The Effect of Combining Herbal Therapy with Conventional Chemotherapy on the Incidence of Chemotherapy Side Effects in 2nd Stage Breast Cancer Patients

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Abstract: The purpose of this study is to identify the effect of the combination of herbal mixture and conventional chemotherapy on minimizing the incidence of chemotherapeutic side effects for 2nd stage breast cancer. Forty adult female patients aging 20 to 65 years old diagnosed with breast cancer stage (II), receiving chemotherapy for at least one month and will continue to receive it for 3 months- were selected randomly and divided equally into study and control groups. They were free from any associated co-morbid diseases as diabetes, renal, cardiac. The patients were interviewed in the oncology outpatient clinic. Study group patients were instructed about the importance of taking herbal capsules regularly with chemotherapeutic cycles, on a scheduled dose of 1 capsule three times per day for 3months. Complete assessment for both groups as baseline data to assess the chemotherapeutic side effects, laboratory investigations and the nutritional status of the patients were done, and then after 45days and after 3 months. The results revealed that (45%) of cancer breast women were in age group 49-65 years. The greater proportion of the sample (62.5%) breast fed and lactated for three times and more through their life. The least affected systems with chemotherapeutic side effects and the most affected systems when combined herbal to conventional therapy were: liver functions and endocrine studies, renal functions, reproductive system, urinary system, and weight changes. While psychological status, nervous system, and skin, hair, and nails were the most affected systems with the side effects of chemotherapy, and they were the least affected systems when combined herbal to conventional chemotherapy. Also it was found that there was significant difference between the study and control groups in relation to second and third assessments related to all body systems. It is recommended that herbal education should be introduced in nursing and medical curriculum. Further researches related to these herbal components to measure its efficacy on minimizing the side effects of chemotherapy for breast cancer and/ or other types of cancer. Further researches are also needed on larger number of sample. Clinical studies should be done to identify the effect of these herbals on different cancer therapies, different chemotherapeutic protocols, specifically pre or post mastectomy.

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Introduction

Breast cancer is the second most common type of cancer after lung cancer, and the fifth most common cause of cancer death. Egyptian National Cancer Institute (NCI) [(9)] , reported that breast cancer is the most common cancer among women, representing 18.9% of total cancer cases (35.1% in women and 2.2% in men) among series of 10556 patients during the year 2001, with an age-adjusted rate of 49.6 per 100 000 population. Breast cancer in Egyptian patients has a younger age distribution with the majority of patients occurring at 30–60 years of age. In Alexandria over the year 2006, 1183 patients diagnosed with breast cancer (1132 patients were females and 51 patients were males) [(10)].

The type of treatment for breast cancer varies with the location, type and severity of the tumor. Therapy options for breast cancer include surgery, chemotherapy, radiation therapy, biological therapy and hormonal therapy [(63)].). The treatment can be physically exhausting for the patient. Current chemotherapeutic techniques have a range of side effects mainly affecting the fast-dividing cells of the body. Important common side-effects include: Bone marrow suppression, digestive system changes as nausea and vomiting, appetite loss and weight

changes, taste changes, constipation, diarrhea, hair loss, fatigue, heart damage and nervous system changes [14, 15].Recently, there is a call for returning to the nature by using herbals with proven efficacy in prevention, treating, and minimizing the consequences of many diseases.Health care in the twenty-first century requires that nurses recognize the shift of thinking toward the incorporation of alternative and complementary approaches to care. Nurses at all levels and in every area of practice are answering the call to use new methods to care for the ill patients and to enhance the health of those who are well [7].

Complementary and alternative medicine (CAM) is widely embraced by cancer patients due to largely patients' demands for integration of herbal therapies into their cancer treatment. Integrated medicine is a holistic approach to cancer care, with some herbal medicines showing proven efficacy as adjuvant to conventional medical treatments. At the present time there is little evidence of a systematic process of evaluation or dialogue between mainstream medicine and herbal medicine practitioners [16].Herbal Medicine is one of the oldest types of medicine which is dating back to the ancient cultures of Egypt, China, and India, and possibly even pre-historic times for healing purposes [17]. It encompasses the use of natural sources as plants and natural products for healing or therapeutic purposes [16, 17].

