



The effect of ginger and chamomile consumption on the severity and frequency of chemotherapy induced nausea and vomiting: a Review of Randomized Clinical Trials

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Abstract

Objective: This study was conducted to investigate the effect of ginger and chamomile consumption on the intensity and frequency of nausea and vomiting caused by chemotherapy.

Methods: To write this literature review, All published randomized clinical trials between January 2003 and July 2023, were systematically searched using Google Scholar, Scopus, Med-Line, Science Direct, Up To Date, Web Of Science, Magiran, SID, and Pub-Med search databases with “nausea and vomiting, chemotherapy, chamomile, ginger, herbal plants, herbal medicine Complementary medicine and alternative medicine” as keywords.

Result: After reviewing 250 articles, 20 articles were selected, in which 9 studies showed positive effect of ginger consumption and 9 studies showed no effect of ginger use of nausea and vomiting caused by chemotherapy. About chamomile, two studies indicated its positive effect and one study indicated that it had no effect.

Conclusion: In half of the studies, ginger consumption had a positive effect and in half of the studies it had no positive effect on reducing nausea and vomiting caused by chemotherapy, and chamomile consumption in two studies had completely contradictory results and in one study it had a positive effect on nausea. so we can't certainly say if they are effective or not.

Keywords: nausea and vomiting, chemotherapy, chamomile, ginger, complementary medicine.

Introduction

Although chemotherapy is a necessary and common treatment for cancer patients, it has some serious side effects that can be fatal for these patients both during and after treatment. Nausea and vomiting caused by chemotherapy (CINV) with a prevalence of 54 to 96% is one of the most severe side effects of treatment and one of the major concerns of cancer patients (1, 2), which causes Malnutrition and has negative effects on Immune system, reduces the quality of life of the patient and has negative effects on treatment (3). There are five types of nausea and vomiting caused by chemotherapy, which are acute, delayed, anticipated, sudden and resistant. The acute type develops within 24 hours after the start of chemotherapy. The delayed type occurs after 24 hours of chemotherapy and may last up to 7 days. The anticipated type occurs in patients who have experienced severe nausea and vomiting in previous chemotherapy. The sudden type occurs within 5 days of chemotherapy despite appropriate prophylaxis, and the resistant type occurs in subsequent cycles of chemotherapy. The prevalence of untreated nausea and vomiting is about 70-80% (4, 5). Nausea caused by chemotherapy causes many problems, including electrolyte disorders, dehydration, changes in the immune system, nutritional disorders, and esophageal rupture.

sometimes these problems are so severe that lead patients not to continue their treatment. Even with the widespread use of chemical anti-nausea and vomiting drugs such as serotonin receptor antagonists and neurokinin receptor antagonists, nausea and vomiting continue (6). In addition, the widespread use of industrial anti-emetic drugs has side effects such as extrapyramidal complications, hypotension, headache, etc. Due to the limited effect and dangerous complications caused by the use of industrial drugs, use of non-chemical and non-industrial treatments such as medicinal plants, which have fewer side effects, has increased(7, 8). According to the statistics of the World Health Organization, about 80% of the world's population currently uses herbal compounds for treatment and complementary and alternative treatments are used with standard treatments in cancer patients (9, 10).

Ginger is one of the herbal medicines that is effective in the treatment of nausea and vomiting and is used in the preparation of anti-nausea drugs in the German Pharmacopoeia(11). The rhizome powder of the ginger plant (*Zingiber Officinale* or Ginger) has been used for a long time in the past to treat digestive disorders such as nausea and vomiting, indigestion and diarrhea and recently has also used to relieve nausea caused by disorders such as motion sickness, seasickness, various surgeries such as reproductive system and glandular surgery and nausea during pregnancy(6). Ginger has special compounds such as *Gingerols* and *Shagaols*. These compounds have antioxidant, anti-inflammatory, antimicrobial, anti-cancer, neuroprotective and anti-depressant properties (12), which can treat nausea and vomiting by several mechanisms such as accelerating gastric emptying and by acting antagonistically to serotonin receptors(6). The use of ginger has been considered as an anti-nausea and vomiting agent since ancient times due to its favorable effects in the treatment and prevention of nausea, its use in the field of medical sciences is in the form of capsules, tea and so on(13). Chamomile is one of the dark medicinal herbs and has had a special place in ancient medical texts as well as in Iranian medicine. This plant has anti-inflammatory, antispasmodic, antibacterial and anti-flatulent properties and is used in diseases such as nervous, digestive and respiratory disorders. it can also be used to control nausea and vomiting, stomach ulcers, and to relieve pain and fever(14, 15).

