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# Water-Soluble Vitamin Levels and Supplementation in Chronic Online Hemodiafiltration Patients

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**Introduction:** Supplementation of water-soluble vitamins is a common practice in hemodialysis patients, but dosages are largely based on conventional hemodialysis techniques. The aim of this study was to assess the status of water-soluble vitamins in patients on hemodiafiltration (HDF), and attempt to determine optimal dose of vitamin supplements.

**Methods:** This monocentric study included 40 patients on thrice-weekly chronic HDF. At baseline, all patients received 2 tablets of Dialvit containing B and C vitamins after each dialysis session. Predialysis samples of B and C vitamins were measured in both blood ($n = 40$) and a subgroup of dialysate ($n = 6$) samples. A second blood sample was obtained in 24 patients 3 months after dose adjustment of the vitamin supplement.

**Results:** At baseline, B-vitamin levels were high with, respectively, 0.4%, 10.0%, and 89.6% of patients in the low, normal, and high reference range. For vitamin C, most patients were in the normal range (5.0%, 82.5%, and 12.5% in low, normal, and high reference range). Three months after dose reduction, B vitamin levels decreased but stayed mostly at or above the normal range (1.4%, 25.7%, 72.9% in low, normal, and high reference range). Three patients (12.5%) developed vitamin C deficiency on low-dose substititon.

**Conclusion:** This study shows that the levels of most vitamins are above the normal range in patients on HDF receiving a classic dose of vitamin supplements, vitamin C excepted. Our study suggests that the classic dose of postdialysis vitamin B supplements may be reduced.

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Hemodialysis is a life-saving technique that removes uremic toxins and restores acid-base, fluid, and electrolyte homeostasis. Worldwide, the past decade has witnessed a trend toward increased use of high-flux filters and HDF. This technique is more effective in the removal of middle-sized molecules than conventional hemodialysis (CHD), and possibly improves survival if large convective volumes are achieved.[1] However, HDF may lead to increased losses of essential substances such as albumin and micronutrients.[2] Hemodialysis patients are also at risk for water-soluble vitamin deficiencies. Indeed, due to their low molecular weight (<1 kDa), losses of such vitamins may occur during hemodialysis sessions. Besides, absolute and functional vitamin deficiencies can result from malnutrition, diminished gastrointestinal absorption, and abnormal renal metabolism in the hemodialysis population.[3,4] Water-soluble vitamin supplementation has therefore become a common practice in chronic hemodialysis patients.[5] Nevertheless, prophylactic vitamin supplementation is heterogeneous within and across countries,[6] ranging from 4% in the United Kingdom to 72% in the United States, possibly because official guidelines are lacking or contradictive (Kidney Disease Improving Global Outcomes,[7] Kidney Disease Outcomes Quality Initiative,[8] Best Practice guidelines[3]). If vitamins are provided during dialysis sessions, it is usually a combination of B-group vitamins and vitamin C (ascorbic acid). Moreover, vitamin supplementation doses and schedules are largely based on studies performed in patients on CHD.[9] Despite a few studies on vitamins C, B9 (folic acid), and vitamin B12

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(cobalamin),[10–15] there is a lack of knowledge specific to HDF-associated losses of water-soluble vitamins. Although water-soluble vitamins are relatively small molecular weight molecules, losses are possibly higher in HDF as compared with CHD. Morena *et al.*[14] reported a reduction in circulating vitamin C of 45% (8–230 mg) and 30% per session in HDF and CHD, respectively. Diffusive transport was responsible for two-thirds, whereas convection accounted for up to 30% of the loss of vitamin C. As the convective volume was relatively low (maximal 15 liters) compared with current practice, one may expect even greater losses in the clinical setting. Besides, water-soluble vitamins are partly bound to albumin,[16] and albumin losses occur more often in HDF.[2] To the best of our knowledge, there are no data concerning dialysate losses of vitamins B2 (riboflavin), B3 (niacin), B5 (pantothenic acid), B6 (pyridoxine), and B8 (biotine or B7) in HDF. As a consequence, the optimal vitamin supplementation regimen for patients with chronic HDF remains largely unknown.

The aims of this study were therefore (i) to assess the status of water-soluble vitamins in patients with chronic hemodialysis receiving HDF and vitamin supplements, (ii) to quantify vitamin losses during HDF, and (iii) to assess what could be the optimal dose of vitamin supplements in patients with HDF.

