B-6 vitamers and 4-pyridoxic acid in the plasma, erythrocytes, and urine of postmenopausal women1–3

Priscille G Massé, J Dennis Mahuren, Carole Tranchant, and Juliana Dosy

ABSTRACT

Background: Although many studies have reported reduced vitamin B-6 status with aging, little information is available about the specific effects of menopause.

Objective: We aimed to examine vitamin B-6 metabolism in premenopausal and early postmenopausal women.

Design: We examined dietary intake and vitamin B-6 metabolites in the plasma, erythrocytes, and urine of 30 premenopausal women (x ± SD age: 41.9 ± 4.8 y) and 30 women (aged 54.0 ± 3.8 y) who were 4.0 ± 1.4 y past menopause.

Results: Vitamin B-6 intake in the postmenopausal group (1.97 ± 0.40 mg/d) was significantly greater than that in the premenopausal group (1.63 ± 0.50 mg/d). Plasma pyridoxal phosphate (PLP) and pyridoxal concentrations and erythrocyte PLP, pyridoxal, and pyridoxamine phosphate concentrations were in the normal range in both groups and did not differ significantly between the 2 groups. Plasma and erythrocyte 4-pyridoxic acid (4-PA) concentrations were significantly higher in the postmenopausal group than in the premenopausal group, which may have been due at least partly to the slightly higher vitamin B-6 intake of the former group. Erythrocyte 4-PA was correlated (r = −0.37, P < 0.01) with serum estradiol in both groups. Urinary 4-PA did not differ significantly between the 2 groups. The serum phosphate concentration was higher in the postmenopausal group than in the premenopausal group, and it was correlated (r = 0.40, P < 0.01) with plasma PLP. Inhibition of alkaline phosphatase by the increased phosphate may help to increase plasma PLP.

Conclusion: Menopause may not necessarily be associated with a decrease in vitamin B-6 status. Am J Clin Nutr 2004;80:946–51.

KEY WORDS Vitamin B-6, menopause, aging

INTRODUCTION

The quantitative determination of the plasma and erythrocyte content of vitamin B-6 (pyridoxine) has been challenging because of the existence in vivo of multiple forms of this vitamin. In effect, this vitamin is metabolized in humans to several vitamers and is excreted in the urine primarily as 4-pyridoxic acid (4-PA). In persons consuming a self-selected, nonvegetarian diet, pyridoxal 5'-phosphate (PLP), pyridoxal, and 4-PA are the major vitamin B-6 compounds found in blood plasma (1). Plasma PLP concentration has been the most frequently used direct measure of vitamin B-6 status (2). After acknowledging that studies of older persons have been quite limited, the Food and Nutrition Board concluded that the estimated average requirement for vitamin B-6 is increased in the elderly, and the recommended dietary allowance for women aged >50 y was set at 1.5 mg/d (2). The elderly frequently have low vitamin B-6 status (3, 4).

In addition to estrogen deficiency, postmenopausal women experience a panoply of other hormonal and metabolic events. The most documented one in recent years has been bone mineral loss (osteoopenia), which leads to osteoporosis (low bone density) and eventually bone fracture. Vitamin B-6 deficiency can modulate bone metabolism. Studies in chicks and rats showed the essential role of vitamin B-6 in the structural integrity of collagen molecules in connective tissue, biomechanical properties (strength), and healing of bone whose organic matrix is composed primarily of collagen (5–7). Vitamin B-6–deficient bone is more fragile because of osteoporosis-type lesions and uncoupling (ie, there is too much resorption for the newly formed bone) (8, 9). Reynolds et al (10) reported that half of their hip fracture patients were vitamin B-6 deficient (plasma PLP: <13 nmol/L). Whether low PLP is a causal factor or a consequence of these processes is unknown.

Alkaline phosphatase (ALP), an enzyme located on the external surface of cells and in plasma, influences the metabolism of both bone and vitamin B-6. One function of ALP is to hydrolyze PLP to pyridoxal, which allows uptake into cells. Reduced ALP activity in hypophosphatasia results in significant elevation of plasma PLP concentrations (11). Under physiologic conditions in plasma, hydrolysis of PLP by ALP is influenced by the concentration of inorganic phosphate, which is an inhibitor of ALP (12). Reduced inhibition of ALP activity might contribute to the low PLP values observed in persons with hypophosphatemic rickets (13). These effects of physiologic concentrations of inorganic phosphate on ALP activity are seen only when the assay is assayed in undiluted plasma. The dilution of plasma in clinical assays reduces the phosphate concentrations, which minimizes the inhibitory effects of phosphate.

