Blood concentrations of vitamins B1, B6, B12, C and D and folate in palliative care patients: Results of a cross-sectional study

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Abstract

Objective: The main purpose of palliative care is symptom relief. Frequently, the symptoms of patients requiring palliative care are the same as common symptoms of vitamin deficiency (e.g. pain, weakness, fatigue, depression). The study aim was to investigate whether patients in palliative care are vitamin deficient.

Method: This was a monocentre cross-sectional study. Patients attending the palliative care unit of a general hospital in Germany from October 2015 to April 2016 were examined for vitamin blood concentrations and symptoms. Data were analysed using univariate analysis and bivariate correlations.

Results: Data were available from 31 patients. Vitamin D3 deficiency (<62.5 nmol/L) affected 93.5% of patients, vitamin B6 deficiency (<4.1 ng/mL) 48.4%, vitamin C deficiency (<4.5 mg/L) 45.2%, vitamin B1 deficiency (<35 µg/L) 25.8% and vitamin B12 deficiency (<193 pg/mL) 12.9%. There was a significant negative correlation between vitamin B1 ranges and pain ($r = -0.384$) and depression ($r = -0.439$) symptoms.

Conclusion: All patients showed a deficiency in at least one of the measured vitamins; 68% had concurrent deficiencies in >1 vitamin. A follow-up study using validated questionnaires and a larger sample is needed to investigate the effects of targeted vitamin supplementation on quality of life and symptom burden.

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Introduction

The main aim of palliative care is to provide relief from pain and other distressing symptoms, thereby improving the quality of life (QOL) of patients facing problems associated with life-threatening illness. A recent nationally representative, longitudinal cohort study of community-dwelling US residents aged 51 years and older revealed that the goal of pain relief was not achieved during the last year of life.[1] According to this study, the prevalence of pain and other critical symptoms during the final year of life increased despite efforts to improve end-of-life care. Between 1998 and 2010, the final-year-of-life prevalence of any pain in all decedents had actually increased by 11.9% (95% confidence interval (CI), 3.1% to 21.4%), and the prevalence of depression and periodic confusion lasting at least 1 month increased by 26.6% and 31.3%, respectively.[1]

According to their metabolic function, vitamins such as B1, B6, folate, B12, C and D are associated with characteristic deficiency symptoms. Unspecific deficiency symptoms, which can also occur in subclinical deficiency conditions, include weakness, fatigue, pain, shortness of breath and loss of appetite.[2–4] These symptoms are consistent with common symptoms of patients requiring palliative care. The symptoms of seriously ill people cannot be explained solely by vitamin deficiency, but it may be useful to investigate the frequency of vitamin deficiency in patients with severe illness to better understand the contribution of vitamin deficiency, if any, to symptom burden. In addition, the potential need for supplements could be identified.

Malnutrition in palliative care patients owing to reduced food intake, malabsorption or metabolic disorders is common[5–7] and may result in vitamin deficiencies. However, except for studies on vitamin D, this problem has been inadequately investigated.[8–14] At present, study data are mainly available from cancer patients, and non-cancer patients are still underrepresented in palliative care.[15] However, the number of non-cancer patients in palliative care is increasing.[16–18] Folate and vitamin B12 have been mainly investigated in anaemic palliative care and cancer patients;[8] to the best of our knowledge, there are no studies on vitamin B6 (pyridoxal phosphate) concentrations in palliative care patients. Only three studies have considered the possible association between vitamin concentration and symptoms (vitamin B1 and cognitive dysfunction;[9] vitamin D and fatigue, anorexia and QOL[10,19]). Furthermore, most studies have focused only on a single vitamin. Palliative care patients may be deficient in multiple vitamins, which would have even more pronounced effects on QOL.

Other important issues that should be addressed are optimum vitamin concentrations and their influence on the health of the individual. Although therapeutic vitamin treatment is often administered for clinical deficiency states, some subclinical ailments may also require treatment of vitamin deficiency.[2–4,20]

Our primary objectives were to a) determine whether patients in palliative care are deficient in folate and vitamins B1, B6, B12, C and/or D and b) investigate whether there are linear correlations between vitamin plasma or serum concentrations and symptoms.

