Vitamin B$_1$, B$_2$, B$_6$, and C status in hospital inpatients$^{1,2}$


ABSTRACT The status of vitamin B$_1$, B$_2$, B$_6$, and C was investigated in 656 hospital inpatients by means of a dietary interview, biochemical studies, and clinical investigation. The daily intake was lower than the Recommended Dietary Allowance for vitamin B$_1$ in 57%, B$_2$ in 47%, B$_6$ in 53%, and C in 9% of the patients; it was less than half the Recommended Dietary Allowance in 19, 12, 15, and 3%, respectively. A biochemical deficiency was observed in 25% of the patients for vitamin B$_1$, in 11% for B$_2$, in 25% for B$_6$, and in 14% for C. On the basis of the parameters selected for this study, the biochemical vitamin status, the dietary vitamin intake, and the clinical symptoms correlated significantly with each other except in the case of vitamin B$_6$. Am. J. Clin. Nutr. 33: 2595-2600, 1980.

The aim of this study was to determine the extent to which biochemical vitamin deficiencies occur among hospital inpatients in a developed, west European country (France), and their relationship to dietary vitamin intake, clinical symptoms, and individual disease.

Materials and methods

Over a period of 2 years, 656 inpatients (see Table 1) in the Hôpital de la Conception, Marseille, were investigated by means of a dietary interview, clinical examination, and biochemical studies. The control group consisted of subjects undergoing a check-up examination. Of the 241 female subjects, 17 were pregnant. The mean age was 47.3 years, mean weight 61.7 kg, and mean height 164 cm.

Dietary interview

The mean daily vitamin intake was calculated by means of a dietary questionnaire completed daily for the week preceding the clinical examination and taking the blood sample (1-11). Using the Recommended Dietary Allowances (RDA, National Research Council) (12), the subjects were divided into three vitamin intake groups: normal (>80% RDA), marginal (50-80% RDA), and deficient (<50% RDA) (see Table 2).

Clinical investigation

For each subject an 80-point anamnestic and clinical data sheet was completed, including especially data that concerned the disease state or that might reflect a vitamin deficiency. Weight, physical activity, general condition, consumption of alcohol and tobacco are among the other parameters recorded (see Table 3) (2, 13, 14).

Biochemical studies

A venous blood sample was taken from each subject into a heparinized tube on the final day of the dietary interview (between the 8th and the 14th day of the hospitalization). The sample was centrifuged, frozen immediately and dispatched for analysis.

Vitamin B$_1$ status was assessed by means of an enzyme activation test. The activity of the vitamin B$_1$ dependent enzyme, erythrocyte transketolase (ETK), was assessed before and after in vitro addition of the coenzyme, thiamin-pyrophosphate. The activation coefficient (activation coefficient of ETK is the ratio of the stimulated activity to the original activity; it is regarded as a measure of the vitamin B$_1$ status (15-21)). Vitamin B$_2$ was assessed using the in vitro stimulation of erythrocyte glutathione reductase activity by flavin adenine dinucleotide (aEGR) (22-25). Vitamin B$_6$ was assessed using the in vitro stimulation of erythrocyte glutamate oxaloacetate transaminase by pyridoxal 5'-phosphate (aEGOT) (26-28). The vitamin C status was assessed by measuring the plasma level of ascorbic and dehydroascorbic acids by a microfluorimetric method (29, 30). The average values for vitamin status are shown in Table 4: Values higher than 1.22 for ETK, 1.19 for aEGR, 1.69 for aEGOT (activation tests), and lower than 0.20 mg/100 ml for plasma ascorbic acid, were considered as deficient.

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Results

Vitamin intake

The incidence of normal, marginal, and deficient daily vitamin intake which was demonstrated by the dietary interview is shown in Table 5.

Clinical investigation

Certain clinical findings were especially common, namely: total tooth loss (16%), periodontosis (22%), caries (16%), ocular signs (18%), debility and anorexia (20 to 30%). See further comments in "Correlations" and "Discussion".