Several studies have been conducted all around the world regarding the effect of ginger in different forms on the nausea and vomiting caused by chemotherapy, but there are limited studies regarding the use of chamomile. The aim of this study was reviewing the studies conducted to investigate effect of various types of ginger and chamomile on nausea and vomiting caused by chemotherapy.

Materials and methods

This literature review has been composed of the period between January 2003 and July 2023 by using Google Scholar, Scopus, Med-Line, Science Direct, Up To Date, Web Of Science ,Magiran, SID, and Pub-Med search databases with “nausea and vomiting, chemotherapy, chamomile, ginger ,herbal plants , herbal medicine Complementary medicine and alternative medicine” as keywords.

The Inclusion criteria in this study was all clinical trials and semi-experimental studies conducted on humans that used ginger in its various oral forms, or chamomile in its various forms to investigate their effect on nausea and vomiting caused by chemotherapy. The excluding criteria was articles not related to the topic, descriptive or qualitative studies. After reviewing 250 articles, 20 articles that met the inclusion criteria were selected.

Table 1- Included Studie

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|---------------------------|----------|-----------------------------|-----|---|---|---|
| Ansari, 2016(16) | Iran | RCT | 119 | Capsules (powdered dried ginger) with a daily dose of 1 gr (500 mg twice a day) for 3 days | placebo (Granisetron , Aperpitant) | Ginger has no effect on the severity of nausea and vomiting. |
| Arslan, 2015(17) | Turkey | RCT | 60 | Ginger powder with yogurt with a dose of 500 mg twice a day for 3 days | placebo (ranitidine and dexamethasone) | Reduction in the severity of nausea. (p < 0.05) Reduction in the frequency of vomiting. (p < 0.05) |
| Borhan, 2017(18) | Iran | RCT | 60 | Chamomile extract , two hours before chemotherapy with a dose of 25 mg/ kg | Sterile Water for Injection | Reduction of nausea No effect on vomiting frequency |
| Bossi, 2017(8) | Italy | RCT | 244 | Gelatin soft gel capsules(each capsule containing ginger with a daily dose of 40 mg) used 80 mg twice a day for 42 to 56 days. | Placebo (NK-1 receptor antagonist, 5-HT3 receptor antagonist, Dexamethasone, Sunflower oil(| No effect on nausea and vomiting |
| Das, 2020(19) | India | RCT | 100 | Ginger tea for 5 weeks | placebo | Reduction in nausea and vomiting |
| Fahimi, 2011(20) | Iran | RCT | 36 | Capsules(powdered dried ginger) with a daily dose of 1 gr (500 mg twice a day) for 3 days | Placebo (5-HT3 antagonist, Corticostreoid, Lactose) | No effect on the severity and frequency of nausea and vomiting |
| Kadhim, 2021(21) | iraq | RCT | 60 | Ginger tea with a dose of 1500 mg daily for 5 days | Not mentioned | Ginger had no effect on acute and delayed nausea and vomiting, but it reduced the severity of nausea. (p < 0.05) |
| Li X, 2018(22) | China | RCT | 140 | Capsules (powdered dried ginger) with a daily dose of 500 mg (250 mg twice a day) for 5 days | Placebo (5-HT3 RAs, Corn starch(| No effect on acute and delayed nausea and vomiting |
| Manusirivithaya, 2004(23) | Thailand | Cross-over double blind RCT | 43 | Capsules(powdered dried ginger) with a daily dose of 1 gr (250 mg four times a day) for 5 days | placebo (metoclopramide) | No effect on nausea and vomiting in the acute phase and an effect equivalent to metoclopramide in the delayed phase |
| Ghanbari 2013(24) | Iran | Cross-over | 31 | Capsules(powdered dried ginger) | Placebo (Ketril, Dexametasone, | Reducing the intensity and |