Method

Study design

In this monocentre cross-sectional study, we examined patients shortly after admission to a palliative care unit. Frequency of vitamin deficiency was investigated by examining one blood sample at the start of palliative care. The number of patients in the hospital palliative care unit during the study period determined the sample size.

The secondary outcome was to determine whether there were any linear correlations between plasma/serum vitamin concentrations and the most common symptoms, homocysteine (Hcy) concentration, nutritional risk screening (NRS) score, inflammation (concentration of C-reactive protein (CRP)) and performance (Karnofsky score). As symptoms in this heterogenic patient group are biased by many factors (e.g. age, underlying disease for palliative care) and the sample was small, linear correlation analysis was only conducted to identify preliminary indications of possible links between specific vitamin deficiencies and symptoms for a subsequent study with a larger sample. Ethical approval was obtained from the University of Rostock ethics committee (A2015-0107 04/09/2015).

Study sample

Data were collected from patients attending the palliative care unit of the general hospital Warnow-Klinik, Bützow, Germany, from October 2015 to April 2016, who complied with the inclusion criteria (≥ 18 years; Karnofsky score $\geq 30\%$, performance status according to the Eastern Cooperative Oncology Group (ECOG) ≤ 3, capable of providing written informed consent).

Patients with very poor performance status (ECOG 4 or Karnofsky score $<30\%$) were excluded for ethical reasons (e.g. to avoid additional stress, discomfort and blood loss). All participants agreed with the study participation, data processing and publication of the data, and provided written informed consent.

Assessment of symptoms, performance and nutritional status

The following symptoms were assessed by physicians at admission, graded using a 4-point scale (none, mild, medium, severe) and converted to an ordinal scale (0–3): pain, nausea, vomiting, shortness of breath, constipation, weakness, loss of appetite, fatigue, depression, anxiety, tension, periodic confusion, disturbed wound healing and decubitus.

Each patient was questioned about their vitamin supplement intake in the week prior to admission (name of product(s) or substance(s) and dosage) using a written questionnaire.

The recording of symptoms, NRS, CRP and Karnofsky scores are part of the routine basic examination on admission to the Warnow-Klinik hospital.

Additionally, to examine how specific vitamin deficiencies correlated with symptoms and performance, NRS was used to validate the association with nutritional status, and CRP was chosen to screen for a possible association with inflammation.

Hcy plasma concentrations were measured because hyperhomocysteinemia is considered an independent risk factor for cardiovascular and cerebrovascular diseases, and data suggest that it is an important indicator for overall health status.[21]

Deficiencies in folate, vitamin B12 and/or vitamin B6 affect Hcy metabolism, resulting in hyperhomocysteinemia.[21]

Measurement of vitamins and homocysteine

From each patient, one blood sample was drawn in the early morning (fasting). The testing laboratory (Biovis Diagnostik MVZ GmbH, Limburg-Offheim, Germany) has DIN EN ISO 15189:2014 accreditation and has successfully participated in proficiency testing. Vitamin B1 was estimated in plasma by reversed phase high-performance liquid chromatography (HPLC) (IC2201rp) and subsequent fluorescence detection,[22] vitamin B6 in plasma by reversed phase HPLC (IC2100rp) and subsequent fluorescence detection,[23] folate in erythrocytes by electrochemiluminescence - cobas 6000 system (Roche Diagnostics GmbH, Penzberg, Germany),[24] vitamin B12 in serum by electrochemiluminescence - cobas 6000 system (Roche Diagnostics GmbH, Penzberg, Germany),[25] vitamin C in plasma by reversed phase HPLC (IC2900rp) and subsequent UV detection,[26] 25-OH-vitamin D3 in serum by liquid chromatography (Shimadzu Prominence LC system, Shimadzu Corporation, Kyoto, Japan) and mass spectroscopy (QTRAP® 5500 system), and Hcy in plasma by electrochemiluminescence - cobas 6000 system (Roche Diagnostics GmbH, Penzberg, Germany).[27] The intra- and inter-assay coefficients were within acceptable ranges.

