

Blood Pressure Values in Children with Intrauterine Growth Retardation

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Abstract

Background: Low birth weight has been shown to be strongly related to hypertension in adult life.

Objectives: To determine whether blood pressure is higher in children with intrauterine growth retardation than in control subjects.

Methods: Blood pressure was measured in 58 children aged 4–6 years with IUGR and in 58 age-matched controls. The control children, whose birth weight was appropriate for gestational age, were also matched for gestational age.

Results: The children with IUGR had significantly higher mean values of systolic ($P < 0.05$) and diastolic blood pressures ($P < 0.05$) and mean arterial pressure ($P < 0.05$). Significant differences in blood pressure values were found between preterm IUGR ($n = 21$) and preterm controls ($P < 0.05$).

Conclusions: These data indicate that children with IUGR may be at higher risk of hypertension already in childhood.

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High blood pressure is a recognized risk factor for ischemic heart disease and stroke. According to recent studies, one important determinant of hypertension in adult life is poor growth *in utero*. Epidemiological data indicate that hypertension is more common in adults who were smaller than normal at birth [1–3], and that adult systolic blood pressure is inversely related to birth weight [1,3,4]. Most theories explaining the biological mechanisms that underlie the association between birth weight and blood pressure focus on the long-term structural consequences of the *in utero* environment, such as reduced number of nephrons [5,6], altered arterial compliance [7] and fetal exposure to glucocorticoid excess [8]. This has been supported by a series of animal and human studies [9,10]

that have shown an association between intrauterine growth retardation and reduced nephron number, which may be a predisposing factor for hypertension [11].

A negative relationship between birth weight and higher blood pressure has been reported also in children [3,4,12–14] and adolescents [15]. However, none of the studies conducted so far has been directed at children with IUGR. The present study was undertaken to determine whether young children with a history of IUGR are already at risk of hypertension.

Materials and Methods

Subjects

This investigation is part of a long-term prospective follow-up study designed to determine school-age developmental/cognitive outcome in infants with IUGR [16]. Since September 1989, all infants born at the Serlin Maternity Hospital (now Tel Aviv Sourasky Medical Center) with a birth weight under the 5th percentile for gestational age according to the Israeli percentile curves [17] have been examined annually until age 9 years at the Child Development Center. Children with genetic syndromes, major malformations or congenital infection were excluded. The remaining children had mainly vascular-induced IUGR of a late-onset, asymmetric type.

For the present study, blood pressure values in all children with IUGR aged 4 to 6 years ($n = 58$) were analyzed. Findings were compared with those in 58 gender and age-matched appropriate-for-gestational-age children attending regular public kindergartens and schools. Since 36% ($n = 21$) of the IUGR children were preterm (gestational age < 37 weeks), the control group was matched for gestational age as well. Gestational age was calculated by the last menstrual period.

Methods

Blood pressure was measured as a routine procedure at the Child Development Center. The same nurse, who was trained for that purpose, performed all the measurements in both the IUGR children and the controls. The nurse was unaware of the aim of the study.

A standard clinical sphygmomanometer with appropriate cuff size was used, with the cubital fossa supported at heart level.

IUGR = intrauterine growth retardation

Measurements were performed in a controlled environment, in the seated position, after 5 minutes of rest [18]. Systolic pressure was determined by the onset of the “tapering” Korotkoff sounds, and diastolic pressure was defined as the fifth Korotkoff sound (K5). We performed two consecutive measurements three times with 5 minute intervals between each pair, for a total of six measurements. The average of the six measurements of the systolic and diastolic blood pressure was used in the analysis. Mean arterial pressure was computed as the sum of the diastolic pressure and one-third of the pulse pressure.

Body weight and height were measured in all children. Height for age was determined by the height percentile according to standard growth curves.

Blood pressure was rated as normal, high-normal or high (hypertension) by height percentile, on the basis of the normative tables published in 1996 by the National High Blood Pressure Education Program [18]. “Normal” blood pressure was defined as a systolic and diastolic pressure of less than the 90th percentile for age and gender, “high-normal” blood pressure as a systolic or diastolic pressure greater than or equal to the 90th percentile but less than the 95th, and “hypertension” as an average systolic or diastolic pressure greater than or equal to the 95th percentile for age and gender on at least three separate occasions.

Details on birth weight and gestational age were obtained from hospital charts. A family history (first and second-degree relatives) of hypertension, renal disease and diabetes mellitus was obtained by interview with the parents using a guided questionnaire.

Statistical analysis

Between-group differences in mean systolic and diastolic blood pressures, and mean arterial pressure, as well as age, birth weight, gestational age, body weight, height and height percentile were compared by the unpaired *t*-test. Differences between premature IUGR and controls and between full-term IUGR and controls were also measured by the unpaired *t*-test.

The frequency of children with hypertension and high-normal blood pressure in each group was compared using the chi-square test, as was the frequency of hypertension and renal disease in the family.

