Chronic alcoholics are typically malnourished. The authors suggest that injections of vitamin C may be needed in detoxification therapy for ethanol withdrawal to normalize vitamin C blood levels in some alcoholic patients “in order to enhance repair of tissue damage caused by chronic ethanol ingestion” and “for utilization of other vitamins and nutrients.” —*R.D.M.*

Vitamin C Utilization Status in Chronic Alcoholic Patients after Short-Term Intravenous Therapy

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Summary: Blood (leukocytic) ascorbic acid (vitamin C) levels were estimated in 25 chronic alcoholics (M=21, F=4; Age: mean ± S.D. = 46.28 ± 8.78; range 28-61 years) on admission before starting any treatment and on the sixth day following intravenous therapy with vitamin C — 500 mg daily for 5 days. Twenty-four out of 25 patients (96%) were found to be deficient in blood vitamin C (mean ± S. D. = 68.44 ± 28.13; range = 28–148; normal range for control population = 120–300 nmol / 10^8 W.B.C.). The status of blood vitamin C was significantly improved after the replenishment therapy with I / V vitamin C 500 mg daily for 5 days (mean ± S.D. = 108.32 + 34.98 nmol / 10^8 W.B.C.: range = 54-282.5; t = 3.76; P =< 0.001). Still the levels did not return to within the normal range in 16 patients out of 25 (64%).

In view of the biochemical deficiency of vitamin C in chronic alcoholics, it is suggested that conventional detoxification therapy for ethanol withdrawal syndrome should include polyvitamins including ascorbic acid. It is further suggested that more prolonged replenishment therapy with vitamin C, preferably by intravenous route, may be needed to normalize its blood levels in some chronic alcoholic patients.

INTRODUCTION

Malnutrition— clinical and/or biochemical at the subcellular level is well-known in chronic alcoholic patients [11, 12]. Deficiency of vitamin C which is an important element of nutrition is also well documented in these patients [1, 6]. Man cannot synthesize L-ascorbic acid (the biologically active form of vitamin C) and has to rely absolutely on its exogenous supply through diet [1]. There are two studies reported so far where oral supplementation of vitamin C (250 mg daily) was given for a short period (one week) in one [5] without normalisation of blood vitamin C levels and for longer period (3 months) in the other with daily oral supplementation with 175 mg vitamin C where the blood levels returned to normal [10].

In view of these observations on the oral supplementation therapy, we assessed the blood vitamin C status in 25 chronic alcoholic in-patients both before and after treating them with intravenous vitamin C 500 mg (L-ascorbic acid) daily for five consecutive days.

MATERIALS AND METHODS

Patients

Twenty five chronic alcoholics (M = 21; F = 4; mean age ± S. D. = 46.28 ± 2.78; age range = 28–61 years) were randomly selected on admission for the study. Daily amount of ethanol intake was more than 100 g and the duration of drinking ranged from 5–20 years. They were drinking up to the time of admission. There was nothing clinically suggestive of scurvy in our patients or any other condition which might lead to vitamin C deficiency but clinical stigmata of ethanol-induced liver damage viz hepatomegaly, palmar erythema, spider naevi, were present in some of them. Patients were totally abstinent from ethanol during the course of therapy. None had delirium tremens (D. Ts).

Methods

10 mls of blood was collected on each occasion from each patient both on admission and on the sixth day following treatment with I/V vitamin C for five days, placed into a sequestrene bottle and kept on ice. Within half an hour of collection, 11 mls blood was put in duplicate into a diluent containing sodium chloride, EDTA as anti-coagulant and dextran (to bring about rouleaux formation of the red cells) which causes them to settle down rapidly on standing. The leukocytes and platelets from the buffy layer, which remain suspended are recovered from the supernatant fluid by centrifugation and re-dissolved in TCA. The ascorbic acid content of the buffy layer is determined by forming a derivative with 2, 4-dinitrophenylhydrazine, which when treated with 65% sulphuric acid gives a reddish coloured compound; this compound is the measured at 520 nm (nano meter) in the spectrophotometer and the ascorbic acid content is expressed as nmol/10^8 W.B.C. [4]. As we are interested in assessing the blood vitamin C levels in chronic alcoholics in order to monitor their improvement after intravenous therapy, we prefer to use the ascorbic content of the buffy layer (containing both leukocytes and platelets) as an acceptable index of blood vitamin C status. In the patients under study, the ± 2 S. D. of platelet counts was near to the lower end of the reference range for control population and hence, it is not likely to make significant difference in the ascorbic acid levels.

Treatment

All patients were treated with intravenous "Parentrovite" (High Potency) — No. I and II, Bencard (U. K.) — one injection daily in the morning for five consecutive days. Contents of each injection are: ascorbic acid (as sodium ascorbate) — 500 mg, anhydrous dextrose — 1000 mg, thiamine hydrochloride — 250 mg, riboflavine — 4 mg, pyridoxine hydrochloride — 50 mg and nicotinamide —160 mg.

In addition, they were given a hypno-sedative — chlormethiazole ("Heminevrin" — Astra) in a reducing dosage over the same period to treat ethanol withdrawal syndrome. All drugs were well-tolerated. Chlormethiazole is not known to antagonize the effect of vitamin C (ascorbic acid).

RESULTS

Results are given in the Table.

