly different from the controls

		Controls matched for:	
	SGA (n=18)	Weight (n=18)	Gestation (n=18)
Median (range) birth weight (g)	978 (608–1380)	917 (552–1404)	1590 (966–2468)
Median (range) gestation (weeks)	31 (28–34)	26 (23–29)	30 (26–34)
No of survivors	15	13	18
No with patent ductus arteriosus	5	5	5
No with acute renal failure	1	3	1
Characteristics at the time of measurement Day 1 (n=18)			
Mean (SD) arterial oxygen tension (kPa)	8·6 (2·1)	9·3 (1·8)	9·3 (2·4)
Mean (SD) arterial blood pressure (mm Hg)	35·4 (6·9)	34·1 (8·1)	39·6 (8·1)
No receiving inotropic support	2	3	0
No receiving artificial ventilation	10	18	15
No with umbilical arterial catheter	8	18	15
Day 3 (n=11)			
No receiving inotropic support	0	2	0
No receiving artificial ventilation	6	11	4
No with umbilical arterial catheter	8	18	15
Day 7 (n=8)			
No receiving inotropic support	0	2	0
No receiving artificial ventilation	1	5	2
No with umbilical arterial catheter	4	5	1

During the first week, the difference in renal artery blood flow velocity between the SGA infants and their gestation matched controls became more marked (fig 2; day 7; SGA 17 cm/s, gestation matched controls 28 cm/s, p<0·001).

Although mean blood flow velocity was lower in the SGA infants than in their weight matched controls on all three occasions, at no time was the difference statistically significant. There were no statistically significant differences in pulsatility index or in serum urea or creatinine concentrations between the three groups (fig 3). The fall in serum creatinine during the study period was less in the SGA infants (from 92 to 80 μmol/l) than in their gestation matched controls (from 100 to 62 μmol/l), but this difference was not statistically significant.

Discussion

In SGA infants, the renal artery blood flow velocity is lower than in appropriately grown infants of equivalent gestation. These findings cannot be explained by other clinical differences between the two groups, such as blood pressure, blood gases, or incidence of patent ductus arteriosus.

The most likely explanation for the reduced renal blood flow velocity in the SGA infants is reduced blood flow to the kidney. Although volume flow is dependent on both blood flow velocity and vessel diameter, the latter was too small to allow accurate measurement by ultrasound. It is unlikely, however, that the renal arteries of the SGA infants had a larger diameter than those of their controls. Indeed, all measurable cardiovascular structures, including the aorta and umbilical arteries, are smaller in SGA infants.[7]

Reduction in renal blood flow may be the result of increased renal vascular resistance. There were no significant differences in pulsatility index, however, between the SGA infants and their gestation matched controls. An alternative explanation is that the renal mass of the SGA infants was smaller, which would account for reduced blood flow with apparently normal vascular resistance. Blood flow per unit renal mass might then be similar in the SGA and the appropriately grown infants.

Glomerular filtration rate and sodium clearance have been shown to rise with an increased protein intake,[8] possibly driven by an increase in the nitrogenous excretory load on the kidneys. As there were no significant differences in serum urea between our study groups, it is unlikely that this mechanism could explain the differences we observed.

Serum creatinine concentrations in the SGA infants were not significantly raised, and SGA infants were not more likely to develop acute renal failure. If renal blood flow was reduced as the result of postglomerular vasoconstriction, however, there may have been only minor changes in glomerular filtration rate as increased glomerular capillary pressure would have resulted in an increased filtration fraction. Such changes have been observed as an angiotensin mediated effect in congestive cardiac failure in animals.[9]

