

Vitamin and mineral nutrition in chronic alcoholics including patients with Korsakoff's psychosis

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1. A group of 129 patients with chronic alcoholism were assessed for their nutritional status with respect to certain minerals and vitamins, and compared with control subjects.
2. In all subjects the plasma values were normal for calcium, magnesium and zinc.
3. As in other studies a seasonal variation was found in the plasma levels of 25-hydroxyvitamin D in the control subjects and the alcoholic subjects; in all seasons lower levels were found in the alcoholics than in the controls, but none of the alcoholic patients had results in the range found in osteomalacia.
4. The alcoholic subjects had low levels of ascorbic acid both in the plasma and in the leucocytes.
5. Although vitamin A and β -carotene levels were within the reference range, the results in alcoholics were found to be lower than in the control subjects.
6. We suggest that subclinical vitamin deficiencies other than thiamine deficiency contribute to the cerebral impairment frequently found in alcoholism.

Various vitamin and mineral deficiencies have been described in patients who take excessive quantities of alcohol (Baines, 1978; Prasad, 1966; Mullier, 1979; Comar & Bronner 1964). These may be subclinical and contribute to cerebral impairment (Guthrie & Elliott, 1980). Alcoholic patients have also been reputed to have low blood levels of zinc and magnesium. The disturbance of Zn metabolism could reflect malabsorption or destruction of Zn metallo-enzymes (Walravens, 1980). The hypomagnesaemia could result from malabsorption, malnutrition or defects in renal tubular reabsorption (Heaton *et al.* 1962; Nordin, 1976).

Malnutrition in alcoholics is important clinically and, in combination with toxic effects, may be responsible for the many complications seen in alcoholic patients. Vitamin and mineral deficiencies have been implicated in the aetiology of Wernicke-Korsakoff syndrome (Victor *et al.* 1971), cerebellar syndrome (Graham *et al.* 1971), myopathy (Perkoff *et al.* 1967; Pittman & Decker, 1971) and polyneuritis (Fennelly *et al.* 1964; Erbslon & Abel, 1970; Victor *et al.* 1971).

Cerebral impairment in alcoholics, short of the classical Wernicke-Korsakoff syndrome, has recently been reported from many countries (Tarter, 1971; Carlsson *et al.* 1973; Ornstein, 1977; Eckardt *et al.* 1978). Recent research in Tayside reported a significant relationship between this early cerebral impairment and a malnutrition index (Guthrie *et al.* 1980) and, in addition, there was some evidence that recovery from this complication of alcoholism might be impeded by malnutrition (Guthrie, 1980). Recovery from fatty liver disease may also be impeded by vitamin deficiency (Olson *et al.* 1953).

The object of this work was to determine the incidence of vitamin and mineral deficiencies in a group of alcoholics and controls, to compare findings with other studies and to extend the previous studies by including vitamin A and β -carotene estimations. Also, we felt it was important to do all the assays on the same group of patients.

SUBJECTS AND METHODS

Three groups of subjects were chosen for this study.

Group 1. 108 admissions to Tayside Area Alcoholism Unit (eighty-five male and twenty-three female) with a mean age of 47 years (range 26–67). The Unit is not selective in first admission policy, and takes patients from all agencies in Tayside (population 400 000) although the majority come directly from general practitioners. The patients were consecutive admissions but those with possible brain damage from factors other than alcohol or vitamin deficiency were excluded from the study (Guthrie & Elliott, 1980).

Group 2. Twenty-one hospitalized patients with Korsakoff's psychosis from hospitals within Tayside (thirteen male and eight female), with a mean age of 57 years (range 42–72).

Group 3. Thirty-two regular blood donors in Tayside (thirty male and two female), with a mean age of 38 years (range 24–61).

Blood samples from the three groups were obtained by venepuncture, placed on ice and delivered to the laboratory within 2 h of being taken. Vitamin A and β -carotene were determined in serum by a procedure based on the methods of Neeld & Pearson (1963), Varley (1969) and Dugan *et al.* (1964). Plasma and leucocyte ascorbic acid were determined by the method of Denson & Bowers (1961) modified by employing Dextran T500 (Pharmacia) for leucocyte separation as suggested by McCraw & Sim (1969). Analyses of vitamin D were carried out by measuring plasma 25-OHD, the major circulating metabolite (Preece *et al.* 1974).

