

The role of herbal medicine in the side effects of chemotherapy

El papel de la medicina herbal en los efectos secundarios de la quimioterapia

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Abstract

Nowadays, significant progress has been made in the treatment of cancer. Chemotherapy is one of the most common treatments in cancer management. The use of chemotherapy drugs is generally associated with various serious and non-medical complications. Nausea and vomiting with Chemotherapy are among the most severe side effects and of major concern for patients with cancer. Due to the limited effect and dangerous side effects of taking anti-emetic drugs, herbal medicine has been welcomed by patients as one of the most active and complementary Drugs in this field. The contradictory results in this area led the researcher to carry out the present study with the aim of systematically reviewing the effects of medicinal plants on chemotherapy-induced nausea and vomiting. In this structured review, all studies during the years 2008-2018 using keywords chemotherapy, chemotherapy side effects, medicinal herbs, nausea and vomiting and drug side effects from internal and external databases. The data were analyzed using meta-analysis method; the selected articles were collected according to inclusion criteria and finally were examined more closely. After searching the data-

bases and extracting a large number of articles by title and abstract, 360 articles were reviewed and finally 18 articles were reviewed. The herbal remedies used to prevent and treat chemotherapy-induced nausea were ginger, chamomile, mint, cardamom, and onion, respectively. Early detection of side effects in patients can prevent forced discontinuation of treatment or reduce the dose of medications to control side effects that will reduce the effectiveness of treatment. Therefore, it is possible to improve the condition of patients and reduce the side effects of chemotherapy by providing appropriate educational facilities and programs on how to use these herbs. These interventions have also been studied in patients with a wide range of cancers, while each type of cancer has its own chemotherapy protocol and differs in severity from nausea to other protocols. As a result, it is not easy to judge the efficacy of different types of herbs on chemotherapy-induced nausea and to generalize the results to other cancers, so further research is recommended by the researcher.

Key words: Nausea, vomiting, complications, chemotherapy, herbal medicine.

Resumen

Hoy en día, se han logrado avances significativos en el tratamiento del cáncer. La quimioterapia es uno de los tratamientos más comunes en el manejo del cáncer. El uso de medicamentos de quimioterapia generalmente se asocia con varias complicaciones graves y no médicas. Las náuseas y los vómitos con quimioterapia se encuentran entre los efectos secundarios más graves y de mayor preocupación para

los pacientes con cáncer. Debido al efecto limitado y los efectos secundarios peligrosos de tomar medicamentos antieméticos, los pacientes han acogido con satisfacción la medicina herbal como una de las píldoras más activas y complementarias en este campo. Los resultados contradictorios en esta área llevaron al investigador a los investigadores a llevar a cabo el presente estudio con el objetivo de revisar sistemáticamente los efectos de las plantas

medicinales sobre las náuseas y los vómitos inducidos por la quimioterapia. En esta revisión estructurada, todos los estudios realizados en Irán y en el extranjero durante los años 2008-2018 utilizaron palabras clave quimioterapia, efectos secundarios de la quimioterapia, hierbas medicinales, náuseas y vómitos y efectos secundarios de medicamentos de bases de datos internas y externas. Los datos se analizaron utilizando el método de metanálisis; Los artículos seleccionados se recopilaron según los criterios de inclusión y finalmente se examinaron más de cerca. Después de buscar en las bases de datos y extraer una gran cantidad de artículos por título y resumen, se revisaron 360 artículos y finalmente se revisaron 18 artículos. Los remedios herbales utilizados para prevenir y tratar las náuseas inducidas por la quimioterapia fueron jengibre, manzanilla, menta, cardamomo y cebolla, respectivamente. La detección temprana de los efectos secundarios en los pacientes puede prevenir la interrupción forzada del tratamiento o reducir la dosis de medicamentos para controlar los efectos secundarios que reducirán la efectividad del tratamiento. Por lo tanto, es posible mejorar la condición de los pacientes y reducir los efectos secundarios de la quimioterapia al proporcionar instalaciones y programas educativos apropiados sobre cómo usar estas hierbas. Estas intervenciones también se han estudiado en pacientes con una amplia gama de cánceres, mientras que cada tipo de cáncer tiene su propio protocolo de quimioterapia y difiere en severidad de náuseas a otros protocolos. Como resultado, no es fácil juzgar la eficacia de diferentes tipos de hierbas en náuseas inducidas por quimioterapia y para generalizar los resultados a otros tipos de cáncer, por lo que el investigador recomienda más investigación.

