ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2021 May 21; 27(19): 2251-2433

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

Contents

Weekly Volume 27 Number 19 May 21, 2021

EDITORIAL

FRONTIER

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Cohort Study

World Journal of Gastroenterology

Weekly Volume 27 Number 19 May 21, 2021

Contents

World Journal of Gastroenterology

Weekly Volume 27 Number 19 May 21, 2021

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Pietro Fusaroli, MD, Associate Professor, Department of Medical and Surgical Sciences, University of Bologna/Hospital of Imola, Via Montericco 4, Imola (BO) 40026, Italy. pietro.fusaroli@unibo.it

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2020 edition of Journal Citation Report® cites the 2019 impact factor (IF) for *WJG* as 3.665; IF without journal self cites: 3.534; 5-year IF: 4.048; Ranking: 35 among 88 journals in gastroenterology and hepatology; and Quartile category: Q2. The *WJG*'s CiteScore for 2019 is 7.1 and Scopus CiteScore rank 2019: Gastroenterology is 17/137.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yu-Jie Ma*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Ze-Mao Gong*.

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORS-IN-CHIEF
Andrzej S Tarnawski, Subrata Ghosh

EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/1007-9327/editorialboard.htm

PUBLICATION DATE
May 21, 2021

COPYRIGHT
© 2021 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

© 2021 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com

World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2021 May 21; 27(19): 2366-2375

DOI: 10.3748/wjg.v27.i19.2366

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Retrospective Study

Changes in the nutritional status of nine vitamins in patients with esophageal cancer during chemotherapy

Lan-Qing Liang, Ling-Ling Meng, Bo-Ning Cai, Ze-Ping Cui, Na Ma, Le-Hui Du, Wei Yu, Bao-Lin Qu, Sheng-Qiang Feng, Fang Liu

ORCID number: Lan-Qing Liang 0000-0003-4840-6117; Ling-Ling Meng 0000-0003-4674-5297; Bo-Ning Cai 0000-0003-2358-4806; Ze-Ping Cui 0000-0002-4589-7187; Na Ma 0000-0002-7045-6623; Le-Hui Du 0000-0002-6865-8461; Wei Yu 0000-0002-5024-8675; Bao-Lin Qu 0000-0002-8911-3460; Sheng-Qiang Feng 0000-0002-3996-0872; Fang Liu 0000-0002-8563-4664.

Author contributions: Liang LQ and Meng LL contributed equally to this work; Liang LQ and Meng LL designed and performed the research and wrote the paper; Liu F designed the research and supervised the report; Cui ZP and Ma N designed the research and contributed to the analysis; Du LH, Yu W and Feng SQ provided clinical advice; Qu BL and Cai BN supervised the report.

Supported by Health Bureau of the Department of Logistics and Security of the Central Military Commission of China, No. 17BJZ47.

Institutional review board statement: The study was reviewed and approved by the Medical Ethics Committee of the General Hospital of the Chinese People's Liberation Army, No. S2019-198-02.

Lan-Qing Liang, Ling-Ling Meng, Bo-Ning Cai, Ze-Ping Cui, Na Ma, Le-Hui Du, Wei Yu, Bao-Lin Qu, Fang Liu, Department of Radiotherapy, Chinese PLA General Hospital, Beijing 100853, China

Sheng-Qiang Feng, Department of Health Service, The Guard Bureau of Joint Staff Department of Chinese PLA, Beijing 100017, China

Corresponding author: Fang Liu, MD, Associate Chief Physician, Department of Radiotherapy, Chinese PLA General Hospital, No. 28 Fuxing Road, Haidian District, Beijing 100853, China. liufangfsq@163.com

Abstract

BACKGROUND

Many studies have investigated the relationships between vitamins and esophageal cancer (EC). Most of these studies focused on the roles of vitamins in the prevention and treatment of EC, and few studies have examined the changes in vitamin nutritional status and their influencing factors before and after chemotherapy for EC. Chemotherapy may have a considerable effect on EC patients' vitamin levels and hematological indicators.

AIM

To research the nutritional status of multiple vitamins in EC patients during chemotherapy and to assess its clinical significance.

METHODS

EC patients admitted to our center from July 2017 to September 2020 were enrolled in this study. Serum concentrations of nine vitamins (A, D, E, B_9, B_{12}, B_1, C, B_2 and B_6), hemoglobin, total protein, albumin, blood calcium, blood phosphorus concentrations and body mass index (BMI) were measured in all EC patients. The changes in nine vitamins, hematological indicators and BMI were compared before and after two cycles of chemotherapy. The possible influential factors were analyzed.