Normal vitamin ranges are set by reference to vitamin levels in healthy persons; the 'optimal range' is a reference range that is based on concentrations associated with optimal physiological metabolic processes. In principle, it may be more appropriate to use optimal ranges for some vitamins, as apparently healthy patients often show deficient vitamin concentrations.[28] However, a standard method of estimating these ranges does not exist.

Statistical analysis

The software IBM SPSS Statistics for Windows, version 21 (IBM Corp., Armonk, NY, USA), was used for the statistical analyses, which comprised univariate analysis (data distribution, dispersion and measure of spread) of the vitamin, Hcy and CRP concentrations and bivariate correlation analysis between vitamin concentrations and Hcy, CRP, NRS, Karnofsky score and symptom intensity, respectively.

Normal distribution of data was tested using the Shapiro–Wilk test. Pearson correlation coefficients were calculated for numerical and parametric data; Spearman's rho values were calculated for graded or non-parametric data.

Results

In the observational period, 31 patients fulfilled the inclusion criteria and were invited to participate in the study; no patients refused to participate or dropped out. The ECOG scores of two patients were classified as 4 (bedridden), but after consultation with the attending physician these patients were included. As they were bedridden to prevent falls, the Karnofsky score for both patients was ≥30%. Demographic data, NRS, CRP, glomerular filtration rate and performance status are shown in Table 1.

The predominant disease for palliative care was cancer (77.4%). About one-third of patients were at risk of malnutrition (NRS ≥3). Plasma concentrations of CRP and Hcy were in the normal range in four (12.9%) and two (6.5%) patients, respectively. Three patients (9.7%) had recently used vitamin supplements (parenteral vitamin B1, a multivitamin preparation or vitamin D3). The patient taking weekly vitamin D3 supplementation was the only one

Table 1. Demographic data and clinical characteristics of the 31 study patients.

Age, years: mean ± SD	73.23 ± 11.54
Range	49–92
Sex	Number of patients (%)
Female/male	11 (35.5)/20 (64.5)
Vitamin supplement user	Number of patients (%)
Yes/no	3 (9.7)/28 (90.3)
Primary disease for palliative care	Number of patients (%)
Oncological/non-oncological disease	24 (77.4)/7 (22.6)
NRS, nutritional risk screening	Number of patients (%)
NRS <3 points	21 (67.7)
NRS ≥3 points	10 (32.3)
Performance score	Number of patients (%)
ECOG 2	18 (58.1)
ECOG 3	11 (35.5)
ECOG 4	2 (6.5)
Median ECOG score: 2	
Karnofsky score	Number of patients (%)
30	4 (12.9)
40	4 (12.9)
50	14 (45.2)
60	6 (19.4)
70	3 (9.7)
Median	50
Barthel score**	
Mean ± SD	74.35 ± 24.59
Median/range	85.00/25–100
Symptom intensity score (0–3)	Median, mode, minimum, maximum
Tension	3, 3, 0, 3
Weakness	2, 3, 1, 3
Anxiety	2, 2, 0, 3
Pain	2, 2, 0, 3
Shortness of breath	2, 2, 0, 3
Fatigue	2, 2, 0, 3
Loss of appetite	2, 2, 0, 3
Constipation	1, 1, 0, 3
Depression	1, 0, 0, 3
Confusion/Disorientation	0, 0, 0, 3
CRP* [mg/L]	
Mean ± SD	65.34 ± 81.32
Median/range	23.2/0.70–296.80
GFR [mL/min/1.73m^2]	Number of patients (%)
Below normal (100–140)	26 (83.9)
Within normal range	5 (16.1)

CRP: C-reactive protein; ECOG: Eastern Cooperative Oncology Group; GFR: glomerular filtration rate; SD: standard deviation. *Normal range for CRP: 0.0–5.0 mg/L. **Measures dependence in activities of daily living: 80–100 independent, 60–79 minimally dependent; 40–59 partially dependent, 20–39 very dependent.

whose vitamin D3 concentrations were in the normal range. A fourth patient reported no recent vitamin supplementation, but he had received parenteral vitamin B1, and vitamin C and oral vitamin D3 supplements, during the previous year. He showed well above-normal vitamin D3 concentrations.