Biochemical studies

Some of the subjects had received vitamin therapy (namely B1: 65 subjects; B2: 32; B6: 75; C: 45), and some blood samples could not be analyzed for technical reasons (namely B1: 76; B2: 62; B6: 51; C: 35). These subjects have therefore been excluded; the results from the remainder (B1: 515; B2: 562; B6: 530; C: 576) are compiled in Table 6.

Correlations

The correlation (χ² test) between the biochemical vitamin status and the dietary vitamin intake was highly significant (P < 0.001) for vitamins B1, B2, and C; no correlation was found for vitamin B6 (see Table 7).

A correlation was found between the biochemical vitamin status and the number of malnutrition symptoms (list, see Table 8). There was an increased impairment of the vitamin status in those subjects with three or more symptoms, when compared (χ² test) with those with two or fewer symptoms: vitamin B1 (P = 0.1), vitamin B2 (0.02 < P < 0.05), and vitamin C (P < 0.001).

It is interesting to observe that there was a significantly higher number of patients (P < 0.001) with a plasma ascorbic acid between 0.20 and 0.40 mg/100 ml than of patients with a plasma level higher than 0.40 mg/100 ml, in the group having more than two malnutrition symptoms.

Symptoms were seldom found to be specific for a particular vitamin deficiency. Significant correlations (probably coincidental) were found only between a biochemical vitamin C deficiency and the presence of anorexia and conjunctival hypervascularization, and between a biochemical vitamin B1 deficiency and the presence of debility and conjunctival hypervascularization. A correlation was found between the daily vitamin intake and the number of symptoms. There was a significantly reduced intake of the vitamin B1, B2, and C in subjects with seven or more symptoms when compared with those with two to six symptoms (P < 0.001) in subjects with two to six symptoms when compared with those with one or no symptoms (P < 0.001).

A biochemical deficiency of vitamin B1, B2 (P < 0.05), or vitamin C (P < 0.001) was found more frequently in elderly, obese, or sedentary subjects. A vitamin C deficiency was found more frequently in the male than in the female subjects (P < 0.02).

An attempt to evaluate whether a corre-
tion exists between alcohol consumption and the vitamin status showed that, whereas subjects consuming more than 70 g of alcohol daily were significantly more vitamin C deficient than abstainers ($P < 0.01$), alcohol consumption had no apparent effect on the status of vitamin $B_1$, $B_2$, and $B_6$ in the present study. Nevertheless, it should be mentioned that the amount of alcohol ingested, as declared by the patient, is subject to reservation. Moreover in the group of alcoholics with evident clinical deterioration characterized by chronic liver disease, as described below, there was a higher incidence of vitamin $B_2$

TABLE 3
Clinical parameters used in study on nutritional status

| Body weight | Current or prior disease and/or surgery | Level of physical activity | Dietitian’s estimate of vitamin intake from food or supplement | Cardiovascular symptoms (e.g., blood pressure, pulse rate) | Hematology | Clinical symptoms which could evoke hypovitaminosis: General status (e.g., anorexia, asthenia, muscular cramps) | Neuropsychiatric (e.g., depression, polyneuritis) | Ophthalmological (e.g., photophobia, conjunctival hyperemia, vasculitis) | Dermatological (e.g., dermatitis, delayed cicatrization) | Oral symptoms (e.g., cheilosis, stomatitis) | Mucosal conditions (e.g., rhinitis, glossodynia) | Dental conditions (e.g., caries, parodontosis) | Genital conditions (e.g., impotence, testicular atrophy) | Extent of smoking habit and/or alcohol consumption | History of drug therapy |

TABLE 4
Average values for biochemical vitamin status

<table>
<thead>
<tr>
<th>Status</th>
<th>Vitamin $B_1$</th>
<th>Vitamin $B_2$</th>
<th>Vitamin $B_6$</th>
<th>Vitamin C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
</tr>
<tr>
<td>Marginal</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
</tr>
<tr>
<td>Deficient</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
<td>1.66–1.69</td>
</tr>
</tbody>
</table>

