RESEARCH ARTICLE

Effect of Ginger and Chamomile on Nausea and Vomiting Caused by Chemotherapy in Iranian Women with Breast Cancer

Fateme Sanaati[1], Safa Najafi[2]*, Zahra Kashaninia[3], Masoud Sadeghi[4]

Abstract

Background: Chemotherapy-induced nausea and vomiting (CINV) places a significant burden on the patient. Herbal agents are the most commonly complementary therapies used among the public. This study was done to determine the effect of ginger and chamomile capsules on nausea and vomiting in cases undergoing chemotherapy for breast cancer (BC). Materials and Methods: In a randomized, double-blind and clinical trial study, 65 women with BC undergoing chemotherapy were referred to Breast Cancer Research Center, Tehran, Iran, between May 2013 to June 2014. Regimen for ginger group for 5 days before and 5 days after chemotherapy was: 2 times a day and 500 mg capsules of powdered ginger root in addition to a routine antiemetic regimen consisting of dexamethasone, metoclopramide and aprepitant (DMA) capsules. Chamomile group similarly was: 2 times a day and 500 mg capsules of Matricaria chamomilla extract in addition to a routine antiemetic regimen consisting of DMA capsules. Control group, routine antiemetic regimen consisting of DMA capsules. Results: There were no significant differences between the ginger, chamomile and control groups regarding age. Drugs used for chemotherapy were identical and duration of disease was also matched (1-4 months). Ginger and chamomile were both significantly effective for reducing the frequency of vomiting, there being no significant difference between the ginger and chamomile groups. Moreover, unlike the chamomile, ginger significantly influenced the frequency of nausea. Conclusions: According to the findings of this study, it should be declared that taking ginger capsules (1 g/day) might relieve CINV safely. Nurses dealing directly with cancer patients should be responsible for providing educational programs for patients and their families about how to deal with their drug regimens and associated side effects.

Keywords: Breast cancer - chemotherapy - ginger - chamomile - vomiting - nausea

Asian Pac J Cancer Prev, **17 (8)**, 4125-4129

Introduction

Breast cancer (BC) is a very common health problem in Iranian women (Amirifard et al., 2016). Nowadays, cancer therapy consists of surgery, radiotherapy, chemotherapy and biological therapy as well as some other methods, whereas in the locally advanced stage, chemotherapy such as Trastuzumab therapy is often the only effective method of cancer therapy (Payandeh et al., 2015). Chemotherapy-induced nausea and vomiting (CINV) places a significant burden on the patient.

There are multiple classes of medications developed to treat this symptom in a large number of patients (Carelle et al., 2002; Sun et al., 2005). The incidence of vomiting has been significantly reduced through combinations of anti-emetic medications, but efforts to control nausea have been less successful. Affecting upwards of 60% of patients (Bloechl-Daum et al., 2006), CINV has also been shown to significantly impact on patient quality of life. Moreover, although it happens rarely, CINV can be so severe that it can lead to dose reduction or treatment discontinuation, and subsequently increase the risk of disease progression (Bloechl et al., 2006; Ballatori et al., 2007; Vidall et al., 2011). This is of particular concern as nausea and vomiting in oncology patients can adversely affect food intake, increasing the risk of malnutrition during treatment. Previous studies report one in two patients in this setting as malnourished (Carelle et al., 2002). The cumulative effect of pretreatment and treatment-related malnutrition can be one of compromised immune function, decreased performance status, poor response to treatment, and sometimes treatment discontinuation (Davidson et al., 2012; Van Cutsem and Arends, 2005; Tong et al., 2009).

Herbal therapy is the most commonly complementary

*[1]Department of Nursing, University of Welfare and Rehabilitation Sciences, [2]Breast Cancer Research Centre, Jahad Daneshgahi, Tehran University of Medical Sciences, [3]Department of Nursing, University of Welfare and Rehabilitation Sciences, Tehran, [4]Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran *For correspondence: safa3n@yahoo.com*

