ANXIOLYTIC AND ANTIEMETIC EFFECTS OF AROMATHERAPY IN CANCER PATIENTS ON ANTICANCER CHEMOTHERAPY

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Summary

Aromatherapy is a rapidly growing branch of complementary and alternative medicine. It involves the use of essential oils to attempt to cure, mitigate or to prevent certain symptoms of disease. The aim of this study was to assess the potential impact of aromatherapy in the treatment of anxiety and chemotherapy induced nausea and vomiting in cancer patients. Sixty cancer patients undergoing chemotherapy were recruited from the Kerala state of India. Patients were split into two groups (i) experimental group (n=30) receiving aromatherapy-based massage prior to and during the period of chemotherapy and (ii) the control group (n=30) not in receipt aromatherapy massage. Anxiety was assessed in both groups prior to and 24 hours post chemotherapy. The level of nausea and vomiting were assessed in patients over a 24 hour period following chemotherapy. A significant mean reduction in anxiety was observed in those receiving aromatherapy compared to controls (8.0±2 vs 3.2±1.4, p-value<0.001). In addition, nausea was found to be decreased significantly in the experimental group compared to controls (1.30±0.4 vs 1.73±0.6, p-value<0.01). A lower grade of vomiting was also observed in the group receiving aromatherapy compared to untreated controls (0.4±0.6 vs 0.9±0.8, p-value<0.01). Overall, this study demonstrates significant anxiolytic and antiemetic effects with aromatherapy massage when used as an adjuvant to standard antiemetics in cancer patients undergoing chemotherapy. Our findings suggest that aromatherapy is of some value to medical professionals when attempting to ameliorate common side effects such as nausea, vomiting and anxiety associated with anticancer chemotherapy.

Key words: Anticancer chemotherapy, Emesis and Anxiety, Aromatherapy, Essential oils

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Introduction

Cancer represents a major health burden worldwide. A major source of this burden lies in the current difficulties associated with the prevention, diagnosis and treatment of different types cancers. In terms of treatment, there are different methods available including surgery, chemotherapy, radiation therapy, immunotherapy, monoclonal antibody therapy and hormone therapy. Chemotherapy in particular is widely used as a method to destroy cancer cells in affected patients. However, side effects to chemotherapeutic agents can emerge in patients due to the damage incurred to normal healthy cells and tissue during treatment. The range of side effects of chemotherapy are broad and can include nausea and vomiting, diarrhea or constipation, malnutrition, hair loss, memory loss, myelosupression, infections and sepsis, weight loss and hemorrhage[1]. Treating these side effects in affected patients represents a significant challenge to health care professionals in this area.

Chemotherapy Induced Nausea and Vomiting (CINV) is one of the most common and distressing side effects of anticancer chemotherapy. This is despite of the advances made in antiemisis management such as the development of 5-HT_3 inhibitors, antihistaminics and dopamine (D_2) antagonists. Chemotherapeutic agents can damage healthy host cells which can lead to release of neurotransmitters which stimulate the chemotherapeutic trigger zone resulting in nausea and vomiting. Local gastrointestinal toxicity also contributes to nausea and vomiting. Anticipatory anxiety about chemotherapy and its possible side effects can also lead to nausea and vomiting. Anticipatory nausea and vomiting prior to chemotherapy is often associated with a memory of poorly controlled nausea and vomiting[2]. Furthermore, 20-30% of patients who have CINV, develop anticipatory nausea and vomiting for subsequent chemotherapy cycles[3,4]. CINV can present in two forms, acute and delayed. Acute CINV manifests within 24 hours of chemotherapy while delayed CINV can occur within 2-5 days. The most important variables associated with the risk of developing CINV include the emetogenic potential of the chemotherapeutic regimen adopted, the antiemetics used, and individual patient factors. Chemotherapeutic agents like cisplatin, cyclophosphamide, doxorubicin epirubicin and cyclophosphamide are considered highly emetogenic (>90%). As CINV can be very severe and distressing, many patients may wish to quit the chemotherapy treatment. In addition, patients may also suffer from varying levels of anxiety at all stages during the diagnosis and treatment of cancer.