Symptoms

Weakness was the only symptom present in all patients (score >0). Together with the symptom tension, it had the highest median intensity (3 = severe). Anxiety, pain, shortness of breath, fatigue and loss of appetite were next; all had a mean intensity value of 2 (moderate). Constipation, depression and confusion/disorientation occurred occasionally in some patients. A total of 64.5% of patients had moderate-to-severe pain and 51.6% had at least one episode of depression.

Concentrations of vitamins and homocysteine

The univariate data analysis of vitamins and Hcy plasma concentrations is shown

in Table 2. The vitamin deficiency frequencies are shown in Figure 1, and boxplots of vitamin concentrations in Figure 2a–f. The most frequent deficiency was that of vitamin D3, which affected 93.5% of patients. The mean (± standard deviation) concentration of 35.85 (±53.89) nmol/L vitamin D3 is 43% below the lower limit of the normal range (≥62.5 nmol/L).

Vitamin B6 or C deficiencies were present in nearly half of the study population (48.4% and 45.2%, respectively). Two (6.5%) patients had values within the optimal range for vitamin B6, and none had vitamin C concentrations within the optimal range. Four (12.9%) patients displayed 'scurvy' vitamin C concentrations (≤1.8 mg/L).

Vitamin B1 deficiency was present in 25.8% of patients. An optimal range for vitamin B1 was not available from the laboratory that conducted the analyses. Folate concentrations in erythrocytes were in the normal range for all patients, but 16 (51.6%) had values below the optimal concentration.

Vitamin B12 serum values were below normal in 4 (12.9%) patients, below

Table 2. Analysis of vitamin and homocysteine concentrations.

		Vitamin B1 [µg/L]	Vitamin B6 [ng/mL]	Folate [ng/mL]	Vitamin B12 [pg/mL]	Vitamin C [mg/L]	Vitamin D 3 [nmol/L]	Hcy [µmol/L]
Normal range*		35–99	4.1–43.7	480–1210	193–982	4.5–24.5	62.5–170	<12
Optimal range*		not known	10.0–43.7	>750	600–982	13.9–24.9	75–200	<10
Mean		43	5.1	847	968	5.4	35.9	20
SEM		2	0.8	59	276	0.5	9.7	1
95% CI	lower	39	3.4	726	403	4.4	16.1	18
	upper	48	6.8	968	1532	6.5	55.6	23
Median		42	4.1	716	460	5.3	23.2	19
SD		12	4.6	331	1539	2.8	53.9	7
Minimum		24	1.1	547	144	1.6	10.0	9
Maximum		87	26.3	1968	7685	12.3	312.0	36
	25	35	2.4	620	230	3.1	14.6	16
Percentiles	50	42	4.1	716	460	5.3	23.2	19
	75	50	5.8	957	853	7.5	38.9	25