Results

Table 1 summarizes the demographic data, perinatal parameters and family history. There were no significant differences between the IUGR and control groups in mean age, male:female ratio, gestational age, and family history of hypertension, renal disease and diabetes mellitus. Mean birth weight was significantly lower in the children with IUGR than in the controls ($P < 0.0001$). This was true for current weight and height ($P < 0.0001$). Mean height percentile was significantly lower in IUGR children (36 ± 0) than in controls (55 ± 31), as was expected ($P < 0.005$). Diastolic, systolic and mean blood

Table 1. Characteristics of IUGR and control groups

	IUGR (n=58)	Controls (n=58)	P
Age (yr)	4.5 ± 0.6	4.7 ± 0.6	NS
Gender (M:F)	23:35	28:30	NS
Neonatal			
Mean birth weight (g)	1,871 ± 422	2,866 ± 634	<0.0001
Mean gestational age (wk)	37.0 ± 2.6	37.6 ± 2.9	NS
Familial			
Hypertension (1st relatives)	5 (9%)	8 (14%)	NS
Hypertension (2nd relatives)	30 (52%)	33 (57%)	NS
Renal disease	5 (9%)	3 (5%)	NS
Diabetes	27 (47%)	24 (41%)	NS

Table 2. Blood pressure and growth parameters in IUGR and control groups

	IUGR (n=58)	Controls (n=58)	P
Blood pressure			
Systolic BP (mmHg)	93.0 ± 14.9	83.9 ± 10.7	<0.05
Diastolic BP (mmHg)	57.9 ± 9.0	52.7 ± 6.7	<0.05
Mean arterial pressure (mmHg)	69.6 ± 10.2	65.1 ± 7.5	<0.05
Growth measurements			
Weight (kg)	15.5 ± 3.1	18.3 ± 3.6	<0.0001
Height (cm)	101.7 ± 9.2	108.3 ± 7.3	<0.0001

Table 3. Blood pressure and growth parameters in preterm IUGR and control groups

	Preterm IUGR (n=21)	Preterm controls (n=20)	P
Neonatal			
Mean gestational age (wk)	34.2 ± 2.1	34.1 ± 1.4	NS
Mean birth weight (g)	1,428 ± 384	2,154 ± 444	<0.0001
Blood pressure			
Systolic BP (mmHg)	95.0 ± 14.7	82.7 ± 7.2	<0.005
Diastolic BP (mmHg)	59.2 ± 9.5	49.7 ± 4.0	<0.0001
Mean arterial pressure (mmHg)	71.1 ± 10.4	60.7 ± 4.1	<0.0001
Growth measurements			
Weight (kg)	15.1 ± 3.0	16.0 ± 2.4	NS
Height (cm)	99.7 ± 12.8	103.1 ± 4.4	NS

pressure values were significantly higher in the IUGR group ($P < 0.05$) [Table 2].

In the IUGR group, 8 children (14%) had hypertension and 7 (12%) had high-normal blood pressure, compared to 2 children (3.4%) and 1 child (1.2%), respectively, in the control group ($P < 0.05$).

To exclude the effect of prematurity we compared the premature IUGR children with premature controls [Table 3], and found that differences in blood pressure values remained significant. We also compared full-term IUGR with full-term controls, and found a significant difference in systolic blood

Table 4. Blood pressure and growth parameters in full-term IUGR and control groups

	Full-term IUGR (n=37)	Full-term controls (n=38)	P
Neonatal			
Mean birth weight (g)	2,123 ± 218	3,240 ± 317	<0.0001
Blood pressure			
Systolic BP (mmHg)	91.9 ± 15.1	84.4 ± 12.2	<0.05
Diastolic BP (mmHg)	57.2 ± 8.7	54.3 ± 7.2	NS
Mean arterial pressure (mmHg)	68.7 ± 10.2	64.3 ± 8.5	<0.05
Growth measurements			
Weight (kg)	15.7 ± 3.0	19.5 ± 3.7	<0.0001
Height (cm)	102.9 ± 6.1	111.1 ± 7.1	<0.0001

pressure and mean arterial pressure values, but not in diastolic blood pressure [Table 4].

Discussion

The results of this study suggest that a significant difference in blood pressure can be detected between children with IUGR and normal children, as early as age 4 years. Differences from controls were noted in mean systolic, mean diastolic and mean arterial pressures. This finding is consistent with previous studies showing that in children, as in adults, blood pressure is inversely related to birth weight [4,12–14,19–23]. However, all these studies were carried out on children whose birth weight was within the normal range (2.7–3.4 kg), whereas we studied a specific group of growth-retarded children.

In the present work, blood pressure values were higher in the IUGR group than in the controls, while their weight, height and body surface area were significantly lower. A direct relationship has been found between weight and height and blood pressure already at age 5 years in children with normal birth weight [24,25]. Therefore, we would expect children with IUGR whose somatic growth is reduced [16] to have lower blood pressure. Our finding that children with IUGR have higher blood pressure provides further evidence that this population is at higher risk of future hypertension.

A large number (36%) of the IUGR children were premature, due to induced early labor to prevent further fetal distress in some of them. In order to study the effect of prematurity on blood pressure in this group of IUGR children, we compared the premature IUGR children to premature controls and found no significant differences in blood pressure values [Table 3]. Comparison of the subgroup of full-term IUGR children with the controls [Table 4] showed a significant difference, which apparently was caused by the lower birth weight. This led to the conclusion that the relationship between low birth weight and high blood pressure is independent of the length of gestation, and is linked to fetal growth restriction rather than to premature birth.

In conclusion, the findings of this study suggest that children

with IUGR are at risk of hypertension, and should be followed routinely, starting in childhood.

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