RESULTS

In total, 203 EC patients receiving chemotherapy were enrolled in this study. Varying degrees of vitamin A, D, C and B_2 deficiency and weight loss were found in these patients, and the proportions of vitamin B_2 and vitamin C deficiencies increased significantly after chemotherapy (both $P < 0.05$). Serum concentrations

of vitamins A, C, B_2 and B_6 and BMI before and after chemotherapy were statistically significant (all $P < 0.05$). Multivariate analysis showed that vitamin A levels significantly differed between male and female EC patients, whereas vitamin D concentration significantly differed in EC patients in different stages (all $P < 0.05$). Correlations were observed between the changes in serum concentrations of vitamin A and C before and after two cycles chemotherapy and the change in BMI ($P < 0.05$). Hemoglobin, total protein, serum albumin and blood calcium concentrations significantly decreased in EC patients after chemotherapy (all $P < 0.05$), while the blood phosphorus level significantly increased after chemotherapy ($P < 0.05$). Using the difference in vitamin concentrations as the independent variables and the difference in BMI as the dependent variable, logistic regression analysis revealed statistically significant differences for vitamin A, vitamin D and vitamin C ($F = 5.082$, $P = 0.002$).

CONCLUSION

Vitamin A, D, C and B_2 were mainly deficient in patients with EC during chemotherapy. Multivitamin supplementation may help to improve the nutritional status, chemotherapy tolerance and efficacy.

Key Words: Esophageal cancer; Chemotherapy; Vitamins; Nutritional status; Body mass index

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: This retrospective study investigated the changes in serum vitamins before and after chemotherapy for esophageal cancer. Vitamin deficiencies are common in esophageal cancer patients during chemotherapy and may be associated with the change in body mass index. There were correlations between the changes in vitamin A and C concentrations and the change in body mass index during chemotherapy. Vitamin A level after chemotherapy showed a significant difference between males and females, and the vitamin D level after chemotherapy showed a significant difference among different stages. Vitamin supplementation may reduce the adverse effects of chemotherapy and improve the nutritional status.

Citation: Liang LQ, Meng LL, Cai BN, Cui ZP, Ma N, Du LH, Yu W, Qu BL, Feng SQ, Liu F. Changes in the nutritional status of nine vitamins in patients with esophageal cancer during chemotherapy. *World J Gastroenterol* 2021; 27(19): 2366-2375
URL: https://www.wjgnet.com/1007-9327/full/v27/i19/2366.htm
DOI: https://dx.doi.org/10.3748/wjg.v27.i19.2366

INTRODUCTION

Esophageal cancer (EC) is the ninth most commonly diagnosed cancer and the sixth leading cause of cancer death worldwide[1]. The incidence and mortality rates of EC are highly heterogeneous in terms of gender, histological type, geographic distribution and race[2]. The morbidity and mortality of EC in China are higher than the global averages[3]. Chemoradiotherapy remains the mainstay of treatment for patients with advanced EC. The most common complications during chemoradiotherapy in EC patients include weight loss, malnutrition, bone marrow suppression, electrolyte disturbances, hypoproteinemia and decreased quality of life[4-7]. Multiple vitamins are involved in the pathogenesis, progression and prognosis of tumors and are closely related to the tumor microenvironment. Vitamin testing is valuable in tumor patients as it can identify whether there is a specific vitamin deficiency and/or justify vitamin therapy. Most clinical studies have shown that vitamin nutritional status varies greatly in tumors of different systems[8]. Although many studies have investigated the relationships between vitamins B, A, D and C with EC, most of these studies focused on the roles of vitamins in the prevention and treatment of EC. Few studies have examined the changes in vitamin nutritional status and their influencing factors before and after chemotherapy for EC.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: All authors hereby declare that there is no personal conflict of interest that may cause impact or bias to the results of this study. All authors read and approved the final manuscript.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/Licenses/by-nc/4.0/

Manuscript source: Unsolicited manuscript

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: China

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: February 2, 2021
Peer-review started: February 2, 2021
First decision: March 6, 2021
Revised: March 18, 2021
Accepted: April 13, 2021
Article in press: April 13, 2021
Published online: May 21, 2021

P-Reviewer: Kumar N, Levick C
S-Editor: Fan JR
L-Editor: Filipodia
P-Editor: Ma YJ

Many vitamins have antitumor effects and are closely related to the occurrence, progression, prognosis and recovery of tumors. Vitamin supplementation can lower the risk of tumorigenesis and prevent abnormal DNA methylation changes in tumor cells[9]. With the advances in nutritional therapy in China, nutritional screenings, assessments and interventions have increasingly been applied in tumor patients. The standardized nutritional therapies involve three major macronutrients including carbohydrates, proteins and fats and have specific requirements on micronutrients. Nutritional therapy for tumor patients provides nutrients and energy and focuses on the metabolism-regulating roles of nutrients[10]. Vitamin supplementation is a common nutritional therapy for tumor patients in clinical practice. Serum vitamin levels vary among patients with different tumors. Zhang *et al*[11] analyzed the vitamin nutritional status of approximately 1000 hospitalized tumor patients and found that vitamin B1 concentrations were low in patients with digestive system tumors such as EC and gastric cancer. A study on postoperative nutritional deficiencies in patients with EC or gastric cancer revealed that the incidence of ferritin, folic acid, vitamin B_{12} and vitamin D deficiencies was 42.86%, 9.52%, 6.35% and 36.67%, respectively, and the vitamin levels were significantly improved after nutritional interventions[12]. In another study[13], most patients with advanced tumors had vitamin (particularly vitamins D, B_6 and C) deficiency symptoms during palliative care, and further analysis revealed a correlation between the degree of vitamin deficiency and clinical discomfort in these patients. Most vitamins were found to be negatively associated with the risk of colorectal and gastric cancer in addition to EC in an observational study, yet interventional treatment failed to demonstrate a clear preventive effect in these malignancies [14].

