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Use of Dietary Supplements in Cancer: A Single-Institution Study

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Abstract

Background: Many patients with cancer tend to use vitamin supplements alongside their conventional cancer treatments. They have the presumption that vitamins can help them to feel better or fight the disease.
Objectives: The aim of this study was to determine the use of vitamins among cancer patients in a referral cancer center in Tehran, Iran.
Methods: Two hundred cancer patients who were undergoing outpatient chemotherapy or chemoradiation were chosen. The data on the use of vitamins and if they used vitamins by themselves or based on doctors' prescription were collected by a questionnaire. The type of used vitamin was also recorded.
Results: Among the patients who were being treated with chemotherapy alone (81.5% of the cases), 20.4% reported the regular use of vitamins. This figure for the remaining 18.5% who were undergoing chemoradiation was 23.7%. The interesting finding was that 43.9% of the cases were taking vitamins based on the treating oncologist prescription. More than half (52.5%) of the patients who were taking vitamins had no other medical illness apart from cancer. Multivitamin capsules were the most commonly used medications.
Conclusions: Interestingly, in more than 40% of the cases, vitamin supplements were prescribed by the treating physician. As there is some evidence that vitamins can interfere with chemotherapy and probably radiotherapy, it would be prudent for oncologists to prescribe them more cautiously for cancer patients who are under active treatment.

Keywords: Vitamins, Chemotherapy, Cancer Treatment, Dietary Supplements

1. Background

Vitamins, except vitamin D, cannot be synthesized in the body; thus, there is a need for taking them with food. There is strong evidence that deficiencies in several vitamins are associated with chronic diseases such as atherosclerosis, cancer, and osteoporosis in observational studies (1).

In our practice, we see that some of our patients use vitamins by themselves. They do not tell us about it even when we get the history. We should ask them specifically about vitamins. It is more evident when the patients are referred to our center for radiotherapy. They have received vitamins for such problems like cancer-induced chronic anemia during the course of chemotherapy. If we do not know the use of vitamins, especially anti-oxidant vitamins (A, E, and C), and they continue the usage during radiotherapy, it will interact with the mechanism of radiation-induced free radicals. As is known, the basic mechanism of radiotherapy is through acting the free radicals; therefore, the effectiveness of treatment will decrease.

Moreover, despite that there is no compelling evidence that any dietary supplement can help treat or prevent any type of cancer, it seems that many patients with cancer tend to use vitamin supplements alongside their conventional cancer treatments, such as radiotherapy or chemotherapy, with the presumption that vitamins can help them to feel better or fight the disease (2).

Reducing the symptoms or side effects of cancer treatment such as fatigue, nausea, anemia, etc. seems to be the most important reason for patients to use vitamins. In addition, there is a need for using supplements in some situations. There are principles for supportive care in some cancers in guidelines. For example, supplements such as iron or vitamin B12 should be used in gastric cancer, especially for patients who have subtotal gastrectomy (National Comprehensive Cancer Network, version 2.2018).

While there is still a controversy about whether vitamin supplements have any beneficial effect on cancer treatment, a growing body of evidence shows that some vitamins can affect the efficacy of chemotherapy or radi-

ation therapy. Therefore, if such drugs are misused, they may compromise the effectiveness of treatment (3).

2. Objectives

There are limited data about the use of nutritional supplements in cancer. In our country, no exact data are available about the use of vitamins. In this research, we evaluated the use of nutritional supplements in cancer patients.

3. Methods

The study was performed for six months (January 2017 to July 2017). 200 cancer patients who were undergoing outpatient chemotherapy or chemoradiation at Jorjani Cancer Center and were willing to participate were chosen. Since the treatment was in two disease settings (adjuvant or metastatic), we selected the cases in the first three months of treatment. All the patients admitted to our department signed informed consent forms at the beginning to allow using their data in future research. In our research, another informed consent form related to the topic was also filled out by each patient.

The data were collected by a questionnaire without the name of the cases and just by a code number. In the questionnaire, we recorded the demographic characteristics of the cases that included gender, age, education level, marital status, the type of cancer, metastatic or non-metastatic cancer, and the type of treatment (chemotherapy alone or chemoradiotherapy).