In Egypt, there is a lack in clinical researches investigating the real effect of herbals as a complementary and / or alternative medicine, despite of its safety and benefits in curing chronic diseases or conditions. So the approach today is to use herbals in dealing with these chronic disabilities with other conventional or traditional therapy for managing these disorders [22]

This study emphasizes on identifying the effect of a herbal mixture in a capsule form containing a blend of 5 herbals used in culinary edible purposes. The herbal mixture composed of Ginger rhizome, Nigella Sativa seeds , Boswellia , Curcuma rhizome**,** Cardamom seeds. This study aims to identify the effect of the combination of herbal mixture to conventional chemotherapy on minimizing the incidence of chemotherapeutic side effects for 2nd stage breast cancer. When patients integrate these complementary therapies as herbals into their medical and surgical care, they are creating a more comprehensive treatment plan and helping their own bodies to regain health and vitality [22].

David (2008), reported that, *nigella sativa* (Black Cumin**)** helps treat a broad array of diseases, including some immune and inflammatory disorders , anticancer activity in prostate and colon cancers, as well as antioxidant. Much of the biological activities of its seeds have been reported to provide protection against nephrotoxicity and Hepatotoxicity induced by either disease or chemicals [90].

Ginger is the rhizome of *Zingiber officinale* (Zingiberaceae) contains effective compounds known as gingerols, and volatile oils with antimicrobial effects. The root has antiemetic effects from its carminative and digestive properties which has the ability to enhance GI motility and it reduces the severity and duration of nausea during chemotherapy [94,95]. Ginger has anti-inflammatory effects; by inhibit prostaglandins and thromboxane, antimigraine effects; which inhibit platelet aggregation, antithrombotic effects. Ginger is used most commonly to treat colic, flatulence, and indigestion [95]. It is claimed to treat hypercholesterolemia, burns, ulcers, depression, impotence, and liver toxicity and as an anti-inflammatory for those with arthritis and as an antispasmodic.

Boswellia is a natural oleo-gum resin which consists of resinous portion contains about 60% of Boswellic Acids (BA) (alpha-and beta) which are the active constituents in boswellia [97]. Studies have shown that boswellic acids have an anti-inflammatory action by having an antimicrobial activity and inhibit the complementary system. This acts much like the conventional nonsteroidal anti-inflammatory drugs (NSAIDS). Boswellia inhibits pro-inflammatory mediators in the body, such as leukotrienes and also prevents the breakdown of connective tissue. The mechanism is similar to the action of non-steroidal groups of anti-arthritic drugs. Long-term use of boswellia does not lead to irritation or ulceration of the stomach[98].

Curcuma is a dried rhizome of *Curcuma longa*, family Zingiberaceae. The main active constituent of which is known as curcumin. It protects against free radical damage because it is a strong antioxidant. It also reduces inflammation by reducing histamine levels and possibly by increasing production of natural cortisone by the adrenal glands. It protects the liver from a number of toxic compounds and, it reduce platelets from clumping together, which in turn, improves circulation and helps protect against atherosclerosis (figure 15)[100]Numerous studies have also shown cancer-preventing effects of curcumin. This may be due to its powerful antioxidant activity in the body. A symbol of prosperity, it was considered as a cleansing herb for the whole body [101]. Medically, it was used as a digestive aid and treatment for fever,

infections, dysentery, arthritis, jaundice and other liver problems.. Curcumin is used for the treatment of anorexia, liver disorders, cough, diabetic wounds, rheumatism, and sinusitis. It has been evaluated for its anticarcinogenic and antimutagenic properties [102].

Cardamoms are used to sooth the stomach and treat dyspepsia for its antispasmodic, antiflatulent, and motility- enhancing effects [105]. It is also used for respiratory disorders, asthma, common cold, cough, bronchitis, headache, hoarseness, indigestion, diarrhea, nausea, vomiting and stomach complaints [105, 106]. Cardamom seeds, with their sweet and spicy aroma, are used in aromatherapy to stimulate energy. A few drops of the oil in the bath help fight fatigue. The standardized dose of cardamom is 400 mg-600mg three times per day [106].

The nurse has an important role in assessing and managing many of the problems experienced by the patient undergoing chemotherapy. Therefore, nursing assessment and care focus on identifying and modifying factors that further increase the patient's risk. Suppression of the bone marrow and immune system increase the risk for anemia, infection, and bleeding disorders. Aseptic technique and gentle handling are indicated to prevent infection and trauma. Laboratory test results, particularly blood cell counts, are monitored closely. Any changes in blood test results and signs of infection and bleeding must be reported promptly. The patient and family members are instructed about measures to prevent these problems at home [107].

Aim of the study: The aim of the present work is to identify the effect of the combination of herbal mixture to conventional chemotherapy on minimizing the incidence of chemotherapeutic side effects for 2nd stage breast cancer.