Valid patients n = 31. SEM: standard error of the mean; CI: confidence interval; SD: standard deviation; Hcy: homocysteine. *Ranges were provided by the testing laboratory (Biovis Diagnostik MVZ GmbH).
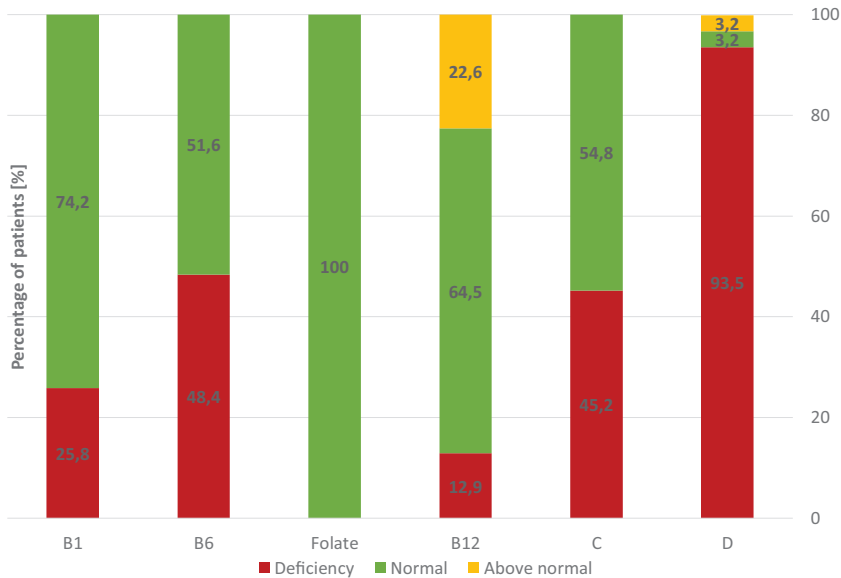
Figure 1. Frequency [%] of patients with vitamin concentrations below normal, in the normal range and above normal
Normal ranges: B1: 35 to 99 µg/L, B6: 4.1 to 43.7 ng/mL, folate: 480 to 1210 ng/mL, B12: 193 to 982 pg/mL, C: 4.5 to 24.5 mg/L, D: 62.5 to 170 nmol/L.

optimal concentrations in 19 (61.3%) patients and above normal in 7 (22.6%) patients.

All patients displayed at least one below-normal vitamin concentration of the six assessed vitamins. Nearly one-third (29%) of the study cohort had two concurrent vitamin concentrations below normal, 22.6% had three, 12.9% had four and 3.2% had five concurrent vitamin concentrations below normal.

Correlation analysis

Only vitamin C and Hcy showed a normal distribution according to the Shapiro–Wilk test. The significant correlations are displayed in Table 3. There were significant correlations between vitamin B12 concentrations and Karnofsky score and weakness (both $P < 0.05$) and between vitamin B12 ranges and weakness ($P < 0.05$). Vitamin B1 ranges showed a significant negative

correlation with both pain ($P < 0.05$) and depression ($P < 0.05$).

Discussion

Although participants showed moderately good health-related QOL overall (median Karnofsky score = 50%; one-third of patients were at risk of malnutrition), a high proportion showed significant vitamin deficiencies, particularly for vitamins D3, B6, C and B1. An association between insufficient vitamin status and symptoms was apparent for vitamin B1 and the symptoms pain and depression. The frequency of the symptoms pain (64.5% had medium-to-severe pain) and depression (51.6%) in our cohort correspond with published data from a larger survey.[15]

