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Vitamin A treatment for night blindness in primary biliary cirrhosis

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Abstract

Three patients with late stage primary biliary cirrhosis were found to have appreciable night blindness. Serum vitamin A concentrations were low in all three patients despite regular intramuscular supplementation in two. All patients responded dramatically to high dose oral supplementation, with full recovery of adaptation to dark and visual fields.

Oral rather than intramuscular vitamin A supplementation seems appropriate in the prevention of ocular complications of vitamin A deficiency in biliary cirrhosis.

Introduction

Vitamins that are soluble in fat are poorly absorbed in cholestatic liver disease, but routine measurements of vitamin A in 20 patients with primary biliary cirrhosis showed that three had pathologically low concentrations despite receiving intramuscular supplementation with vitamin A; two of these three patients had symptomatic night blindness. We report on these three patients.

Patients, methods, and results

We measured serum vitamin A concentrations by high pressure liquid chromatography¹ (normal range 0.7-3.1 $\mu\text{mol/l}$ (20-90 $\mu\text{g}/100\text{ ml}$)) and gave vitamin A supplements intramuscularly (Ro-A-Vit, Roche) or by mouth (vitamin A capsules, Macarthy's). We used a Goldmann perimeter to measure photopic function and an automated perimeter adaptometer to record the course and extent of cone and rod adaptation after an intense xenon flash.²

The table gives details of the patients when they presented initially with primary biliary cirrhosis.

Case 1—This woman presented in 1982 after noticing difficulty in driving at night. Her liver disease had worsened considerably (serum bilirubin concentration 660 $\mu\text{mol/l}$ (38.8 mg/100 ml)). Her visual field was constricted. Adaptation to the dark was absent (figure, curve A), and cone thresholds were raised by more than one log unit.

Dark adaptation curves (case 1) measured with flashing yellow-green test light ($\lambda=530\text{ nm}$) subtending a visual angle of 1° . Data points describe the log relative intensity needed for the test light to be just seen. The maximum intensity of the flash was designated as 0 log units; stimuli that were not seen at all are shown as +0.1. (Curve A, day 0; oral treatment started on day 4; curve B, day 11; treatment stopped on day 40; curve C, day 55; curve D, day 60; treatment restarted on day 61; curve E, day 74.)

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Details of liver disease in patients at time of initial presentation

	Case 1	Case 2	Case 3
Age (years)	58	54	61
Year of presentation	1978	1976	1976
Alkaline phosphatase activity (IU/l) (normal < 130)	520	585	690
Bilirubin ($\mu\text{mol/l}$) (normal < 17)	31	69	36
Mitochondrial antibody	Positive	Positive	Negative
Liver biopsy	Compatible	Compatible	Compatible
Treatment	Penicillamine; vitamin A 100 000 units a month intramuscularly; cholestyramine	Penicillamine; vitamin A 100 000 units a month intramuscularly (until May 1982); cholestyramine	Penicillamine; vitamin A 100 000 units a month intramuscularly; zinc sulphate; cholestyramine

Conversion: SI to traditional units—Bilirubin: $1 \mu\text{mol/l} \approx 58.5 \mu\text{g/100 ml}$.

Her serum vitamin A concentration was $<0.17 \mu\text{mol/l}$ ($5 \mu\text{g/100 ml}$). As dark adaptation and vitamin A concentration had not improved four days after an intramuscular injection of 100 000 U vitamin A, oral vitamin A 50 000 U daily was started. On day 7 the Goldmann field was normal and her serum vitamin A concentration was $0.7 \mu\text{mol/l}$ ($19 \mu\text{g/100 ml}$). Adaptation to dark showed normal cone thresholds, but rod function remained undetectable. On day 11 dark adaptation was within the normal range (figure, curve B) and the serum vitamin A concentration was $1 \mu\text{mol/l}$ ($28 \mu\text{g/100 ml}$). The dose of vitamin A was halved and continued for one month. On day 40 all tests gave normal results. Vitamin A supplements were then withdrawn, and by day 55, although she was asymptomatic, dark adaptation was slowed (figure, curve C) and serum vitamin A concentration was $0.5 \mu\text{mol/l}$ ($14 \mu\text{g/100 ml}$). On day 60 dark adaptation was worse (figure, curve D) and serum vitamin A concentration $0.3 \mu\text{mol/l}$ ($8 \mu\text{g/100 ml}$), although she remained asymptomatic. Vitamin A was restarted at 25 000 U daily, and by day 74 there was full recovery (figure, curve E), with serum vitamin A concentration $1.3 \mu\text{mol/l}$ ($37 \mu\text{g/100 ml}$).