TABLE 5
Vitamin intake in hospital inpatients

<table>
<thead>
<tr>
<th>Vitamin Intake</th>
<th>Criteria</th>
<th>Vitamin $B_1$</th>
<th>Vitamin $B_2$</th>
<th>Vitamin $B_6$</th>
<th>Vitamin C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>$&gt;80%$ RDA</td>
<td>43 (283)</td>
<td>53 (347)</td>
<td>47 (307)</td>
<td>91 (594)</td>
</tr>
<tr>
<td>Marginal</td>
<td>50–80% RDA</td>
<td>38 (245)</td>
<td>35 (226)</td>
<td>38 (248)</td>
<td>6 (39)</td>
</tr>
<tr>
<td>Deficient</td>
<td>$&lt;50%$ RDA</td>
<td>19 (126)</td>
<td>12 (81)</td>
<td>15 (99)</td>
<td>3 (21)</td>
</tr>
</tbody>
</table>

* Percentage of patients.  

and $B_1$ deficiencies, although no case of Wernicke-Korsakof syndrome was seen.

Pathological groups

The group with hepatic disease had the most impaired vitamin status of the three groups (Table 8). Among the 67 patients with hepatic cirrhosis, there was a significantly lower incidence of biochemical vitamin $B_6$ deficiency in those with high serum transaminase levels ($P < 0.001$); this casts doubt on the validity of the EGOT-activation test as used in the present study (Table 8).

The group with gastrointestinal disease had an intermediate vitamin status between the hepatic and the diabetic groups, but it was too heterogeneous to allow any conclusions to be drawn. The diabetic patients had a better vitamin intake (is this related to a careful follow-up of these patients?) and status than the patients with hepatic or gastrointestinal disease. Vitamin deficiencies were more frequently observed in patients with maturity onset diabetes than in those with juvenile diabetes. No correlation was found between the biochemical status of vitamin $B_1$, $B_2$, $B_6$, and the presence of peripheral neuropathy, all of diabetic nature (Table 8).

Discussion

Methods used to assess vitamin status are often called in question without conclusive arguments pro or con. To our knowledge,
TABLE 7  
Correlation vitamin status/vitamin intake (no. of subjects)  

<table>
<thead>
<tr>
<th>Biochemical vitamin status</th>
<th>Vitamin B1</th>
<th>Vitamin B2</th>
<th>Vitamin B6</th>
<th>Vitamin C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N*</td>
<td>M*</td>
<td>D*</td>
<td>N*</td>
</tr>
<tr>
<td>Normal</td>
<td>151</td>
<td>145</td>
<td>49</td>
<td>289</td>
</tr>
<tr>
<td>Marginal</td>
<td>16</td>
<td>17</td>
<td>8</td>
<td>45</td>
</tr>
<tr>
<td>Deficient</td>
<td>45</td>
<td>42</td>
<td>22</td>
<td>25</td>
</tr>
</tbody>
</table>

* Normal.  + Marginal.  & Deficient.

TABLE 8  
Vitamin status according to the type of disease*  

<table>
<thead>
<tr>
<th></th>
<th>B1</th>
<th>B2</th>
<th>B6</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>M</td>
<td>D</td>
<td>N</td>
<td>M</td>
</tr>
<tr>
<td>Controls</td>
<td>62</td>
<td>9</td>
<td>12</td>
<td>29</td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>53</td>
<td>30</td>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>Other liver disease</td>
<td>68</td>
<td>23</td>
<td>0</td>
<td>32</td>
</tr>
<tr>
<td>Maturity onset</td>
<td>69</td>
<td>32</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Insulin-dependant</td>
<td>90</td>
<td>73</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

* Percentage; number of cases is shown in parentheses; N, normal; M, marginal; D, deficient.  +N.B. controls have been recruited among a population of individuals having no apparent disease, however, belonging to a large range of nutritional conditions.

Multipolar studies using simultaneously several types of investigation have not been developed extensively so far, although they are likely to increase the reliability of both the data obtained and the methods chosen. In the present study we compared three different sources of information—nutritional, biochemical, and clinical. Whenever a correlation exists, in one way or another, this may be regarded as a strong evidence that all three represent a reliable method of assessment.