## METHODS

This monocentric study was approved by the local ethics committee of the Canton de Vaud, Switzerland (Swissethics CER-VD, ID-Nr 2017–00518) and conducted according to the principles expressed in the Declaration of Helsinki. Written informed consent was obtained from all participants before entry into the study.

### Subjects' Characteristics and Study Protocol

All 80 patients undergoing dialysis at the outpatient dialysis clinic of the University Hospital in Lausanne were screened for the study. In Lausanne, as in many other Swiss dialysis centers, patients receive a fixed dose of vitamin supplements after each dialysis session (typically 2 tablets of Dialvit; each tablet of Dialvit contains 50 mg of vitamin B1, 10 mg of vitamin B2, 40 mg of vitamin B6, 3 mg of vitamin B9, and 200 mg of vitamin C). When translated to % daily recommended doses (%DRD), this corresponds to 4348% for vitamin B1, 834% for vitamin B2, 400% of vitamin B6, 300% for vitamin B9, and 222% of vitamin C.

Patients undergoing CHD were excluded from the study. Inclusion criteria were age ≥18 years and ability to provide informed consent. Exclusion criteria were concomitant treatment with iron binders, or regular use of self-medication with vitamins, minerals, and food supplements.

### Baseline Vitamin Status

After informed consent, the vitamin status was evaluated in patients with HDF by measuring the predialysis vitamin concentrations on the day of their monthly laboratory check. Two 7.5-ml heparinized blood samples (Sarstedt) were collected; the samples were protected from light, immediately stored on ice, and centrifuged (Eppendorf Centrifuge 5702 R, Hamburg, Germany) within an hour at 2318 relative centrifugal force for 10 minutes at 4°C. Serum was collected in a 2-ml tube (Sarstedt, Micro tube 2 ml) and stored at −80°C before being transferred to the Swiss Vitamin Institute of Epalinges for vitamin analysis. Plasma vitamin C was measured by high-performance liquid chromatography with an electrochemical detector.[17] Vitamins B1, B2, B5, B6, B8, and B9 concentrations were measured with functional assays routinely performed in the laboratory using adapted microbiologic methods on microplates with different bacterial strains.[17]

### Vitamin Losses Throughout a Hemodialfiltration Session

In a subgroup of patients on HDF, we quantified the amount of vitamin losses during an HDF session using continuous sampling of spent dialysate.[18]

Accurate estimation of total vitamin loss in dialysate (diffusive and convective losses) is ideally performed by measuring the vitamin concentrations in the total dialysate effluent volume. In one 240-minute HDF session, the effluent volume can reach 200 liters, raising technical and logistical issues.

Sequential sampling (start, mid-, and end-session) in the dialysate outflow, as described in literature,[14] is prone to significant error, as dialysate effluent is collected in an unsteady fashion.

A dialysate separator was then used in this subgroup of patients. This device allowed us to collect a fraction (approximately 1%) of the dialysate throughout the treatment at a constant flow rate. The measurement of the total amount of the studied vitamines (Total VITdial) being cleared during 1 HDF session is therefore calculated from a small representative sample.[18]

Total VITdial was calculated as following: Total VITdial (nmol or μg) = [TotVIT] × TotDIAL, where *[TotVIT]* is the concentration of a particular vitamine in total spent dialysate (in nmol/L, μg/L) and *TotDIAL* is the total volume of spent dialysate (in liters). TotDIAL is further defined as: TotDIAL (liters) = Dialysate Flow Rate [l/min] × dialysis duration [min] + total convective volume (liters). The total convective volume corresponds to the total postdilutional online

reinjection volume + ultrafiltration volume dedicated to weight loss.

Vitamins B1, B2, B5, B6, B8, and B9 were dosed in the effluent fluid. Vitamin C was not measured because vitamin C is degraded when exposed to UV light and opaque tubing could not be garanteed during the 4-hour collection process.

### Second Vitamin Screening 3 Months After Adaptation of Vitamin Supplements

After the first phase, vitamin dose was adapted according to the results of the baseline visit. After 3 months of dose adaptation, a second predialysis follow-up blood sample of vitamin status was mesured in patients who had not been hospitalized or suffered of any intercurrent illness. The same methods as described previously were applied.