Our center is a referral cancer center that only admits adult patients (above 18-years-old). We evaluated patients older than 20 years. We asked the cases about the use of vitamins either by themselves or by physician's prescription. We filled out the questionnaire for gathering data on vitamin usage, kind of used vitamins, and the duration of usage, if any. Since there are several kinds of vitamin compounds in the drugstores, we divided the used vitamins into three categories: B complex, multivitamins, and other drugs. We had observed that the first two groups were the most commonly used vitamins in the clinics. The data analysis was done using the SPSS version 22 software.

4. Results

The majority of the patients were female (59.7%) and 40.2% had attained at least a high school diploma. The demographic characteristics of the cases are presented in Table 1.

Vitamin use was seen more frequently in the patients who were in their sixth decade of life. Patients with higher education also used vitamins more. Furthermore, single patients used supplements more than married ones (48.1% vs. 20%).

Table 1. The Demographic Characteristics of Patients

Variables	No. (%)
Gender	
Male	81 (40.5)
Female	119 (59.5)
Education	
Under diploma	118 (59)
Diploma	51 (25.8)
University education	31 (84.8)
Marital status	
Single	44 (22)
Married	156 (78)
Metastasis	
Non-metastatic disease	70 (36.3)
Metastatic disease	123 (63.7)
Missing	7 (3.5)
Treatment	
Chemotherapy	162 (81)
Chemoradiation	38 (19)

The three most common cancers were breast, head and neck, and gynecologic cancers. The distribution of cancers is shown in Table 2. There were 10 patients with gastric cancer, four of whom had metastatic disease. One of these metastatic cases used multivitamins by himself due to weakness. The other nine cases did not use any supplement. There were six cervical cancer patients, two of whom with non-metastatic disease used multivitamins prescribed by the physician.

Table 2. The Type of Cancer in Cases

Cancer	Number of Cases
Breast	60
Head and neck	58
Gynecologic	42
Gastrointestinal	28
Sarcoma	2
Lung	6
Urologic	3
Hodgkin lymphoma	1
Total	200

There were 29 cases with anemia. 20 of them did not use vitamins or even iron supplements. Among the other nine cases that used vitamins, the physician had given the supplements to seven of them and the other two patients used vitamins by themselves (including four breast cancers, two endometrial cancers, two laryngeal cancers, and one lung neoplasm).

More than one third (36.3%) of the patients had metastatic disease. Vitamin consumption was more prevalent in these patients compared to non-metastatic cases (25.7% vs. 18.7%). The results are shown in Table 3.

Among the patients who were being treated with chemotherapy alone (81.5% of the cases), 20.4% reported the regular use of vitamins. This figure for the remaining 18.5% who were undergoing chemoradiation was 23.7%. The results are observed in Table 4.

Forty one cases (20.5%) used supplements. 20 cases used multivitamins and nine cases used B vitamins (B complex). 12 patients used other supplements like calcium, vitamin D, etc..

The majority of the patients (66%) who were taking vitamins started using them after the second cycle of chemotherapy (Figure 1). Six cases had started supplements before chemotherapy for at least three months (including three laryngeal, one ovary, one endometrial, and one breast cancer).

The interesting finding was that 43.9% of the cases were taking vitamins based on the treating oncologist prescription. Weakness (22%) and suggestion by family and friends (22%) were other reasons for taking vitamins by the patients. More than half of the patients (52.5%) who were taking vitamins had no other medical illness apart from cancer. We asked the patients about the improvement of symptoms like weakness after using supplements and 16 cases (39%) reported improvements.

Table 3. Vitamin Use by the Type of Metastasis

	Vitamin Use		Total
	Yes	No	
Cancer			
Metastatic			
Count	18	52	70
% within cancer	25.7	74.3	100.0
% of total	9.3	26.9	36.3
Non-metastatic			
Count	23	100	123
% within cancer	18.7	81.3	100.0
% of total	11.9	51.8	63.7
Total			
Count	41	152	193
% within cancer	21.2	78.8	100.0
% of total	21.2	78.8	100.0

Table 4. Vitamin Use by the Type of Treatment

	Vitamin Usage		Total
	Yes	No	
Treatment			
Chemotherapy			
Count	33	129	162
% within treatment	20.4	79.6	100.0
% of total	16.5	64.5	81.0
Chemoradiation			
Count	9	29	38
% within treatment	23.7	76.3	100.0
% of total	4.5	14.5	19.0
Total			
Count	42	158	200
% within treatment	21.0	79.0	100.0
% of total	21.0	79.0	100.0

5. Discussion

While there is no reliable evidence that dietary supplements and vitamins can help prevent or treat cancer, it seems that many cancer patients tend to use them and little data are available on the frequency of their consumption. In addition, the impact of nutritional supplements on chemotherapy and radiotherapy and related toxicities is not clear. This study evaluated the use of different supplements in the adjuvant and metastatic cancer patients in their first three months of treatment. This study was only designed to observe the use of supplements at the time of filling out the questionnaire.

