**Name of Journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 62941

**Manuscript Type:** ORIGINAL ARTICLE

***Retrospective Study***

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

Liang LQ *et al*. Nine vitamins in EC patients

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

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**Received:** February 2, 2021

**Revised:** March 18, 2021

**Accepted:** April 13, 2021

**Published online:**

**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, B9, B12, B1, C, B2 and B6), 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 B2 deficiency and weight loss were found in these patients, and the proportions of vitamin B2 and vitamin C deficiencies increased significantly after chemotherapy (both *P* < 0.05). Serum concentrations of vitamins A, C, B2 and B6 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 B2 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

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; In press

**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.

**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.

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 B12 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, B6 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 B9: 6.8-36.3 nmol/L; vitamin B12: 200-900 pg/mL; vitamin B1: 50-150 nmol/L; vitamin C: 34-114 mmol/L; vitamin B2: 4.26-18.42 mg/L; and vitamin B6: 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 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 ± standard deviation, 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, B2 and B6 concentrations significantly differed before and after chemotherapy (all *P* < 0.05) (Table 3).

***Vitamin deficiencies in EC patients undergoing chemotherapy***

Deficiencies of vitamin A, D, C and B2 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 B2 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, B9, B12, B1, B6) 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).

***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 B2 and vitamin C followed by vitamins A and D.

In the current study, EC patients undergoing chemotherapy were most deficient in vitamin B2 (31.53% and 46.80% before and after chemotherapy, respectively), and vitamin B2 concentration significantly decreased after chemotherapy (*P* < 0.05). Vitamin B1, B9, B12 and B6 deficiency or excess was not found in any of our EC patients. A comparison of vitamin levels before and after chemotherapy suggested that vitamin B6 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 B6 and B9 (also known as folate) can reduce the risk, while higher intake of vitamin B12 may increase the risk[15,16]. A study of residents in Yanting County, Sichuan Province, a high-incidence area of EC in 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 B2 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 B2 deficiency and weight loss were found in EC patients. Statistically significant differences were shown in vitamins A, C, B2 and B6 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 J, 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]

**Footnotes**

**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.

**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.

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**Manuscript source:** Unsolicited manuscript

**Peer-review started:** February 2, 2021

**First decision:** March 6, 2021

**Article in press:**

**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

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

**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 |

**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/m2) |  |  | -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 B9 (nmol/L) | (14.529-23.014) 18.718 | (13.859-22.037) 17.539 | -1.578 | 0.115 |
| Vitamin B12 (pg/mL) | (491.023-598.303) 557.219 | (491.112-590.338) 546.789 | -0.326 | 0.745 |
| Vitamin B1 (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 B2 (μg/L) | (4.182-5.050) 4.501 | (4.105-4.761) 4.284 | -2.631 | 0.009 |
| Vitamin B6 (nmol/L) | (29.702-33.645) 31.747 | (28.875-32.868) 31.363 | -2.351 | 0.019 |

Q1-Q3: Quartiles 1-3.

**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 B2 (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 (*X* ± SD)** | **After chemotherapy (*X* ± 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 |

X: Mean; SD: Standard deviation.

**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 B2 | 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 B9 | -0.016 | 0.824 |
| Vitamin B12 | -0.053 | 0.449 |
| Vitamin B1 | 0.021 | 0.771 |
| Vitamin C | 0.188 | 0.007 |
| Vitamin B2 | -0.102 | 0.149 |
| Vitamin B6 | -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.