Ethnic origin and lung function of infants born prematurely

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Abstract

Background – Ethnic origin has an important influence on the lung function of adults and young children but its effect during infancy, particularly following premature delivery, is unclear.

Methods – The results from infants of pure Afro-Caribbean (subjects) and pure Caucasian (controls) descent, all of whom were born prematurely (median gestational age 28 weeks), were compared. Fifty subjects were each retrospectively matched with a control for gestational age, sex, and requirement for neonatal ventilation. Lung function measurements were performed at similar postnatal ages in each pair. The median postnatal ages of the two groups at the time of study was seven and eight months, respectively. Lung function was assessed by measurement of functional residual capacity (FRC) by a helium gas dilution technique and plethysmographic measurement of thoracic gas volume (TGV) and airways resistance (Raw), from which specific conductance (sGaw) was calculated.

Results – No differences were found between the subjects and controls regarding FRC or TGV, but Raw was higher and sGaw lower in the subjects. The mean Raw of the subjects was 50·3 cm $H_2O/l/s$ and of the controls was 44·1 cm $H_2O/l/s$ (95% confidence intervals of the difference 1·5 to 10·9).

Conclusions – Prematurely born infants of Afro-Caribbean origin have more severe lung function abnormalities at approximately 7–8 months of age than those of Caucasian origin. This merits further investigation.

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Ethnic origin appears to have an important effect on lung function in adults[1] and young children.[2] This has been suggested to be due to differences in body configuration, but no significant differences were found between young children of Afro-Caribbean and Caucasian descent when lung volume was related to sitting rather than standing height.[2] The effect of ethnic origin on lung function of infants, particularly those born very prematurely, is, however, unclear. Compliance, minute ventilation, respiratory frequency, and the ratio of the time to reach peak expiratory flow to total expiratory time were similar in healthy black and white infants measured in the neonatal period by Stocks *et al.*[3] That study included 18 matched pairs of prematurely born infants whose mean gestational age was 33 weeks. Yet, when preterm infants (mean gestational age 35 weeks) were measured at follow up, airways resistance was lower in Afro-Caribbean than in European preterm infants.[4] It is thus possible that differences in lung function due to ethnic origin, although not present immediately after birth,[3] may become apparent later in infancy.[4] The influence of ethnic origin on lung function at follow up of infants born very prematurely, however, is not known.

The incidence[5 6] and severity[7] of respiratory distress syndrome varies between neonates of Afro-Caribbean and Caucasian descent, and these differences are likely to affect lung function at follow up. Thus, if the effect of ethnic origin is to be accurately assessed in a prematurely born population, the patients must be matched not only for gestational age and sex, but also for mechanical ventilation requirement as an index of severity for the initial respiratory illness. We have performed such a matching process using data collected during our prospective follow up study of very prematurely born patients (mean gestational age 28 weeks).

Methods

PATIENTS

From our prospective follow up study, into which patients were recruited over a period of three years, 59 infants of pure Afro-Caribbean descent (subjects) were identified who had had lung function measurements during the first year of life. We then attempted to match the subjects from a pool of 86 infants of pure Caucasian descent (controls) for gestational age, sex, and requirement for ventilation. In the event of there being more than one control matching a subject, the control whose duration of ventilatory requirement most closely matched the subject was chosen. In addition, the lung function measurements of the subject and control had to have been made at a similar postnatal age – that is, within one month. It was not possible to find controls for nine subjects, all of whom were born very prematurely at 23–27 weeks of gestation. None of the controls had delivered at 23 weeks gestation, thus one subject born at 23 weeks could only be matched with a 24-week gestation control. Both the prospective follow up and intervention studies were approved by King's College Hospital Ethics Committee and parents gave informed consent.