Complementary therapies to treat the side effects of cancer treatment have been explored by scientists and medical professionals in recent years. These therapies are varied and include methods such as relaxation techniques, acupuncture,acupressure and guided imagery. Aromatherapy in particular is one of the fastest growing branches of complementary and alternative medicine. It involves the use of essential oils derived from plants in attempting to cure, mitigate or to prevent the symptoms of disease. Essential oils, the pure volatile portion of aromatic plant products, are normally extracted by distillation. Practitioners of aromatherapy consider aromatic essential oils to have a wide range of effects including analgesic, anticonvulsive, antidepressant, antimicrobial, antiseptic, antitoxic, carminative, choleretic, cytophyllatic, cordial, diuretic, hypotensive, sedative and stimulant effects. Commonly used essential oils are lavender oil, sandalwood, jasmine and peppermint oil. Typically, essential oils can be absorbed into the body via the skin or the olfactory system[5]. Commercially available

essential oils have been used for several hundred years and are regularly used for stress management and minor ailments[6].

Several studies have been undertaken to investigate the potential impact of aromatherapy based interventions on the physiological and psychological well-being of cancer patients [7,8,9,10,11,12,13,14,15,16] Results from these studies have been varied and the precise mechanisms of action mediated by essential oils, have not been elucidated. Nevertheless, a number of these studies have demonstrated a positive effect of aromatherapy in treating disease symptoms in cancer patients. For instance, aromatherapy massage had been found to be associated with a short-term benefit(up to two weeks) on anxiety and depression in cancer patients[16]. In addition to reducing anxiety in cancer patients, there is also evidence that treatment with aromatherapy massage may affect the immune system[10]. Aromatic hand massage has also been reported to have a positive effect on pain and depression in patients with terminal cancer[8]. Furthermore, aromatherapy has been reported to reduce the perceived severity of postoperative nausea[7], although as the authors suggest, this is likely related to control of breathing patterns rather than a specific influence mediated directly by aromatic essential oils. In addition to massage, some evidence indicates that essential oils may mediate their effects via the olfactory system of patients. For instance, rosemary and lavender oils have been reported to give rise to objective effects on cognitive performance and subjective effects on mood[13]. It has been reported that humidified essential oils aromatherapy may lead to psychological changes in cancer patients[12].

Overall, there is a considerable gap in our knowledge with respect to the role of aromatherapy in the treatment of the symptoms of cancer patients during anticancer chemotherapy. In particular, hardly any studies have focused on the use of adjuvant aromatherapy in management of chemotherapy induced nausea, vomiting and anxiety. With this in mind, the present study is aimed to assess the effectiveness of aromatherapy as an add-on therapy for treating nausea, vomiting and anxiety in a cohort of cancer patients receiving emetogenic chemotherapy.

Materials and Methods

Patients

Patients receiving anticancer chemotherapy were recruited from the Oncology Department, Amala Cancer Institute and Research Center (ACIRC) at Trishur, in the Kerala state of India. The **inclusion criteria** for this study are (i) patients over 18 years of age and (ii) undergoing highly emetogenic chemotherapy treatment for solid cancer tumors. **Patients were excluded** on the basis of having cancer other than solid tumors, having head and neck cancers or having dermatitis or ulcers in hands and shoulders. In addition, patients with any episodes of retching, vomiting or uncontrolled nausea within 48 hours prior to administration of chemotherapy were excluded. Patients who received radiation therapy in 14 days beforehand and for whom radiation therapy were scheduled during seven days after chemotherapy were also excluded. Those receiving any unscheduled anti-emetic drug within 24 hours of initiation of chemotherapy were not included in this study. Out of the sixty subjects which met the inclusion criteria, thirty were allotted into an experimental group and another thirty were allotted into a control group. The characteristics of patients selected for this study are shown in table 1. This study was conducted following the ACIRC ethical committee clearance. The study was undertaken according to the Helsinki declaration and good clinical practices guidelines. All subjects recruited gave informed consent for participation in this study.

Table 1: Characteristics of study subjects

Selected variables	Experimental group (n=30)		Control group (n=30)	
	n	Percentage	*n*	Percentage
Age				
≤29	1	3.3	1	3.3
30-44	8	26.7	12	40.0
45-59	13	43.3	11	36.7
≥60	8	26.7	6	20.0
Gender				
Male	9	30.0	13	43.3
Female	21	70.0	17	56.7
Marital status				
Married	22	73.3	20	66.7
Single	4	13.3	6	20.0
Widowed	4	13.3	4	13.3
Weight (kg)				
40-49	9	30.0	10	33.3
50-59	15	50.0	17	56.7
60-69	6	20.0	3	10.0
Type of cancer				
Breast	18	60.0	13	43.3
Lungs	4	13.3	6	20.0
Colon	2	6.7	3	10.0
Stomach	2	6.7	4	13.3
Sarcoma	2	6.7	0	-
Ovary	1	3.3	2	6.7
Pancreas	1	3.3	2	6.7
Stage of cancer				
I	1	3.3	0	-
II	15	50.0	11	36.7
III	8	26.7	15	50.0
IV	6	20.0	4	13.3
Cycle of chemotherapy				
I	14	46.7	16	53.3
II	9	30.0	10	33.3
III	6	20.0	3	10.0
IV	1	3.3	1	3.3

Table 1: Characteristics of study subjects
This table shows the characteristics of patients recruited for this study. The number (n) and percentage of individuals in the experimental and control groups and their specific characteristics are indicated in the table.