In a study at the Comprehensive Cancer Center of the University of North Carolina in 2018, a cross-sectional survey of 603 cases with common cancers like breast, colorectal, lung, and prostate was conducted for two years. The percentage of using supplements was 52% in chemotherapy and 51% in radiation therapy cases. They found the common use of non-vitamin non-mineral dietary supplements during initial cancer treatments. About 75% of the cases reported professional sources for prescribing supplements and female and higher educated cases used the supplements more (4). In our study, 43.9% of the cases were using supplements prescribed by physicians. As observed

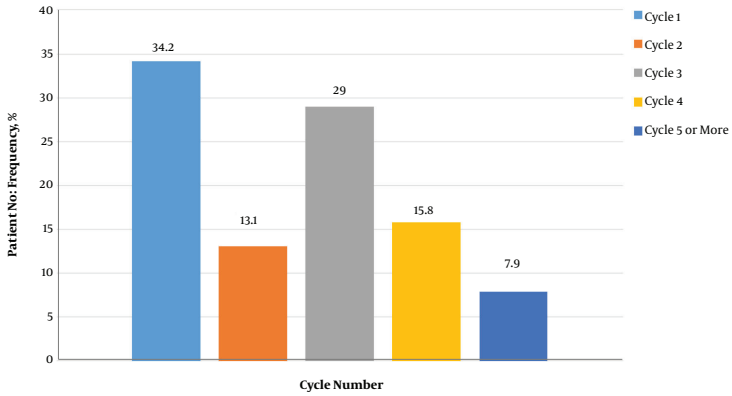

Figure 1. The starting cycle for vitamin usage

in two studies, higher educated cases used dietary supplements more frequently.

A systematic review of 32 studies was conducted in 2008 on vitamin and mineral supplement usage after a diagnosis of cancer. About 14% to 32% of survivors started the supplement use after the cancer diagnosis. Breast cancer patients reported the highest usage whereas the least use belonged to prostate cancer patients. Again, higher education and female gender were two factors associated with more supplement use. It was interesting that about 68% of physicians were unaware of vitamin use among their cancer patients (2). It is the concern of our physicians and the question of our study was based on this observation. About 44% of the cases in our study used supplements by themselves.

There are indications for using some supplements in the course of cancer treatment. For example, in gastric cancer, vitamin B12 and iron should be prescribed after subtotal gastrectomy. For this reason, the cases that had used them before the onset of chemotherapy or chemoradiation were also included. In our study, only had six non-metastatic gastric cancer patients used vitamins before treatment of cancer and two of them had subtotal gastrectomy. Nevertheless, they used no supplements.

In addition, since cancer and underlying morbidities can induce some problems like anemia, there is a need to evaluate patients for these signs and treat them. Although it is known that cancer or induced chronic anemia can affect the tolerance of patients for chemotherapy, it was interesting that only 7 out of 29 anemic cases were treated by physicians. Two anemic patients used iron supplements by themselves. Although there is significant evidence of treating anemia in cervical cancer, only had two out of six cases with this disease used multivitamins. It may prudent to pay more attention to comorbidity of cases (5).

As some vitamins may interfere with the effect of cancer treatment, physicians should ask their patients, especially during radiotherapy. Producing reactive oxygen species (as happens in radiotherapy) and generating free radicals by chemotherapy drugs (by alkylating agents, platinum, and antitumor antibiotics) are among the main mechanisms by which cancer treatment modalities exert their cytotoxic effects. There is some evidence that while antioxidants may protect normal cells from the oxidative damage caused by chemotherapy or radiotherapy (and hence reducing the adverse effects of treatment), non-enzymatic exogenous antioxidants such as vitamins, minerals, and polyphenols may protect tumor cells against the cytotoxic effects of cancer treatment. Although the risks and benefits of antioxidant supplementation are still controversial, a recent meta-analysis concluded that the harm caused by antioxidant supplementation remains unclear for patients during cancer therapy (6).