| | | double blind RCT | | with a daily dose of 1 gr (500 mg twice a day) for 28 days | Metoclopramid , Chickpea powder) | frequency of nausea and vomiting |
|-------------------|-----------|------------------------|-----|---|--|---|
| Panahi, 2012(4) | Iran | RCT | 78 | Capsules(powdered dried ginger) with a daily dose of 1.5 gr (500 mg twice a day) for 4 days | Grainsetron, Dexamethasone | Reduction of acute nausea (p = 0.04) without effect on delayed nausea and acute and delayed vomiting |
| Putri, 2019(15) | Indonesia | RCT | 30 | Aromatherapy with chamomile (the frequency and duration of aromatherapy are not explained in the article) | Prescription antinausea drugs | Reducing nausea P = 0.000 |
| Ryan, 2012(5) | USA | RCT | 375 | Capsules containing ginger extract with three doses of 0.5 , 1 and 1.5 grams daily for 6 days | Placebo (5-HT3 receptor antagonist, Dexamethasone, Extra virgin olive oil) | Reduced the intensity of nausea in the acute phase but it had no effect on the delayed phase)p = 0.017(for 0.5 gr:)p = 0.036(for 1 gr:)p = 0.0001(for 1.5 gr : |
| Sanaati, 2016(10) | Iran | RCT | 45 | Capsules(powdered dried ginger) with a daily dose of 1 gr (500 mg twice a day) for 10 days Capsules(powdered dried Chamomile) with a daily dose of 1 gr (500 mg twice a day) for 10 days | Dexamethasone, Metoclopramide , Aprepitant Dexamethasone, Metoclopramide , Aprepitant | Reducing the frequency of nausea (p = 0.006) Reducing the frequency of vomiting (p < 0.0001) Reducing the frequency of vomiting(P=0.0003) No effect on the severity and frequency of nausea P=0.238 P=0.895 |
| Shokri, 2017(25) | Iran | RCT | 49 | Capsules of powdered dried ginger with a daily dose of 2gr for 6 days | Placebo | No effect on nausea and vomiting |
| Sontakk,2003(26) | India | Cross-over RCT | 50 | Capsules of powdered dried ginger with a daily dose of 1gr for 3 periods | Placebo)Metoclopramide, Ondansetron, Lactulose(| No effect on nausea and vomiting |

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|----------------------------|----------|----------------|-----|---|--|--|
| Uthaipaisanwong, 2020 (۲۷) | Thailand | Cross-over RCT | 47 | Ginger capsules with a daily dose of 2 gr During two periods of 5 days | Placebo (Dexamethasone, Ondansetron, Ranitidine, Dimenhydrinate IV, Corn starch) | Reduction of acute phase nausea (p = 0.03) No effect on delayed nausea and acute and delayed phase vomiting |
| Wazqar, 2021 (۲۸) | Egypt | RCT | 100 | Ginger tea 4 cups a day for 6 days (1 cup = 250 mg) Fresh ginger root is added to 100 ml of boiling water and boiled for 10 minutes and half a teaspoon of honey is added for taste. | Granisetron, Dexamethasone | p < 0.05(Reducing the severity of nausea |
| Yekta, 2012(29) | Iran | RCT | 80 | Capsules of powdered dried ginger with a daily dose of 1gr for 6 days | Granisetron, Dexamethasone | Reduction of anticipated, acute and delayed phase vomiting (p = 0.04, p = 0.04, p = 0.003) |
| Zick S.M. et al., 2009(6) | USA | RCT | 162 | Capsules of powdered dried ginger with a daily dose of 1 or 2gr for 6 days | Placebo(5-HT3 receptor antagonist, Aprepitant, Lactose) | No effect on nausea and vomiting in acute and delayed phase in both doses |

Results Discussion

In conducted studies, different results have been presented. In some studies, it was shown that ginger has positive effect on the severity of nausea. In the study conducted by Ryan on patients with various cancers, it was shown that the consumption of ginger with doses 0.5, 1 and 1.5 gr per day, compared to placebo, significantly reduces the severity of nausea in the acute phase ($P=0.03$)(5). Some studies showed that ginger reduces the severity of nausea in the acute phase, but it did not affect the frequency of nausea and vomiting. Ghanbari et al.'s study was conducted on 44 patients undergoing chemotherapy, The results showed that there was no statistically significant difference in the frequency of nausea and vomiting between the two treatment regimens. But the ginger diet significantly reduced the severity and score of nausea compared to the placebo. ($p = 0.06$ and $p = 0.01$)(24). In some studies, it was shown that ginger affects both the severity and the frequency of nausea. In the study conducted by Yekta et al., it was shown that the severity and frequency of nausea in the predicted phase were significantly lower in the ginger group compared to placebo group ($P = 0.0007$, $P = 0.0008$). the frequency and severity of nausea in the acute phase were significantly less in the ginger group than placebo($P=0.0001$, $P=0.0001$), so the consumption of ginger capsules 1 gr per day from three days before chemotherapy to three days after it, along with the standard anti-nausea treatment, can help to reduce nausea in both the predicted and acute phases (29).