Deficient vitamin B1 concentrations occurred in one-quarter of our patients, which is comparable to results of a previous study.[9] We found an association between
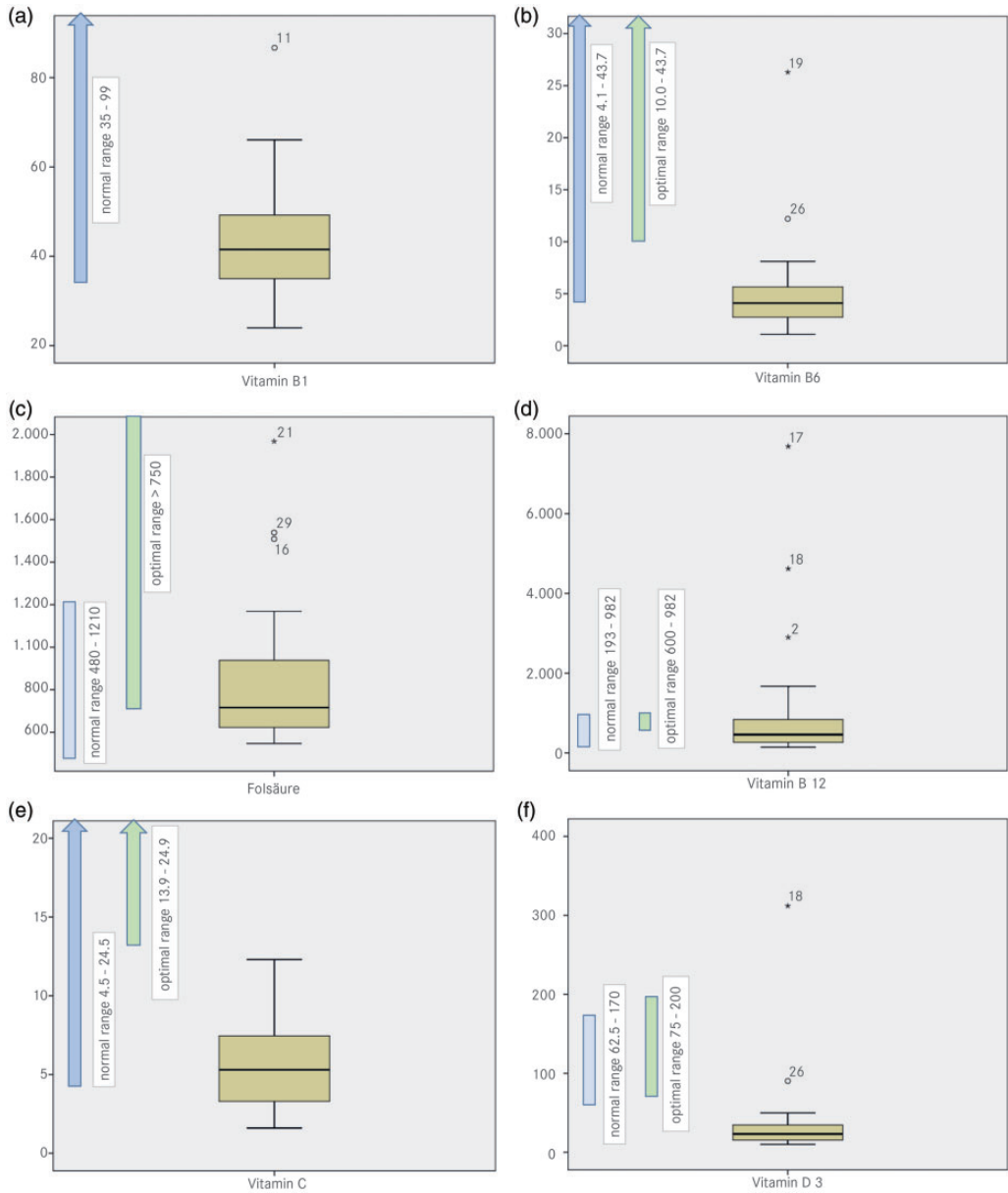
Figure 2. Vitamin concentrations in relation to normal and optimal ranges. (a) B1 (b) B6 (c) folate (d) B12 (e) C (f) D3

Normal and optimal ranges were provided by the testing laboratory (Biovis Diagnostik MVZ GmbH).

Normal vitamin ranges are set by reference to vitamin levels in healthy persons; the optimal range is based on concentrations associated with optimal physiological metabolic processes.

Table 3. Correlation analysis.

Variables	Correlation coefficient (r)	Sig. (P, 2-tailed)
Vitamins and Karnofsky score		
Vitamin B12 concentrations – Karnofsky score	−0.415	0.02
Vitamins and symptoms		
Vitamin B12 concentrations – symptom 'weakness'	0.401	0.025
Vitamin D3 concentrations – symptom 'weakness'	0.495	0.005
Vitamin B12 ranges (below-normal, normal and above-normal) – symptom 'weakness'	0.451	0.011
Vitamin D3 concentrations – symptom 'anxiety'	0.434	0.015
Vitamin D3 ranges (below-normal, normal and above-normal) – symptom 'pain'	−0.373	0.039
Vitamin D3 ranges (below-normal, normal and above-normal) – symptom 'depression'	−0.377	0.037
Vitamin B1 ranges (below-normal and normal) – symptom 'pain'	−0.384	0.033
Vitamin B1 ranges (below-normal and normal) – symptom 'depression'	−0.439	0.014
Vitamins among themselves		
Vitamin C ranges (below-normal and normal) – Vitamin B1 ranges (below-normal and normal)	0.502	0.004
Vitamin C ranges (below-normal and normal) – Vitamin B6 ranges (below-normal and normal)	0.418	0.019
Vitamin D3 ranges (below-normal, normal and above-normal) – Vitamin B1 ranges (below-normal and normal)	−0.445	0.012