Palabras clave: náuseas, vómitos, complicaciones, quimioterapia, fitoterapia.

Introduction

As the world population ages, increasing cancer risk behaviors, especially smoking and exposure to stimuli such as chemicals, radiotherapy, inappropriate eating habits and sedentary lifestyles, have become a global problem¹. According to WHO statistics, the incidence of cancers in developed countries is twice as high in developing countries, but the number of people infected with these diseases annually is higher in developing countries and their disease is far more fatal². Significant advances have been made in the treatment of cancer today. Various therapies, including chemotherapy, radiotherapy, surgery, hormone therapy, immunotherapy, biological therapies, and cryotherapy are used to manage cancer³. The use of chemotherapy drugs is generally associated with various serious and non-serious side effects⁴. The purpose of monitoring side effects is to identify unknown drug-related immune problems, to identify and quantify risk factors as-

sociated with drug use⁵. Adverse drug information can be used to formulate therapeutic guidelines, make decisions about public health policies, and in pharmacoeconomic research⁶. Evaluation of the side effects of chemotherapy drugs in the hospital provides a good insight into the cause, severity, and extent of the preventable side effects and may prevent the recurrence of similar complications in similar patients⁷. Timely diagnosis of adverse events in patients can improve patient acceptance of treatment and prevent forced discontinuation of treatment or dosing of medications to control adverse events that may reduce the efficacy of treatment itself⁸.

The most common side effects of nausea with or without vomiting, diarrhea, hair loss, darkening of the skin and nails, bone marrow suppression, mucositis, dysfunction of the ovaries, hyperuricemia, neuropathy, cardiomyopathy, cystitis hemorrhagic, kidney problems, disorders of electrolyte have been reported⁹.

Nausea and vomiting with Chemotherapy are among the most severe side effects and of major concern for patients with cancer, with a prevalence of 54-96%¹⁰. This complication develops most during the first 24 hours (acute phase) after chemotherapy and has adverse effects on patients' personal and professional lives¹¹.

Chemotherapy induced nausea can cause many problems for patients, and sometimes these problems are so severe that they can be discontinued¹². This complicates the physiological, electrolyte-induced diarrhea, altered immune system, nutritional disorder and even esophageal rupture and affects the quality of life and the continued treatment of patients¹³. These problems are consistent even with the widespread use of anti-inflammatory chemicals and the potentiation of the serotonin receptor antagonists and neurokinin-receptor antagonists¹⁴.

Lack of control of nausea and vomiting also results in high costs, which may not refer to direct or indirect costs. Direct costs include increased hospitalization days and additional costs related to medical and paramedical care, as well as indirect costs such as losing or reducing the income of patients, their family members or careers¹⁵.

On the one hand, the widespread use of industrial vomiting drugs is associated with side effects such as complications, extra pyramidal effects of hypertension, headache, etc.¹⁶. Due to the limited effect and dangerous side effects of these drugs, the tendency towards non-chemical and non-industrial treatments has increased. One of the basic and low-risk measures in this field is the use of herbal medicine as the active ingredient in pomegranate extracts, which has gained much attention over the past decade, according to WHO statistics at present. 80% of the world's population use herbal remedies for treatment¹⁷.

Taking into account factors such as involvement in decision-making, avoidance of toxicity of drugs, lack of health insurance, high cost of drugs, and most importantly, interest in using preventive strategies¹⁸. Although clinical trials

on new drugs provide information about their serious adverse effects, these reports are inadequate and may not accurately reflect the patient population's experience¹⁹. In this regard, the researcher intends to conduct a systematic review of the present study with the aim of systematically reviewing the literature and using the author's experiences and the opinions of experts in the study of the effects of medicinal plants on nausea and vomiting caused by chemotherapy.