therapies used among the public (Olaku and White,2011). Two of the roots of the plant are used as medicine, are ginger and chamomile. Ginger (Zingiber officinale) has a long history in many cultures as a folk-remedy for nausea and gastrointestinal discomfort. Empirical research has demonstrated that ginger may be effective as an anti-nausea agent; in particular (Wu et al., 2008), it has been proposed as a possible candidate for anti-CINV therapy (Wu et al., 2008; Marx et al., 2014). Furthermore, animal studies provide preliminary support for the role of ginger supplementation in the prevention of cisplatin-induced emesis (Sharma et al.,1997; Sharma and Gupta,1998). Few adverse effects from the ingestion of ginger are reported in the literature (Ernst and Pittler,2000). Chamomile is also extensively consumed as a tea or tonic and is used internally to treat anxiety, hysteria, nightmares, insomnia and other sleep problems, convulsions, and even delirium tremens (Martens D,1995). One of chamomile's main roles is as a multipurpose digestive aid to treat gastrointestinal disturbances including flatulence, indigestion, diarrhea, anorexia, motion sickness, nausea, and vomiting. Chamomile used in modern medicine primarily for their spasmolytic, antiphlogistic, antibacterial properties, and as a multipurpose digestive to treat gastrointestinal disturbances including flatulence, indigestion, diarrhea, anorexia, motion sickness, nausea, and vomiting (Shikov et al., 2008) .

This study was done to determine the effect of Ginger and Chamomile capsules on nausea and vomiting in chemotherapy.

Materials and Methods

Patients

This study was approved by Ethics Committee of University of Social Welfare and Rehabilitation Sciences and was registered in Iranian Registry of Clinical Trials (IRCT) with code of IRCT2013020912404N1. In a randomized, double-blind and clinical trial study, 65 women with BC undergoing chemotherapy referred to Breast Cancer Research Center, Tehran, Iran, between May 2013 to Jun 2014.

Criteria

Inclusion criteria: Patients between 20 and 60 years; histological diagnosis of BC, history of receiving at least one chemotherapy injection, receiving single-day cycles of chemotherapy (each cycle separated from next by≥2 weeks); experiencing vomiting in previous sessions, and having normal values of hematologic and biomedical laboratory parameters.

Exclusion criteria: Patients with multiple-day chemotherapy; receiving concurrent radiotherapy with high risk of causing emesis (i.e., total body, hemi body, upper abdomen, and craniospinal radiation); taking therapeutic doses of warfarin, aspirin, or heparin; had a history of bleeding disorder(s) like severe thrombocytopenia; had an allergy to ginger or chamomile or had taken it in the last week; had gastrointestinal disorders and cancers; and had other emesis-inducing diseases, such as hypertension, liver, and renal failure. Also, patients who met the following criteria: forgotten to take capsules ≥3 consecutive times; used other antiemetic drugs or therapeutic methods except the routine antiemetic; had severe gastrointestinal problems during the study; and refusal to continue participating in trial.

Regimens

A. Intervention group 1 (ginger group) for 5 days before and 5 days after chemotherapy was: 2 times a day and 500 mg capsules of powdered ginger root in addition to a routine antiemetic regimen consisting of dexamethasone, metoclopramide and aprepitant (DMA) capsule was consumed.

B. Intervention group 2 (chamomile group) for 5 days before and 5 days after chemotherapy was: 2 times a day and 500 mg capsules of Matricaria Chamomilla extract in addition to a routine antiemetic regimen consisting of DMA capsule was consumed.

C. Control group, routine antiemetic regimen consisting of DMA capsule was consumed.

Method

The patients were randomly allocated to treatment two experimental groups (ginger and chamomile) and one control group using the 20 block random tables. The treatment groups received white capsules of ginger or chamomile manufactured by University Biochemistry Laboratory Shahed, Tehran, Iran. Coding and blinding of the 2 groups were performed privately by the pharmacologist consultant, and all of the samples, data analyzers, and all participants too, were unaware of the real content of the capsules.

The dosage of capsules was selected based on the results of clinical trials conducted by Sontakke et al. (2003) and Ryan et al. (2009). A self-made, two-part self-reporting instrument was used to measure the frequency and severity of nausea and vomiting each member of three groups, after checking the content validity. This instrument was a reliable standard table that has been used in various studies as well (Sontakke et al., 2003; Manusirivithaya et al., 2004; Ozgoli et al., 2009; Zick et al., 2009). First part contained two tables with a 10 cm visual analogue scale (VAS) to record chemotherapy induced nausea and vomiting (CINV), and the second section included 3 questions about the: (a) probable use of other antiemetics; (b) missed cases of capsule taking; (c(probable side effects due to capsules intake. The patients were asked to fill the questionnaires out every night during the study and in any cases of intolerable complications stop the consumption and contact the researchers for more information.