There are some controversies about the efficacy of supplements on chemotherapy or its adverse effects. Branda et al. in 2004 evaluated the effects of vitamin B12, folate, and dietary supplements on chemotherapy-induced mucositis and neutropenia in 49 patients with breast cancer. They concluded that chemotherapy-induced neutropenia might be ameliorated by dietary supplementation with a multivitamin or vitamin E, while high serum folate levels can exacerbate a decrease in neutrophil counts. No significant association was found between oral mucositis and nutritional supplements (7).

A cross-sectional, population-based survey compared the supplement use among patients with cancer and other chronic conditions. Participants reported the use of multivitamins and 27 vitamins, minerals, herbs, and other natural products during the preceding 12 months. The results showed that cases with cancer or other chronic conditions

had a higher prevalence of supplement use than those reporting no illness. Cancer patients used vitamins whereas patients with other chronic conditions used all types of supplements. Supplement use was similar between cancer survivors and cancer-free individuals and it was correlated with being a woman, advancing age, greater physical activity, and more fruit and vegetable intake (8). As in our study, female gender has been as a key factor in using supplements in many studies.

A study was conducted in Turkey to evaluate the prevalence of the use of complementary and alternative medicine (CAM) in patients who visited the outpatient clinic in the medical oncology department. The CAM use included pharmacologic agents like vitamins, dietary supplements, and herbal products or non-pharmacologic methods such as praying, meditation, hypnosis, massage, or acupuncture. Of 1499 cases who filled the survey questionnaire, 1433 (96%) used non-pharmacologic CAM. The most common methods were praying (n = 1,433) and herbal products use (n = 42). Only used 60 cases (4%) pharmacologic CAM and it was not associated with age, gender, or income level. Nevertheless, the level of education and employment status were correlated with the use of them significantly. About 10% of these 60 cases used pharmacologic CAM for more than two years and there was a surprising result that 22 (36%) used them by themselves (9). In this study, the age or gender did not influence the use of supplements that is in contrast to our study.

A meta-analysis from the U.S. Preventive Services Task Force included 19 randomized clinical trials (RCTs) (three for cancer and 16 for fracture outcomes) and 28 observational studies (for cancer outcomes). Although the data from RCTs showed that vitamin D supplementation might reduce cancer risk, the data from observational studies showed the contrary results. The authors concluded that vitamin D and calcium supplements might reduce fracture risks, especially in cases that were institutionalized. This study showed that the effect of special vitamins like vitamin D is unknown on cancer. The patients may have insufficient vitamin D level and may need supplements. Therefore, we should extend our knowledge about the use of these supplements (10).

In a study on 241 patients, it was shown that chemotherapy-induced toxicity did not depend on whether the patients were vitamin D depleted or had sufficient levels (11). This study presented some evidence that vitamin D supplements may not be effective in cancer patients.

Another study reported that 20% - 80% of individuals used dietary supplements after a cancer diagnosis. The most common cancers leading patients to use more supplements were breast, prostate, colorectal, and lung. The reasons for using supplements were improving the quality of life, reducing treatment-related symptoms, medical practitioners' prescription, and family and friends advice (12). These data are similar to our study that family may influence the use of supplements.

Song et al. calculated the amount of nutrients taken from foods and supplements, the percent contribution of supplement nutrients to the total nutrient intakes, and cancer survivors' nutrient intakes relative to the estimated average requirements (EARs) and the tolerable upper intake levels (ULs) among 400 cancer survivors and 10,387 cancer-free individuals, aged $\geq$ 19 years in Korea. It was reported that 33.3% of cancer survivors and 22.1% of cancer-free individuals used dietary supplements. It was revealed that cancer survivors used more riboflavin, folate, and iron from foods ($P < 0.05$ for each) and had higher intakes of calcium ($P = 0.05$) and vitamin C ($P = 0.01$) from foods and supplements compared to cancer-free individuals. In female cancer survivors, those with higher education level, moderate physical activity, low vegetable intake, and high circulating vitamin D levels had higher supplement intake (13). This study showed there was a tendency to higher levels of supplements intake in cancer cases. Since the exact effects of various vitamins on oncologic treatment are unclear, it is important to keep in mind asking patients about supplement use when taking a medical history.

5.1. Conclusion

In our study, more than 40% of cases used vitamin supplements based on the treating physician prescription. Because of the potential negative effects of vitamins on treatment efficacy, it would be prudent to avoid prescribing them for patients under active cancer treatment. Besides, the treating physician should make the patients aware of these potential hazards.