Case 2—This woman presented in 1982 after noticing difficulty in seeing at night. Her liver disease had progressed (serum bilirubin concentration $259 \mu\text{mol/l}$ (15.2 mg/100 ml)). Her serum vitamin A concentration was $<0.17 \mu\text{mol/l}$ ($5 \mu\text{g/100 ml}$), and rod adaptation was grossly slowed (increase of 1.5 log units after 60 minutes). Oral vitamin A 50 000 U daily was started. On day 3 adaptation to dark was normal and her serum vitamin A concentration $1.0 \mu\text{mol/l}$ ($28 \mu\text{g/100 ml}$). The dose of vitamin A was halved, and visual function remained normal. Vitamin A concentrations subsequently remained over $1.05 \mu\text{mol/l}$ ($30 \mu\text{g/100 ml}$).

Case 3—This woman presented in 1982 with a bilirubin concentration of $375 \mu\text{mol/l}$ (22 mg/100 ml). Three weeks after an injection of 100 000 U vitamin A intramuscularly adaptation to dark was very slow (110 minutes). One week after a further injection of 100 000 U vitamin A adaptation to dark was worse and the serum vitamin A concentration was $0.2 \mu\text{mol/l}$ ($6 \mu\text{g/100 ml}$); a week later there was no rod function (vitamin A concentration $<0.17 \mu\text{mol/l}$ ($5 \mu\text{g/100 ml}$)). Oral supplements (25 000 U daily) were started. Seven days later (day 22) she was free of symptoms, although full adaptation to dark required 55 minutes (longer than expected in normal subjects). Her vitamin A concentration was $1.0 \mu\text{mol/l}$ ($29 \mu\text{g/100 ml}$). Further investigation could not be performed because of clinical deterioration.

Discussion

Vitamin A deficiency and slight night blindness commonly occur in primary biliary cirrhosis,³ but severe night blindness seems to occur only at the later stages of the disease. This deterioration may be due either to aggravation of a metabolic defect⁴ or to poor synthesis and release of retinol binding protein.⁵ The failure of intramuscular vitamin A to restore serum concentrations and visual function is surprising and unexplained, but oral vitamin A was effective.

We suggest that patients with advanced primary biliary cirrhosis should be given oral vitamin A. As absorption may be poor treatment should be regulated by monitoring of visual function and serum vitamin A concentrations to limit the risk of toxicity. An adequate initial dose is 25 000 U daily, although lower doses may be effective. Further investigations are needed to identify the prevalence of this serious and preventable complication of primary biliary cirrhosis and to establish the therapeutic range of vitamin A.

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ONE HUNDRED YEARS AGO Our Paris correspondent writes: The plague has broken out in the Ottoman territory, in the Bedra district. A sanitary inspection has ascertained that the plague has now attacked Bedra, Dyessan, Mendeli, and Zorbatia; also affecting the Arab tribes, wandering or settled, camped within this area. Bedra is about ten or fifteen hours' journey from Bagdad; but, at the present time, the inundation which is ravaging Mesopotamia renders communication laborious. The overflowing of the Tigris has converted Bagdad into an island, and couriers take eight days to go from Bagdad to Bedra and return. The danger of the plague spreading is centered in the north. Mendeli is already attacked. The road from Hanneguine to Bagdad serves as the high road, and is traversed by all the pilgrims journeying from Persia to Bagdad. The districts of Diz-foul and Chuster lie to the south-east. If the epidemic reach the Lower Tigris, towards Kout-el-mara, it would probably travel along the innumerable canals which cut up this territory, and would devastate Trak-Arabi southwards, as happened in 1875, when more than twenty thousand inhabitants perished. Should the plague travel to the port of Bassorah, the danger that would result is evident; also the necessity for framing protective measures. Egypt now exacts twenty-four hours' surveillance on all importations from this port, and has rigorously prohibited the importation of rags, or of clothes already worn. It is stated that the plague appeared at Bedra two months ago; but it may really date from several months back. There are no precise data, and no one knows. There is one thing certain: the plague is endemic at Trak-Arabi. Since the terrible epidemic of 1830, it has never been quite stamped out any more than in Kurdistan in Persia. There are yearly epidemics of plague in the Persian Kurdistan. It exists also in the Persian Khorassan, probably in Afghanistan, and certainly in a permanent form southwards of the Anglo-Indian Himalayas. Specialists believe that it exists in Yun-Nan, China. In all the epidemics at Trak-Arabi a diurnal temperature of 40° Centigrade made it disappear. The International Sanitary Council of Constantinople has taken sanitary measures. Dr. Lubiez, of Bagdad, Dr. Saad, of Hanneguine, and Pardálaki, of Bassorah, are on the spot. They tend the plague-stricken, aided by indigenous civil and military medical men. (*British Medical Journal* 1884;i:964.)