In this structured review, all studies at Iran and abroad during the years 2008-2018 using keywords chemotherapy, chemotherapy side effects, medicinal herbs, nausea and vomiting and drug side effects from internal and external databases including Magiran -med lib-SID-iran medex as well as Latin databases such as CINHALL-Pub med, scopus and Elsevier were reviewed and data were analyzed using meta-analysis method and data of selected articles were collected. All articles were reviewed irrespective of the place and place of publication and the way they were done. After reviewing and aggregating all the searched articles, duplicate and unrelated articles were removed. Subsequently, the articles that were included in the study were evaluated according to the inclusion criteria, including: Intervention studies that examined a variety of medicinal plants as a way to prevent and treat chemotherapy-induced nausea. Exclusion criteria included case report and poster data, conferences, descriptive and review articles.

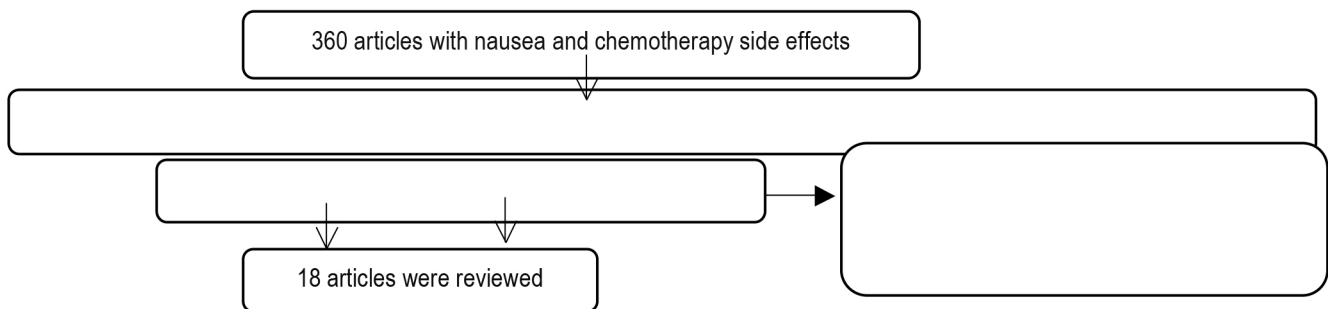
This study had several limitations; the restriction of databases to extract full-text articles limited the access to a large part of the articles despite their title relevance, English language, and intervention. Another limitation was that most of the articles were on acupuncture and electrical stimulation, and there may be articles on chemotherapy-induced nausea and vomiting that may be unavailable due to the lack of full text or English language. They should not be examined. All ethical requirements regarding the correct use of the extracted articles and the rules for publication were respected.

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fter searching the databases and extracting a large number of articles by title and abstract, 360 articles were reviewed, of which 220 were removed because they did not intervene to combat the adverse effects of chemotherapy.

140 articles were examined in more detail, 122 of which did not specifically address the strategies for dealing with chemotherapy-induced nausea. Finally, 18 articles were included in this review study (PRISMA chart).

Finally, the types of herbs that were used as a strategy for the prevention and treatment of chemotherapy-induced nausea were ginger, chamomile, mint, cardamom, garlic, and onion, respectively, and discussed below.



According to what was said types of plants as a way to prevent and treat nausea caused by chemotherapy were used to arrange the use of ginger, chamomile, mint,

cardamom and garlic and onions were. The following article analyzes will be discussed in relation to their impact. The following table shows some of the details of these studies (Table).

| Table I. Some details of the studies studied | | | | |
|-----------------------------------------------------------------------------------------------------------------------|------------------|-----------------------------------------------------------|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Authors | Herb | Cancer type | Outcome criteria | Effectiveness |
| Internal: Najafi, Montazeri, Ghanbari, Cosmic, Industrial External: Lete, Zick, Manusirivithaya, Leopold, Sontakke | Ginger | Breast and Leukemia | VAS (Visual Analogue Scale) | Taking one gram daily of capsules containing ginger root powder can reduce the number of nausea and vomiting caused by chemotherapy. |
| Borhani and sanati | Chamomile | Breast Colorectal Lung Leukemia The testicles | VAS (Visual Analogue Scale) | It reduces nausea caused by chemotherapy but has no significant effect on reducing chemotherapy vomiting. |
| Ahdadi | Mint | Breast | VAS (Visual Analogue Scale) | It reduced nausea in patients, but vomiting showed no effect of ice containing peppermint extract. |
| Pooter and khalili | Cardamom | Digestive system | VAS (Visual Analogue Scale) | Cardamom inhaled aromatherapy helped standard anti-nausea and vomiting drugs reduce the severity of chemotherapy-induced nausea, but failed to reduce the number of nausea, vomiting, and retching in the acute phase of chemotherapy. |
| Fakhari | garlic and onion | Digestive system | VAS (Visual Analogue Scale) | |