Keywords:

Herbal Mixture: in form of capsules containing 5 natural herbals (Nigilla Sativa– Cardamom m–Ginger–Curcuma–Boswellia serrata gum) .

Material & Methods

Materials:

Research design: A Quasi experimental research design was utilized in this study.

Settings:

Oncology out-patient clinics of Alexandria Main University Hospital.

Sample :

Forty adult female patients who were diagnosed with breast cancer and were receiving chemotherapy for at least one month and will continue to receive it for 3 months were included in the study. The subjects were selected randomly and divided equally into study and control groups, 20 patients in each group. Patients `age ranged from above 21 to below 65 years , they were diagnosed with breast cancer of the same type, stage II, on chemotherapy for at least 4 months basis. The subjects included were one month post 1st chemotherapeutic cycle of the same protocol. Either pre-or post operative and they were free from any associated co-morbid diseases as diabetes, renal, cardiac, hypertension.

Tools: Two tools were used**:**

Tool: Breast cancer women's assessment questionnaire sheet:

This questionnaire was developed by the researchers based on literature review and specialist opinion. It was divided into three parts.

(A). Chemotherapeutic side effects schedule sheet; it was adopted from Sitizia, (1999) [116].This part includes a list of chemotherapeutic side effects. Its grade of severity ranged from one to four (not present, mild, moderate, and severe). These side effects were divided according to body parts and systems.

Facio-maxillary, integumentary system, gastrointestinal system, musculoskeletal system, neurological system, cardiovascular system, respiratory system, urinary system, reproductive system, psychological status

(B). Laboratory investigations: Complete blood count (CBC), renal and liver functions tests, and fasting blood glucose level.

(C). Quality of life standard scale: This part includes two questions which assess the standard of life for all patients -control and study groups- over the three months of the study. For study group they assess the standard of life pre and post administering the herbal capsules. These two questions are part of The European Organization for Research and Treatment of Cancer quality of life questionnaire version 3,0 (EORTC QLQ-C30 Version 3.0): it is the most recent version, composed of 30 questions, for assessing the health related quality of life (QOL) of cancer patients participating in international clinical trials research, developed by The European Organization for Research and Treatment of Cancer (EORTC) in Arabic language in 1995.these two questions (likert

scale) are scored positively (i.e. 7 indicated excellent is the best and 1 indicated very poor is the worst) [47, 117].

***In addition to**: Patient's Sociodemographic data as:

Name **,**age, educational level, occupation, marital status, number of children, type and number of child's feeding, date and type of first dose of chemotherapy.

Chemotherapeutic protocol prescribed by oncologist for both groups, for each cycle, includes:

- Endoxane with 500 cc glucose 5%.
- Adriamycin with 100 cc saline 9%.
- Fluorouracil with500 cc saline 9%.

* The doses of these drugs are calculated according to the patient's weight and height.

* Before starting these drugs, there was a starting bottle contains 100 cc saline 9% with one ampoule of Zantac, one ampoule Decadrone and another one of Emax

Tool II: Nutritional assessment check list:

It was developed to detect nutritional health status of the breast cancer patients which includes:

*** Anthropometric measures**: anthropometric measurements provide an objective assessment of nutritional status it includes patient's body weight, height, triceps skin fold (TSF) mid – upper arm circumference. (MAC) and mid upper arm muscle circumference (MAMC) as well as body mass index (BMI). Each of these measurements was taken according to the standard procedures recommended by Jelliffe (1998) [118].

1- Body weight: - it should be recorded on admission and monitored regularly. Weight was taken by asking every patient to stand on the center of a bath spring scale without moving or touching any thing. The reading was recorded to the nearest 1 kilogram [119].

2- Standing height: - Height was measured by asking the patients to stand on the floor bare head and feet .she stands erect with shoulders and back of the head in the upright position and looking straight ahead, both heels and scapula are in contact with the wall. The measurement was taken by a measuring tape. The reading was recorded to the nearest 0.1 cm [112].

3- Body mass index (BMI): - calculation of body mass index, is a way of classifying weight. It was estimated by the following equation: $BMI_{(kg/m2)} = \{weight_{(kg)} / height_{(meter)\,2}\}$ [119].

4- Triceps skin fold thickness (TSF):-it is an index of total body fat, the assessment of subcutaneous body fat by skin fold measurements is accurate. The measurement was done using the skin fold calipers. The site of measurement selected is the same mid point used to measure mid – upper arm circumference [112].

