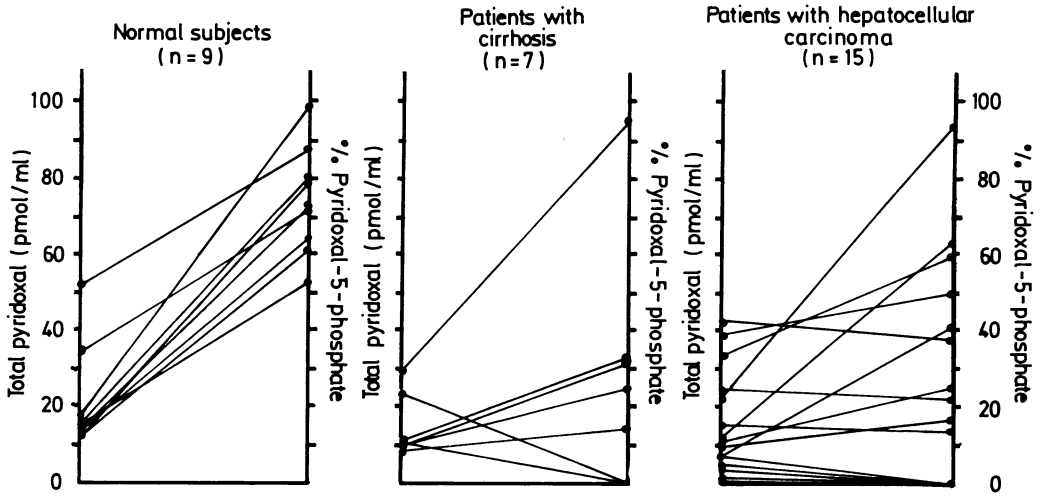
SHORT REPORTS

Vitamin B6 concentrations in patients with chronic liver disease and hepatocellular carcinoma

Vitamin B6 is the generic term for three closely related and interconvertible compounds. Most of the vitamin B6 obtained from the diet is rapidly converted by the liver to its active coenzyme, pyridoxal-5-phosphate, which has a central role in the metabolism of amino acids. Patients with chronic liver disease are commonly deficient in pyridoxal-5-phosphate, and this may be due to decreased conversion of vitamin B6 to pyridoxal-5-phosphate, although increased breakdown of pyridoxal-5-phosphate[1 2] or decreased intake or poor absorption of dietary vitamin B6 may be responsible.



Total pyridoxal concentrations and proportion of existing pyridoxal-5-phosphate in patients and controls.

Recently a method permitting estimation of concentrations of pyridoxal-5-phosphate from direct measurement of plasma total pyridoxal and free (that is, non-phosphorylated) pyridoxal concentrations was described,[3] and we applied this to patients with chronic liver diseases. Because of the high risk of hepatocellular carcinoma in patients with chronic liver disease we also studied patients with hepatocellular carcinoma with or without associated cirrhosis.

Patients, methods, and results

We studied 17 patients with cirrhosis (cryptogenic, two; chronic active, five; alcoholic, five; primary biliary, two; haemachromatosis, two; Wilson's, one), 10 of whom had histologically confirmed hepatocellular carcinoma; five patients with hepatocellular carcinoma but without cirrhosis; and nine healthy control subjects. None gave a history of dietary supplementation with vitamin B6 during the previous six months. The age range was 30-55 in the normal subjects, 18-69 in the patients with uncomplicated cirrhosis, and 20-68 in the patients with hepatocellular carcinoma. Total and free pyridoxal concentrations were measured by the method of Smith *et al*[3] and serum α fetoprotein by radioimmunoassay (AFP-RIA, Amersham, United Kingdom).

Total pyridoxal concentrations ranged from 10 to 51 pmol/ml in the nine normal subjects, a range similar to that reported by Smith *et al*.[3] Although seven of the patients with hepatocellular carcinoma had concentrations below the lowest values recorded in the control group, there was no significant difference overall between either patient group and the control subjects (figure). The concentrations of pyridoxal-5-phosphate, however, were much lower in the patients with uncomplicated liver disease, being unrecordable in seven ($p < 0.01$, Wilcoxon's rank sum test). The proportion of total pyridoxal existing as active pyridoxal-5-phosphate was more than 50% in all control subjects but less than 50% in all patients with liver disease apart from one with cirrhosis and three with hepatocellular carcinoma. None of the patients with uncomplicated cirrhosis had increased serum and α fetoprotein concentrations, and in the patients with hepatocellular carcinoma there was no correlation between α fetoprotein and pyridoxal-5-phosphate concentrations.

Comment

The normal concentrations of total pyridoxal in most of the patients with cirrhosis suggest that deficient intake and poor absorption of vitamin B6 are not the major cause of the deficiency of pyridoxal-5-phosphate in such patients found in this and other studies. This deficiency may be due either to failure of hepatic conversion of vitamin B6 or to enhanced degradation of pyridoxal-5-phosphate. Although in this study there was no relation between α fetoprotein concentrations and pyridoxal-5-phosphate deficiency, experimental studies have shown that dietary deprivation of vitamin B6 may lead to increased α fetoprotein concentrations and preneoplastic nodules in baboons.[4] The possibility that vitamin B6 deficiency is a risk factor for the development of hepatocellular carcinoma in cirrhosis cannot be excluded, particularly as seven of the patients had lower concentrations of pyridoxal-5-phosphate than any normal subject.