Footnotes

Conflict of Interests: None declared.

Funding/Support: There is no financial support for this study.

Patient Consent: All patients admitted to our department signed informed consent forms at the beginning. In the consent form, the patients allowed that their data could be used for future research. In our research, another informed consent form related to the topic was also filled out by each patient.

References

1. Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: High-dosage vitamin E supplementation may

increase all-cause mortality. *Ann Intern Med*. 2005;**142**(1):37–46. doi: 10.7326/0003-4819-142-1-200501040-00110. [PubMed: 15537682].
2. Velicer CM, Ulrich CM. Vitamin and mineral supplement use among US adults after cancer diagnosis: A systematic review. *J Clin Oncol*. 2008;**26**(4):665–73. doi: 10.1200/JCO.2007.13.5905. [PubMed: 18235127].
3. Fritz H, Flower G, Weeks L, Cooley K, Callachan M, McGowan J, et al. Intravenous vitamin C and cancer: A systematic review. *Integr Cancer Ther*. 2014;**13**(4):280–300. doi: 10.1177/1534735414534463. [PubMed: 24867961].
4. Luo Q, Asher GN. Use of dietary supplements at a comprehensive cancer center. *J Altern Complement Med*. 2018;**24**(9-10):981–7. doi: 10.1089/acm.2018.0183. [PubMed: 30247972].
5. Candelaria M, Cetina L, Duenas-Gonzalez A. Anemia in cervical cancer patients: Implications for iron supplementation therapy. *Med Oncol*. 2005;**22**(2):161–8. doi: 10.1385/MO:22:2:161. [PubMed: 15965279].
6. Yasueda A, Urushima H, Ito T. Efficacy and interaction of antioxidant supplements as adjuvant therapy in cancer treatment: A systematic review. *Integr Cancer Ther*. 2016;**15**(1):17–39. doi: 10.1177/1534735415610427. [PubMed: 26503419]. [PubMed Central: PMC5736082].
7. Branda RF, Naud SJ, Brooks EM, Chen Z, Muss H. Effect of vitamin B12, folate, and dietary supplements on breast carcinoma chemotherapy–induced mucositis and neutropenia. *Cancer*. 2004;**101**(5):1058–64. doi: 10.1002/cncr.20484. [PubMed: 15329916].
8. Miller MF, Bellizzi KM, Sufian M, Ambs AH, Goldstein MS, Ballard-Barbash R. Dietary supplement use in individuals living with cancer and other chronic conditions: A population-based study. *J Am Diet Assoc*. 2008;**108**(3):483–94. doi: 10.1016/j.jada.2007.12.005. [PubMed: 18313431].
9. Yalcin S, Hurmuz P, McQuinn L, Naing A. Prevalence of complementary medicine use in patients with cancer: A Turkish comprehensive cancer center experience. *J Glob Oncol*. 2018;(4):1–6. doi: 10.1200/JGO.2016.008896. [PubMed: 30241173]. [PubMed Central: PMC6180833].
10. Wang L, Sesso HD, Glynn RJ, Christen WG, Bubes V, Manson JE, et al. Vitamin E and C supplementation and risk of cancer in men: Post-trial follow-up in the Physicians' Health Study II randomized trial. *Am J Clin Nutr*. 2014;**100**(3):915–23. doi: 10.3945/ajcn.114.085480. [PubMed: 25008853]. [PubMed Central: PMC4135500].
11. Kitchen D, Hughes B, Gill I, O'Brien M, Rumbles S, Ellis P, et al. The relationship between vitamin D and chemotherapy-induced toxicity - a pilot study. *Br J Cancer*. 2012;**107**(1):158–60. doi: 10.1038/bjc.2012.194. [PubMed: 22588559]. [PubMed Central: PMC3389405].
12. Marian MJ. Dietary supplements commonly used by cancer survivors: Are there any benefits? *Nutr Clin Pract*. 2017;**32**(5):607–27. doi: 10.1177/0884533617721687. [PubMed: 28813230].
13. Song S, Youn J, Lee YJ, Kang M, Hyun T, Song Y, et al. Dietary supplement use among cancer survivors and the general population: A nation-wide cross-sectional study. *BMC Cancer*. 2017;**17**(1):891. doi: 10.1186/s12885-017-3885-1. [PubMed: 29282002]. [PubMed Central: PMC5745960].