5- Mid-upper arm circumference (MAC):-mid – arm circumferences measures muscle mass and subcutaneous fat, although it is not a useful measurement by it self, it is used as a part of the procedure for calculating arm muscle circumference (MAMC). [119].

6- Mid arm muscle circumference (MAMC):- it was calculated from the MAC and TSF measurements by the following equation: $MAMC_{(cm)} = MAC_{(cm)} - \{3.14 \times TSF_{(cm)}\}$.

The value is recorded and compared with standard reference value [119].

II-METHODS:

1. Permission to conduct the study was obtained from responsible authorities of the general director of the Alexandria University Hospital and the head of oncology department in the Main University hospital.

2. An ethical approval was taken from the ethical committee of the Faculty of Nursing Alexandria University for carrying out this study.

3. The researchers have undergone a special training about the route for preparing and fixing the herbal capsules about one month, under the supervision of a specialist trainer in the pharmacognosy department who was one of the supervisors of the thesis, the herbal mixture was mixed then prepared in the form of capsules. The dose was adjusted to be 1 capsule three times per day for 3 months for the study group in conjunction with chemotherapy protocol .Control group will be on chemotherapy protocol only.

4. Aflatoxins study: The mixture was subjected to aflatoxins test to insure its safety and puerility.

5. Herbal materials: The dose of herbal calculated and fixed according to the reference's recommended doses as *nigella sativa* seeds is 500 mg /three times per day, curcumin is 500 mg /three times per day, cardamom is 500 mg /three times per day, boswellia is 300 mg /three times per day, ginger is 2 gm /three times per day.

6. Research Tools The tools were developed based on the recent relevant literature. Tool I was developed by the investigators. Content validity was tested by ten experts in the filed of nursing and oncology field. Tool II was taken according to the standard procedures recommended by jelliffe (1998) [118]. Reliability for Tool I and Tool II were done by using test- re test.

7. Pilot study A pilot study was carried out before starting the data collection. It was applied on 10 patients with breast cancer who fulfill the study criteria to test feasibility and applicability of both tools and necessary modification were done.

9. Patient's consent Patient's written consent to participate in the study was then obtained. Every patient was informed that confidentiality will be assured, and she had the right to discontinue from the study at any time she wants.

The researchers interviewed every patient from the first day of the second cycle of receiving chemotherapy. Each patient was interviewed individually and each interview took approximately one hour. For the study group patient and her family were instructed about the importance of taking herbal capsules regularly, and illustrate the aim of the study as well as the scheduled dose which is 1 capsule three times per day for 3months on an individual basis. Numbers of sessions were adopted according to chemotherapeutic protocol till 3 months.

11. Assessment phase (for both groups) firstly General data about the patient has been collected as name, age, address, marital status, level of education, occupation, and date of first dose of chemotherapy.

12. Implementation Phase (for both groups) two tools (I&II) were used for both groups as baseline data to assess the chemotherapeutic side effects, laboratory investigations as well as the nutritional status of the patients. Then these two tools were also applied for both groups after 45days then after 3 months of administering the herbal capsules to detect their effect on chemotherapeutic side effects and the nutritional status of the patients. Laboratory investigations data was obtained from the patient's hospital sheet at the scheduled times. Nutritional assessment weight has been measured at the first assessment then at the second and third one; percent of weight changes is calculated using the following formula. {(first weight – current weight) / first weight} x 100 =% weight change.

13. Evaluation Phase (for both groups):

I. Side effects of chemotherapy in relation to all body systems were evaluated by using tool I & II after 45 days and then repeated after 3 months.

II. The standard ranges that used for laboratory investigations are [66]:

RBC (4.2 – 6.1) x 10^6 cells /ul	HGB (12- 18) g/dl
HCT (37 -52) %	MCV (80-99) fL
MCH (27 – 31) pg	MCHC (33- 37) g/dl
WBC (5.2 – 12.4) x 10^3 cells/ul	Neutro (40 -74) %
Lympho (19- 48) %	Mono (3.4 – 9) %
Eso (0 – 7) %	
Platelets count (150 – 450) x 10^6 cells /ul	Baso (0.5 -1.5) %
Blood urea Nitrogen (7 – 18) mg/dl	Creatinine (0.6- 1.3) mg/dl
Total Bilirubin (.3-1.9)mg/dl	SGPT (15 – 37) u/l
SGOT (30 – 65) u/l	
Fasting Blood Glucose (70 -110).	

III. Weight changes less than 2 kilos is considered mild changes, more than 2 kilos as moderate changes and more than 5 kilos is severe changes. Weight, height mid arm circumference and skin fold thickness was compared with the normal standard. Of the corresponding sex and age [119].