Ginger

Ginger is one of the herbal remedies that is effective in the treatment of nausea and vomiting and does not cause any particular side effects and is used in the manufacture of anti-nausea drugs in the German Pharmacopoeia. The major pharmacological activity of ginger, under the scientific name *Zingiber officinale*, is its active ingredients, including gingerols and shagaols. These compounds have anti-vomiting, anti-inflammatory, anti-inflammatory, anti-inflammatory, anti-stress, anti-cancer, reducing prostaglandins and relieving digestive problems. Ginger products exert an anti-vomiting effect through several mechanisms. For example, gingerol and shagols reduce gastric contractions but increase gastrointestinal (gastrointestinal) activity. They also have anti-serotonin effects and exert destructive effects on free radicals that cause vomiting. In the study of Ebrahimi et al.²⁰ the only side effect of ginger reported by some patients was heart failure, with no significant difference between the two groups. As a result, it can be deduced that ginger is safe and harmless. Clinical trials have provided contradictory results on the effects of ginger on nausea caused by chemotherapy, which makes it difficult to judge its efficacy, as Sontakke²¹ indicated the anti-nausea effects of this drug. This is metoclopramide. Ryan²² and Lete²³ also acknowledged its positive anti-marital effects, but in contrast Zick²⁴ and Manusirivithaya²⁵ rejected its effects.

On the Use of Ginger in Cancer Patients Sonaki et al.²¹ study of 50 cancer patients undergoing chemotherapy called ginger, an anti-vomiting agent in chemotherapy-induced nausea and vomiting, found that ginger in nausea and vomiting control. More effective than metoclopramide and there is some research that contradicts findings, Leopold et al.²⁶ investigating the effect of ginger

on postoperative nausea and vomiting on 180 women undergoing genital laparoscopic surgery. The effects of ginger on postoperative nausea and vomiting were different and the severity of the severity was lower and vomiting as compared to controls was observed in the group receiving. In addition, a study of 43 patients with chemotherapy for cancer patients undergoing chemotherapy with the aim of determining the anti-vomiting effects of ginger on nausea and vomiting showed that ginger was effective in reducing late nausea and vomiting due to chemotherapy²⁴. Such results may be due to the small size of the statistical population, the limitation of the number of samples and the lack of utilization of the desired product, since the characteristics of previous studies are such that it can affect their results. Each study, for example, examined the effect of the ginger plant on patients with a wide range of cancers, while each type of cancer had its own chemotherapy protocol and severely induced nausea. Other protocols are different, so it is not easy to judge the efficacy of ginger on chemotherapy-induced nausea and to generalize the results to other cancers.

This study is in the study of Ebrahimi et al.²⁰ in breast cancer patients treated with one-day chemotherapy courses and in many similar internal studies²⁷⁻³¹ with the conditions listed in Table 1 having a significant effect on Control of nausea and vomiting was the study samples. Thus, by comparing the results and generalizing the results, it is recommended that more extensive research be conducted in the future on patients with other types of cancers as well as on cancer patients undergoing several days of chemotherapy, which will be more likely to be different. Based on the results of the research, it can be stated that daily consumption of 1 g capsules containing ginger root powder can reduce the number of nausea and vomiting

caused by chemotherapy. Therefore, it is possible to improve the condition of patients and reduce the side effects of chemotherapy by providing appropriate educational facilities and programs on how to use this capsule. Chamomile

Chamomile

Chamomile is one of the prominent medicinal herbs of chicory and has a special place in ancient medical and medicinal texts as well as in Iranian and Islamic medicine. Various species of this plant and its essential oils have been identified and used in pharmacy.

In a study, Borhani et al.³² investigated the effect of this medicinal plant on nausea and vomiting caused by chemotherapy. According to the results of this study, chamomile extract reduces nausea caused by chemotherapy but has no significant effect on reducing chemotherapy vomiting; on the other hand, Sanaati et al.³². The severity of nausea in patients with chemotherapy not treated with chemotherapy was only effective in the frequency of vomiting, which is different from the results of this study and may be related to the research method or the characteristics of the subjects.

