Value of acetylated haemoglobin assay in fetal assessment

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Summary

Acetylation of fetal haemoglobin, probably a post-translational, intracellular, enzyme-mediated reaction, depends upon an adequate supply of glucose and oxygen to the fetus and the nature of the diabetes (if present) in the mother. These complicating factors limit the general usefulness of acetylated fetal haemoglobin assay in fetal assessment.

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Unlike the formation of glycosylated or acetylated[1] haemoglobin in the adult, the formation of acetylated fetal haemoglobin (Hb F_1) appears to be enzyme-mediated.[2,3] It has been suggested that Hb F_1 be used to assess gestational age in newborns from normal mothers,[4] or to assess fetal exposure to glucose during the last weeks of pregnancy.[5]

A Whatman DE52 cellulose column procedure,[2,3,6] which separates acetylated from glycosylated fetal haemoglobin (Hb F_{1a}), was used to investigate factors influencing the formation of Hb F_1 in non-diabetic, gestational diabetic (GD) and established diabetic (ED) pregnant women.

Subjects, methods and results

Maternal and mixed cord blood samples were obtained from 12 non-diabetic, 12 GD and 8 ED mothers and their neonates immediately after delivery.[6] Maternal total glycosylated haemoglobin (Hb A_1) was determined by a microcolumn kit procedure, Hb F_1 by a previously documented gradient elution procedure[2,3,6] and percentage oxygen saturation of cord blood haemoglobin on an IL-co-oximeter (model 282).

There was no significant difference in gestational age at delivery (Dubowitz examination[7]), maternal Hb A_1 at delivery, or cord blood Hb F_1 and percentage O_2 saturation between the three groups of patients[6] (and unpublished data). Birth weight ratio (calculated using charts appropriate for our patient population) was significantly higher ($P < 0,05$; Student's t-test) in our GD patients.[6] Hb F_1 correlated with cord blood percentage O_2 saturation (Fig. 1A) in a combined group of non-diabetic and ED patients. There was no correlation in GD patients ($N = 9$; $r = 0,2$; P = NS). Hb F_1 also correlated with maternal Hb A_1 (Fig. 1B) and this was significant in non-diabetic subjects ($N = 10$; $r = 0,48$; $P < 0,05$; linear regression). There was no correlation between Hb F_1 and major fetal haemoglobin component at term (Hb F_0) or birth weight ratio in any of the patient groups studied.

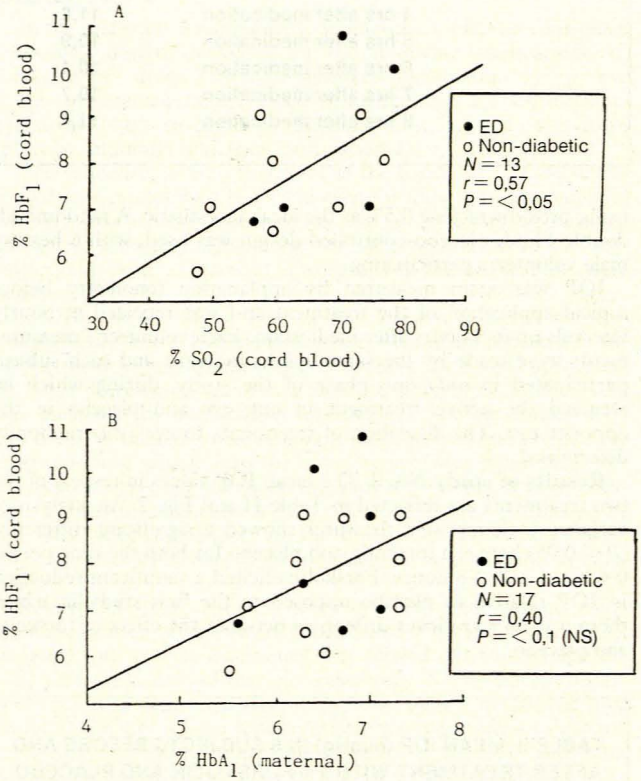

Fig. 1. Percentage Hb F_1 in cord blood v. cord blood percentage oxygen saturation (% SO_2) (A) and maternal percentage Hb A_1 in non-diabetic and ED mothers. (B). (It was not possible to examine all patients for all variables. The graphs show the total results obtained.)