IV. Interpretation and evaluation of anthropometric measurements:

(1) Evaluation of Body Mass Index: [125].

Under weight	<19
Normal weight	19 - < 25
Over weight	25 - < 30
Mild obesity	30 - < 35
Moderate obesity	35 - < 40
Severe obesity	40

(2) Evaluation of MAC, TSF, and MAMC: [119]

Measurement	Standard
MAC (cm)	29.0

TSF (mm) 16.5
MAMC (cm) 23.5

14. Statistical analysis:

Data was analyzed using PC with statistical Package for Social Sciences version 13.0.The 0.05 level was used as the cut off value for statistical significance and the following statistical measures were used.

A. Descriptive statistics:*Count and percentage and Minimum, Maximum, Arithmetic mean($\overline{X}$), Standard deviation(SD):*

Analytical statistics:the following were used:

1. ***Chi square: (χ^2):***
   Fisher Exact Test:
   Monte Carlo Exact Test:
2. ***Student t-test:***
   a. *The pooled variance t-test:* If the variances of the two groups are equal.
   b. *The separate variance t-test:* If the variances of the two groups are not equal.

   Levene test is used to test the hypothesis that the two population variances are equal.
3. ***One way Analysis Of Variance (ANOVA):***
   It is used for testing the difference between more than 2 groups mean.In case of significant ANOVA f test the Post Hoc Sheffe test was used for multiple comparison of each of couple of groups.

RESULTS

Table (I): Distribution of the study and control groups regarding to biosociodemographic characteristics.

Item	Study		Control		Total		Test of significant
	n	%	n	%	n	%	
Age:							
27-	6	30%	2	10%	8	20%	**FET** = 0.274
38-	7	35%	7	35%	14	35%	
49-65	7	35%	11	55%	18	45%	**P**= 2.793
Education:							
- High level	0	0%	0	0%	0	0%	
- Moderate	4	20%	6	30%	10	25%	**FET** = 0.443
- Lower than moderate	1	5%	3	15%	4	10%	**P**= 1.951
- illiterate	15	75%	11	55%	26	65%	
Occupation:							
- Working	1	5%	7	35%	8	20%	
-Non working	19	95%	13	65%	32	80%	**FETp** = 0.044*
Marital status:							
- Married	18	90%	12	60%	30	75%	**FET** = 0.025*
- single	2	10%	2	10%	4	10%	
-widowed	0	0%	6	30%	6	15%	**P**= 7.371
type of breast feeding:							
- breast feeding	12	60%	13	65%	25	62.5%	**FET** = 0.744
- bottle feeding	8	40%	7	35%	15	37.5%	**P**= 0.107
Frequency of breast feeding:							
- less than 3 times	8	40%	7	35%	15	37.5%	**FET** = 0.744
- 3 times and more	12	60%	13	65%	25	62.5%	**P**= 0.107
Total	20	100	20	100	40	100	

n: number of patients FET: fisher's exact test P: level of significant ≤ 0.05

Table (II): Effect of herbal and conventional therapy on the side effects of chemotherapy regarding to all body systems among the study and control groups.

Item	n=20 Study			n=20 Control			t- test		
	$\overline{X}$ ± SD			$\overline{X}$ ± SD					
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd

Eye, ear, mucous membranes.	52.3 ± 8.5	37.0 ± 8.8	28.0 ± 6.7	47.3 ± 9.4	55.4 ± 8.0	64.5 ± 5.6	1.760	6.902	18.502
Skin and nails.	47.2 ± 12.6	39.4 ± 11.1	33.1 ± 8.9	40.6 ± 7.5	49.4 ± 9.7	62.8 ± 6.9	2.008	3.029	11.841
Weight changes.	18.1 ± 8.6	13.1 ± 4.9	16.9 ± 6.1	6.3 ± 9.5	13.8 ± 9.0	18.1 ± 12.5	4.146	0.273	0.402
Gastro intestinal system.	49.8 ± 7.7	32.0 ± 5.2	17.3 ± 3.4	38.0 ± 7.7	44.3 ± 9.2	53.3 ± 7.1	4.836	5.170	20.365
Musclo skeletal system.	47.2 ± 11.0	34.7 ± 10.4	24.4 ± 8.3	47.8 ± 8.9	55.3 ± 9.6	68.1 ± 6.0	0.197	6.515	18.996
Nervous system.	47.2 ± 13.8	37.5 ± 12.5	32.5 ± 10.3	38.3 ± 9.0	45.6 ± 7.6	53.8 ± 7.1	2.289	2.483	7.603
Respiratory system.	46.7 ± 11.2	31.3 ± 7.2	23.5 ± 4.9	45.2 ± 3.6	50.6 ± 8.6	65.8 ± 4.8	0.555	7.728	27.506
Urinary system.	34.2 ± 7.8	22.7 ± 6.3	15.6 ± 6.6	31.9 ± 6.1	38.5 ± 6.3	48.3 ± 6.3	1.033	7.956	16.082
Reproductive system.	26.0 ± 8.2	18.5 ± 5.8	13.5 ± 5.9	19.4 ± 4.9	22.1 ± 4.5	27.9 ± 5.3	3.114	2.154	8.159
Psychological status.	51.6 ± 9.3	38.8 ± 5.2	30.3 ± 6.5	43.8 ± 8.1	50.0 ± 7.6	65.0 ± 9.2	2.837	5.467	13.813