In the current study, we analyzed the effects of chemotherapeutic drugs on EC patients' vitamin levels and hematological indicators by detecting the changes in nine vitamins and hematological indicators (*e.g.*, hemoglobin, total protein, serum albumin and electrolytes) before and after chemotherapy, with an attempt to provide evidence for clinical vitamin supplementation and nutritional therapies. Our findings may be valuable for the implementation of tailored nutritional interventions, which will help to reduce chemotherapy-related complications, alleviate treatment resistance and improve chemotherapy efficacy.

MATERIALS AND METHODS

Subjects

In total, 203 EC patients (181 men and 22 women) aged 37-78 yrs (mean: 60.03 ± 7.95 years) who were receiving chemotherapy in our center between July 2017 and September 2020 were enrolled in this study. The vast majority of subjects had esophageal squamous cell carcinoma (n = 192, 94.58%), and 166 patients (81.77%) were in stage III-IV (Table 1). The inclusion criteria were as follows: (1) pathologically confirmed esophageal malignancies, with indications for chemotherapy, regardless of gender; (2) aged 18-80 years; (3) an expected survival of > 6 mo; and (4) a Karnofsky performance status score of ≥ 70 points. The exclusion criteria included: (1) contraindications to chemotherapy; (2) coexisting tumors in other systems; (3) coexisting primary blood diseases or endocrine diseases; (4) coexisting cardiopulmonary dysfunction; and (5) coexisting psychiatric disorders.

Methods

Determination of vitamin concentrations and hematological indicators: Vitamin levels were measured using electrochemiluminescence with an LK3000VI vitamin detector (Tianjin Lanbiao Electronic Technology Development Co., Ltd., Tianjin, China) pre- and postchemotherapy in EC patients. The normal thresholds were as follows: hemoglobin: 137-179 g/L in males and 116-155 g/L in females; total protein: 55-88 g/L; serum albumin: 35-50 g/L; blood calcium: 2.09-2.54 mmol/L; blood phosphorus: 0.89-1.60 mmol/L; vitamin A: 0.52-2.20 mmol/L; vitamin D: 25-200 nmol/L; vitamin E: 10-15 mg/mL; vitamin B_9: 6.8-36.3 nmol/L; vitamin B_{12}: 200-900 pg/mL; vitamin B_1: 50-150 nmol/L; vitamin C: 34-114 mmol/L; vitamin B_2: 4.26-18.42 mg/L; and vitamin B_6: 14.6-72.9 nmol/L.

Chemotherapy regimens: Of these 203 EC patients, 168 were treated with induction chemotherapy, 15 with postoperative adjuvant chemotherapy and 20 with postrelapse chemotherapy. The specific regimens were as follows: (1) squamous cell carcinoma: paclitaxel + platinum; (2) adenocarcinoma: oxaliplatin + fluorouracil; and (3) small cell

Table 1 Baseline data of esophageal cancer patients (*n* = 203)

Clinical features	*n*	(%)
Gender		
Males	181	89.16
Females	22	10.84
Age		
< 60 yr	94	46.31
≥ 60 yr	109	53.69
Tumor stage		
II	16	7.88
III	98	48.28
IV	68	33.50
Uncertain	21	10.34
Pathologic type		
Squamous cell carcinoma	192	94.58
Nonsquamous cell carcinoma	11	5.42
Treatment		
Induction chemotherapy	168	82.76
Postoperative adjuvant chemotherapy	15	7.39
Postrelapse chemotherapy	20	9.85
Primary tumor site		
Cervical	14	6.90
Upper thoracic	28	13.79
Middle thoracic	77	37.93
Lower thoracic	84	41.38

carcinoma: etoposide + platinum. All of these regimens were repeated every 3 wk.

Statistical methods

SPSS 24.0 statistical software was used for analyzing the data. Normally distributed data were expressed as mean ± SD, and intergroup comparisons were based on the paired-sample *t*-test. Non-normally distributed data were expressed as quartiles and medians, and the rank sum test was applied for comparisons between two groups. The Spearman method was used to test for correlations between the changes in multiple vitamin serum concentrations (the independent variables) and body mass index (BMI) (the dependent variable) during chemotherapy using. P value < 0.05 was regarded as statistically significant.