Some studies showed that ginger did not reduce the severity of nausea in the acute phase, but it reduced the frequency of nausea and vomiting. The results of the study conducted by Sanaati et al. showed that the severity of nausea in the acute phase between the two groups did not differ significantly ($P=0.238$), so ginger has no effect on the severity of nausea, while the frequency of nausea ($P=0.006$) and the frequency of vomiting ($P=0.0001$) was significantly less in the intervention group with ginger than the control group. This study also measured the effect of chamomile on nausea and vomiting caused by chemotherapy and it was shown that chamomile has no effect on the severity and frequency of nausea ($P=0.895$, $P=0.238$), but it decreased the frequency of vomiting ($P=0.003$)(10). In some studies, it was shown that the consumption of ginger cannot reduce the severity of nausea in the acute phase. The study conducted by Zick showed that in cancer patients undergoing chemotherapy, the consumption of ginger could not reduce the

severity of nausea compared to the control group in the acute phase ($P=0.5$) and the reason is probably related to the use of chemotherapy drugs with strong cytotoxic effects such as cisplatin(6). In the study

conducted by Bossi, it was shown that in cancer patients under Chemotherapy with a high dose of cisplatin, the consumption of ginger at a dose of 160 mg daily compared to the control group couldn't reduce the severity of nausea in the anticipated and delayed phase (8). In the study conducted by Manusirivithaya, in patients with ovarian and cervical cancers treated with cisplatin, daily consumption of 1 gr of ginger couldn't reduce the severity of nausea in acute phase ($P=0.9$) and the reason can be the high nausea intensity of Cisplatin, but in the delayed phase, it has an effect equivalent to metoclopramide (23). In some studies, it was observed that ginger is effective in reducing episodes of acute phase vomiting, but its effect decreases by time. In the study of Sontakke et al., it was shown that the frequency of vomiting episodes in the second 12 hours of the study showed a significant increase compared to the first 12 hours, which is attributed to the decrease in the antiemetic effects of ginger by time(26). On the other hand, some studies indicated that ginger can be effective in the delayed phase of nausea and vomiting caused by chemotherapy. For example, Levine et al.'s study showed that the consumption of ginger along with protein in the meal reduces delayed nausea (30). Borhan et al.'s study showed that chamomile reduces nausea but has no effect on reducing the frequency of vomiting. Its results were exactly opposite to the results obtained by Sanaati et al. Putri et al.'s study showed that chamomile aromatherapy reduces nausea in patients undergoing chemotherapy ($P=0.000$). In table 1 you can read the conducted studies in detail.

Conclusions

The oral consumption of ginger in different forms, in some studies, has reduced the frequency of nausea and vomiting. In some studies, it has reduced the severity of nausea and vomiting, and in some studies, it reduced both frequency and severity of nausea and vomiting. In some studies, ginger consumption was only effective on nausea in the acute phase and was ineffective on nausea in the delayed phase and it was effective on vomiting in the acute and delayed phase. In some studies, ginger did not have any effect on the intensity and frequency of nausea and vomiting. In the studies that investigated the effect of chamomile on nausea and vomiting caused by chemotherapy(10), there were also different results. These differences could be because of the type of cancer which was not the same in these studies, therefore the chemotherapy drug used was different. Considering that each type of cancer has its own chemotherapy drug and the drugs differ from each other in terms of the severity of nausea, as a result, it is not possible to easily judge the effectiveness of ginger and chamomile on nausea and vomiting caused by chemotherapy. The other reason for different results of these studies, is the different types and shapes of ginger and chamomile used in the studies and also because different doses of ginger have been used in different studies. The period of use is also different. In some studies, ginger was given before chemotherapy and in some after it.

In our review, in 9 studies, it was concluded that the consumption of ginger does not have any effect on nausea and vomiting caused by chemotherapy and in 9 studies, ginger had positive effects on patients undergoing chemotherapy. In 3 studies about Chamomile, one study showed that Chamomile aromatherapy reduced nausea and two studies had opposite results to each other, so we cannot surely recommend the use of ginger and Chamomile in the treatment of nausea and vomiting caused by chemotherapy, and more extensive studies are still needed to prove the effectiveness of ginger and chamomile. It is recommended that in future studies, each study be conducted on patients with the same type of cancer and with the same chemotherapy drugs, and also the effectiveness of ginger and chamomile be checked according to the time of their use (whether before or after chemotherapy).

Conflict of Interest

The authors declare there is no conflict of interest.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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