t: t-test

1st, 2nd, 3rd : assessments

Table (II) cont.

Item	**n=20 Study**			**n=20 Control**			**t- test**		
	(X^- ± SD)			**(X^- ± SD)**					
	1st	**2nd**	**3rd**	**1st**	**2nd**	**3rd**	**1st**	**2nd**	**3rd**
Hematological tests	48.8± 16.3	41.9 ± 17.7	25.8± 15.6	36.2± 13.7	50.0 ± 12.0	57.3±12.3	2.652	1.635	7.070
Renal functions studies	45.0 ± 22.4	2.5 ± 11.1	10.0± 22.5	37.5 ± 39.3	52.5 ± 19.7	92.5 ±18.3	0.742	9.871	13.413
Liver functions and endocrine studies	51.3 ± 18.9	25.0 ± 18.1	6.3± 11.1	37.5 ± 23.6	35.0 ± 20.5	45± 15.4	2.028	1.633	9.131
Total	43.0 ± 5.6	30.9 ± 4.4	23.2 ± 3.4	37.4 ± 4.9	43.9 ± 5.3	54.3 ± 3.6	**T_1** 3.369 **P** 0.002* **T_2** 8.420 **P** 0.000* **T_3** 27.781 **P** 0.000*		

Significant relation at P level ≤ 0.05

1st, 2nd, 3rd : assessments

Table (III): Ranking of all body systems that affected with the chemotherapeutic side effects post herbal and conventional therapies (3rd assessment) among two groups.

study		**control**	
Body system	**(X^- ± SD) of 3rd assessment**	**Body system**	**(X^- ± SD) of 3rd assessment**
Liver functions and endocrine studies	6.3± 11.1	Weight changes	18.1 ± 12.5
		Reproductive system	27.9 ± 5.3

Renal functions studies	10+ 22.5		
Reproductive system.	13.5 + 5.9	Liver functions and endocrine studies	45.0+ 15.4
Urinary system.	15.6 + 6.6	Urinary system.	48.3 + 6.3
Weight changes.	16.9 + 6.1	Gastro intestinal system	53.3 + 7.1
Gastro intestinal system.	17.3 + 3.4	Nervous system.	53.8 + 7.1
Respiratory system.	23.5 + 4.9	Hematological tests	57.3+12.3
Musclo skeletal system.	24.4 + 8.3	Skin and nails.	62.8 + 6.9
Hematological tests	25.8+ 15.6	Eye, ear, mucous membranes.	64.5 + 5.6
Eye, ear, mucous membranes.	28.0 + 6.7	Psychological status.	65.0 + 9.2
Psychological status.	30.3 + 6.5	Respiratory system	65.8 + 4.8
Nervous system.	32.5 + 10.3	Musclo skeletal system.	68.1 + 6.0
Skin and nails	33.1 + 8.9	Renal functions studies	92.5 +18.3

Table (IV) : Effect of herbal and conventional therapy on the side effects of chemotherapy regarding to health and life style among the study and control groups.