### Parameters

The spKt/V was calculated with the Daugirdas formula.[19] Normalized polymerase chain reaction (nPCR) was used to reflect protein catabolism and intake, and calculated using interdialytic urea kinetics.[20]

Dialysis vintage was defined as the time between the start of renal replacement therapy and the baseline visit. HDF vintage was the time between the introduction of this specific treatement method and the baseline visit. Blood flow was the average blood flow of the dialysis session on the sampling day. Substitution volume was the postdilutional online reinjection volume on the day of the study visit. Epurated blood volume was the total volume of blood treated by 1 HDF session and equaled the blood flow × dialysis time. Ultrafiltration volume was the net filtered volume dedicated to the adequate control of the patient volume condition. Charlson comorbidity index was calculated based on comorbidity data obtained from a chart review.[21]

### Statistical Analysis

Values of the whole group are given as means and their SDs, or as median (interquartile range), as appropriate. Circulating vitamin levels were compared with the standard reference range of the general population as published by Schupbach *et al*.[22] To compare the means before and after a dialysis session or of the effluent volume, we used analysis of variance for repeated measures. Further pairwise comparisons were carried out using Student's *t*-test or Fisher's least significant difference. Associations between circulating vitamin levels and several baseline characteristics were assessed using Spearman's rank correlation. All *P* values are 2-sided and values $< 0.05$ were considered to be significant. Analyses were performed using STATA software version 12.1 (StataCorp, College Station, TX).

**Table 1.** Patient characteristics

| Clinical characteristics | Mean ± SD or *n* (%) |
|---|---|
| Age (y) | 56.1 ± 15.7 |
| Female (%) | 10 (25) |
| Ethnicity (%) | |
| White | 30 (75) |
| African | 4 (10) |
| Asian | 5 (12.5) |
| South American | 1 (2.5) |
| Weight (postdialysis) (kg) | 73.07 ± 14.3 |
| Height (cm) | 168.6 ± 9.1 |
| Body mass index (kg/m$^2$) | 26.4 ± 5.3 |
| Former transplantation (%) | 6 (15) |
| Charlson comorbidity index | 5 ± 2.4 |
| Diabetes (%) | 16 (40) |
| Hypertension (%) | 31 (77.5) |
| Vascular acces (%) | |
| Native arteriovenous graft | 11 (27.5) |
| Prosthetic arteriovenous graft | 18 (45) |
| Permanent hemodialyis catheter | 11 (27.5) |
| Dialyzer F × 1000 (%) | 35 (87.5) |
| Weekday (Monday) (%) | 22 (55) |
| Hemodiafiltration vintage (mo) | 15.6 ± 17.6 |
| Sp kt/V; ekt/V | 1.8 ± 0.3; 1.6 ± 0.3 |
| Blood flow (ml/min) | 361 ± 31 |
| Weekly dialysis time (min) | 711 ± 27 |
| Substution volume (liters) | 22.0 ± 6.2 |
| Epurated blood volume (liters) | 84.9 ± 9.4 |
| Ultrafiltration (ml) | 2012 ± 1065 |

## RESULTS

A total of 40 patients on chronic HDF were enrolled in the study. Patient and dialysis characteristics are listed in Table 1.

Results of baseline laboratory values (electrolytes, creatinine, urea, and proteins) are shown in Supplementary Table S1. Concerning potassium and phosphate, most patients (90% and 70%, respectively) were within the range recommended by the Kidney Disease Improving Global Outcomes guidelines. Mean nPCR value was 1.07 ± 0.27 g/kg per day, suggesting sufficient protein intake.

Results of the different predialysis hydrosoluble vitamin concentrations are listed in Table 2. The large majority of patients were above the normal reference intervals for B vitamins (B1, B2, B5, B6, B8, B9) with 0.4%, 10.0%, and 89.6% in the low, normal, and high reference range, respectively. For vitamin C, most patients were in the range that is considered normal for the healthy population,[22] with 5.0%, 82.5%, and 12.5% in the low, normal, and high reference range.