Study Design
The Lydia E. Hall Core Care Cure Model[16,17] was adopted in this study. The study was conducted in three steps. In the step I, assessment of anxiety level of both experimental and control groups was performed. In step II, aromatherapy was carried out for the experimental group while the control group did not receive any intervention. In step III, post test scores of anxiety level of both groups was assessed using the same scale. In addition, the incidence of

nausea and vomiting were assessed. Both pre-test and post-test assessment of anxiety in the experimental and control group was carried out while CINV was only assessed following aromatherapy treatment.

Psychological examination

Anxiety in both experimental and control groups were assessed using Beck Anxiety Inventory [18] prior to chemotherapy. Following the pre-test, members of the experimental group were given a short explanation about aromatherapy massage followed by treatment. No intervention was undertaken for the control group. Post-test assessment was done following 24 hours of chemotherapy. Overall patient scores for each patient classified them into categories of low anxiety (score range 0-21), moderate anxiety (score range 22-35) and severe anxiety (score >36). Nausea and vomiting of both experimental and control groups were assessed following chemotherapy. Nausea was assessed using the 'National Cancer Institute-Criteria for grading severity of nausea - Version 3 (NCI CTCAE, 2006)[19]. Vomiting was assessed by counting the number of episodes of vomiting following chemotherapy for 24 hours. The enrolled patients and bystanders were instructed to note down each episode of vomiting and this was correlated with the nurse's record. Pre-test and post-test assessment of anxiety was performed for both experimental and control group.

Aromatherapy procedures

Aromatherapy was administered one hour before chemotherapy and was subsequently continued every hour until the completion of chemotherapy. Aromatherapy[6] was performed as follows[6]: six drops of lavender oil was applied over the shoulders, neck and hands and massaged in circular motion for ten minutes. In addition to massage, patients were provided with cotton dipped in lavender oil for inhalation during aromatic massage treatments.

Statistical analysis

Data was analyzed by directly comparing the experimental cohort receiving aromatherapy with the control cohort not receiving aromatherapy. Both the experimental and control group sample scores (anxiety and CINV) were compared using students't' test.

Results

This study was undertaken to determine the effectiveness of aromatherapy in ameliorating anxiety and chemotherapy induced nausea and vomiting among cancer patients receiving highly emetogenic anticancer agents. Statistical analyses demonstrated a marked reduction in nausea, vomiting and anxiety in each case following aromatherapy intervention.

Reduction in anxiety following aromatherapy

Anxiety levels were calculated by means of the Beck Anxiety Inventory prior to chemotherapy. Levels were found to be similar between the experimental and control groups (28.3±4.2vs 28.4±4.2, Table 2A). Reductions in anxiety levels were observed in both groups 24 hours following chemotherapy. In the case of the control group, anxiety levels dropped significantly from 28.4±4.2 prior to chemotherapy as compared to 25.2±3.8 post-chemotherapy ($p < 0.001$, table 2A). A significant reduction in anxiety levels was also observed in the experimental group with levels dropping from a value of 28.3±4.2 to 20.3±3.7 ($p < 0.001$, table-2A). Overall this

gives rise to a significantly larger mean reduction in anxiety levels in the experimental group versus controls (8.0±2 vs 3.2±1.4, $p < 0.001$, table-2B). This indicates that addition of aromatherapy intervention prior to chemotherapy is associated with a significant reduction in anxiety levels in cancer patients on chemotherapy compared to those not treated with aromatherapy.

(A)

Groups	**Pre-test Anxiety**		**Post-test Anxiety**		**Mean difference**		**'t'**	**df**	**Significance**
	Mean	SD	Mean	SD	Mean	SD			
Experimental	28.3	4.2	20.3	3.7	8.0	2.0	21.365	28	p<0.001
Control	28.4	4.2	25.2	3.8	3.2	1.4	12.309	28	p<0.001

(B)

Groups	**Mean reduction**		**Differences of means**	**'t'**	**df**	**Significance**
	Mean	SD				
Experimental	8.0	2.0	4.8	10.769	58	p<0.001
Control	3.2	1.4				

Table-2: **Reduction in anxiety levels following aromatherapy intervention.**

Table 2A shows the pre-test and post-test levels of anxiety and mean reduction of anxiety scores in the both experimental (n=30) and control groups (n=30). Comparisons of the mean anxiety scores pre- and post- aromatherapy intervention was determined for both groups by means of the student 't' test. Table 2B compares reductions in mean anxiety levels in both cohorts also using the student 't' test.