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Prevalence of antibody to HTLV-III in haemophiliacs in the United Kingdom

Haemophiliacs receiving treatment with blood coagulation factor are at risk of infection with human T cell lymphotropic virus type III (HTLV-III) (or lymphadenopathy associated virus),[1] the agent thought to cause the acquired immune deficiency syndrome (AIDS).[2 3] Studies carried out in different parts of the United Kingdom have shown that many haemophiliacs now have

Antibody to HTLV-III in relation to severity of coagulation defects and age of patients suffering from haemophilia A and haemophilia B

Age (years)	Factor VIII/IX concentration (IU/100 ml) <2 Patients tested	<2 No (%) positive for HTLV-III	2-10 Patients tested	2-10 No (%) positive for HTLV-III	>10 Patients tested	>10 No (%) positive for HTLV-III	Total* Patients tested	Total* No (%) positive for HTLV-III
				Haemophilia A				
<5	40	5 (12)	15	5 (33)	2	0	60	11 (18)
5-9	91	32 (35)	45	6 (13)	12	0	149	39 (26)
10-14	104	71 (68)	49	18 (37)	19	2 (11)	174	92 (53)
15-19	163	106 (65)	57	18 (32)	23	1 (4)	243	125 (51)
20-29	340	230 (68)	117	26 (22)	44	3 (7)	506	261 (52)
30-39	232	152 (66)	76	15 (20)	38	3 (8)	349	170 (49)
40-49	148	93 (63)	52	13 (25)	30	4 (13)	232	110 (47)
50-59	86	44 (51)	40	4 (10)	23	2 (9)	150	50 (33)
60-69	48	16 (33)	41	8 (20)	21	1 (5)	112	26 (23)
≥70	15	3 (20)	22	5 (23)	8	3 (38)	45	11 (24)
Total*	1268	752 (59)	516	118 (23)	220	19 (9)	2025	896 (44)
				Haemophilia B				
<5	6	0	7	0	0	0	14	0
5-9	18	0	10	1 (10)	3	0	31	1 (3)
10-14	12	0	12	0	3	0	28	0
15-19	23	(9)	13	1 (8)	5	1 (20)	41	4 (10)
20-29	46	7 (15)	31	0	4	0	82	7 (9)
30-39	32	1 (3)	10	1 (10)	5	0	47	2 (4)
40-49	16	1 (6)	8	0	2	0	27	1 (4)
50-59	14	2 (14)	12	2 (17)	4	0	31	4 (13)
60-69	5	1 (20)	9	0	2	0	16	1 (6)
70+	2	0	2	0	1	0	5	0
Total*	174	14 (8)	115	5 (4)	29	1 (3)	324	20 (6)

*Includes patients whose age or coagulation factor concentration, or both, were unknown.

antibody to HTLV-III in their blood.[4 5] We report the results of a survey of the prevalence of antibody to HTLV-III in patients suffering from haemophilia A, haemophilia B, and von Willebrand's disease in the United Kingdom.

Patients, methods, and results

In June 1985 each of the 109 haemophilia centres in the United Kingdom was sent a computer printout of the names of patients who had been treated at that centre from 1980 to 1984. The directors of the centres were asked to indicate those patients who had been tested for antibody to HTLV-III and the date and result of the most recent test and to return the annotated printouts to the Oxford haemophilia centre by 9 August 1985. All information on named patients was handled in Oxford in strictest confidence by only one person. The information submitted for computer analysis in Oxford did not contain patients' names and did not mention HTLV-III.

Information on 2609 patients was received from 81 centres (74%). Tests for antibody to HTLV-III were performed on 2025 patients with haemophilia A, of whom 896 (44%) were found to be positive; 20 (60%) of 324 patients with haemophilia B who were tested were positive, and 11 (5%) of 215 patients with von Willebrand's disease who were tested were positive. The table shows a detailed analysis of the results from patients with haemophilia A and B according to age and severity of the disease.

To see whether prevalence of antibody varied with the type of factor used in treatment patients with haemophilia A were categorised into those who had received only commercial factor VIII, those who had received only National Health Service factor VIII, those who had received only cryoprecipitate, and those who had received any combination of these products from 1980 to 1984. Only a few patients had received a single type of treatment material during the five years. Of these, 166 had received only cryoprecipitate; two (1·2%) had antibody to HTLV-III. The risk was greater in those treated with NHS factor VIII concentrates obtained from a large pool (20 of 198 tested were positive) and greatest for those treated with commercial concentrates (44 of 97 tested were positive). In those who received more than one type of material the prevalence of antibody was greater if the patient had received commercial concentrate.

Comment

Nearly 60% of patients with severe haemophilia in this study had antibody to HTLV-III. The prevalence of antibody was greater in patients who had received commercial factor VIII concentrate with or without other blood products, though it is clear from this study and others that some batches of NHS factor VIII that have not been heated also contain HTLV-III. The overall prevalence of antibody in patients with haemophilia B (6%) was much lower than that in patients with haemophilia A (44%) and was closer to the prevalence in patients with haemophilia A treated with only NHS factor VIII (10%). All factor IX that is in the United Kingdom is produced for the NHS at blood product laboratories at Elstree and Edinburgh.

This is the first national survey of the HTLV-III antibody state of haemophiliacs in the United Kingdom and will serve as a baseline for future surveys. We plan to repeat the survey at regular intervals to study the change in prevalence with time and to see what effect the introduction of heat-treated concentrates will have on antibody prevalence.

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