Only 2 patients showed vitamin levels below the reference range: one patient for vitamin C and the other

**Table 2.** Predialysis vitamin concentrations

| Vitamin | Ref range | Mean (SD) | Deficient | Normal *n* (%) | High |
|---|---|---|---|---|---|
| Vitamin B1[a] | 10–53 (nmol/l) | 207.8 (±138.2) | – | 4 (10) | 36 (90) |
| Vitamin B2[a] | 18–180 (nmol/l) | 257.7 (±143.7) | – | 10 (25) | 30 (75) |
| Pantothenic acid | 160–588 (nmol/l) | 1515.6 (±1321.5) | – | 2 (5) | 38 (95) |
| Vitamin B6[a] | 6.5–69 (nmol/l) (women)<br>10–111 (nmol/l) (men) | 177.3 (±65.0) | 1 (2.5) | 3 (7.5) | 36 (90) |
| Biotin | 0.3–3.8 (nmol/l) | 7.4 (±3.8) | – | 5 (12.5) | 35 (87.5) |
| Folic acid[a] | 7–31 (nmol/l) | 169.5 (±54.9) | – | – | 40 (100) |
| Vitamin C[a] | 26–97 (μmol/l) | 64.9 (±39.3) | 2 (5) | 33 (82.5) | 5 (12.5) |

[a]Substituted vitamins.
Predialysis vitamin concentrations measured during the first phase (all patients on 2 tablets of Dialvit postdialysis thrice weekly).

patient for vitamins C and B6. When confronted with these results, the 2 vitamin-deficient patients admitted not taking the vitamin supplements administered at the end of each dialysis session.

## Vitamin Losses Throughout a Hemodialfiltration Session

Vitamin losses in the dialysate were measured in 6 patients; all 6 were taking 2 tablets of Dialvit thrice weekly at the moment of the dialysate collection. Vitamin blood levels before and after the dialyis session were obtained (Figure 1). Results of total vitamin losses in dialysate are reported in Table 3. Data are represented as absolute loss (nmol and μg) and related to food intake as in DRD. Levels of vitamin B2 could not be measured in 3 samples. Vitamin B8 value was annulated for 1 sample for technical reasons (abnormally high value). Mean values of blood flow were 375 ml/min (± 42 ml/min), dialysate flow 515 ml/min (± 17 ml/min), substitution volume 16.7 l (± 8.7 l), dialysate time 230 minutes (± 15 ml/min), and ultrafiltration 1300 ml (± 724 ml). Mean sampling volume was 1541 ml (± 122 ml) of a mean total effluent volume of 139 l (± 10 l), which corresponds to 1.1% of the total effluent volume (see Supplementary Table S2). Compared with DRDs of vitamin intake, average vitamin losses were estimated at 84% of DRD for vitamin B1, 197% of DRD for vitamin B2, 148% of DRD for vitamin B5, 37% of DRD for vitamin B8, and 67% of DRD for vitamin B9. Low dialysis losses were detected for vitamin B6, estimated at 1% of DRD.

## Associations Between Vitamin Status and Baseline Clinical Characteristics

In univariate analysis (Spearman), there were no associations between the levels of circulating vitamins and basic patient characteristics such as age, gender, and body mass index. No significant associations were found between vitamin levels and other patient parameters, such as weight, Charlson comorbidity index, hospitalization in the past 3 months, ethnicity, and diabetes (with the exception of vitamin B6, rho −0.39, $P = 0.014$).

The dialysis parameters Kt/V, substitution volume, epurated blood volume, and vascular access were also not associated with vitamin status, except for panthtenic acid that tended to increase with increasing dialysis vintage (r = 0.39, $P = 0.014$).

Finally, plasma nutritional parameters showed significant associations with some vitamins. Vitamin C was positively associated with pre-albumin, creatinine, and urea, as well as a trend toward positive association with nPCR. Vitamin B6 was positively associated with nPCR, protein, albumin, and creatinine. Vitamin B5 was positively associated with nPCR, protein, creatinine, and urea. Vitamin B8 was positively associated with pre-albumin and creatinine (summary of associations in Supplementary Table S3). There were no associations with dry weight or body mass index. These results remained unchanged after adjustment for age and sex in multivariate linerar regression analysis. However, when applying multiple testing rules (Bonferoni), no significant associations ($P$ values <0.001) were found.

