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RELATIONSHIP BETWEEN ORAL BIOTIN SUPPLEMENTATION AND ANAEMIA AND DRY SKIN IN REGULAR HAEMODIALYSIS PATIENTS

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Summary

The effect of oral biotin supplementation (6mg daily for 11 weeks) on anaemia and dry skin was evaluated in 20 haemodialysis patients. The pre-treatment haematocrit of the supplemented group (27.4±2.5%) gradually increased to 31.4±3.1% ($p<0.05$) after 11 weeks of treatment and plasma concentrations of biotin were significantly increased from 2.7±0.4ng/ml to 233.2±55.8ng/ml. Biotin did not improve the dryness of the skin. These results suggest that biotin supplementation could be a useful method of improving the anaemia of regular haemodialysis patients.

Introduction

Although biotin deficiency has been virtually ignored in the treatment of regular haemodialysis patients, a recent paper by Yatzidis [1] on the use of biotin for uraemic neuroencephalopathy prompted us to examine the place of oral biotin supplementation for the anaemia and dry skin often seen in regular haemodialysis patients.

Materials and methods

Twenty stable haemodialysis patients (32 to 63 years) were randomly selected from 60 outpatients on regular haemodialysis at our unit. They had been on haemodialysis for 24 to 130 months using hollow fibre cuproammonium rayon kidneys at a blood flow rate of 250ml/min and a dialysate flow rate of 450ml/min for 5.5 to six hours thrice weekly. None of our patients received a blood transfusion or a biotin-containing vitamin preparation in the previous nine years. The patients were divided alphabetically into two groups: 10 patients (group I) received oral supplementation with 6mg biotin daily in three divided doses for 11 weeks in addition to their routine medication. Patients in group II were not given biotin and served as controls. In addition 10 normal subjects were used for

comparison (group III). Blood samples were taken from the arterial line immediately before and after haemodialysis in all 20 patients on four occasions: just before biotin supplementation was started (day 0), during treatment (6 weeks), at the end of treatment (11 weeks) and after treatment (25 weeks) for estimation of plasma biotin. Pre-haemodialysis haematocrit, red blood cell count, haemoglobin, creatinine, blood urea nitrogen, and electrolytes were measured twice monthly for 25 weeks. Plasma biotin was measured by bioassay using Lactobacillus plantarum. Humidity of the abdominal skin was measured 5cm distal to the umbilicus using a dermal humidometer before, during and after treatment with biotin. All results are expressed as mean values ± standard error (SEM) of the mean and analysed using the Student's 't' test for unpaired data.

Results

Plasma biotin before treatment and in unsupplemented haemodialysis patients were slightly higher than those of healthy controls (Table I). Plasma biotin concentrations changed minimally after haemodialysis in unsupplemented patients which

TABLE I. Plasma biotin in haemodialysis (HD) patients with and without biotin supplementation and healthy controls (mean ±SEM)

		Plasma biotin levels (ng/ml)			
		Pre-treatment		Post-treatment	
Group		Day 0	6 weeks	11 weeks	25 weeks
I Biotin 6mg	Pre-HD	2.7±0.4	189.3±48.7	233.2±55.8	5.8±0.6
	Post-HD		112.1±29.5	148.7±37.2	
II None	Pre-HD	2.2±0.5	4.3±1.1	4.5±1.2	
	Post-HD		3.2±1.1	4.2±1.1	
III Healthy controls		0.4±0.1			

may suggest that biotin is bound to protein or other metabolites in these patients. In contrast plasma biotin was significantly increased by oral biotin administration to 233.2±55.8ng/ml. About 30 per cent being removed by a five hour dialysis. This observation may suggest that some of the orally given biotin is unbound to protein or other substances and easily dialysed from the circulation. Fourteen weeks after stopping oral biotin blood values had fallen to 5.8±0.6ng/ml, similar to pre-treatment levels. The pre-treatment mean haematocrit of the supplemented group (27.4±2.5%) gradually but steadily increased to 31.4±3.1 per cent ($p<0.05$) after treatment for 11 weeks, while unsupplemented patients showed no change in haematocrit. Six weeks after stopping biotin supplementation the haematocrit fell slightly to 29.5±2.6 per cent and remained stable thereafter (Figure 1). The mean skin humidity scores of haemodialysis patients (0.5±0.01, 0.4±0.01) was markedly lower than healthy controls (8.2±1.5) and was not improved by biotin.