RESULTS

Variation in BMI and hematological parameters in EC patients during chemotherapy

BMI declined after chemotherapy in 133 cases (65.52%). The number of patients with anemia increased from 119 before chemotherapy to 182 after chemotherapy. The differences in these proportions were statistically significant (P < 0.05) (Table 2).

Vitamin levels in EC patients pre- and postchemotherapy

Vitamin A, C, B_2 and B_6 concentrations significantly differed before and after chemotherapy (all P < 0.05) (Table 3).

Table 2 Changes in body mass index and hematological indicators in esophageal cancer patients before and after chemotherapy [*n* (%)]

Item	Before chemotherapy	After chemotherapy	χ^2/*Z*	*P* value
Body mass index (kg/m^2)			-2.646	0.008
< 18.5	25 (12.32)	22 (10.84)		
18.5-23.9	103 (50.74)	123 (60.59)		
> 23.9	75 (36.95)	58 (28.57)		
Hemoglobin (g/L)			55.710	< 0.001
Decreased	119 (58.62)	182 (89.66)		
Normal	84 (41.38)	21 (10.34)		
Serum albumin (g/L)			2.717	0.099
Decreased	34 (16.75)	47 (23.15)		
Normal	169 (83.25)	156 (76.85)		
Serum calcium (mmol/L)			4.780	0.029
Decreased	21 (10.34)	36 (17.73)		
Normal	182 (89.66)	167 (82.27)		
Blood phosphorus (mmol/L)			2.382	0.123
Decreased	23 (11.33)	13 (6.40)		
Normal	180 (88.67)	190 (93.60)		

Table 3 Vitamin concentrations in esophageal cancer patients before and after chemotherapy

Item	Before chemotherapy (Q1-Q3) median	After chemotherapy (Q1-Q3) median	*Z*	*P* value
Vitamin A (μmol/L)	(0.561-0.980) 0.741	(0.528-0.858) 0.678	-3.465	0.001
Vitamin D (nmol/L)	(33.618-49.939) 41.383	(33.235-46.473) 38.832	-1.599	0.110
Vitamin E (μg/mL)	(10.898-11.673) 11.267	(10.905-11.867) 11.298	-1.678	0.093
Vitamin B_9 (nmol/L)	(14.529-23.014) 18.718	(13.859-22.037) 17.539	-1.578	0.115
Vitamin B_{12} (pg/mL)	(491.023-598.303) 557.219	(491.112-590.338) 546.789	-0.326	0.745
Vitamin B_1 (nmol/L)	(75.056-97.909) 84.070	(75.826-93.322) 83.095	-1.477	0.140
Vitamin C (μmol/L)	(34.324-38.543) 36.075	(33.299-37.849) 35.259	-3.824	< 0.001
Vitamin B_2 (μg/L)	(4.182-5.050) 4.501	(4.105-4.761) 4.284	-2.631	0.009
Vitamin B_6 (nmol/L)	(29.702-33.645) 31.747	(28.875-32.868) 31.363	-2.351	0.019

Q1-Q3: Quartiles 1-3.

Vitamin deficiencies in EC patients undergoing chemotherapy

Deficiencies of vitamin A, D, C and B_2 were detected pre- and postchemotherapy, and the proportion of each of these four vitamin deficiencies increased after chemotherapy. In particular the proportions of vitamin C and B_2 deficiencies (24.46% *vs* 38.85%) increased significantly (both $P < 0.05$) (Table 4). Three EC patients had excessively high vitamin A concentrations before chemotherapy, which decreased to normal levels in 2 cases and to vitamin A deficiency in 1 case after chemotherapy. None of the other five vitamin (E, B_9, B_{12}, B_1, B_6) deficiencies were detected during chemotherapy.

Changes in hematological indicators in EC patients pre- and postchemotherapy

Hemoglobin, total protein, serum albumin and blood calcium concentrations significantly decreased, and blood phosphorus concentrations significantly increased after chemotherapy (all $P < 0.05$) (Table 5).

Table 4 Vitamin deficiencies in esophageal cancer patients before and after chemotherapy, *n* (%)

Item	Before chemotherapy		After chemotherapy		χ^2	*P* value
	Normal	Deficiency	Normal	Deficiency		
Vitamin A (μmol/L)	163 (81.50)	37 (18.50)	158 (79.00)	42 (21.00)	0.485	0.486
Vitamin D (nmol/L)	194 (95.57)	9 (4.43)	191 (94.09)	12 (5.91)	0.235	0.629
Vitamin C (μmol/L)	155 (76.35)	48 (23.65)	133 (65.52)	70 (34.48)	6.682	0.010
Vitamin B_2 (μg/L)	139 (68.47)	64 (31.53)	108 (53.20)	95 (46.80)	9.677	0.002

Table 5 Changes in hematological indicators in esophageal cancer patients before and after chemotherapy

Item	Before chemotherapy (mean ± SD)	After chemotherapy (mean ± SD)	*t*	*P* value
Hemoglobin (g/L)	130.070 ± 16.484	115.010 ± 14.584	15.342	< 0.001
Total protein (g/L)	66.572 ± 5.726	64.499 ± 5.528	5.032	< 0.001
Serum albumin (g/L)	38.880 ± 4.138	37.546 ± 3.719	4.355	< 0.001
Blood calcium (mmol/L)	2.240 ± 0.128	2.207 ± 0.132	2.835	0.005
Blood phosphorus (mmol/L)	1.130 ± 0.200	1.180 ± 0.184	-2.818	0.005

SD: Standard deviation.