In addition, Reynolds et al (10) proposed that low vitamin B-6 in hip fracture patients might reduce the activity of ornithine decarboxylase, which produces putrescine, a metabolic regulator.
The rationale for the present study was threefold: 1) postmenopausal women are at risk of both cardiovascular disease and osteoporosis, which may be aggravated by inadequate vitamin B-6 status; 2) over the last decade or so, a novel function of this vitamin has emerged as a factor that modulates the actions of steroid and other hormones (14); and 3) vitamin B-6 metabolism in menopause has not yet been thoroughly studied. It thus appears well justified and opportune to verify whether this metabolism is impaired in the context of the steroid hormone (estrogen) depletion that characterizes the menopausal state.

SUBJECTS AND METHODS

Subjects

More than 200 women from a homogeneous white population living in an urban area of Canada responded to various kinds of advertisements—media, conferences, posters in public places, and E-mails to the university and the local hospital community. Women who were postmenopausal for 3 to 5 y and premenopausal women (aged 30–45 y) with regular menstruation were eligible to participate in the study, provided they fulfilled the other selection criteria. Participants were required to be non-smokers, active, nonobese, and in subjectively good health; to have no history of renal, hepatic, or vascular disease; to have taken no medication or vitamin B supplementation on a regular basis for the previous 12 mo and not to be currently taking either oral contraceptive (premenopausal group) or hormone replacement therapy (postmenopausal group); and not to be following a special or vegetarian diet. An initial screening by telephone excluded ineligible women.

The 60 meticulously selected subjects (30 postmenopausal, 30 premenopausal) attended an information meeting and gave written informed consent. All were asked to complete a general questionnaire and to keep a 3-d food diary, after which blood and vitamin B-6 concentrations in serum. Blood was allowed to clot for 1 h at 37 °C and then centrifuged at 2000 × g for 10 min. An enzyme immunoassay (Abbott IMX; Abbott Laboratories, Chicago) was used for the analytic determination of serum estradiol concentrations. Folate and cobalamin concentrations were determined by using immunoassays (Advia Centaur; Bayer Corporation, Tarrytown, NY). Hemoglobin (18) and total serum protein (19) were also analyzed.

Biochemical analyses

After a 10–12-h fast, whole blood was collected by venipuncture in the morning: in premenopausal subjects, this was done during the ovulation phase of the spontaneous menstrual cycle (from day 12 to day 16 after the first day of the most recent menses), in the other women, it was done at any time. Evacuated 10-mL tubes were used for collecting antecubital venous samples for assay of the concentrations of estradiol, folate, and cobalamin (vitamin B-12) in serum. Blood was allowed to clot for 1 h at 37 °C and then centrifuged at 2000 × g for 4 °C for 10 min. An enzyme immunoassay (Abbott IMX; Abbott Laboratories, Chicago) was used for the analytic determination of serum estradiol concentrations. Folate and cobalamin concentrations were determined by using immunoassays (Advia Centaur; Bayer Corporation, Tarrytown, NY). Hemoglobin (18) and total serum protein (19) were also analyzed.

Vitamin B-6 status and evaluation of cofactors

The 10-mL tube containing heparin into which the blood sample was drawn was wrapped in aluminum paper to protect its vitamin B-6 content from light during transportation from the outpatient clinic to the laboratories, after which it was centrifuged immediately (within 15 min) at low speed (1000 × g at 4 °C for 10 min) to obtain the plasma. Plasma and erythrocyte B-6 vitamer and 4-PA concentrations in urine were measured by using cation-exchange HPLC (20). The evaluation of vitamin B-6 status included the measurement of the nonphosphorylated pyridoxal metabolite and PLP and the assessment of total vitamin B-6 aldehydes (PLP + pyridoxal) to allow the consideration of complex interactions between ALP and inorganic phosphate (12, 21); these measurements were performed by using a Metra assay kit (Quidel, Mountain View, CA) for ALP and a routine autoanalyzer method (Vitros Slides; Johnson & Johnson Clinical Diagnostics, Rochester, NY) for inorganic phosphate. The concentration of creatinine was measured in urine specimens obtained from subjects in the fasting state between 0800 and 1000 on the day of the blood test by using a colorimetric technique based on the Metra assay. Urinary 4-PA was expressed per millimole of creatinine.