Mint

Mint is commonly used as a flavoring in food, tea, toothpaste, washing solutions and medications. Menthol in peppermint acts as a gastric relaxant which reduces nausea and vomiting by relaxing the stomach muscles and gastric wall anesthesia. Peppermint also has a calming effect. Aromatherapy with mint also has a psychological effect and reduces nausea and vomiting. In a study by Haddadi et al.³⁴, ice containing peppermint extract was used as a noninvasive, simple, inexpensive, and non-invasive method along with medication to improve nausea in breast cancer patients. Ice cold causes vasoconstriction in the peripheral parts of the gastrointestinal tract (esophagus and stomach) and reduces the entry of chemotherapeutic agents into these areas, reducing irritation of the gastrointestinal tract and reducing nausea and vomiting. In the present study, the intervention reduced nausea in the patients, as well as the patients' satisfaction, but in the case of vomiting it showed no effect of ice containing peppermint extract. Therefore, it is suggested to apply conditional nausea (before chemotherapy starts) and delayed nausea to other cancer groups.

Cardamom

The scientific name for cardamom is "Elettaria cardamomum". The main chemical components of cardamom include Cineole, Limonene, Terpenyl Acetate, Sabinene, and Linalool. Cardamom is a family of ginger and is commonly known as the spice queen. Cardamom is used to relieve dyspepsia, cough and itching, prevent and treat gastrointestinal disorders, sore throat, lung congestion and oral infections. One of its uses is to relieve nausea and vomiting. Cardamom inhaled aromatherapy can help standard anti-nausea and vomiting medications reduce the severity of nausea caused by chemotherapy. In this regard, Khalili

et al.'s³⁵ study of cardamom aroma was used for this purpose. According to the findings of this study, cardamom inhalation aromatherapy was able to help standard anti-nausea and vomiting medications in reducing the severity of chemotherapy-induced nausea but failed to reduce The number of nausea, vomiting and retching help in the acute phase of chemotherapy. in the study of Potter et al.³⁶, deep breathing more than orange essential oil reduced nausea and retention following stem cell infusion, whereas bergamot aromatherapy did not reduce nausea in children and adolescents under stem cell infusion.

Garlic and onion

Scientific evidence suggests that the medicinal and biological effects of garlic and onions are due to the high amount of soluble compounds in these plants. These special ingredients make garlic and onions. Flavonoids are abundant in onions, but not in garlic. Biological properties of garlic and onion ingredients such as lectin, prostaglandin, fructan, pectin, adenosine, vitamins B6, B2, B1, E, nicotinic acid, fatty acid, glycolipid, phospholipid acid have been essential amino acids for decades. So far, the biological importance and medicinal properties of anti-fungal, antibacterial, anti-tumor, anti-thrombotic and hypocholesteroleptic properties of saponins such as B chlo-rogenin have been recognized. Garlic and onions in addition to these biological activities, absorption of AGE from the small intestine can protect patients against the side effects of anti-tumor drugs such as: vomiting, nausea, gastritis, gastric ulcer, bleeding and intestinal ulcer. Onion consumption can also stimulate the gastrointestinal process and increase the rate of absorption of food and decrease the time of passage through the gastrointestinal tract and help improve nausea and vomiting³⁷.

Conclusions

Timely diagnosis of adverse events in patients can improve patient acceptance of treatment and prevent forced discontinuation of treatment or dosing of medications to control adverse events that may reduce the efficacy of treatment itself. Considering the different body systems, the most common complication in gastric cancer patients was gastrointestinal complications, especially nausea and vomiting. Also, in some patients no treatment was taken to control the complication; however, as noted, many of these complications were promptly diagnosed, correct dose adjustment based on body surface area, kidney and liver function, and weight of the patient and liver. Preventive measures are minimized. Therefore, it is possible to improve the condition of patients and reduce the side effects of chemotherapy by providing appropriate educational facilities and programs on how to use these herbs. Researchers have also studied these interventions in patients with a wide range of cancers,

while each type of cancer has its own chemotherapy protocol and differs in severity from nausea to other protocols, thus it is not easy to judge the efficacy of different types of herbs on chemotherapy-induced nausea and to generalize the results to other cancers easily, so further research is recommended by the researcher.

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