Item	n=20 Study			n=20 Control			FET / P
	1st %	2nd %	3rd %	1st %	2nd %	3rd %	
Health grade: - Bad	30%	0%	0%	0%	5%	45%	
- Accepted	70%	0%	0%	35%	65%	55%	
- Moderate	0%	65%	0%	65%	30%	0%	**FET**$_1$= 23.356 **P**$_1$ = 0.000* **FET**$_2$= 25.761 **P**$_2$ = 0.000* **FET**$_3$ = 44.879 **P**$_3$= 0.000*
- Good	0%	35%	20%	0%	0%	0%	
- Very good	0%	0%	80%	0%	0%	0%	
Life style: - Bad	35%	0%	0%	0%	0%	35%	
- Accepted	65%	0%	0%	25%	65%	65%	**FET**$_1$= 28.429 **P**$_1$ = 0.000*
- Moderate	0%	70%	0%	75%	35%	0%	**FET**$_2$= 23.356 **P**$_2$ = 0.000*
- Good	0%	30%	30%	0%	0%	0%	
- Very good	0%	0%	70%	0%	0%	0%	**FET**$_3$ = 44.691 **P**$_3$= 0.000*

Significant relation at P level $\leq$ 0.05

1st, 2nd, 3rd : assessments

Table (V): Effect of herbal and conventional therapy on the side effects of chemotherapy regarding to anthropometric measurements among the study and control groups.

Item	Assess.	Study group		Control group		t- test	P
		Range	Mean ±SD	Range	Mean ±SD		
Weight	1st	54.0 – 95.0	73.6 ± 11.0	60.0- 86.0	74.6 ± 8.9	0.317	0.753
	2nd	55.0 – 96.0	74.8 ± 11.1	59.0 – 85.0	73.2 ± 8.4	0.514	0.610
	3rd	56.0 – 98.0	76.9 ± 11.1	58.0 –83.0	71.1 ± 7.8	1.915	0.063
Height	1st	150.0 - 173	163.6 ± 6.3	150.0 – 175.0	166.1 ± 5.9	2.904	0.006*
	2nd	150.0 - 173	163.6 ± 6.3	150.0 – 175.0	166.1 ± 5.9	2.904	0.006*
	3rd	150.0 - 173	163.6 ± 6.3	150.0 – 175.0	166.1 ± 5.9	2.904	0.006*
Mid arm circumference	1st	26.0 – 36.0	31.0 ± 2.6	23.0 – 31.0	28.6 ± 2.0	3.312	0.002*
	2nd	26.0 - 37	31.5 ± 2.7	23.0 – 30.5	28.0 ± 1.8	4.650	0.000*
	3rd	27 – 37.5	32.1 ± 2.7	23.0 – 30.0	27.6 ± 1.8	6.284	0.000*
Mid arm muscle circumference	1st	21.1 – 29.7	25.4 ± 2.1	18.2 – 25.3	23.3 ± 1.6	3.517	0.001*
	2nd	21.2 – 30.4	25.8 ± 2.2	18.2 – 25.0	22.9 ± 1.5	4.845	0.000*
	3rd	20.9 – 30.7	26.3 ± 2.3	18.2 – 24.5	22.4 ± 1.6	6.212	0.000*
Triceps skin fold	1st	15.5 - 21	17.5 ± 1.9	15.0 – 20.0	16.8 ± 1.1	1.526	0.137
	2nd	15.0 – 22.0	17.8 ± 2.1	15.0 – 19.5	16.5 ± 1.0	2.564	0.016*
	3rd	16.0 – 23.0	18.4 ± 2.2	15.0 – 19.0	16.2 ± 1.0	4.185	0.000*
Body mass index	1st	22.4 – 34.4	27.3 ± 3.0	21.7 – 29.7	26.2 ± 2.7	1.307	0.199
	2nd	22.8 – 34.8	27.8 ± 3.0	22.4 – 29.0	25.6 ± 2.5	2.432	0.020*
	3rd	23.3 – 35.5	28.6 ± 3.0	22.2 – 28.3	25.0 ± 2.3	4.280	0.000*

Significant relation at P level ≤ 0.05

Table (XXI): Relation between age and chemotherapeutic side effects of all body systems among breast cancer women post herbal and conventional therapy.

Item	Side effects ($\bar{X}$ ± SD)					
	n = 20 Study			n = 20 Control		
	1st	2nd	3rd	1st	2nd	3rd
Age :						
27-	42.8 ± 2.7	29.3 ± 4.3	22.8 ± 3.6	36.9 ± 10.3	42.4 ± 11.4	53.3 ± 6.2
38-	44.4 ± 3.1	32.0 ± 2.1	23.9 ± 2.6	35.5 ± 2.7	41.9 ± 3.9	52.9 ± 3.9
49-65	41.8 ± 8.9	31.0 ± 6.0	22.7 ± 4.2	38.6 ± 5.1	45.3 ± 5.1	55.2 ± 3.0

F	0.364	0.576	0.238	0.854	0.908	0.900
P	0.700	0.573	0.790	0.443	0.422	0.425

Significant relation at P level ≤ 0.05; 1st, 2nd, 3rd: assessments

Table (XX): Relation between occupation and chemotherapeutic side effects of all body systems among breast cancer women post herbal and conventional therapy.

