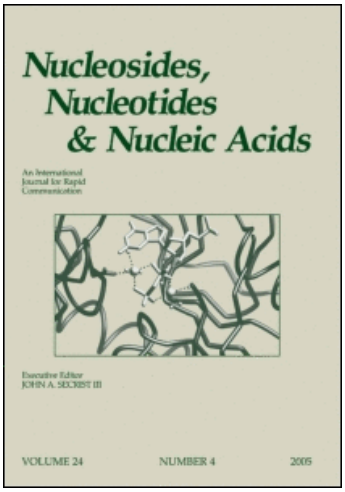

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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

A. D. Laurence[a]; M. Layton[b]; J. A. Duley[c]; H. A. Simmonds[c]
[a] University College, London, UK [b] Imperial College, London, UK [c] Guy's Hospital, London, UK

Online publication date: 27 October 2004

To cite this Article Laurence, A. D. , Layton, M. , Duley, J. A. and Simmonds, H. A.(2004) 'Elevated Erythrocyte CDP-Choline Levels Associated with β-Thalassaemia in Patients with Transfusion Independent Anaemia', Nucleosides, Nucleotides and Nucleic Acids, 23: 8, 1265 — 1267
To link to this Article: DOI: 10.1081/NCN-200027535
URL: http://dx.doi.org/10.1081/NCN-200027535

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 23, Nos. 8 & 9, pp. 1265–1267, 2004

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

A. D. Laurence,[1,*] M. Layton,[2] J. A. Duley,[3] and H. A. Simmonds[3]

[1]University College, London, UK
[2]Imperial College, London, UK
[3]Guy's Hospital, London, UK

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.□□□ ± 48 μM) and CDP-ethanolamine (34.6 μM ± 34.5 μM), mean control <3 μM. 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-ethanolamine; CDP-choline phosphotransferase; Haemolytic anaemia; Basophilic stippling.

*Correspondence: A. D. Laurence, University College, London, UK.

DOI: 10.1081/NCN-200027535
1525-7770 (Print); 1532-2335 (Online)

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.[3] 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.[3]

RESULTS

The β-thalassaemia patients had elevated concentrations of CDP-choline (86.□□□ ± 48 μM) and CDP-ethanolamine (34.6 μM ± 34.5 μM), compared with

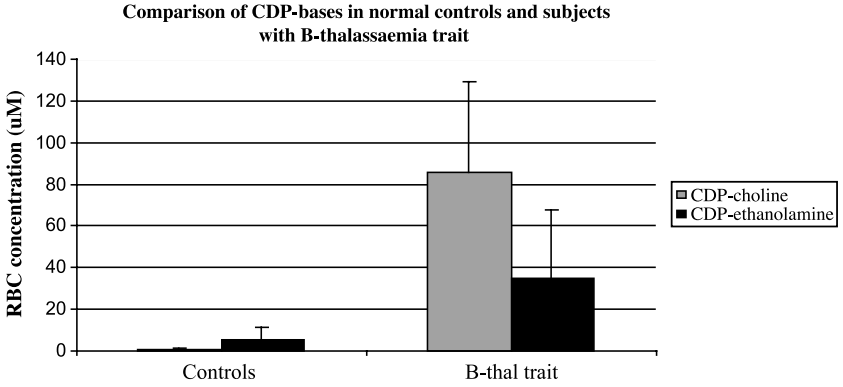

Figure 1.

less than 3 μM 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.

REFERENCES

1. Paglia, D.E.; Valentine, W.N.; Nakatani, M.; Rauth, B.J. Selective accumulation of cytosol CDP-choline as an isolated erythrocyte defect in chronic hemolysis. Proc. Natl. Acad. Sci. U. S. A. **1983**, *80*, 3081–3085.
2. Laurence, A.; Duley, J.A.; Simmonds, H.A.; Layton, M.; Rose, S.J.; Kelly, S.J. Erythrocyte CDP-choline accumulation in haemolytic anaemia and renal failure (RF). Adv. Exp. Med. Biol. **1998**, *431*, 155–159.
3. Simmonds, H.; Duley, J.; Davies, P. Analysis of purines and pyrimidines in blood, urine and other physiological fluids. In *Techniques in Diagnostic Human Biochemical Genetics: A Laboratory Manual*; Hommes, F.H., Ed.; Wiley-Liss: New York, 1991; 397–424. Vol. Chapter 25.