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Table 1 Patient characteristics

	Afro-Caribbean (n = 50)	Caucasian (n = 50)	p
Males (n)	24	24	NS
Birthweight (g)	1138 (506–1866)	1094 (560–1950)	NS
Gestational age (weeks)	28 (23–35)	28 (24–35)	NS
Received surfactant (n)	10	11	NS
Ventilated (n)	42	42	NS
Duration of ventilation (days)	2·5 (0–63)	4·5 (0–75)	NS
Maximum peak inspiratory pressure (cm H_2O)	20 (0–35)	20·5 (0–31)	NS
Maximum inspired oxygen concentration (%)	50 (0–95)	67 (0–95)	NS
Duration of oxygen dependency (days)	7 (0–370)	12 (0–180)	NS
Parental smoking (n)	12	10	NS
Bronchiolitis (n)	5	4	NS
Symptomatic (n)	29	24	NS

Median (range) values are given where relevant.

STUDY DESIGN

The smoking habits of the parents were determined and recorded as positive if the parents were smoking at the time of the lung function measurements. As part of the prospective follow up study lung function measurements were made at approximately six monthly intervals
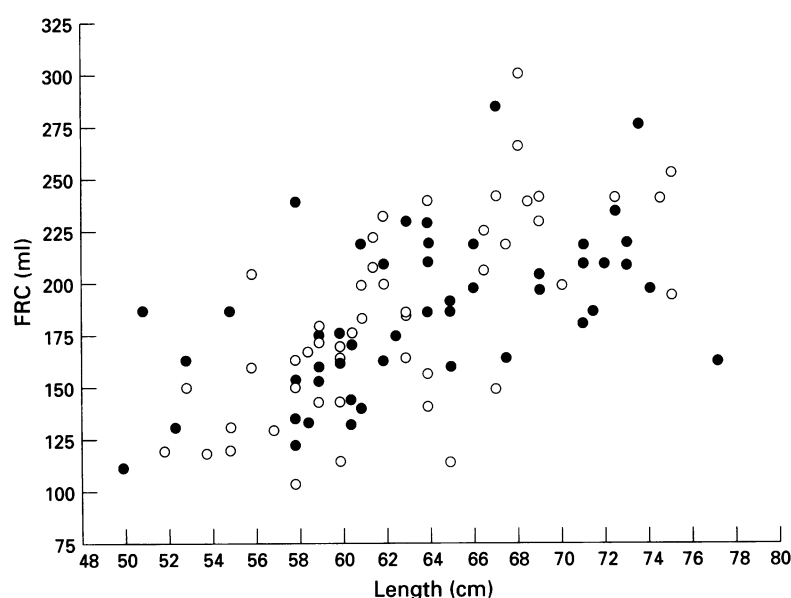

Figure 1 Functional residual capacity (FRC) (ml) versus length (cm). ● = Afro-Caribbean origin; ○ = Caucasian origin. Individual data plotted.
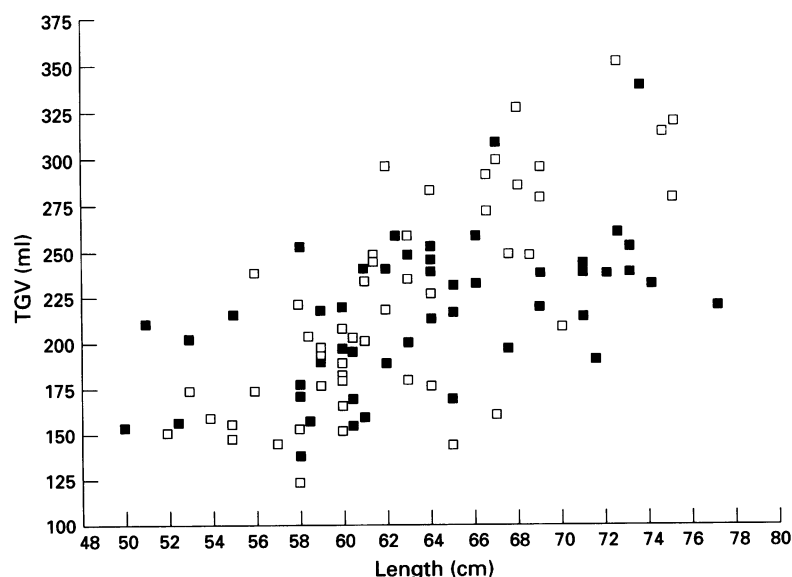

Figure 2 Thoracic gas volume (TGV) (ml) versus length (cm). ■ = Afro-Caribbean origin; □ = Caucasian origin. Individual data plotted.

during infancy. In addition, diary cards were kept by parents of their child's respiratory problems. For the purposes of this study infants were described as symptomatic if they had wheezed and/or coughed on at least three days per week over a four week period, or at least three days following upper respiratory tract infections during the period between discharge from hospital and the first lung function measurements.