Statistical Analysis

Professional blind interviewers collected and recorded the information and then data entry and analysis, were performed by a professional blind statistician. Data were analyzed using SPSS software version 16 and the application of descriptive and inferential statistics. The Chi-squared test was applied to compare the 2 groups regarding demographic characteristics, such as age (continuous variable) and education (ranked qualitative variance). To examine differences in the frequency and

severity of nausea and vomiting, inferential statistics of the linear logarithm model with Poison and paired t-test function were applied. After completing the data analysis the consultant pharmacologist broke the codes and introduced the groups.

Results

Out of 65 patients, 20 patients (8 patients in the intervention group with ginger; 7 patients in the intervention group with chamomile; and 5 patients in the control group) interrupted their participation (7 for general weakness and canceling of the chemotherapy; 6 because of unwillingness to continue the study; 6 for not filling the tools; and 1 due to die). Sampling time was extended to maintain the sample size (45 persons).

There were no significant differences between the ginger; chamomile and control groups regarding age variable (P = 0.45). Most participants of all three groups had Diploma and were homogenous (P = 0.19) according to Table 1.

Used Drugs for chemotherapy were identical (same severity of nausea) and duration of disease was also matched (1-4 months). The findings indicated no significant differences between the groups in terms of state profiles.

Table 2 indicates that ginger and chamomile are ineffective on intensity of nausea (P=0.238) while both are effective on the frequency of vomiting (P<0.0001), though there is no significant difference in the ginger and chamomile groups (Table 3)

Moreover, unlike the chamomile (P=0.895) (Table 4), ginger effects on the frequency of nausea (P=0.006) (Table 5).

Table 1. Baseline Characteristics of the Randomized Groups

Variables	Ginger N=15	Chamomile N=15	Control N=15
Age, n(%)			
20-30	1(6.7)	1(6.7)	1(6.7)
31-40	6(40)	1(6.7)	6(40)
41-50	7(46.7)	12(80)	7(46.7)
51-60	1(6.7)	1(6.7)	1(6.7)
Education			
High school	1(6.7)	1(6.7)	1(6.7)
Diploma	10(66.7)	10(66.7)	9(60)
University	4(26.7)	4(26.7)	5(33.3)

There was no significant different between groups and P-value was considered significant at P < 0.05 by Chi-square test

Table 2. Effects of the Groups on Components Using the Generalized Estimating Equations (GEE) Model

Component	Chi-square statistics	Degree of freedom	P-value
Intensity of nausea[a]	2.867	2	0.238
Number of nausea	7.376	2	0.025
Number of vomiting	20.812	2	<0.0001

[a]Intensity of nausea was evaluated by using Visual analog scale: (0 = no nausea, 3-1 = mild, 6-4 = moderate 9-7 = severe, 10 = very severe)

Discussion

BC is the most frequent malignancy among females and is a leading cause of death of middle-aged women (Payandeh et al., 2015). Advances in our understanding of the pathophysiology of CINV), the identification of patient risk factors, and the development of new antiemetics have led to significant improvements in CINV prevention (Jordan et al., 2014). In addition to controversial reports, there are few studies about the effect of ginger extract on the CINV. It seems that characteristics of those studies could affect their results. For example, they have targeted wide range and kind of cancers (Manusirivithaya et al., 2004; Zick et al., 2009). Meanwhile, each of them has special therapeutic protocol and each protocol has also its own special emetogenicity in comparison to the others. Hence, we can't easily approve or refuse the effectiveness of ginger plant on CINV and also we

Table 3. Effects of the Groups on Nausea and Vomiting Using the Generalized Estimating Equations (GEE) Model

Component	Model coefficient	Standard error of the coefficient	Statistics	Degree of freedom	P-value
Nausea					
Ginger	0.746	0.2996	6.195	1	0.013
Chamomile	0.025	0.1932	0.017	1	0.896
Control	Basic	-	-	-	-
Vomiting					
Ginger	1.303	0.5597	16.924	1	<0.0001
Chamomile	1.145	0.4911	5.437	1	0.02
Control	Basic	-	-	-	-

Table 4. Paired Sample t-test Comparison of Number of Nausea

Group	Mean difference	Standard error of the coefficient	Degree of freedom	P-value
Ginger-Control	1.5845	0.5787	1	0.006
Chamomile-Control	0.0769	0.5851	1	0.895
Chamomile-Ginger	1.6615	0.5282	1	0.002