Factors affecting vitamins and hematological indicators in EC patients

After adjustment for covariates of each indicator before chemotherapy, vitamin A levels after chemotherapy showed a significant difference between males and females. Vitamin D levels after chemotherapy showed a significant difference among different tumor grades (both $P < 0.05$). No statistically significant differences were shown for the other baseline data (all $P > 0.05$) (Table 6).

Correlation between vitamin concentrations and BMI during chemotherapy in EC patients

There were correlations between the changes in serum vitamin A and C concentrations and the change in BMI before and after chemotherapy ($P < 0.05$) (Table 7).

Regression analysis of vitamins and BMI in EC patients

Using the difference in vitamin concentrations as the independent variables and the difference in BMI as the dependent variable, logistic regression analysis revealed statistically significant differences for three vitamins ($F = 5.082$, $P = 0.002$) (Table 8).

DISCUSSION

It was found that EC patients had different degrees of vitamin deficiency during chemotherapy, and the hemoglobin, total protein, serum albumin concentration and blood calcium concentration significantly decreased after chemotherapy. In addition, the proportions of patients with weight loss, anemia and hypoproteinemia also significantly increased. Our subjects were most deficient in vitamin B_2 and vitamin C followed by vitamins A and D.

In the current study, EC patients undergoing chemotherapy were most deficient in vitamin B_2 (31.53% and 46.80% before and after chemotherapy, respectively), and vitamin B_2 concentration significantly decreased after chemotherapy ($P < 0.05$). Vitamin B_1, B_9, B_{12} and B_6 deficiency or excess was not found in any of our EC patients. A comparison of vitamin levels before and after chemotherapy suggested that vitamin B_6 concentrations decreased significantly after chemotherapy but were still within the normal range. It has been reported that B vitamin intake is correlated with the risk of EC. Appropriate supplementation with vitamins B_6 and B_9 (also known as folate) can reduce the risk, while higher intake of vitamin B_{12} may increase the risk[15,16]. A study of residents in Yanting County, Sichuan Province, a high-incidence area of EC in

Table 6 Factors affecting various indicators in esophageal cancer patients during chemotherapy

Item	Gender (Males/females)		Age (≥ 60 yr/< 60 yr)		Tumor grades (grades II/III/IV)		Tumor location (cervical/upper, middle, lower thoracic)	
	F	*P* value	F	*P* value	F	*P* value	F	*P* value
Body mass index	0.014	0.904	0.042	0.837	0.672	0.512	0.718	0.542
Hemoglobin	0.044	0.834	0.757	0.385	0.747	0.475	0.195	0.900
Serum albumin	0.707	0.402	3.387	0.067	0.210	0.811	2.554	0.057
Vitamin A	5.407	0.021	0.059	0.809	0.151	0.860	0.692	0.558
Vitamin D	0.594	0.442	0.326	0.568	6.899	0.001	0.324	0.808
Vitamin C	3.774	0.053	0.537	0.464	2.633	0.075	2.261	0.083
Vitamin B_2	0.178	0.674	0.863	0.354	0.381	0.684	2.273	0.081

The descriptive statistics of each indicator before and after chemotherapy are shown in Tables 3 and 5.

Table 7 Relationships between the differences in vitamins before and after chemotherapy and the difference in body mass index before and after chemotherapy in esophageal cancer patients

Difference in vitamin concentration	Difference in BMI	
	r	*P* value
Vitamin A	0.240	0.001
Vitamin D	-0.080	0.259
Vitamin E	-0.095	0.177
Vitamin B_9	-0.016	0.824
Vitamin B_{12}	-0.053	0.449
Vitamin B_1	0.021	0.771
Vitamin C	0.188	0.007
Vitamin B_2	-0.102	0.149
Vitamin B_6	-0.078	0.269

BMI: Body mass index.

Table 8 Regression analysis of the relationships between the concentrations of various vitamins and body mass index in 203 esophageal cancer patients

Independent variables (differences)	Dependent variable (difference in BMI)		
	B (coefficient)	*t*	*P* value
Constant	0.365	4.978	< 0.001
Vitamin A	0.304	1.877	0.062
Vitamin D	-0.009	-2.355	0.020
Vitamin C	0.026	1.793	0.074

BMI: Body mass index.