Reduction in chemotherapy induced nausea and vomiting following aromatherapy.

Nausea was measured in patients following chemotherapy using the National Cancer Institute-Criteria for grading severity of nausea - Version 3. Nausea was found to be significantly decreased in the experimental group receiving aromatherapy compared to controls (1.30±0.4 vs 1.73±0.6, $p < 0.01$, table 3). The incidence, severity, and frequency of vomiting in patients following chemotherapy was also significantly lower in the group receiving aromatherapy compared to untreated controls (0.4±0.6 vs 0. 9±0.8, $p < 0.01$, table 4) thus demonstrating the beneficial effects of aromatherapy treatment compared to those not receiving it.

Post test grade	Nausea								t	Significance
	Experimental				Control					
	f	%	Mean	SD	*f*	%	Mean	SD		
0	0	0			0	0				
1	22	73.3			10	33.3				
2	8	26.7	1.3	0.4	18	60.0	1.73	0.6	3.33	p<0.01
3	0	0			2	6.7				
Total	30	100			30	100				

Table-3: Effectiveness of aromatherapy in reducing chemotherapy induced nausea.
This table shows the grading of nausea in both experimental and control groups following aromatherapy intervention. Mean grades of nausea were compared between the two cohorts using the students 't' test.

Post test grade	Vomiting								t	Significance
	Experimental				Control					
	f	%	Mean	SD	*f*	%	Mean	SD		
0	19	63.3			10	33.3				
1	10	33.3			16	53.3				
2	01	3.4	0.4	0.6	02	6.7	0.9	0.8	3.23	p<0.01
3	0.0	0.0			02	6.7				
Total	30	100			30	100				

Table-4: Effectiveness of aromatherapy in reducing chemotherapy induced vomiting.
This table shows the grading of vomiting episodes in both experimental and control groups following aromatherapy intervention. Mean grades of vomiting episodes were compared between the two cohorts using the student 't' test.

Discussion

This study provides evidence that aromatherapy-based treatment ameliorates chemotherapy induced nausea, vomiting and anxiety in cancer patients. In particular, following chemotherapy, anxiety levels were found to be reduced in patients who had received aromatherapy prior to and during their course of treatment. This finding is consistent with previous studies which have also demonstrated a reduction in anxiety in cancer patients on treatment with aromatherapy[10,16]. However, the present study highlights the positive impact of aromatherapy on the psychological

well-being of patients when intervention takes place just prior to and during chemotherapy treatment. The psychological impact of anxiety on patients suffering from cancer can be severe. In particular, anticipatory anxiety about chemotherapy treatment may contribute to nausea and vomiting in affected patients. In this study we observed that over a twenty four hour period, a two fold reduction in vomiting in those receiving aroma therapy as compared to controls. In this respect, the association between aromatherapy treatment and reduced anxiety in cancer patients observed in this study indicates that aromatherapy is definitely useful as a short term adjuvant antiemetic therapy for cancer patients receiving chemotherapy.in reducing anxiety and in turn, side effects of chemotherapy such as nausea and vomiting.

The precise mechanism by which aromatherapy may ameliorate the side effects of chemotherapeutic treatment is unclear. Some studies suggest that essential oils may exert positive influences on patient's well-being on entering the body through the olfactory system or through absorption via the skin. However, intervention through massage therapy alone and/or control of breathing patterns may account for the observed antiemetic and anxiolytic affects observed in this study rather than through direct effects mediated by aromatic essential oils. In addition, it is possible that the observed reductions in the side effects of chemotherapy may be partly due to the effect of aromatherapy in lowering anxiety levels in patients prior to and during chemotherapy.

Overall, this study provides further evidence in support of the view that aromatherapy-based treatments may be of considerable value to medical professionals while treating cancer patients receiving chemotherapy. Further studies are required to establish the precise mechanism(s) of action involved in these treatments and in turn establishing optimal procedures for methods of administration of this treatment.

Conclusions

The potential use of aromatherapy-based on complementary and alternative medicine in treating symptoms of serious diseases such as cancer and the side effects associated with its chemotherapy have been investigated by medical professionals in recent years. The findings in this current study support to the view that aromatherapy represents an effective add-on therapy in the prevention and / or reduction of side effects such as anxiety, nausea and vomiting suffered by cancer patients while on highly emetic chemotherapy.

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