## Dose Supplementation Assessment

A total of 24 patients remained free of complications between baseline and the 3-month follow-up period. For the second dose-assessment phase, Dialvit was reduced to 1 tablet after each session in all patients with baseline hydrosoluble vitamin levels above normal range. After 3 months of this low-dose substitution, a follow-up blood sample of vitamin status was measured (see Table 4). B vitamin levels were lower but mostly stayed above the normal range (1.4%, 25.7%, and 72.9% in low, normal, and high reference range). However, 3 patients (12.5%) had developped vitamin C deficiency on low-dose substititon (87.5% in normal range). Comparison of the vitamin levels are displayed in Figure 2; significant reductions occured in the concentrations of vitamins C, B1, B6, B8, and B9. There was no significant change for vitamins B2 and B5. Vitamin B2 levels were stable despite supplementation. Of the 2

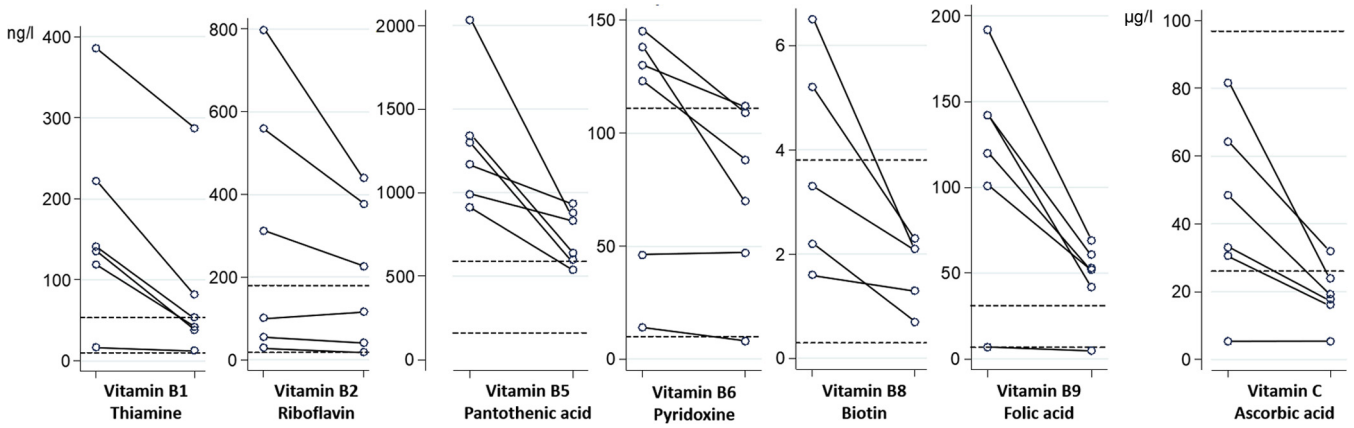


**Figure 1.** Vitamin loss throughout a HDF session (before and after blood levels).

other vitamins that were not supplemented, B5 levels were stable, but suprisingly B8 was lower at the follow-up measurement. Three patients developed vitamin C deficiency; 1 patient developed vitamin B1 and B8 deficiency.

The 3 patients who developed vitamin C deficiency were all in a stable clinical condition and otherwise good nutritional status; however, 1 patient suffered from uncontrolled hyperthyroidism and another suffered from alcoholic hepatic cirrhosis.

The patient who showed deficiency for vitamins B1 and B8 showed severe denutrition at the time of the second vitamin screening. This patient had undergone heart transplantation 26 years ago and mecanic aortic heart valve replacement 4 years before the study. He had been on hemodialysis for 2 years and experienced 2 episodes of bacterial endocarditis in the past year with prolonged hospitalizations. At the time of the study, he was still treated with prophylactic oral amoxicillin. He had no clinical sign of thiamin deficiency. We have assessed the effect of circulating amoxicillin, at an estimated physiological concentration of 33 µg/l, on the results of vitamin B1 and B8 concentrations as measured by microbiological assays. In this experiment, despite a noticed downestimation of the vitamin concentrations due to the inhibitory effect of the antibiotic on the microbiological assays, this effect is unlikely to explain on its own the observed deficiencies of vitamins B1 and B8 in this patient (data not shown).

## DISCUSSION

This monocentric study in patients on chronic HDF on thrice-weekly postdialysis vitamin supplementation showed that under these conditions, HDF is not associated with hydrosoluble vitamin deficiency, despite the removal of considerable amounts in the dialysate. On the contrary, for most vitamins (B1, B2, B8, B6, B9, and B5), patients showed vitamin levels higher than the reference range, except for vitamin C. Vitamin levels remained within the reference range after lowering the usual supplementation dose, vitamin C excepted.