China, found that riboflavin intake was markedly deficient, and riboflavin supplements in high-risk groups reduced the incidence of EC[17]. In a multicenter study in China, whole blood riboflavin was tested in 764 EC patients (and in controls), and the analysis revealed that whole blood riboflavin levels were not significantly correlated with the prevalence of EC. However, high whole blood riboflavin level was more

favorable for the survival of elderly EC patients aged 50-70 yrs[18]. Therefore, B vitamin supplementation in EC patients undergoing chemotherapy is beneficial to improve vitamin nutritional status and reduce complications.

In our research, the proportion of vitamin C deficiency cases was 23.65% and 34.48%, before and after chemotherapy, respectively. The difference was statistically significant, and vitamin C was the most deficient vitamin after chemotherapy. Thus, chemotherapy may have a considerable effect on vitamin C levels in EC patients. A meta-analysis showed a negative correlation between dietary vitamin C intake and EC risk and concluded that a high level of vitamin C may prevent EC[19]. Vitamin C supplementation was found to downregulate nuclear factor kappa B activity and significantly decrease proinflammatory cytokine levels in EC patients treated with neoadjuvant radiotherapy[20].

In the current study, vitamin A and D deficiencies were found in EC patients both before and after chemotherapy, and their proportions increased following chemotherapy. However, the changes in the proportions were not statistically significant after chemotherapy. Further stratified analysis of the baseline data showed that the change in vitamin A concentration during chemotherapy might be associated with gender, while vitamin D might differ among different tumor stages. Vitamins A and D are mainly derived from food sources. EC itself can affect the intake and absorption of food, and chemotherapy drugs further damage the nutritional status of patients, resulting in more significant vitamin deficiencies in patients after treatment. In the current study, we further analyzed the difference between vitamin concentrations and BMI in EC patients before and after chemotherapy and found that vitamins A and C were significantly correlated with the change in BMI. Regression analysis of multiple vitamins and BMI revealed a statistically significant overall model for three vitamins (A, D and C). Therefore, body weight, vitamin levels and hematological indicators interact with each other during chemotherapy in EC patients, and the supplementation of macronutrients and micronutrients are equally important. Developing holistic care is the key to nutritional therapy for tumor patients.

There were different degrees of vitamin A and D deficiencies in EC patients treated with chemotherapy, and a higher proportion of vitamin A deficiency than vitamin D deficiency and no vitamin E deficiency was detected during our observation. A meta-analysis suggested that vitamin A levels were negatively correlated with EC risk[21], and further studies are needed to confirm whether it affects the prognosis of EC patients. Vitamin D has been found to inhibit tumor cell proliferation, induce cell differentiation, promote apoptosis and suppress angiogenesis[22]. A meta-analysis did not observe an association between vitamin D levels and the development of esophageal lesions[23]. Another study reported that appropriate vitamin D supplementation in postoperative EC patients improved quality of life and disease-free survival, and further multivariate analysis found that vitamin D supplementation was an independent prognostic factor for disease-free survival but was not associated with overall survival[24].

This study had some limitations: (1) the sample size was not large due to the single center retrospective design of the study; (2) a control group was not included, and it is unclear whether vitamin supplementation is beneficial in EC patients undergoing chemotherapy; (3) the results might be biased due to different disease states and chemotherapy regimens; and (4) some patients might have received targeted therapy or immunotherapy during chemotherapy, which may have had an impact on the study results. In addition, no data on response rate or overall survival were included in our analysis, and the relationship between vitamin nutritional status and prognosis in EC patients requires further investigation in multicenter prospective studies.

CONCLUSION

Vitamin deficiencies (mainly vitamins A, D, C and B_2 deficiencies) are common in EC patients during chemotherapy and may be associated with the change in BMI. In addition, chemotherapy drugs decrease hematological indicators such as hemoglobin and albumin. Appropriate nutritional interventions and vitamin supplementation can reduce the adverse effects of chemotherapy, improve overall nutritional status of patients and improve drug tolerability and quality of life.

ARTICLE HIGHLIGHTS

Research background

Few studies have examined the changes in vitamin nutritional status and their influencing factors during chemotherapy for esophageal cancer (EC). Most vitamins were found to be negatively associated with the risk of colorectal and gastric cancer in addition to EC, yet interventional treatment failed to demonstrate a clear preventive effect in these malignancies. In our study, the effects of chemotherapeutic drugs on EC patients' vitamin levels and hematological indicators were analyzed.

Research motivation

We analyzed the effects of chemotherapeutic drugs on EC patients' vitamin levels and hematological indicators by detecting the changes in nine vitamins and hematological indicators before and after chemotherapy, with an attempt to provide evidence for vitamin supplementation. Many oncologists believe that vitamin testing is valuable in tumor patients as it can identify whether there is a specific vitamin deficiency and/or justify vitamin therapy. Our findings may be valuable for the implementation of tailored nutritional interventions.

Research objectives

To explore multiple vitamin levels and the possible influential factors in EC patients treated with chemotherapy. Varying degrees of vitamin deficiency and weight loss were found in these patients. Vitamin supplementation may reduce the adverse effects of chemotherapy.