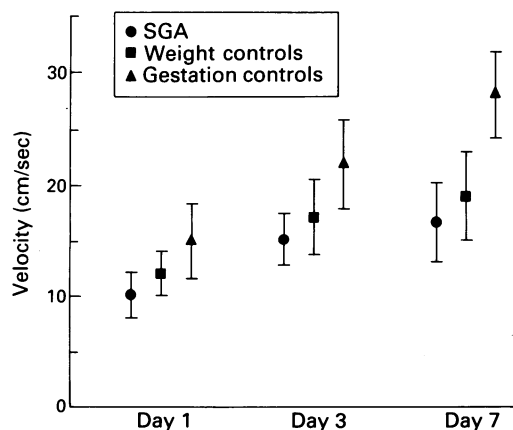Epidemiological studies have suggested an association between low birth weight and

Figure 2 Changes in renal artery blood flow velocity during the first week of life for SGA infants and their weight matched and gestation matched controls. Means and 95% confidence intervals are shown.
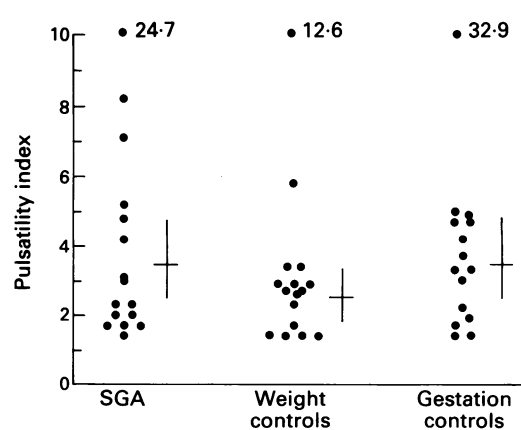

Figure 3 First day renal artery pulsatility index measurements from SGA infants and their weight matched and gestation matched controls. Geometric means and 95% confidence intervals are shown.

hypertension in later life.[10] Our findings suggest that in fetal growth retardation there is impaired renal perfusion that persists during the neonatal period, even after the hypoxia, which may have caused this impairment, has been relieved. It is possible that impaired perfusion of the kidneys during a critical stage of development may lead to impaired renal growth and a permanent readjustment of the mechanisms that control blood pressure.

1 Skidmore R, Woodcock JP, Wells PNT, Bird D, Baird RN. Physiological interpretation of Doppler shift waveforms – III. *Ultrasound Med Biol* 1980; **6:** 227–31.

2 Bilardo CM, Nicolaides KH, Campbell S. Doppler measurements of the fetal and uteroplacental circulations: relationship with umbilical venous blood gases measured at cordocentesis. *Am J Obstet Gynecol* 1990; **162:** 115–20.

3 Vyas S, Nicolaides KH, Campbell S. Renal artery flow velocity waveforms in normal and hypoxic fetuses. *Am J Obstet Gynecol* 1989; **161:** 168–72.

4 Vyas S, Nicolaides KH, Bower S, Campbell S. Middle cerebral artery flow velocity waveforms in fetal hypoxaemia. *Br J Obstet Gynaecol* 1990; **97:** 797–803.

5 Kempley ST, Gamsu HR, Vyas S, Nicolaides KH. Effects of intrauterine growth retardation on postnatal visceral and cerebral blood flow velocity. *Arch Dis Child* 1991; **66:** 1115–8.

6 Gosling RG, King DH. Arterial assessment by Doppler-shift ultrasound. *Proc R Soc Med* 1974; **67(b):** 447.

7 Meyer RA, Siddiqi TA, Korfhagen JC, Khoury J, Mimouni F, Miodovnik M. The effect of intrauterine growth retardation on fetal cardiac size and function [Abstract]. *Pediatr Res* 1990; **27:** 236A.

8 Herin P, Zetterstrom R. Studies in the renal response to various protein intakes in preterm infants. *Acta Paediatr Scand* 1987; **76:** 447–52.

9 Ichikawa I, Pfeffer JM, Pfeffer MA, Hostetter TH, Brenner BM. Role of angiotensin II in the altered renal function of congestive cardiac failure. *Circ Res* 1984; **55:** 669–75.

10 Law CM, Barker DJP, Bull AR, Osmond C. Maternal and fetal influences on blood pressure. *Arch Dis Child* 1991; **66:** 291–5.