To the best of our knowledge, this is the first study that simultaneously measured a panel of hydrosoluble vitamins in patients on HDF. Tight regulation of vitamin status is important, as deficiencies or concentrations superior to upper recommended levels can lead to important clinical consequences. Lack of vitamin B1 may lead to Beriberi or Wernicke encephalopathy, whereas lack of vitamin B6 is associated with stomatitis, glossitis, cheilosis, irritability, confusion, and depression. Deficiencies are the consequence of either reduced intake or increased losses during hemodialysis sessions. In our HDF study, dialysate losses were

**Table 3.** Exploratory dialysate loss study

| Dialysate loss (mean, SD) | nmol | µg | % DRD | Blood level reduction (%) |
|---|---|---|---|---|
| Vitamin B1 | 3625 (4911) | 961 (1301) | 84 (113) | 49 |
| Vitamin B2 | 6294 (2956) | 2367 (1111) | 197 (93) | 34 |
| Pantothenic acid | 33730 (9682) | 7387 (2120) | 148 (42) | 43 |
| Vitamin B6 | 647 (389) | 109 (66) | 1.1 (0.7) | 27 |
| Biotin | 46 (33) | 11.2 (8.1) | 37 (27) | 12 |
| Folic acid | 1518 (777) | 669 (343) | 67 (34) | 60 |

The amount of vitamins removed during 1 dialysis session in a subgroup of 6 patients is shown. Absolute vitamin losses are presentend in nmol and µg and translated to daily recommended doses (DRDs).

**Table 4.** Vitamin values after dose adjustment (1 instead of 2 tablets postdialysis thrice weekly in all remaining participants)

| Vitamin | Ref range | Mean (sd) | Deficient | Normal *n* (%) | High |
|---|---|---|---|---|---|
| Vitamin B1[a] | 10–53 (nmol/l) | 112.9 (±59.4) | 1 (4.2) | 4 (16.7) | 19 (79.2) |
| Vitamin B2[a] | 18–180 (nmol/l) | 244.3 (±133.9) | – | 11 (45.8) | 13 (54.2) |
| Pantothenic acid | 160–588 (nmol/l) | 1399.9 (±663.1) | – | 1 (4.2) | 23 (95.8) |
| Vitamin B6[a] | 6.5–69 (nmol/l) (women)<br>10–111 (nmol/l) (men) | 116.9 (±30.7) | – | 10 (41.7) | 14 (58.3) |
| Biotin | 0.3–3.8 (nmol/l) | 5.0 (±3.9) | 1 (4.2) | 11 (45.8) | 12 (50) |
| Folic acid[a] | 7–31 (nmol/l) | 94.2 (±23.9) | – | – | 24 (100) |
| Vitamin C[a] | 26–97 (µmol/l) | 39.9 (±13.7) | 3 (12.5) | 21 (87.5) | – |

[a]Substituted vitamins.

important. Compared with the DRDs of vitamin intake, average vitamin losses during 1 HDF sesison ranged between 27% DRD for B8 to 113% DRD for vitamin B1. In contrast, vitamin B6 was hardly removed during dialysis in our study, with losses estimated at 0.7% DRD.

The only clinical factors that were moderately associated with baseline vitamin status were parameters of poor nutrition status, such as nPCR, pre-albumin, creatinine, and urea. It is well known that dialysis patients are at high risk for malnutrition because of restricted diet, diminished gastrointestinal absorption, and comorbid conditions; however, associations were weak and no longer significant after Bonferoni correction.

The main reason for vitamin deficiency was low adherence to postdialysis vitamin intake (Dialvit). This was nicely illustrated by the fact that the only 2 patients with multiple deficiencies at baseline admitted, when confronted with the results, that that they did not take Dialvit. They assured the medical team that they would swallow the pills at home but instead, they threw them away. They had no signs of vitamin deficiency, and their results normalized at follow-up once they started taking Dialvit. This strongly suggests that vitamin supplementation is essential in HDF.

As hydrosoluble vitamins are predominantely eliminated by renal clearance, toxic levels may also occur in end-stage renal disease in case vitamin supplementation is excessive. Toxic levels have been described for vitamin B8, with symptoms such as depression, somnolence, hyperesthesia, anorexia, and dermatosis.[15,16] In the case of vitamin B6, peripheral neuropathy, dermatoses, photosensitivity, dizziness, and nausea have been reported, whereas overdose of vitamin C can lead to oxalosis. Although no clinical signs of toxicity were observed, most patients in our study had excessive vitamin levels, strongly suggesting that actual dosing schedules need revision.