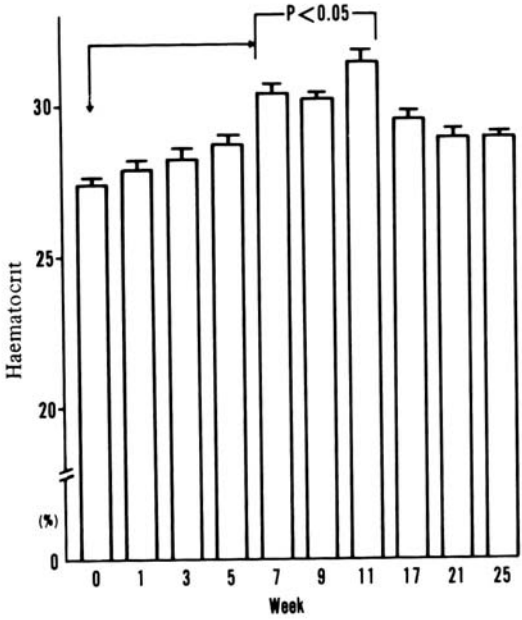

Figure 1. Haematocrit changes in haemodialysis patients with biotin supplementation (mean ±SEM). The pre-treatment mean haematocrit gradually but steadily increases to 31.4± 3.1 per cent ($p<0.05$)

Discussion

Biotin deficiency in man is very rare because biotin is widely distributed in food, the daily intake being approximately 60 to 100μg. Biotin is also synthesized by intestinal flora but the availability of this source has not yet been quantified. In a recent paper Yatizidis [1] suggested that for a number of reasons an acquired biotin-deficiency can easily occur in patients maintained on regular haemodialysis. Routine dietary restriction decreases the intake of biotin and various supplementary vitamin preparations given to these patients were completely biotin-free. In addition, biotin is loosely and poorly bound to serum protein and therefore easily depleted during dialysis. For these reasons, we have studied the effects of biotin on the anaemia and dry skin of regular haemodialysis patients. Our results clearly show that the haematocrit gradually but steadily increased to a mean of 31.4±3.1 per cent from 27.4±2.5 per cent after treatment with biotin, 6mg daily over 11 weeks. Although the way in which biotin increases the haematocrit in haemodialysis patients is not fully understood, the essential nature of biotin-dependent carboxylase enzymes in mammalian metabolism such as glyconeogenesis and fatty-acid synthesis suggest that impairment of one or more of these pathways could produce a clinical picture characterized by a disruption in metabolism and acid-base

balance [2]. The resulting metabolic acidosis could cause a progressive anaemia by bone marrow depression. In addition, accumulation of various metabolites such as isovaleric acid could contribute to the anaemia in these patients [3]. Partly because of the difficulty in assaying the extremely small quantities of biotin in biological fluids the biokinetics in haemodialysis patients are poorly understood. To our knowledge only two papers describing blood biotin in haemodialysis or peritoneal dialysis patients have previously been published [4,5]. Since then biotin has been virtually ignored in the treatment of regular haemodialysis patients with the exception of two reports by Yatzidis et al [1,6] who concluded that biotin supplementation could be of a clinical benefit in the prevention and treatment of neuroencephalopathy in regular dialysis patients. Unfortunately, these authors did not mention the pre- and post-treatment plasma biotin of their patients.

Our study has shown that blood biotin in haemodialysis patients is slightly higher than normal controls. As biotin is excreted by the kidney an increased plasma concentration may occur in renal failure. The fact that there was no change in plasma biotin before and after haemodialysis in unsupplemented patients may indicate that biotin is bound to plasma protein or other uraemic metabolites in unsupplemented patients. Biotin, a vitamin of the B complex, is an essential co-factor for the four major carboxylases; pyruvate, propionyl-CoA, methylcrotonyl-CoA and acetyl-CoA carboxylase. These enzymes play a significant role in the metabolism of fat and carbohydrate and are available to humans in a wide variety of foods or from enteric synthesis, although the significance of the latter source has not been determined [7]. The most prominent finding in our study was the low concentration of unbound biotin in the plasma of uraemic patients which was increased by the administration of 6mg of biotin daily. Although it is important to consider biotin deficiency in the differential diagnosis of skin disease, our results showed no beneficial effect of biotin supplementation on the dry skin of haemodialysis patients, suggesting that this problem is caused by a mechanism unrelated to biotin deficiency.

In conclusion, the plasma free concentration of biotin in haemodialysis patients is low and supplementation using 6mg biotin orally for 11 weeks significantly increased free biotin and haematocrit.

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