Table 5. Paired Sample t-test Comparison of Number of Vomiting

Group	Mean difference	Standard error of the coefficient	Degree of freedom	P-value
Ginger-Control	0.108	0.2474	1	<0.0001
Chamomile-Control	0.8394	0.2814	1	0.003
Chamomile-Ginger	0.2686	0.1989	1	0.177

can't generalize the results to other types of cancer. On the other hand, no studies have examined the effect of chamomile on the CINV. Therefore, this study was carried out to address those issues that have been less studied. Only women with BC were attended to increase the accuracy and generalizability of the results because BC is the most common type of cancer among women in Iran and in the world (Sontakke et al., 2003; Ryan et al., 2009) and almost the same chemotherapy protocol is used to treat it. In this study, the results indicate that ginger and chamomile are ineffective on intensity of nausea while both influence on the frequency of vomiting. Moreover, unlike the chamomile (P>0.05), ginger effects on the frequency of nausea significantly. Similar to our findings, Zick et al. (2009) reported that in cancer patients undergoing chemotherapy, ginger capsules could not relieve the CINV in acute and delayed (P>0.05) phases in comparison to the control group that could be probably due to the use of cisplatin as a high cytotoxic agent. Moreover, Manusirivithaya et al. (2004) expressed that there was no significant differences between ginger and placebo groups related to the complete control of acute and delayed vomiting that could be concerned using cisplatin in chemotherapy protocol. In contrast, Ryan et al. (2009) indicated that in cancer patients undergoing chemotherapy the use of ginger (5.0, 1 and 5.1 g/day) reduced the intensity of nausea in acute phase (P<0.05). Sontakke et al. (2003) indicated that in cancer patients undergoing chemotherapy the antiemetic effect of metoclopramide was equivalent to ginger (1g/day) in acute phase (58% versus 62%, respectively). Similar to our findings, Nanthakomon and Pongrojpaw (2006), reported that in cancer patients undergoing chemotherapy, ginger capsules reduced the frequency of nausea and vomiting significantly. The results of other studies about the effect of ginger extract on pregnancy-induced vomiting (PINV) are the same as ours. As Ozgoli et al. (2009) stated, the use of ginger (1g/day (significantly reduced the cases of PINV. In addition, Jenabi et al. (2009) revealed that taking ginger powder (1 g/day) significantly relieved PINV.

There is no published study about the effect of chamomile on the CINV. This study was only performed on women with BC undergoing single-day courses of chemotherapy. This matter has its own privileges, but also limitations. The most important limitation of this study was that our results were only devoted and applicable for patients with BC, and thus we cannot generalize the results to other types of cancers. So, it should be suggested that to conduct more widespread studies about the effect of ginger and chamomile on the different types of cancers and also to assess the effect of ginger and chamomile on patients undergoing multiple-day chemotherapy to achieve more accurate information about the efficacy of these herbs.

In conclusions, according to the findings of this study, it should be declared that taking ginger capsules (1 g/day) might relieve the CINV safely. Nurses are dealing directly with cancer patients and are responsible for providing educational programs for patients and their families about how to deal with their drug regimens and its side effects. Therefore, nurses should introduce and teach those patients to take these capsules, as the effectiveness and safety of ginger are confirmed.

Acknowledgements

This study was carried out with the financial support of research deputy of University of Social Welfare and Rehabilitation Sciences and with the favor of Breast Cancer Research Center of University of Tehran. Hereby we would like to express our appreciation to all the dear participants and personnel of Breast Cancer Research Center.

This study was registered at http://www.irct.ir (registration number IRCT2013020912404N1).

References

Amirifard N, Sadeghi E, Payandeh M, et al (????). Relationship between HER2 proto-oncogene status and prognostic factors of breast cancer in the west of Iran. *Asian Pac J Cancer Prev*, **17**, 295-8.

Ballatori E, Roila F, Ruggeri B, et al (2007). The impact of chemotherapy-induced nausea and vomiting on health-related quality of life. *Supportive Care in Cancer*, **15**, 179-85.

Bloechl-Daum B, Deuson RR, Mavros P, Hansen M, Herrstedt J(2006). Delayed nausea and vomiting continue to reduce patients' quality of life after highly and moderately emetogenic chemotherapy despite antiemetic treatment. *J Clin Oncol*, **24**, 4472-8.

Carelle N, Piotto E, Bellanger A, et al(2002). Changing patient perceptions of the side effects of cancer chemotherapy. *Cancer*, **95**, 155-63.

Davidson W, Teleni L, Muller J, et al (2012). Malnutrition and chemotherapy-induced nausea and vomiting: implications for practice. *Oncol Nurs Forum*, **39**, 340-5.