Statistical analyses

INSTAT software (version 2.0; GraphPad Software, San Diego) was used for statistical analysis. All data are reported as means ± SDs. The significance of differences between mean values of normally distributed data was then determined by using a two-tailed unpaired Student’s t test. The Mann-Whitney test was used for plasma PLP and pyridoxal, which were not normally

Anthropometric measurements

Height was measured with the use of a portable vertical measuring board and recorded to the nearest 0.1 cm. A standard balance-beam scale was used for measuring body weight, which was recorded to the nearest 0.5 kg. Subjects were weighed while wearing indoor clothing but no shoes. Body mass index (BMI; in kg/m²) was calculated from measured weight and height.

Waist and hip circumferences were measured to the nearest 0.1 cm by using a flexible, plastic-coated measuring tape. For waist measurement, the tape was applied around the narrowest part of the torso, between the ribs and iliac crest. For hip measurement, it was applied around the maximum posterior extension of the buttocks (15). Fat-free lean tissue mass was assessed according to Lee et al (16). Their anthropometric prediction model, the first developed in vivo by using state-of-the art body-composition methods, is based on corrected muscle circumference of the arm, thigh, and calf. The limb circumferences were corrected for subcutaneous adipose tissue thickness.

Dietetic evaluation

To estimate energy and nutrient intakes, all subjects were asked to keep a food record for 3 nonconsecutive days including one weekend day. They were instructed to maintain their usual food intakes on the recording days and to record all foods and beverages immediately after consumption. For each subject, the energy and pertinent nutrient intakes were determined by using FOOD ANALYST PLUS software [version 2.04 (CD-ROM); Hopkins Technology, Hopkins, MN], which contained the latest US Department of Agriculture nutrient database. A 3-d mean was calculated for each dietary nutrient to compare the 2 groups and to assess nutritional adequacy by comparison with current nutrition recommendations (2, 17). The vitamin B-6 intake has been expressed in terms of absolute units (mg) and per gram of protein consumed.

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TABLE 1
Descriptive and basic anthropometric characteristics of postmenopausal and premenopausal women

<table>
<thead>
<tr>
<th></th>
<th>Premenopausal group</th>
<th>Postmenopausal group</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 30)</td>
<td>(n = 30)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>41.9 ± 4.8</td>
<td>54.0 ± 3.8</td>
<td></td>
</tr>
<tr>
<td>Time since menopause</td>
<td>NA</td>
<td>4.0 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66.2 ± 11.4</td>
<td>66.6 ± 8.1</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.1 ± 4.0</td>
<td>25.5 ± 3.0</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.77 ± 0.08</td>
<td>0.78 ± 0.05</td>
<td>&lt;0.80–0.82</td>
</tr>
<tr>
<td>Lean tissue mass (kg)</td>
<td>42.5 ± 3.7</td>
<td>38.3 ± 4.1</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> NA, not applicable.
<sup>2</sup> ± SD (all such values).
<sup>3</sup> Significantly different from premenopausal group: <sup>4</sup> P < 0.0001, <sup>5</sup> P < 0.001.
<sup>6</sup> From reference 23.
<sup>7</sup> From reference 24.