Valid patients n = 31. The table displays only significant correlations between Karnofsky score and vitamins, symptoms and vitamins, and vitamins among themselves. Correlation analyses were conducted for vitamin concentrations (continuous data) and ranges (categories). For the parametric measurements of vitamin C and Hcy, Pearson correlation coefficient was used; for all other measurements, Spearman's rho values were calculated.

depression and pain and vitamin concentrations only for vitamin B1. However, this may be because patients with vitamin B1 deficiency often had multiple vitamin deficiencies. Seven of the eight patients with below-normal vitamin B1 concentrations also displayed below-normal vitamin C and vitamin D3 concentrations, and five were also deficient in vitamin B6. Mental changes and neuropathy are symptoms of vitamin B1 deficiency.[3] Pain and depression are both symptoms of subclinical vitamin C[29] and D[30,31] concentrations, and depression occurs in patients with vitamin B6 deficiency.[3] It is possible that multiple vitamin deficiency contributes to pain and depression symptoms in palliative care patients.

As targeted vitamin supplementation to prevent deficiency states is easy to achieve and inexpensive, a follow-up study is warranted to investigate the therapeutic effects of vitamins on symptom relief.

To the best of our knowledge, this study is the first to examine the concentration of vitamin B6 in palliative care patients. Nearly 50% of our patients displayed deficient vitamin B6 concentrations. Although no correlation between vitamin B6 deficiency and symptoms was detected, a targeted treatment for vitamin B6 deficiency should be investigated, as vitamin B6 is the most important coenzyme in amino acid metabolism. It is involved in the synthesis of various neurotransmitters, such as serotonin, noradrenalin,

dopamine, gamma-aminobutyric acid, and of myelin, collagen, haemoglobin and other functional proteins.[3,32]

Surprisingly, erythrocyte folate concentrations were in the normal range; however, only half the patients had an optimal concentration. The mandatory fortification of staple foods with folic acid, which is common in many countries, cannot explain these data, as this practice is not established in Germany although some products are available. The adequate folate concentrations in our sample of patients with life-threatening illness is also surprising in light of data from the Federal Ministry for Risk Assessment of Germany (Bundesministerium für Risikobewertung, BfR), which has estimated that two-thirds of the German population are deficient in folate.[33] German women of child-bearing age have a median erythrocyte folate concentration of 266 ng/mL,[33] which is far less than the median in our study cohort (716 ng/mL). However, our data are in accord with data from a New Zealand study that also found normal red blood cell folate concentrations in palliative care patients.[8]

Vitamin B12 concentrations were more frequently above normal (22.6%) than below normal (12.9%). Similar data were derived from a large study of cancer patients in palliative care,[34] which concluded that there was a functional vitamin B12 deficiency despite the high vitamin B12 values. This conclusion was based on the presence of elevated concentrations of Hcy or methylmalonic acid.[35] Although the exact cause is unknown, the involvement of oxidative stress is likely, as reactive oxygen species oxidize the cobalt atom of vitamin B12, preventing conversion to the active coenzymes (methyl- and adenosylcobalamin). Therefore, vitamin B12 supplementation in cases of above-normal concentrations seems to be warranted.[35] Several studies have demonstrated that above-normal vitamin B12 concentrations are associated with high CRP concentrations, which predicts increased mortality in palliative care cancer patients.[36–41] In our study cohort, a linear negative association between vitamin B12 concentrations and the Karnofsky score was found, with reduced performance in patients with above-normal vitamin B12 concentrations. This is consistent with our finding of a positive correlation between vitamin B12 concentrations and weakness, which disappeared following exclusion of above-normal vitamin B12 values. The reason for the elevated vitamin B12 concentrations in severely or critically ill patients is still unclear, although several plausible causes (kidney, liver or myeloproliferative diseases and IgG-B12-immune complexes) have been discussed.[36,37,42–44]

