

Whole Blood Selenium Levels and Selenium Supplementation in Patients Treated in a Family Doctor Practice in Golßen (State of Brandenburg, Germany): A Laboratory Study

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Abstract

Introduction: The supply of selenium (Se) varies widely in Germany. Therefore, a laboratory study was conducted in patients treated at a family doctor practice in Brandenburg, Germany, to determine whether there is a general Se deficiency in this area; specifically, whether Se concentrations differ with age, sex, or presence of cancer. Moreover, we tested the effects of a Se supplementation on whole blood Se levels (WBSL). **Methods:** In 2006, WBSL were analyzed in 871 patients (496 females, 375 males, median age: 67 years). Of these, 143 (78 females, 65 males) had cancer and were in an aftercare situation. From 2006 to 2012, 317 patients (76 with tumors, 241 without tumors) received continuous Se supplementation with sodium selenite (300 µg per day) and annual WBSL measurements. WBSL were compared by Student's *t* test for paired and independent samples. **Results:** The initial WBSL of all patients was 97.2 ± 20.7 µg/L (mean \pm SD). WBSL did not differ with regard to age or sex, but patients with cancer had the lowest WBSL. Se supplementation increased mean WBSL in both patients with (to 128.5 µg/L) and without (to 119.52 µg/L) cancer ($P < .001$). **Discussion:** Patients with cancer displayed significantly lower WBSL than patients without cancer, indicating a negative effect of tumors on Se uptake, absorption, or metabolism. Significant influences of age or sex were not observed. Selenite supplementation efficiently improved WBSL to concentrations considered necessary for health benefits.

Keywords

whole blood selenium levels, selenium supplementation, sodium selenite, patients with tumors, patients without tumors

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Introduction

It is well known that selenium (Se) intake varies widely around the world. In the United States, higher Se levels are measured in serum than in Europe.^{1,2} In relation to the optimal activity of Se-dependent proteins, such as the glutathione peroxidases and selenoprotein P, serum Se values should be between 100 and 130 µg/L (equivalent to 125–163 µg/L in whole blood).^{3–7} This is not the case in Europe. In Germany, the mean Se serum values are between 60 and 80 µg/L (equivalent to 75–100 µg/L in whole blood).^{8–12}

In Germany, an inhomogeneous Se supply, with different Se values depending on the diet, is assumed in different regions.^{13–18} Therefore, in a family doctor's practice in 2006

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in the state of Brandenburg, Germany, initial Se levels in whole blood were determined in patients with different diseases. Then, some patients were given supplemental sodium selenite, and whole blood Se level (WBSL) measurements were performed annually. Sodium selenite was chosen because experiences from studies indicate that it was safe at daily doses of 500 to 1000 µg for limited periods of time.^{19,20}

Patients and Methods

Data Collection

The blood collection, the recording of patient data, and the monitoring of the Se values were continuously performed by the family doctor together with a staff nurse. On completion of the full data set, the information was transferred into SPSS for statistical evaluation.

Decision From the Local Institutional Review Board

The Ethics Committee of the Medical Association of the state of Brandenburg decided that no formal ethical approval for this analysis is required as only retrospective data from anonymized subjects have been processed (decision letter from September 12, 2018).

Patients

In 2006, an initial measurement of the Se value in whole blood was carried out in 871 patients (496 females, 375 males) with a median age of 67 (range 30-96) years. Of these, 143 (78 females, 65 males) were patients with cancer in an aftercare situation. The exact patient data in this regard are shown in Tables 1 and 2.

Se supplementation was recommended to 317 patients after a Se deficit had been established by analysis of WBSL (Table 3). Regular checks of WBSL were performed at 12-month intervals. Se supplementation was provided by sodium selenite pentahydrate (300 µg Se per day). The prescription drug selenase 300[®] from the pharmaceutical company biosyn, Fellbach, Germany, was used throughout the study. The quality of this pharmaceutical preparation is guaranteed by continuous quality control and batch release as well as by usual drug safety measures (pharmacovigilance). Compliance with the recommendation to taking the prescription drug selenase 300[®] was monitored by the family doctor during the regular patient visits. The Se drugs were given as part of routine clinical practice and not as part of an organized clinical trial.

Measurement of Whole Blood Selenium

Levels of whole blood Se were measured using atomic absorption spectroscopy according to the method of Winnefeld et al.²¹

Table 1. Characteristics of Patients.