Ensiyeh J, Sakineh MA(2009). Comparing ginger and vitamin B6 for the treatment of nausea and vomiting in pregnancy: a randomised controlled trial. *Midwifery*, **25**, 649-53.

Ernst E, Pittler M (2000). Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. *Br J Anaesthesia*, **84**, 367-71.

Jordan K, Schaffrath J, Jahn F, Mueller-Tidow C, Jordan B (2014). Neuropharmacology and management of chemotherapy-induced nausea and vomiting in patients with breast cancer. *Breast Care*, **9**, 246-53.

Manusirivithaya S, Sripramote M, Tangjitgamol S, et al (2004). Antiemetic effect of ginger in gynecologic oncology patients receiving cisplatin. *Int J Gynecological Cancer*, **14**, 1063-9.

Martens D (1995). Chamomile: the herb and the remedy. *J Chiropractic Academy Homeopathy*, **6**, 15-8.

Marx W, McCarthy AL, Ried K, et al(2014). Can ginger ameliorate chemotherapy-induced nausea? Protocol of a randomized double blind, placebo-controlled trial. *BMC Complement Altern Med*, **14**, 134.

Nanthakomon T, Pongrojpaw D (2006). The efficacy of ginger in prevention of postoperative nausea and vomiting after major gynecologic surgery. *J Med Assoc Thai*, **89**, S130-6.

Olaku O, White JD(2011). Herbal therapy use by cancer patients: a literature review on case reports. *Eur J Cancer*, **47**, 508-14.

Ozgoli G, Goli M, Simbar M(2009). Effects of ginger capsules on pregnancy, nausea, and vomiting. *J Alternative Complementary Med*, **15**, 243-6.

Payandeh M, Sadeghi M, Sadeghi E, Aeinfar M (2015). Clinicopathology figures and long-term effects of tamoxifen plus radiation on survival of women with invasive ductal carcinoma and triple negative breast cancer. *Asian Pac J*

Cancer Prev, **16**, 4863-7.
Payandeh M, Sadeghi M, Sadeghi E (2015). Differences in prognostic factors between early and late recurrence breast cancers. *Asian Pac J Cancer Prev*, **16**, 6575-9.
Ryan J, Heckler C, Dakhil S, et al (2009). Ginger for chemotherapy-related nausea in cancer patients: A URCC CCOP randomized, double-blind, placebo-controlled clinical trial of 644 cancer patients. *J Clin Oncol*, **27**, 9511.
Sharma S, Kochupillai V, Gupta S, Seth S, Gupta Y(1997). Antiemetic efficacy of ginger (Zingiber officinale) against cisplatin-induced emesis in dogs. *J Ethnopharmacol*, **57**, 93-6.
Sharma SS, Gupta YK (1998). Reversal of cisplatin-induced delay in gastric emptying in rats by ginger (Zingiber officinale). *J Ethnopharmacol*, **62**, 49-55.
Shikov AN, Pozharitskaya ON, Makarov VG, Kvetnaya AS (2008). Antibacterial activity of chamomilla recutita oil extract against helicobacter pylori. *Phytotherapy Res*, **22**, 252-3.
Sontakke S, Thawani V, Naik M(2003). Ginger as an antiemetic in nausea and vomiting induced by chemotherapy: a randomized, cross-over, double blind study. *Indian J Pharmacol*, **35**, 32-6.
Sun CC, Bodurka DC, Weaver CB, et al(2005). Rankings and symptom assessments of side effects from chemotherapy: insights from experienced patients with ovarian cancer. *Supportive Care Cancer*, **13**, 219-27.
Tong H, Isenring E, Yates P (2009). The prevalence of nutrition impact symptoms and their relationship to quality of life and clinical outcomes in medical oncology patients. *Supportive Care Cancer*, **17**, 83-90.
Van Cutsem E, Arends J(2005). The causes and consequences of cancer-associated malnutrition. *Eur J Oncol Nurs*, **9**, 51-63.
Vidall C, Dielenseger P, Farrell C, et al (2011). Evidence-based management of chemotherapy-induced nausea and vomiting: a position statement from a European cancer nursing forum. *Ecancermedicalscience*, **5**, 211.
Wu KL, Rayner CK, Chuah SK, et al(2008). Effects of ginger on gastric emptying and motility in healthy humans. *Eur J Gastroenterol Hepatol*, **20**, 436-40.
Zick SM, Ruffin MT, Lee J, et al (2009). Phase II trial of encapsulated ginger as a treatment for chemotherapy-induced nausea and vomiting. *Supportive Care Cancer*, **17**, 563-72.