TABLE
Vitamin C Utilization Status in Chronic Alcoholic Patients

Patient No.	Age	Sex	Leukocylic Ascorbic Acid (Vit. C) N=120-300 nmol/108 W.B.C. Pre-Treatment	Post Treatment
1	50	M	62	87
2	44	M	74	54
3	42	M	53	64
4	36	M	59	121
5	45	M	91	126
6	50	M	65	96
7	30	M	84	90
8	61	M	28	85.3
9	39	M	76.3	78
10	58	M	65	94
11	59	M	53	64
12	46	F	78.6	81
I3	53	F	35	113
14	40	M	99.7	137
15	33	M	90.2	87
16	42	M	51	170
17	52	M	68	109
18	46	F	101	162
19	28	M	148	130
20	50	M	67.6	114.3
21	52	F	109.7	167.2
22	58	M	32.2	115.7
23	48	M	29.7	84.4
24	44	M	52	185
25	51	M	42.1	282.5
Mean	46.28	M=21	68.64	108.32
± S.D.	8.78	F=4	28.13	34.98

(t = 3.76; P = < 0.001; Highly Significant)

Blood vitamin C content was found to be reduced in 24 out of 25 patients (96%) (mean ± S. D.= 68.64 ± 28.12; range = 28–148); normal range for control population = 120–300 nmol/l0^8 W.B.C.). The status of blood vitamin C was significantly improved after replenishment therapy with I/V vitamin C 500 mg daily for 5 days (mean ± S. D. 108.32 ± 34.98 nmol/l0^8 W. B. C.; range = 54–282.5; t = 3.76; p = < 0.001). Still the levels did not return to within the normal range in 16 out of 25 patients (64%).

Discussion

In this study 24 out of 25 patients (96%) were found to be deficient in blood vitamin C and even after intravenous therapy for 5 days (500 mg daily), the levels returned to within the normal range only in 9 while the levels still remained low in 16 patients (64%) (Table).

Overt clinical manifestations of vitamin C deficiency are very rarely seen in chronic alcoholic patients [1]. But blood levels do indicate the status of the vitamin at the subcellular level. Malnutrition is a state of imbalance between supply and demand of the biologically active forms of different nutrients including vitamins at the subcellular levels [12]. Biochemical correction of low vitamin concentrations at the subcellular level as reflected by their blood status is likely to enhance repair of tissue damage inflicted by chronic ethanol ingestion. On the contrary, if the normalisation of low blood vitamin levels is not adequate, repair of ethanol-induced tissue damage may be delayed or inadequate. In such circumstances, prolonged replenishment therapy by suitable routes of administration may be needed.

Ethanol is known to have direct toxic effect on the enterocytes of the gastrointestinal tract and thus may interfere with the intestinal absorption of various nutrients including vitamins [13]. That is why oral therapy with vitamins may not be able to normalise their blood levels. This might be the reason why short-term treatment with oral vitamin C failed to correct the blood vitamin status in the first study [5] and took as long as 3 months to correct it in the other [10].

The full biochemical functions of ascorbic acid are still unknown. It is thought to be involved in the biosynthesis of cholesterol and corticosteroid, metabolic oxidation of amino acids including tyrosine, collagen metabolism, conversion of folic acid to folinic acid, gastro-intestinal absorption of iron, transmission from the plasma protein-transferrin to the organ protein ferritin in spleen and bone marrow, cyclic nucleotide metabolism, stimulation of the phagocytic activity of leukocytes and the reticulo-endothelial system thereby enhancing the development resistance to infection, formation of antibodies and in cerebral metabolism [7, 12]. It is also reported in animal studies to have a protective action against acetaldehyde — the first metabolite of ethanol metabolism [8, 9]. It seems that vitamin C may protect the tissue against the toxic effects of acetaldehyde even in humans. Acetaldehyde is known to produce condensation products in liver and also in brain in combination with dopamine stimulating tetra- hydroisoquinoline (TIQ) derivatives which then act probably on the opiate deceptors in brain (endorphine and encephalins) and also with metabolites of serotonin producing beta carboline compounds — these are the probable biochemical basis of addiction and mental changes in alcoholics respectively [2, 3]. It is a conjecture that vitamin C might have a role here related to the development of addiction. Of course, this hypothesis needs to be confirmed.

Whether, in the absence of clinically recognizable symptoms of scurvy, low vitamin C levels are deleterious to man remans still unproven [1]. Man cannot synthesize L-ascorbic (vitamin C) and has to rely on an adequate dietary intake for its requirement [1]. As alcoholics are usually malnourished due to low dietary intake of nutrients including vitamins, their intestinal malabsorption and insufficient hepatic transformation to their respective active metabolites [11, 12], it is important to correct the underlying biochemical deficiency at the subcellular level in order to improve the chances of repair of physical damage in different organs inflicted by chronic ethanol ingestion.

It is, therefore, advisable to include polyvitamins including vitamin C in conventional detoxification therapy for ethanol withdrawal syndrome. In view of our observations, it is further suggested that more prolonged replenishment therapy with vitamin C preferably by intravenous route may be needed to normalize its blood level in some alcoholic patients in order to enhance repair of tissue damage caused by chronic ethanol ingestion. As a reducing agent, it is probably needed for utilization of other vitamins and nutrients as well. Polyvitamin deficiency seems to be a biochemical reality in chronic alcoholics.

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