For the measurements of calcium, phosphate and alkaline phosphatase (*EC* 3.1.3.1) activity, the Vickers Multichannel 300 analyser was used. The Ca assay was based on that of Kessler & Wolfman (1964) and Gitelman (1967), the phosphate method on Lawrence (1974) and Hurst (1964) and the alkaline phosphatase method on Kind & King (1954).

The analyses of Zn (Parker *et al.* 1967) and Mg (Willis, 1961) were done by atomic absorption spectrophotometry using the Jarrell Ash 810 instrument for the former and the Perkin-Elmer 303 for the latter.

RESULTS

The results in Table 1 show that there were no significant differences in the Ca, Mg and Zn content of the plasma in the three groups studied. No subject showed low levels of plasma Ca and only one (male) showed reduced levels of Zn. Only nine male subjects (9%) showed low levels of Mg and such deficiency was not found in the female subjects. Phosphate and alkaline phosphatase levels were also within the normal ranges. Only one person had low levels of plasma phosphate; six subjects had raised alkaline phosphatase (three males and three females).

Vitamin A and β -carotene levels in alcoholics and patients with Korsakoff's psychosis were lower than in controls but the differences were not significant. No seasonal variation was observed in serum vitamin A and β -carotene content in any of the three groups studied. Both in the alcoholic subjects and in those with Korsakoff's psychosis, reduced levels of β -carotene were found in fifty-five male subjects (56%) and in ten female subjects (32%). Low levels of vitamin A were found to be present in only 10–12% of the subjects and no sex differences were observed.

The results in Table 1 also show low levels of plasma and leucocyte ascorbic acid in alcoholic subjects. Leucocyte counts in the alcoholics were found to be lower than those of the control group ($P < 0.01$); however both results were within the reference range. Leucocyte ascorbic acid values were low in fifteen male subjects (15%) and in four female subjects (13%).

Table 2 shows plasma 25-OHD levels in all groups studied. It clearly indicates low levels

Table 1. *Biochemical findings in patients with alcohol related illnesses*
(Mean values and standard deviations; no. of subjects in parentheses)

	Reference range	Controls (32)		Alcoholics		Korsakoff's psychosis (21)	
		Mean	SD	Mean	SD	Mean	SD
Vitamin A ($\mu\text{mol/l}$)	0.50-2.10	1.51	0.46	1.40	0.35 (87)	1.29	0.33
β -Carotene ($\mu\text{mol/l}$)	1.12-3.72	2.15	0.68	1.41	0.62 (85)	1.24	0.47
Plasma ascorbic acid ($\mu\text{mol/l}$)	23.0-85.0	—	—	17.4	13.8 (15)	—	—
Leucocyte ascorbic acid ($\mu\text{mol}/10^8$ cell)	0.12-0.30	0.21	0.09	0.10	0.07 (20)	—	—
Leucocyte count ($10^9/l$)	4.0-10.0	6.1	3.3	5.7	2.2 (20)	—	—
Calcium (mmol/l)	2.15-2.65	2.43	0.13	2.40	0.10 (85)	2.41	0.10
Magnesium (mmol/l)	0.70-1.15	0.81	0.05	0.81	0.08 (87)	0.79	0.05
Zinc ($\mu\text{mol/l}$)	10.0-19.0	13.9	3.2	14.7	4.0 (83)	14.5	2.1
Phosphate (mmol/l)	0.80-1.55	1.05	0.16	1.16	0.21 (81)	1.11	0.18
Alkaline phosphatase (KAU ^a /100 ml)	3.0-14.0	7.6	1.6	9.4	3.6 (77)	10.1	2.4

• KAU, King-Armstrong units.