The fact that the correlation was the strongest for vitamin C does not alter the concept according to which the plasma level of this vitamin is more representative of the recent intake than of cellular saturation. From the large number of patients investigated with this parameter here, it seems, however, that cases in which the recent intake is in contradiction with the storage are seldom likely to occur. In fact, low plasma vitamin C coincided not only with low intake but also with a higher number of malnutrition symptoms.

It is interesting to observe that the transketolase and the glutathione activation coefficients were in good agreement with the dietary levels of vitamin B1 and B2, respectively. In contrast, no correlation was found for vitamin B6 (see Table 7). For the assay of glutamate oxaloacetate transaminase we have used a two point automatic procedure according to P. Trinder and J. F. Kirkland adapted to erythrocytes (31). Despite the fact that there is some criticism of the use of glutamate oxaloacetate transaminase for assessing vitamin B6 status in humans (32) we have restricted ourselves to this method, since it was not possible to include any more tests in the trial. We hoped, therefore, to get at least some information on the applicability of the glutamate oxaloacetate transaminase test. Tentative guidelines to interpret the biochemical values are given in Table 3. We have derived the normal data of aETK, aEGR, and αEGOT from values found in a group of healthy young blood donors. By comparing the results of the tryptophan load test with the results of the transaminase test performed under the same conditions, in a group of children of 8 to 11 years, Buzina and Bru-
(32) have proposed a cutoff point of 2.0. In epidemiological studies, Ritzel and Brubacher (34) found in a normal healthy male population a decrease of the mean aEGOT-values with age, whereas in females the aEGOT-values increase. In the same population a highly significant negative correlation was found between mean aEGOT-values and alcohol consumption: in subgroups with high alcohol intake more often low values of aEGOT were found than in subgroups with a low alcohol intake (35). It seems therefore that even in a normal population the aEGOT value is not only a function of the vitamin B6 status but of a series of other factors.

Regarding the coincidence between the different vitamin deficiencies, an additional confirmation is gained that they are usually associated in humans. The correlation observed between the vitamin deficiencies and the malnutrition symptoms, on the other hand, suggest that in cases of deficiency, mostly marginal, a higher general morbidity, rather than a specific clinical deficiency syndrome is to be expected.

The present results seem to be in agreement with the observations reported by several authors such as Butterworth (36), Prevost and Butterworth (37), Bistrian et al. (38), Hill et al. (39), Weinsier et al. (40), on the questionable level of hospital nutrition. Although it was not possible to determine to what extent the nutritional conditions of the prehospitalization period contributed to the impaired vitamin status, it should be pointed out that a treatable deficiency was found in a large proportion of hospitalized patients.

Conclusions

As demonstrated by the biochemical studies, a marginal or deficient status of vitamin $B_1$, $B_6$, and $C$ occurs in about 30% of hospital inpatients in a country regarded as having good nutrition. The group particularly prone to vitamin deficiency was the group of patients with hepatic diseases and, to a lesser extent, those with gastroenterological disorders, the elderly, the obese, and those with a high alcohol intake.

As demonstrated by the dietary interview, a lowered vitamin intake was mainly responsible for the impaired vitamin $B_1$, $B_2$, and $C$ status. Good aEGOT results (normal in 71%) occurred in spite of a poor vitamin $B_6$ intake (marginal or deficient in 53%).

The classical signs of severe vitamin deficiency were seldom observed, but rather an increase in the number of nonspecific symptoms, suggesting that general morbidity and loss of appetite are related to the impairment of vitamin status.

A statistical correlation exists between the different types of investigation for vitamin $B_1$, $B_2$, and $C$, thus confirming the adequacy of the methods selected.

The authors are grateful to Prof. J. Vague of the Endocrinology Department (Hôpital de la Conception, Marseille) for allowing us to study his patients, and to Dr. Vuilleumier (Hoffmann-La Roche, Basle) for carrying out the vitamin assays.

References