The correlation of Hb F_1 with maternal Hb A_1 in non-diabetic subjects agrees with the findings of Poon *et al.*,[5] whose patients were either non-diabetic ($N = 14$) or established diabetics ($N = 10$), i.e. not gestational diabetics. Glucosylated haemoglobin (Hb A_{1C}) was determined by immuno-electrophoresis ($N = 24$; $r = 0,4$; $P < 0,05$). Our own results showed a significant correlation in non-diabetics ($N = 10$), but no correlation with ED patients either in isolation ($N = 7$), or when plotted with non-diabetics ($N = 17$). We could not demonstrate a significant correlation of the cord blood $\frac{\text{Hb } F_1}{\text{Hb } F_1 + \text{Hb } A_0}$ ratio with gestational age in any of the patient groups studied, in contrast with Peterson *et al.*[4] In our ED patients, Hb F_1 significantly correlated with cord C-peptide ($N = 8$; $r = 0,86$; $P < 0,001$; linear regression[6]). This correlation was absent in our non-diabetic and GD patients. There was no correlation between maternal Hb A_1 and cord C-peptide or birth weight ratio in any of the groups studied.[8]

Comment

While an excellent correlation ($N = 17$; $r^2 = 0,80$) of the $\frac{\text{Hb } F_1}{\text{Hb } F_1 + \text{Hb } A_0}$ ratio to gestational age (days) was demonstrated by Peterson *et al.*,[4] our results and those of Poon *et al.*[5] suggest

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that other factors may affect this correlation and limit the usefulness of this approach in diabetic pregnancy. The fetal exposure to glucose would appear to influence the formation of Hb F_1 as shown by the correlation of Hb F_1 with maternal Hb A_1[5] (Fig. 1B, correlation significant in non-diabetic group) and the correlation of Hb F_1 with cord C-peptide in ED patients.[6] Furthermore, the oxygenation status of the fetus would also appear to influence formation of Hb F_1 in neonates born to ED and non-diabetic mothers (Fig. 1A). Since a general reduction in oxygen levels of cord blood has been shown[9] as term is approached, and we demonstrated a direct correlation between Hb F_1 and percentage O_2 saturation in ED and non-diabetic patients, this may explain the negative correlation of Hb F_1 with gestational age shown by Peterson *et al.*[4] in non-diabetic patients. The formation of Hb F_1 in our non-diabetic and ED patients would seem to depend on the presence of glucose (Fig. 2), insulin (Hb F_1 versus cord C-peptide; $P < 0{,}001$ in our ED patients[6]) and an adequate oxygen supply (Fig. 1). This is consistent with the suggestion that the formation of Hb F_1 in fetal erythrocytes is enzyme-mediated and uses glucose as a precurser for the acetyl moiety in Hb F_1.[6] The usefulness of Hb F_1 as a measure of gestational age[4] or of fetal exposure to glucose[5] appears to be limited by these complicating factors and by the nature of diabetes in the mother, as the correlations shown were absent in our GD patients.

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Chronic cough and cough mixtures in a private paediatric practice

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Summary

A survey of 256 private practice paediatric patients with chronic cough revealed that 50% were asthmatic, 28% had upper respiratory infections including bronchiolitis and bronchopneumonia, while 22% had whooping cough despite being fully immunised. Diagnosis and management are discussed. The only cough mixture of real value appears to be a bronchodilator.

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Chronic cough is a common problem in private paediatric practice. The patient usually presents after a number of cough mixtures and often antibiotics have been found to be ineffective. It is therefore of value to determine the causes and management. Chronic cough is defined as a cough of at least 3 weeks' duration.

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Patients and methods

A retrospective survey for 1984-1985 from examination of patients' records was undertaken in a private practice in Cape Town, which caters mainly for patients in the southern suburbs who are virtually all from the coloured and white race groups.

Results

The study group consisted of 256 patients aged 3 months to 15 years with chronic cough. Of these 129 (50%) were asthmatic; 71 (28%) had recurrent upper respiratory tract (URT) infections including bronchiolitis and bronchopneumonia; and 56 (22%) had whooping cough. Of the asthmatics 55% were under 4 years of age, of the recurrent URT infections 63% were aged 6 months - 4 years and 61% of the whooping cough patients were 1 - 4 years old.

The 256 patients included 1 case of pulmonary tuberculosis, 1 of bronchiectasis following whooping cough and 1 patient with a persistently atelectatic right middle lobe. There were no cases of inhaled foreign body, cystic fibrosis or psychogenic cough.

Diagnosis

This was made in most instances clinically from the nature of the cough, a detailed history and examination. Although asthmatics typically cough and wheeze recurrently, they often present with a