TABLE 2
Pertinent biochemical data for postmenopausal and premenopausal women

<table>
<thead>
<tr>
<th></th>
<th>Premenopausal group</th>
<th>Postmenopausal group</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 30)</td>
<td>(n = 30)</td>
<td></td>
</tr>
<tr>
<td>Serum estradiol (pmol/L)</td>
<td>649 ± 273</td>
<td>134 ± 91</td>
<td>&lt;217</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>13.5 ± 1.7</td>
<td>14.4 ± 1.3</td>
<td>12–16</td>
</tr>
<tr>
<td>Plasma protein (g/L)</td>
<td>7.0 ± 0.6</td>
<td>7.0 ± 0.4</td>
<td>5–8</td>
</tr>
<tr>
<td>Serum cobalamin (pmol/L)</td>
<td>273 ± 100</td>
<td>312 ± 127</td>
<td>147–542</td>
</tr>
<tr>
<td>Serum folate (nmol/L)</td>
<td>26.7 ± 5.8</td>
<td>25.6 ± 5.7</td>
<td>6.3–30.6</td>
</tr>
<tr>
<td>Plasma phosphate (nmol/L)</td>
<td>1.01 ± 0.12</td>
<td>1.11 ± 0.13</td>
<td>0.7–1.3</td>
</tr>
<tr>
<td>Plasma alkaline phosphatase (µmol/min/L)</td>
<td>7.2 ± 3.5</td>
<td>6.3 ± 2.4</td>
<td></td>
</tr>
<tr>
<td>Ratio of plasma 4-pyridoxic acid (nmol/L) to pyridoxal (nmol/L)</td>
<td>1.17 ± 0.49</td>
<td>1.31 ± 0.59</td>
<td></td>
</tr>
<tr>
<td>Ratio of erythrocyte 4-pyridoxic acid (nmol/L) to pyridoxal (nmol/L)</td>
<td>0.38 ± 0.29</td>
<td>0.67 ± 0.37</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Determined in our laboratory.
<sup>2</sup> ± SD (all such values).
<sup>3</sup> Significantly different from premenopausal group: <sup>4</sup> P < 0.0001, <sup>5</sup> P < 0.001.

RESULTS

Descriptive data

Sixty women met the inclusion criteria. They came from the same geographic area and had similar socioeconomic and educational backgrounds. They reported having no health problems and using no drugs or supplements on a regular basis. Descriptive and basic anthropometric characteristics of the 2 groups of women are summarized in Table 1.

The last menstruation in the postmenopausal group was reported to be 4.8 ± 3.4 y previously. The 2 groups of women were similarly active, healthy with desirable body weight, and not at risk of cardiovascular disease as judged by BMI and waist-hip ratio (Table 1). Their general nutritional status as assessed by the concentrations of hemoglobin, plasma protein, cobalamin, and folate in blood was adequate (Table 2).

Postmenopausal status was confirmed by serum estrogen concentrations < 217 pmol/L. Plasma ALP activity and plasma PLP concentration in both groups did not differ significantly. However, inorganic phosphate concentrations in postmenopausal women were significantly greater than those in premenopausal women.

At first glance, diets in both groups are comparable, as judged by the contribution (%) of energy macronutrients to total energy and vitamin intakes (Table 3). The dietary intakes were nutritionally adequate in both groups. The vitamin B-6 content of the postmenopausal women’s diet was superior to that of the premenopausal women’s diet. Nutritional recommendations for proteins and total essential and sulfur amino acids were also fulfilled in both groups.

Vitamin B-6 metabolism and correlates

The 4-PA concentrations were significantly higher in the plasma and erythrocytes of the postmenopausal women than in those of the premenopausal women (Figure 1). The concentration in erythrocytes had almost doubled without a noticeable change in other vitamins. Erythrocyte 4-PA was correlated with serum estradiol. The ratio of erythrocyte 4-PA to pyridoxal in the postmenopausal women was almost twice that in the premenopausal women (Table 2). PLP was the predominant B-6 vitamer in plasma and erythrocytes (Figure 1).

Plasma PLP concentrations were within normal limits in both groups and did not differ significantly between groups (Figure 1). Plasma total B-6 aldehydes, which may be a better index of vitamin B-6 nutritional status than is PLP alone, were significantly greater in the postmenopausal group. As noted above, the
postmenopausal group consumed more vitamin B-6 from their diet than did the premenopausal group (Table 3). However, no significant correlation was found between dietary intakes and the concentrations of plasma PLP or plasma total B-6 aldehydes (Table 4). The only significant correlation with dietary intake was that with erythrocyte 4-PA. Table 4 also shows other pertinent correlations, such as the expected positive relations between pyridoxal and 4-PA in plasma and in erythrocytes. A significant negative association was found between lean tissue mass and plasma PLP but not between lean tissue mass and erythrocyte PLP or PMP. Plasma PLP was positively correlated with plasma phosphate.