LUNG FUNCTION TESTS

Infants were seen in the Paediatric Respiratory Laboratory where a medical history was taken, height and weight measured, and the infant examined. Sedation was achieved with oral chloral hydrate (80–100 mg/kg) and lung mechanics were measured in the supine position during quiet sleep. Thoracic gas volume (TGV) and airways resistance (Raw) was measured with an infant whole body plethysmograph (Hammersmith Hospital, Department of Medical Engineering) and specific conductance (sGaw) was calculated from these measurements. Functional residual capacity (FRC) was measured by a helium gas dilution technique. The details of TGV, Raw, and FRC measurements have been described previously.[8] Some of the individual results have already been reported as part of the prospective follow up[8-10] and intervention[11-14] studies.

STATISTICAL ANALYSIS

The 95% confidence intervals of the difference between the means of the lung function results of the two groups were calculated. Differences in the patient characteristics of the two groups were assessed for statistical significance using the Wilcoxon rank sum or χ^2 test as appropriate. As the distribution of the differences in lung function between pairs was not skewed, differences between individual subject and control pairs were assessed for statistical significance using the paired t test.

Results

Fifty Afro-Caribbean and 50 Caucasian infants were studied. There was no significant difference in the characteristics of the two groups (table 1). Twenty two subjects and 19 controls required supplementary oxygen beyond 28 days and, of these, five subjects and four controls had bronchopulmonary dysplasia.[15] No infant, however, was oxygen dependent at the time of the lung function measurements. There was no significant difference in the number of infants who had bronchiolitis, were symptomatic at follow up, or whose parents smoked (table 1).

There were no significant differences in FRC (fig 1) or TGV (fig 2) between the groups regardless of whether lung volume was related to weight or length (table 2). The Afro-Caribbean infants, however, had higher Raw (fig 3) (p<0·05) and lower sGaw (p<0·05) than the Caucasian infants (table 2).

Table 2   *Lung function results*

	Afro-Caribbean	Caucasian	95% CI of difference between means	p
Postnatal age (months)	8 (2) 6–12	8·3 (2·1) 6–12		NS
Weight at measurement (kg)	6·65 (1·4) 3·7–10·2	6·3 (1·4) 3·6–9·5		NS
Height at measurement (cm)	63·2 (11·8) 50–77	62·4 (11) 52–75		NS
FRC (ml/kg)	28·7 (5) 20·4–40·6	29·3 (4·6) 19·2–40·3	−2·51 to 1·31	NS
TGV (ml/kg)	33·4 (5·3) 24·1–46	35·3 (5·6) 20·8–48	−4·06 to 0·264	NS
Raw (cm H_2O l^{-1} s^{-1})	50·3 (11·7) 31–96	44·1 (12) 22–77	1·50 to 10·9	<0·05
sGaw (cm H_2O^{-1} s^{-1})	0·098 (0·03) 0·054–0·232	0·116 (0·04) 0·056–0·257	−0·033 to −0·003	<0·05

Values are mean (SD) and ranges.

Discussion

Our finding of a significantly higher Raw and lower sGaw in the Afro-Caribbean infants was surprising as, from previous data,[16] we might have predicted the reverse. Severity of the respiratory distress syndrome, as determined by the level of respiratory support, influences Raw and sGaw at follow up.[9] To avoid such a bias we matched the patients for neonatal ventilation requirement. In addition, fortunately there was no significant difference between the maximum peak inspiratory pressure or inspired oxygen concentration of the subjects and controls. It therefore seems unlikely that ethnic variation in the severity of the initial respiratory disease explained our findings. Exogenous surfactant administration affects lung function at follow up.[17] We did not control for the use of surfactant, but fortunately a similar number of infants in the two groups had been exposed to this treatment.