Table 2. *Plasma levels of 25-hydroxyvitamin D in alcoholics and the control group of subjects*

(Mean values and standard deviations; no. of subjects in parentheses)

Month	Plasma 25-hydroxyvitamin D (nmol/l)					
	Controls		Alcoholics		Korsakoff's psychosis	
	Mean	SD	Mean	SD	Mean	SD
1977 Aug	49.5	11.0 (8)	35.8	13.8 (9)	—	—
Sep	58.0	12.8 (8)	43.5	19.0 (11)	—	—
Oct	58.3	12.3 (8)	34.3	9.0 (19)	—	—
Nov	45.3	18.3 (28)	33.0	18.0 (14)	22.8	— (1)
Dec	48.5	5.8 (7)	35.0	22.5 (5)	22.5	7.0 (4)
1978 Jan	39.0	8.8 (11)	29.3	12.5 (6)	—	—
Feb	25.0	0.5 (2)	23.8	9.5 (7)	21.3	8.5 (7)
Mar	44.8	3.3 (7)	41.8	— (1)	45.3	4.3 (5)

of plasma 25-OHD in alcoholics, and even lower values in patients with Korsakoff's psychosis. The results also show the expected seasonal variation in both the control group and the alcoholic group. The values of plasma 25-OHD levels were found to be significantly different in September and February ($P < 0.001$). The plasma levels of 25-OHD in control subjects were generally higher than those found in alcoholics, throughout the year.

DISCUSSION

Our study shows that blood levels of Ca, Mg and Zn are normal in chronic alcoholism. Our findings for Ca are similar to those of Bogdon & Troiano (1978) but these workers found low levels of Mg and Zn in some of their patients with the most severe delirium tremens

or prolonged hallucinations during alcohol withdrawal. Our study revealed low Mg levels in only two patients with Korsakoff's psychosis and low Zn levels in none. The differences in their results and ours may be related to the severity of the disease. Normal plasma levels of Zn also imply that Zn metallo-enzymes are not reduced significantly in our subjects.

A substantial proportion of our alcoholic patients had low levels of β -carotene and this has not previously been reported. On the other hand a much smaller proportion of the patients had low levels of vitamin A. Since β -carotene is a precursor of vitamin A and this conversion takes place mainly in the liver, it is unlikely that hepatic NADH-dependent enzymes (Marks, 1968) are impaired in alcoholism. It may be significant that plasma vitamin A: β -carotene value in alcoholics was 1:1 compared to a value of 1:1.4 in the control group. It is therefore probable that inadequate intake of food accounts for the low levels of β -carotene. That malnutrition is likely is also suggested by our low results for ascorbic acid which are seen even after allowing for the leucocyte count (Vallance, 1979). Our findings on ascorbic acid are similar to those of Krasner *et al.* (1974). Both in respect of β -carotene and of ascorbic acid, patients with Korsakoff's psychosis might be expected to be more severely affected than the other alcoholics but no significant differences were noted.

It is well established that plasma 25-OHD contents vary with the season (McLaughlin *et al.* 1974; Lund & Sorensen, 1979; Poskitt *et al.* 1979); our findings like those of Lund and co-workers (1977) show that such a trend is also present in the alcoholics. Reduction in the plasma levels of 25-OHD in alcoholics could result from malabsorption, malnutrition or because of an inability of the liver to hydroxylate vitamin D to 25-OHD. Because the seasonal variation in the blood levels of 25-OHD are still seen in the alcoholic subjects, it is unlikely that lack of the hepatic enzyme vitamin D-25-hydroxylase contributes to the low levels of plasma 25-OHD. This conclusion is similar to that of Posner *et al.* (1978) who also found low levels of 25-OHD in patients with alcoholic cirrhosis. We cannot on the basis of the present evidence exclude increased catabolism of vitamin D metabolites or decreased exposure to ultraviolet radiation as factors in the low 25-OHD levels. Malabsorption is much less likely than malnutrition because the vitamin A levels were normal despite low levels of β -carotene and because ascorbic acid levels were low.

Studies carried out on animal brain tissue show that ascorbic acid has a significant effect on the neurotransmitters (Kuo *et al.* 1979) and that this tissue also has vitamin A receptors (Bhat & Rao, 1978; Wiggart *et al.* 1978) as well as vitamin D-dependent Ca binding protein (Taylor, 1977). Our study therefore suggests that cerebral impairment in chronic alcoholism is not only due to thiamine deficiency (Chan, 1978; Henderson *et al.* 1978) but in part could also be due to the other vitamin deficiencies which we have demonstrated. We are now seeking to relate the nutritional findings to quantitative assessments of the degree of cerebral impairment.

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