DISCUSSION

This report specifically compares premenopausal and postmenopausal women by using a statistically valid sample size according to rigorous inclusion criteria. The women’s general nutritional status was adequate. Menopausal status was confirmed biochemically, and blood samples were collected at the same time of the menstrual cycle for each subject in the premenopausal (control) group. Mean dietary protein, essential amino acid, and vitamin B-6 intakes of both groups were superior to the nutritional recommendations, including the more recent suggestion of an intake of 0.02 mg vitamin B-6/g protein (26, 27). Mean plasma PLP concentrations were indicative of vitamin B-6 adequacy, regardless of whether <30 nmol/L (28) or <20 nmol/L (2) was used as the “cutoff” for inadequacy. The values also fell within the range of 20–60 nmol/L reported by Hamfelt et al (29) for healthy middle-aged people. The significant elevations of 4-PA in the plasma and erythrocytes of the postmenopausal women probably reflect the higher dietary intake of that group in comparison with the premenopausal women. The significant correlations between 4-PA and pyridoxal in plasma and erythrocytes are not surprising because 4-PA is produced by the oxidation of pyridoxal. As observed here, erythrocyte PLP concentrations in persons consuming normal diets are usually similar to or lower than those of plasma PLP, but the former increase to much higher values than do those of plasma PLP in subjects taking supplements (2).

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Average (3 d) daily energy and pertinent dietary nutrient intakes of postmenopausal and premenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Premenopausal group (n = 30)</td>
</tr>
<tr>
<td>Energy (MJ)</td>
<td>8.1 ± 2.82 ^2</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>81.8 ± 22.9</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>16.2 ± 4.5</td>
</tr>
<tr>
<td>Essential amino acids (g)</td>
<td>25.7 ± 11.4</td>
</tr>
<tr>
<td>Sulfur amino acids (g)</td>
<td>2.00 ± 0.77</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>233.5 ± 81.2</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>46.2 ± 16.1</td>
</tr>
<tr>
<td>Pyridoxine (mg)</td>
<td>1.63 ± 0.50</td>
</tr>
<tr>
<td>(µg/g protein) ^6</td>
<td>20.6 ± 6.1</td>
</tr>
<tr>
<td>Riboflavin (mg)</td>
<td>1.7 ± 0.4</td>
</tr>
<tr>
<td>Cobalamin (µg)</td>
<td>4.51 ± 3.01</td>
</tr>
<tr>
<td>Folate (µg)</td>
<td>222.2 ± 72.9</td>
</tr>
</tbody>
</table>

^1 Dietary reference intakes for energy, carbohydrate, and protein were from reference 17; those for riboflavin, vitamin B-6, folate, and vitamin B-12 were from reference 2.
^2 ± SD (all such values).
^3 Postmenopausal/premenopausal (all such values).
^4 Significantly different from premenopausal group, P < 0.01.
^5 Recommended dietary allowance (25).

VITAMIN B-6 METABOLISM IN MENOPAUSE

FIGURE 1. Vitamin B-6 metabolism in the urine, erythrocytes, and plasma of postmenopausal women (n = 30, ■) and premenopausal women (control; n = 30, □). PLP, pyridoxal phosphate; PL, pyridoxal; total vitamin B-6 aldehydes, PLP + PL; PMP, pyridoxamine phosphate; 4-PA, 4-pyridoxic acid. Vitamin B-6 compounds other than 4-PA were not detected in the routine HPLC procedure used. *P < 0.02, **P < 0.0001.
Studies of the effect of age on plasma PLP have yielded conflicting results. Hamfelt and Söderhjelm (29) reviewed several reports indicating that P-PLP declined with age. Pannemans et al (30) found markedly lower plasma PLP concentrations in elderly (x ± SD age: 70 ± 1 y) subjects than in younger (aged 29 ± 1 y) adults consuming the same diet. Most of the previous studies on the effects of aging used a wider age range and older subjects than are used in the present study. The participants in the study by Bor et al (31) ranged in age from 38 to 80 y. Those investigators found a tendency for a decrease in the plasma PLP concentration and an increase in the plasma 4-PA concentration. Studies of menopausal age are very scarce and controversial. In a small group (n = 8) of postmenopausal women (aged 55.3 ± 4.0 y), Lee and Leklem (32) reported significantly lower plasma PLP values and slightly higher urinary 4-PA concentrations than were found in 5 young women (aged 24.4 ± 3.2 y) when a normal diet was consumed. The present study is in agreement with Wright et al (33), who found a tendency for plasma PLP concentrations to increase with age. Leinert et al (34) also found that this B-6 vitamer increased after menopause. Those investigators attributed the change to hormonal influences and not to diet, and they referred to studies on oral contraceptives to support their thesis.

