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Elevated Erythrocyte CDP-Choline Levels Associated with β-Thalassaemia in Patients with Transfusion Independent Anaemia

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ABSTRACT

The accumulation of CDP-ethanolamine as well as CDP-choline in a small cohort of patients with normal UMPH1 and no defined cause for their anaemia suggested a defect in both phosphotransferases. Here we report 10 patients with transfusion independent β -thalassaemia; 8 being pure heterozygotes and 2 heterozygotes also for Hb E. Mean CDP-choline (86. \square \square \pm 48 μ M) and CDP-ethanolamine (34.6 μ M \pm 34.5 μ M), mean control <3 μ M. Elevated CDP-choline in patients with no defined cause for their haemolytic anaemia was previously suggested as a possible indicator of CDP-choline phosphotransferase deficiency. Here we associate it with transfusion independent β -thalassaemia.

Key Words: Beta-thalassaemia trait; CDP-choline; CDP-choline phosphotransferase; Haemolytic anaemia; Basophilic stippling.

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INTRODUCTION

Haemolytic anaemia with basophilic stippling is characteristic of pyrimidine 5′-nucleotodase (UMPH1) deficiency. ^[1] The selective accumulation of CDP-choline in high concentrations in the erythrocytes of a patient with haemolytic anaemia and a normal UMPH1 activity was first reported by Paglia et al. ^[1] A defect in CDP-choline phosphotransferase which catalyses the last stage of lecithin biosynthesis was suggested. The selective accumulation of CDP-choline is thought to occur in the erythroblast as CDP-choline phosphotransferase has been shown to be inactive in the mature erythrocyte. The accumulation of CDP-ethanolamine as well as CDP-choline in a small cohort of patients with normal UMPH1 activity and either unexplained haemolytic anaemia, or secondary to chronic renal failure, led us to postulate the existence a defect in both phosphotransferases. ^[2]

METHODS

Two groups of patients contributed to the study: Ten healthy controls and ten patients with β -thalassaemia intermedia, all having transfusion independent disease. Eight were typed as simple β -thalassaemia heterozygotes and a further two patients were heterozygous for β -thalassaemia and Haemoglobin E. All had normal UMPH1 activity.

Erythrocyte nucleotide extracts were prepared from venous blood separated and washed as described previously. TCA-soluble components in the supernatant following centrifugation were back-extracted with water-saturated diethyl ether, and frozen at -20° C if not analysed immediately by anion exchanges HPLC with in-line diode-array detection as described. Electron as described.

RESULTS

The β -thalassaemia patients had elevated concentrations of CDP-choline (86. $\square\square\square \pm 48 \mu M$) and CDP-ethanolamine (34.6 $\mu M \pm 34.5 \mu M$), compared with

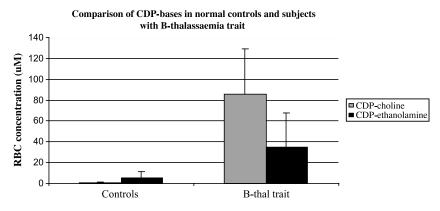


Figure 1.

less than 3 μ M in controls (Fig. 1) and was significant for both components (p = 0.002 for CDP-choline, p = 0.02 for CDP-ethanolmine).

DISCUSSION

The patients in this report with transfusion independent β -thalassaemia. all had CDP-choline levels in excess of their CDP-ethanolamine (p = 0.002). These findings contrast with our earlier results in patients also with normal UMPH1 and raised CDP-choline/ethanolamine but no other cause of their anaemia where this ratio was reversed, [2] Elevated erythrocyte CDP-choline in patients with no defined cause for their haemolytic anaemia was suggested first by Paglia [1] as an indicator of CDP-choline phosphotransferase deficiency. The accumulation of CDP-ethanolamine as well as CDP-choline in our small cohort of patients with normal UMPH1 activity and either unexplained haemolytic anaemia, or secondary to chronic renal failure, led us to postulate a defect in both phosphotransferases. Correction of the haematological profile following successful renal transplantation in one renal failure patient implied possible heterozygosity for this defect. [2]

The elevated concentrations of both CDP-choline and CDP-ethanolamine found here in a group of patients with transfusion independent β -thalassaemia raises the possibility that elevated erythrocyte CDP-choline/CDP-ethanolamine is either a consequence of the haemolysis of β -thalassaemia or a consequence of a number of different haemolytic anaemias. Work is ongoing to characterise a variety of haemolytic anaemias and to identify any similar association with elevated CDP-choline/ethanolamine concentrations.

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