Specific conductance changes with postnatal age,[4] but we do not feel that this explains our results as matched subjects and controls were of similar postnatal age. In addition, the patients were measured at a time when the change in sGaw with respect to age is relatively small.[4]

Very few of our patients had suffered from bronchiolitis, so our results cannot be explained by the well recognised impact of that illness on subsequent lung function.[18] There were no significant differences between the two groups in the number of infants whose parents smoked or who were symptomatic at follow up. There

was, however, a trend regarding both factors which was unfavourable to the Afro-Caribbean infants. Both parental smoking[19] and symptom status[20] are known to affect lung function at follow up, and these two factors may have acted synergistically to produce a higher Raw in our subjects.

No significant differences were found between the groups in lung volume, either assessed by measurement of TGV or FRC. There was a trend for lower volumes in Afro-Caribbean infants, although this did not reach statistical significance even when the results were related to body length.[2] This lack of significance may be due to a type II error, as in older children it has been suggested that most of the racial differences in pulmonary function follow from racial differences in lung size.[21]

Previous differences in Raw between ethnic groups have been ascribed to differences in nasal resistance.[16] In that study, however, only 13 Negro infants and 30 Caucasians were studied, and the two groups were not matched for gestational or postnatal age or requirement for ventilatory support. In addition, the median gestational age (35 weeks) of the population was very much higher than that of the present study. The accurate measurement of nasal resistance may be problematical as large differences between individual neonates,[22] and even between each nasal passage,[23] have been documented. Nevertheless, assessment of nasal resistance in a very immature population would be interesting. If a lower nasal resistance was found in prematurely born patients of Afro-Caribbean descent[16] this would emphasise the difference in airways resistance seen in this study between the two ethnic groups. The aetiology and long term implications of the lung function abnormalities in Afro-Caribbean infants born very prematurely merit further investigation.

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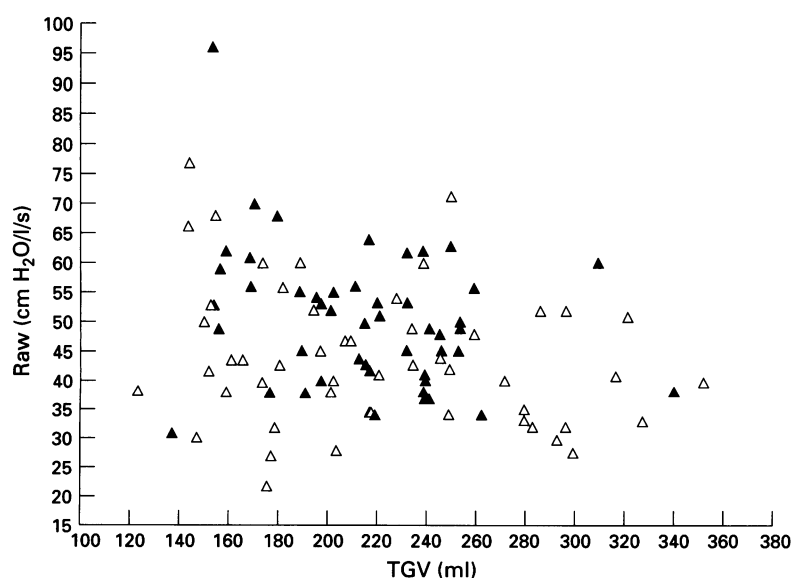6 Collaborative Group on Antenatal Steroid Therapy. Effect of antenatal dexamethasone administration on the pre-

Figure 3   *Airways resistance (Raw) (cm $H_2O/l/s$) versus TGV (ml). ▲ = Afro-Caribbean origin; △ = Caucasian origin. Individual data plotted.*

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