As was the case with studies of the effects of aging on vitamin B-6 metabolism, attempts to correlate various vitamin B-6 metabolites with dietary intake have yielded conflicting results. Whereas it is established that even small changes in vitamin B-6 intakes will increase plasma PLP concentrations under well-controlled conditions (35), population surveys do not always find a significant correlation between vitamin B-6 intakes and plasma PLP concentrations. This lack of correlation probably reflects a relatively narrow range of intakes, errors in estimates of intakes, or failure to consider the complex interactions between ALP, inorganic phosphate, and plasma PLP (12). Although Bates et al (36) found a strong correlation between plasma PLP or 4-PA concentrations and vitamin B-6 intakes in subjects >65 y old, their data show only a small change in plasma PLP concentrations as intakes increase from 1 to 2 mg/d. In view of the errors involved in estimating dietary intakes, it is obvious why population studies might fail to detect a correlation between dietary intakes and plasma PLP concentrations if the range of intakes is limited. In the present study, only erythrocyte 4-PA concentrations were correlated with dietary vitamin B-6 intakes.

There also was a significant negative correlation between serum estradiol and erythrocyte 4-PA concentrations, which could simply reflect the higher dietary intakes of the postmenopausal (low-estrogen) group. However, metabolic changes may also be a factor. Urinary 4-PA increased in aged rats, particularly females, in parallel with increases in liver pyridoxal oxidase and pyridoxal dehydrogenase activity (37). Muscle PLP concentrations in the rats decreased along with a decrease in glycogen phosphorylase. Because muscle represents the largest vitamin B-6 pool in the body, Bode et al (37) suggested that the increased 4-PA excretion might represent a reduced vitamin B-6 requirement. In the aged rats, PLP decreased in both muscle and plasma. In the current study, a negative correlation was found between plasma PLP concentrations and lean muscle mass. As observed in both the present study and previous investigations (38–41), menopause is associated with a decrease in lean tissue mass. According to Wang et al (39), the highest rate of lean tissue mass loss, or sarcopenia, occurs during the earliest years of menopause, concomitant with a marked decrease in total bone mass. Bone mineral loss in postmenopausal women in the present study, as assessed by reduced bone mineral density, has recently been reported (42). The elevation of serum inorganic phosphate found in postmenopausal women that is inherent to bone loss (ie, resorption) (43–45), which is a consequence of estrogen deficiency, could also contribute to increased plasma PLP concentrations because plasma concentrations of inorganic phosphate may inhibit ALP under physiologic conditions. This is true even though the usual in vitro clinical assays using diluted plasma may not detect that inhibition (12). The possible interaction between PLP and inorganic phosphate is supported by the significant positive correlation found between these 2 variables.

In conclusion, the onset of menopause is not necessarily associated with a decrease in vitamin B-6 status. The decrease in indicators seen in other studies involving a wider age range may

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Table 4

Pertinent correlations between variables adjusted for age difference

<table>
<thead>
<tr>
<th>Diet</th>
<th>Lean tissue mass</th>
<th>Serum estradiol</th>
<th>Plasma Erythrocyte</th>
<th>Plasma alkaline phosphatase</th>
<th>Plasma phosphate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLP</td>
<td>0.11</td>
<td>−0.30</td>
<td>0.12</td>
<td>−0.08</td>
<td>0.40</td>
</tr>
<tr>
<td>Pyridoxal</td>
<td>0.20</td>
<td>0.02</td>
<td>0.33</td>
<td>−0.18</td>
<td>0.12</td>
</tr>
<tr>
<td>4-Pyridoxic acid</td>
<td>0.04</td>
<td>−0.12</td>
<td>0.18</td>
<td>−0.37</td>
<td></td>
</tr>
<tr>
<td>B-6 aldehydes</td>
<td>0.09</td>
<td>−0.26</td>
<td>0.26</td>
<td>−0.18</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte PLP</td>
<td>0.08</td>
<td>−0.24</td>
<td>0.37</td>
<td>−0.37</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte PMP</td>
<td>0.13</td>
<td>−0.12</td>
<td>0.18</td>
<td>−0.37</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte pyridoxal</td>
<td>0.20</td>
<td>0.02</td>
<td>0.33</td>
<td>−0.37</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte vitamin B-6 aldehydes</td>
<td>0.18</td>
<td>0.26</td>
<td>0.37</td>
<td>−0.37</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte 4-pyridoxic acid</td>
<td>0.10</td>
<td>0.20</td>
<td>0.33</td>
<td>−0.37</td>
<td></td>
</tr>
</tbody>
</table>

1 PLP, pyridoxal phosphate; PMP, pyridoxamine phosphate; vitamin B-6 aldehydes, PLP + pyridoxal.
2 P < 0.05.
3 P < 0.01.
VITAMIN B-6 METABOLISM IN MENOPAUSE

reflect dietary and metabolic changes associated with aging in
general, but not necessarily those related to menopause.