Research methods

Vitamin nutritional status was measured using the electrochemiluminescence method with an LK3000VI vitamin detector before and after two cycles of chemotherapy in EC patients. Statistical analysis was performed using the SPSS 24.0 software package. The latent correlations between multiple vitamin levels (the independent variables) and body mass index (the dependent variable) during chemotherapy were analyzed using the Spearman method.

Research results

Varying degrees of vitamin A, D, C and B_2 deficiency and weight loss were found in EC patients. Statistically significant differences were shown in vitamins A, C, B_2 and B_6 levels and body mass index before and after chemotherapy. Multivariate analysis showed that vitamin A levels significantly differed between male and female EC patients, whereas vitamin D concentrations significantly differed in EC patients in different stages. Correlations were observed between the changes in serum vitamin A and C levels pre- and postchemotherapy and the variation in body mass index.

Research conclusions

Varying degrees of vitamin deficiency and weight loss were found in EC patients undergoing chemotherapy. Vitamin supplementation may help to improve the nutritional status, chemotherapy tolerance and efficacy. To detect the concentrations of vitamins is valuable for EC patients.

Research perspectives

A multicenter prospective study should be performed to reveal the suitable vitamin replenishment programs and potential effects on treatment outcomes and the adverse effects of chemotherapy in EC patients. Thus, randomized control studies and intervention are needed to verify our finding.

REFERENCES

1 **Bray F**, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; **68**: 394-424 [PMID: 30207593 DOI: 10.3322/caac.21492]

2 **Chen R**, Zheng RS, Zhang SW, Zeng HM, Wang SM, Sun KX, Gu XY, Wei WW, He J. [Analysis of incidence and mortality of esophageal cancer in China, 2015]. *Zhonghua Yu Fang Yi Xue Za Zhi* 2019; **53**: 1094-1097 [PMID: 31683393 DOI: 10.3760/cma.j.issn.0253-9624.2019.11.004]

3 **Malhotra GK**, Yanala U, Ravipati A, Follet M, Vijayakumar M, Are C. Global trends in esophageal