The reduction of Dialvit from 2 to 1 tablet in our study led to significant lower levels of vitamins B1, B6, B8, and B9 at the second follow-up visit 3 months later, whereas levels of vitamins B2 and pantothenic acid did not change. However, in several patients (12.5%), vitamin C levels were inferior to the deficiency threshold. The larger effect on vitamin C is in line with the work of Morena *et al.*[14] that described one-third of vitamin C loss was attributed to the convective component of HDF. These data suggest that the performed dose reduction is a first step in the right direction, but further studies are necessary to assess the optimal vitamin doses. Ideally, the composition of

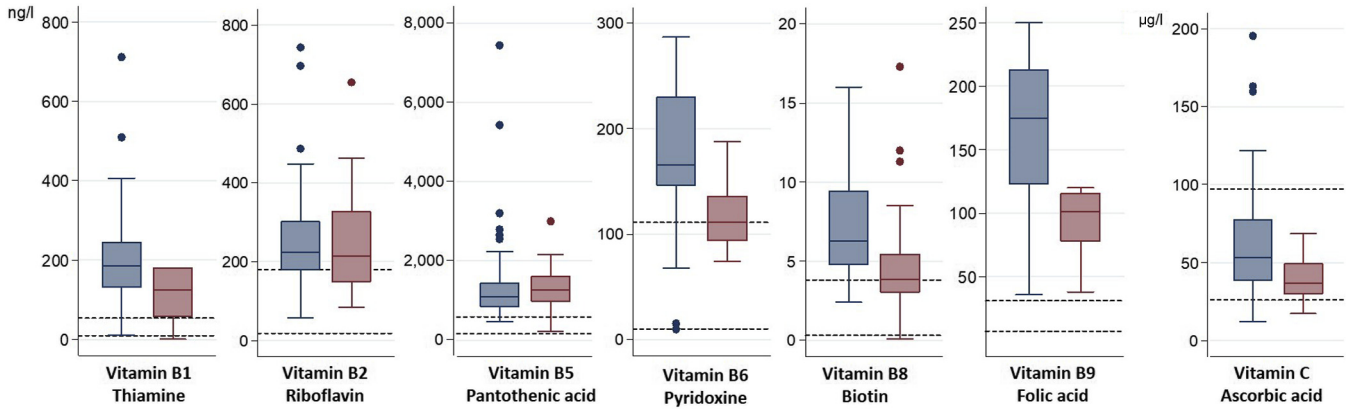


**Figure 2.** Predialysis vitamin levels at baseline with standard vitamin substition of 2 Dialvit tablets (blue) and follow-up vitamin levels after 3 months of lowered dose vitamin substitution of 1 Dialvit tablet (red).

multivitamin pills should be adapted to the actual trend of increased use of HDF.

This study has several limitations. First, we included mainly white patients; therefore, results may be different for various ethnicities. Second, we did not obtain information on dietary intake or nutritional habits. Finally, the number of subjects was relatively low and we did not include a CHD control group. Instead, we compared our results with data previously published in the international litterature; however, the vitamin levels on standard vitamin supplementation were systematically above the usual range, except in patients who did not take Dialvit after their dialysis sessions. We therefore believe that a greater number of patients would not have fundamentally changed our main finding, namely that most levels of hydrosoluble vitamins are above the normal range under current vitamin substitution.

Among its strengths we mention that this study is, to the best of our knowledge, the first to explore simultaneously a complete panel of hydrosoluble vitamins in patients with HDF. These findings were completed with quantitative dialysate loss of these vitamins. We further prospectively adjusted vitamin doses to assess optimal dosing regimen.

In conclusion, hydrosoluble vitamin B and/or C deficiency is rare in patients on HDF and only occurs in patients who do not take the postdialysis vitamin substitution. Although many vitamins are partly cleared by HDF, the actual doses can be safely reduced, vitamin C excepted. Further studies are necessary to assess the optimal vitamin substitution dose for patients on HDF.

## DISCLOSURE

All the authors declared no competing interests.

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## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

**Table S1.** Predialysis biological values.

**Table S2.** Dialysis parameters for exploratory dialysate loss study in 6 patients.

**Table S3.** Spearman associations of vitamin levels and markers of nutritional status.

**STROBE Statement.**

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