Subnormal plasma concentrations of vitamin C (<4.5 mg/L) were found in nearly half our patients, and 13% showed a clinical deficiency (concentrations associated with scurvy). The proportion of patients with subnormal vitamin C concentrations was lower than that reported in other studies that included only cancer patients in palliative care (62%[14] and 72% deficiency[13]). One explanation could be a higher frequency of concomitant chemotherapy in other study groups, which may generate oxidative stress, causing reduced vitamin C concentrations.[45–47] The frequency of chemotherapy was not documented in our study group. Because 22.6% of the patients received palliative care owing to a non-oncological disease, it can be assumed that the frequency of chemotherapy was lower compared with purely oncological studies.

The mean vitamin D3 concentration was only half the minimum requirement (≥62.5 nmol/L). The median value was still lower, and below values reported in similar studies.[11,12] One explanation could be the time of evaluation (October to April), when solar radiation (UV index <3) in Germany is low.

The high proportion of patients with vitamin D3 deficiency matches well with data from a German cross-sectional study of 1,343 patients visiting general practices for various health problems[48] The German cross-sectional study also revealed that the proportion of patients with deficient vitamin D3 concentrations increases with age,[48] which might explain why a higher proportion of our cohort had deficient vitamin D3 concentrations; the mean age of participants was 73 years, compared with 58 years in the German cross-sectional study. The positive correlation between vitamin D3 blood concentrations and the symptoms weakness, anxiety, pain and depression should be interpreted as non-meaningful owing to two outlying high values: the rest of the patients displayed severe deficiency. Weakness and pain are well-known symptoms of vitamin D deficiency.[49,50] Furthermore, vitamin D deficiency has been linked to an increased incidence of depression.[49] A recent study of 30 patients in palliative care with advanced solid cancer found vitamin D3 deficiency in 90% of patients. A positive correlation between serum vitamin D concentration and patient-reported absence of fatigue and physical and functional well-being has also been reported.[19]

To our knowledge, the use of vitamin supplements in palliative care patients has not yet been investigated. Less than 10% of our patients took supplements. This proportion is lower than in patients undergoing acute oncological treatment (28% in melanoma patients and 31% in breast cancer patients).[51,52] The rural location and low socioeconomic status of the region in which the study centre is located may also help to explain these findings.[53,54]

Study strengths and weaknesses

Strengths of the study were the simultaneous measurement of several vitamins, the investigation of vitamin B6 concentrations, the focus on the potential use of vitamin supplements and the measurement of normal and optimal ranges for vitamins in palliative-treated patients for the first time.

A weakness of this study is the small sample size, which could limit the representativeness of our findings. In this study, vitamin concentrations were only determined at one time (admission day to intensive care unit), so no control or follow-up values were available. Symptoms were measured using a simple 4-point scale (none, mild, medium, severe). A follow-up study is needed that measures blood values at several points in time, and that uses validated questionnaires to evaluate symptoms and QOL.

Conclusion

Although median Karnofsy performance score of the study population was 50%, and only one-third of patients were at risk of malnutrition, all patients exhibited below-normal concentrations of at least one vitamin; 68% of patients had concurrent deficiencies of several vitamins.

Almost all patients displayed a vitamin D3 deficiency. Vitamin B6 and C deficiency affected nearly half the population. A quarter of patients had vitamin B1 below-normal concentrations, and 13% had deficient vitamin B12 concentrations.

Because patients in palliative care are severely vitamin deficient, targeted vitamin supplementation of such patients is warranted. A follow-up interventional study is needed to determine vitamin status and to investigate the effects of targeted vitamin supplementation on QOL and symptom burden.

Declaration of conflicting interests

this cross-sectional study. CV is employed part-time by Pascoe Pharmazeutische Präparate GmbH (Giessen, Germany).

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