We gratefully acknowledge the assistance of the staff of Hôpital GL
Dumont Outpatient Clinic and Laboratories (Moncton, Canada). We thank
Rejeanne Dallaire for her valuable help with the diet computer analysis.
We greatly appreciate the full cooperation of the subjects because, without them,
this study could not have been carried out.

PGM planned the study concept and design, gathered and summarized all
data into tables and figures, interpreted the data, and wrote the manuscript.
JD contributed to the preparation of the materials and recruitment of subjects,
centrifuged and stored blood samples, and collected dietetic and anthropo-
metric data. CCT conducted the literature research, computed data, per-
formed statistical analyses, and helped edit the manuscript. JDM provided the
vitamin B-6 data. None of the authors had any conflicts of interest.

REFERENCES

1. Lumeng L, Liu A, Li TK. Plasma content of B-6 vitamers and its relationship

2. Vitamin B-6. Standing Committee on the Scientific Evaluation of Di-
etary Reference Intakes. Dietary Reference Intakes: Thiamin, Ribofla-
vin, Niacin, Vitamin B-6, Folate, Vitamin B-12, Pantothenic Acid, Bi-
150–95.

status of elderly men and women according to place of residence.


5. Massé PG, Colombos VE, Gerber F, Howell DS, Weiser H. Morphologi-
cal abnormalities in vitamin B-6 deficient tarsometatarsal chick carti-

6. Massé PG, Rimnac CM, Yamauchi M. Pyridoxine deficiency affects

7. Dodds RA, Dunham J, Bitskensky L, Chayen J. Abnormalities in fracture

8. Massé PG, Prüitzer KPH, Mendes MG, Boskey AL, Weiser H. Vitamin B₆
deficiency experimentally-induced bone and joint disorder: microscopic,

9. Benke PJ, Fleshwood HL, Pitot HC, Osteoporotic bone disease in the

10. Reynolds TM, Marshall PD, Brain AM. Hip fracture patients may be
vitamin B-6 deficient. Controlled study of serum pyridoxal 5'-phos-

11. Whyte MP, Mahuren JD, Vrabel LA, Coburn SP. Markedly increased

12. Coburn SP, Mahuren JD, Jain M, Zubovic Y, Wortsman J. Alkaline phos-
thosphate (EC:3.1.3.1) in serum is inhibited by physiological concentrations of

13. Reynolds RD, Lorenc RS, Wieczorek E, Pronicka E. Extremely low

14. Tully DB, Allgood VE, Cidlowski JA. Modulation of steroid receptor-

Lohman TG, Roche AF, Martorell R, eds. Anthropometric standardiza-


54. Leinert J, Simon I, Hotzel D. Methods and their evaluation for the estimation

61. Leinert J, Simon I, Hotzel D. Methods and their evaluation for the estimation

70. Leklem JE, Miller LT. The metabolism of small doses of vitamin B-6 in men. J

75. Massé PG, Vielma U, Rice ME, et al. The effects of menopause on
pyridoxal 5'-phosphate deficiency: a cross-sectional study of 655 healthy

80. Massé PG, Vielmeier JP, Weiser H. Pyridoxine status as assessed by the
concentration of B-6 aldehyde vitamers. Int J Vitam Nutr Res 1989:

101. Massé PG, Vielmeier JP, Weiser H. Pyridoxine status as assessed by the
concentration of B-6 aldehyde vitamers. Int J Vitam Nutr Res 1989:

107. Meisler SG, Jilkes SR, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

110. Meisler SG, Jilkes SR, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

114. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

118. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

122. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

126. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

130. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

134. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

138. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

142. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

146. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy

150. Schmidt P, Haufroid V, and the Menopause Study Group. The effects of
menopause on vitamin B-6 status: a cross-sectional study of 655 healthy