	Women	Men
Number (N = 871)	496	375
Age, years (median)	67 (20-96)	68 (19-93)
Without malignoma (n = 728)	418	310
With malignoma (n = 143)	78	65
Age, years (without malignoma)	67 (20-96)	68 (19-93)
Age, years (with malignoma)	68 (20-91)	66 (24-86)

Table 2. Distribution of the Most Common Tumor Entities (Shown as Number of Cases).

Colon cancer	24
Breast cancer	23
Lung cancer	13
Rectal cancer	12
Prostate cancer	10
Skin cancer	10

Table 3. Comparison of Patients With Versus Without Selenium Supplementation.

	Without Selenium Supplementation, n	With Selenium Supplementation, n
Patients (all)	554	317
Women	317	179
Men	237	138
With malignoma	67	76
Without malignoma	487	241

Statistics

All data were stored and analyzed using the SPSS statistical package 15.0 (SPSS Inc, Chicago, IL). Descriptive statistics were computed for continuous and categorical variables. The statistics computed included mean and standard deviations (SDs) of continuous variables and frequencies and relative frequencies of categorical factors. WBSL were compared by Student's *t* test for paired and independent samples. All *P* values were 2-sided statistical tests, and values of *P* < .05 were considered to be statistically significant.

Results

The initial mean WBSL of all patients was 97.2 µg/L (SD: 20.65). For patients with cancer, the mean value was 91.6 µg/L (SD: 25.26) in contrast to 98.9 µg/L (SD: 19.26) for patients without cancer (*P* = .003). The lowest mean value (87.9 µg/L [SD: 22.76]) was measured in male cancer patients. More results, including the influences of age or sex, are shown in Table 4.

The number of patients concerning initial WBSL distribution depending on the presence of a tumor is given in Table 5.

Table 4. Initial Mean Whole Blood Selenium Level Depending on the Influence of Age, Sex, and the Presence of a Tumor.

Age ≤30 years (n = 26)	100.8 µg/L (SD: 25.7)	
Age 31-50 years (n = 133)	97.5 µg/L (SD: 20.8)	
Age 51-70 years (n = 380)	97.4 µg/L (SD: 20.0)	
Age >70 years (n = 332)	96.4 µg/L (SD: 21.0)	<i>P</i> = .864
Women (n = 496)	97.8 µg/L (SD: 20.6)	
Men (n = 375)	96.4 µg/L (SD: 20.4)	<i>P</i> = .3
Patients with tumors (n = 143)	91.6 µg/L (SD: 25.3)	
Patients without tumors (n = 728)	98.9 µg/L (SD: 19.3)	<i>P</i> = .003
Women with tumors (n = 78)	94.9 µg/L (SD: 26.9)	
Women without tumors (n = 418)	98.4 µg/L (SD: 19.2)	<i>P</i> = .234
Men with tumors (n = 65)	87.9 µg/L (SD: 22.8)	
Men without tumors (n = 310)	98.1 µg/L (SD: 19.4)	<i>P</i> = .001

Table 5. Overview of Initial Whole Blood Selenium Levels (WBSL) in Patients With or Without Tumors in Relation to the Recommended Range.

	Number of Patients With WBSL Below Recommended Range (125-163 µg/L)	Number of Patients With WBSL Within Recommended Range (125-163 µg/L)	Number of Patients With WBSL Above Recommended Range (125-163 µg/L)
Patients with tumors (n = 143), n (%)	n = 133 (93.0%)	n = 8 (5.6%)	n = 2 (1.4%)
Patients without tumors (n = 728), n (%)	n = 673 (92.4%)	n = 53 (7.3%)	n = 2 (0.3%)

Table 6. Highest WBSL Reached With Se Supplementation Compared With Initial WBSL Depending on the Presence of a Tumor.

	Initial WBSL in Patients With Se Supplementation	Highest WBSL Reached With Se Supplementation	<i>P</i> (Student's <i>t</i> Test for Paired Samples)
Patients with tumors	91.7 µg/L (SD: 27.3) (n = 76)	133.4 µg/L (SD: 17.9) (n = 38)	<.001
Patients without tumors	87.4 µg/L (SD: 17.3) (n = 241)	119.5 µg/L (SD: 18.8) (n = 39)	<.001

Abbreviations: WBSL, whole blood selenium level; Se, selenium.

Table 7. Time Resolved Analysis of WBSL in Se Supplemented Patients With Tumors.