cancer. *J Surg Oncol* 2017; **115**: 564-579 [PMID: 28320055 DOI: 10.1002/jso.24592]
4 **Ohnuma H**, Sato Y, Hayasaka N, Matsuno T, Fujita C, Sato M, Osuga T, Hirakawa M, Miyanishi K, Sagawa T, Fujikawa K, Ohi M, Okagawa Y, Tsuji Y, Hirayama M, Ito T, Nobuoka T, Takemasa I, Kobune M, Kato J. Neoadjuvant chemotherapy with docetaxel, nedaplatin, and fluorouracil for resectable esophageal cancer: A phase II study. *Cancer Sci* 2018; **109**: 3554-3563 [PMID: 30137686 DOI: 10.1111/cas.13772]
5 **Ma L**, Luo GY, Ren YF, Qiu B, Yang H, Xie CX, Liu SR, Liu SL, Chen ZL, Li Q, Fu JH, Liu MZ, Hu YH, Ye WF, Liu H. Concurrent chemoradiotherapy combined with enteral nutrition support: a radical treatment strategy for esophageal squamous cell carcinoma patients with malignant fistulae. *Chin J Cancer* 2017; **36**: 8 [PMID: 28077159 DOI: 10.1186/s40880-016-0171-6]
6 **Verzicco I**, Regolisti G, Quaini F, Bocchi P, Brusasco I, Ferrari M, Passeri G, Cannone V, Coghi P, Fiaccadori E, Vignali A, Volpi R, Cabassi A. Electrolyte Disorders Induced by Antineoplastic Drugs. *Front Oncol* 2020; **10**: 779 [PMID: 32509580 DOI: 10.3389/fonc.2020.00779]
7 **Smyth EC**, Lagergren J, Fitzgerald RC, Lordick F, Shah MA, Lagergren P, Cunningham D. Oesophageal cancer. *Nat Rev Dis Primers* 2017; **3**: 17048 [PMID: 28748917 DOI: 10.1038/nrdp.2017.48]
8 **Jain A**, Tiwari A, Verma A, Jain SK. Vitamins for Cancer Prevention and Treatment: An Insight. *Curr Mol Med* 2017; **17**: 321-340 [PMID: 29210648 DOI: 10.2174/1566524018666171205113329]
9 **Nasir A**, Bullo MMH, Ahmed Z, Imtiaz A, Yaqoob E, Jadoon M, Ahmed H, Afreen A, Yaqoob S. Nutrigenomics: Epigenetics and cancer prevention: A comprehensive review. *Crit Rev Food Sci Nutr* 2020; **60**: 1375-1387 [PMID: 30729798 DOI: 10.1080/10408398.2019.1571480]
10 **Shi HP**. Cancer is a metabolic disease. *Zhongliu Daixie Yu Yingyang Dianzi Zazhi* 2018; **5**: 111-116 [DOI: 10.16689/j.cnki.cn11-9349/r.2018.02.001]
11 **Zhang XS**, Liu ZH, Peng Y, Yang XY, Zhang Y, Xu Q, Liu YH. Analysis of vitamin nutritional status in hospitalized cancer patients. *Zhongguo Zhongliu Linchuang Yu Kangfu* 2018; **25**: 1448-1451 [DOI: 10.13455/j.cnki.cjcor.2018.12.11]
12 **Veeralakshmanan P**, Tham JC, Wright A, Bolter M, Wadhawan H, Humphreys LM, Sanders G, Wheatley T, Berrisford RJ, Ariyarathenam A. Nutritional deficiency post esophageal and gastric cancer surgery: A quality improvement study. *Ann Med Surg (Lond)* 2020; **56**: 19-22 [PMID: 32566222 DOI: 10.1016/j.amsu.2020.05.032]
13 **Zhang X**. Analysis of vitamin deficiency in palliative care cancer patients. *Heilongjiang Yixue* 2020; **44**: 437-438
14 **Masri OA**, Chalhoub JM, Sharara AI. Role of vitamins in gastrointestinal diseases. *World J Gastroenterol* 2015; **21**: 5191-5209 [PMID: 25954093 DOI: 10.3748/wjg.v21.i17.5191]
15 **Ma JL**, Zhao Y, Guo CY, Hu HT, Zheng L, Zhao EJ, Li HL. Dietary vitamin B intake and the risk of esophageal cancer: a meta-analysis. *Cancer Manag Res* 2018; **10**: 5395-5410 [PMID: 30464635 DOI: 10.2147/CMAR.S168413]
16 **Qiang Y**, Li Q, Xin Y, Fang X, Tian Y, Ma J, Wang J, Wang Q, Zhang R, Wang F. Intake of Dietary One-Carbon Metabolism-Related B Vitamins and the Risk of Esophageal Cancer: A Dose-Response Meta-Analysis. *Nutrients* 2018; **10** [PMID: 29954131 DOI: 10.3390/nu10070835]
17 **Li JB**, Zou XN, Wang HY, Tao DM, Qiao YL, Gu YK, Zheng SF. Effect of riboflavin-fortified-salt intervention on esophageal preancerous lesions among population with high risk in Yanting County. *Zhongguo Zhongliu Fangzhi Zazhi* 2009; **16**: 325-328 [DOI: 10.16073/j.cnki.cjcpt.2009.05.002]
18 **Li SS**, Tan HZ, Xu YW, Wu ZY, Wu JY, Zhao XK, Wang LD, Long L, Li EM, Xu LY, Zhang JJ. [The association between the whole blood riboflavin level and the occurrence, development and prognosis of esophageal squamous cell carcinoma]. *Zhonghua Yu Fang Yi Xue Za Zhi* 2019; **53**: 1124-1129 [PMID: 31683399 DOI: 10.3760/cma.j.issn.0253-9624.2019.11.010]
19 **Bo Y**, Lu Y, Zhao Y, Zhao E, Yuan L, Lu W, Cui L, Lu Q. Association between dietary vitamin C intake and risk of esophageal cancer: A dose-response meta-analysis. *Int J Cancer* 2016; **138**: 1843-1850 [PMID: 26355388 DOI: 10.1002/ijc.29838]
20 **Abdel-Latif MMM**, Babar M, Kelleher D, Reynolds JV. A pilot study of the impact of Vitamin C supplementation with neoadjuvant chemoradiation on regulators of inflammation and carcinogenesis in esophageal cancer patients. *J Cancer Res Ther* 2019; **15**: 185-191 [PMID: 30880777 DOI: 10.4103/jcrt.JCRT_763_16]
21 **Li K**, Zhang B. The association of dietary β-carotene and vitamin A intake on the risk of esophageal cancer: a meta-analysis. *Rev Esp Enferm Dig* 2020; **112**: 620-626 [PMID: 32543872 DOI: 10.17235/reed.2020.6699/2019]
22 **Rouphael C**, Kamal A, Sanaka MR, Thota PN. Vitamin D in esophageal cancer: Is there a role for chemoprevention? *World J Gastrointest Oncol* 2018; **10**: 23-30 [PMID: 29375745 DOI: 10.4251/wjgo.v10.i1.23]
23 **Zgaga L**, O'Sullivan F, Cantwell MM, Murray LJ, Thota PN, Coleman HG. Markers of Vitamin D Exposure and Esophageal Cancer Risk: A Systematic Review and Meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2016; **25**: 877-886 [PMID: 27030602 DOI: 10.1158/1055-9965.EPI-15-1162]
24 **Wang L**, Wang C, Wang J, Huang X, Cheng Y. Longitudinal, observational study on associations between postoperative nutritional vitamin D supplementation and clinical outcomes in esophageal cancer patients undergoing esophagectomy. *Sci Rep* 2016; **6**: 38962 [PMID: 27958342 DOI: 10.1038/srep38962]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com

© 2021 Baishideng Publishing Group Inc. All rights reserved.