Control Measurement After	Initial WBSL in Patients With Se Supplementation	WBSL Reached With Se Supplementation	<i>P</i> (Student's <i>t</i> Test for Paired Samples)
1 year	91.7 µg/L (SD: 27.3) (n = 76)	121.7 µg/L (SD: 23.2) (n = 76)	<.001
2 years	91.4 µg/L (SD: 30.1) (n = 60)	127.5 µg/L (SD: 25.8) (n = 60)	<.001
3 years	92.3 µg/L (SD: 34.8) (n = 38)	133.4 µg/L (SD: 17.9) (n = 38)	<.001
5 years	93.1 µg/L (SD: 41.5) (n = 26)	128.5 µg/L (SD: 19.9) (n = 26)	<.001

Abbreviations: WBSL, whole blood selenium level; Se, selenium.

Se supplementation increased the mean WBSL in both patients with cancer (from 91.7 to 133.4 µg/L) and in patients without cancer (from 87.4 to 119.52 µg/L; *P* < .001; Tables 6-8).

During supplementation, no Se-related side effects were observed or reported by the patients.

Discussion

With the data presented here, the initial WBSL of a larger patient population from the state of Brandenburg, Germany,

are available for the first time. The mean WBSL of 97.2 µg/L (corresponding to approximately 77 µg/L in serum) of all patients does not reach the range of 100 to 130 µg/L in serum necessary for the optimal activity of selenoproteins. For patients with tumors, the mean WBSL was even lower at 91.6 µg/L (corresponding to approximately 73 µg/L in serum). This confirms that with normal nutrition, only a suboptimal supply of Se is guaranteed in Germany.^{1,2} Se deficiency in patients with cancer is well known, confirming existing data.⁸⁻¹²

In our study, Se supplementation was initially given to 317 patients. Normalized Se status could be achieved both

Table 8. Time Resolved Analysis of WBSL in Se Supplemented Patients Without Tumors.

Control Measurement After	Initial WBSL in Patients with Se Supplementation	WBSL Reached With Se Supplementation	P (Student's t Test for Paired Samples)
1 year	87.4 µg/L (SD: 17.3) (n = 241)	113.5 µg/L (SD: 20.2) (n = 241)	<.001
2 years	84.2 µg/L (SD: 17.5) (n = 92)	117.9 µg/L (SD: 18.3) (n = 92)	<.001
3 years	84.5 µg/L (SD: 18.2) (n = 39)	119.5 µg/L (SD: 18.8) (n = 39)	<.001
5 years	84.5 µg/L (SD: 17.5) (n = 24)	119.5 µg/L (SD: 18.8) (n = 24)	<.001

Abbreviations: WBSL, whole blood selenium level; Se, selenium.

in patients with cancer and in patients without malignancies. In comparison to organic Se compounds, sodium selenite used in our study did not lead to an increase in the mean WBSL >135 µg/L, even after several years of continuous use, although patients' Se levels did increase. This confirms already known data that the Se values above normal range are not reached, because excess Se is excreted through the pulmonary and renal systems.²² With the longer use of organic Se compounds, blood levels of more than 200 µg/L could be achieved, which are unlikely to have further Se-related effects on health.^{2,23}

Neither the initial Se levels nor Se supplementation showed significant differences between women and men.

It is noteworthy that the cancer patients achieved higher WBSL on Se supplementation than the noncancer patients. A potential reason for this difference may lie in a higher motivation of cancer patients to adhering to the recommended supplementation regimen, which might have caused a better compliance in this group of subjects.

In order to achieve the optimal activity of selenoproteins, patients with tumors who have Se deficiency should receive Se supplementation to protect them from the associated health risks and to improve their quality of life during chemotherapy and radiotherapy.^{19,20,23-34} In addition, determining Se levels in patients with tumors should definitely be recommended as part of clinical routine.

Study Limitations

The data presented in this article need to be interpreted with the due care, as the type of study is a retrospective laboratory analysis and cannot identify causal relationships. In addition, we have no detailed information on compliance of the patients with regard to regular intake of the pharmaceutical preparation, or with regard to potential side effects in response to selenite intake.

Conclusion

Patients with tumors displayed significantly lower WBSL than patients without tumors, indicating a negative effect of tumors on Se uptake, absorption, or metabolism. Significant influences of age or sex were not observed.

Selenite supplementation efficiently improved the WBSL to concentrations considered to provide health benefits and protect patients from Se deficiency-associated health risks.

Authors' Note

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Declaration of Conflicting Interests

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