Item	Side effects (X ± SD)					
	n = 20 Study			n = 20 Control		
	1st	2nd	3rd	1st	2nd	3rd
Occupation:						
- Working	43.2	30.7	22.9	34.0 ± 3.5	40.3 ± 5.0	51.9 ± 3.8
- Non working	43.0± 5.7	30.8 ± 4.5	23.2 ± 3.5	39.2± 4.7	45.8 ± 4.7	55.5 ± 2.9
t-test	0.037	0.029	0.083	2.525	2.429	2.350
P	0.971	0.977	0.935	0.021*	0.026*	0.030*

Significant relation at P level ≤ 0.05

1st, 2nd, 3rd : assessments

Table (XXI): Relation between type and frequency of breast feeding and chemotherapeutic side effects of all body systems among breast cancer women post herbal and conventional therapy.

Item	Side effects (X ± SD)					
	n = 20 Study			n = 20 Control		
	1st	2nd	3rd	1st	2nd	3rd
Type of feeding:						
- Bottle feeding	42.6 ± 2.7	30.4 ± 4.0	23.8 ± 3.4	38.0 ± 6.3	44.5 ± 7.2	54.8 ± 4.3
- Natural feeding	43.3± 7.0	31.1 ± 4.8	22.8 ± 3.6	37.0± 4.3	43.5 ± 4.4	54.0 ± 3.4
t-test	0.242	0.373	0.583	0.391	0.384	0.434
P	0.812	0.714	0.567	0.705	0.705	0.669
Frequency of breast feeding:						
- Less than three	42.7 ± 3.1	29.6 ± 3.9	23.2 ± 3.8	36.2 ± 4.6	43.4 ± 5.2	53.1 ± 4.1
- Three and more	43.2 ± 6.9	31.7± 4.6	23.1± 3.4	38.1± 5.1	44.1± 5.6	54.9± 3.4
t-test	0.200	1.093	0.039	0.834	0.286	1.038
P	0.844	0.289	0.969	0.415	0.778	0.313

Significant relation at P level ≤ 0.05; 1st, 2nd, 3rd : assessments

Table (I): shows distribution of the patients among the study and control groups regarding to biosociodemographic characteristics.It was observed that the majority of patient's age (45%) were in the age group of (49 – 65) years, while (20%) only were in the age group of (27 – 38) years. Regarding to educational level, it is evident that illiterate patients formed the greatest proportion of the sample (65%). There was no statistically significant difference among the study and control groups in relation to age and educational level. P= (0.274 and 0.443), respectively.

As regard the occupation the majority of the patients (80%) were found to be non - working, while (20%) were working. There was a statistically significant difference among the two groups in relation to occupation P= (0.044).In relation to marital status, it was observed that the majority of patients (75%) were married, while (10%) were single. there was a statistically significant difference among the two groups in relation to marital status P= (0.025).Concerning the type and frequency of breast feeding. It was found that the majorities of the sample (62, 5%) were breast fed and lactated their children for three times and more through their life. There was no statistically significant difference among the study and control groups in relation to type and frequency of breast feeding where, P= (0.744).

Table (II): shows the effect of herbal and conventional therapy on the side effects of chemotherapy regarding to all body systems among the study and control groups. This table illustrated that, the side effects of chemotherapy regarding to all body systems for the study group shows a decrease on the second and third assessments (30.9±4.4, and 23.2±3.4), respectively compared with the first assessment (43.0±5.6). In contrast for the control group, it was observed that these side effects showed an increase of its severity on the second and third assessments (43.9±5.3, and 54.3±3.6), respectively compared with the first assessment (37.4±4.9). It was found that there was a significant difference between study and control groups in relation to first, second and third assessments related to all body systems. P = (0.002, 0.000, 0.000), respectively.

Table (III): shows the ranking of all body systems that affected with the chemotherapeutic side effects post herbal and conventional therapies (3rd assessment) among two groups.This table illustrated the actual effect of herbal therapy in relation to the third assessment, it was found that, liver functions and endocrine studies, renal functions studies, reproductive, urinary system, and weight changes were the least affected systems with the side effects of chemotherapy, and they were the most affected systems with combining herbal to conventional chemotherapy (6.3± 11.1), (10.0± 22.5), (13.5 ± 5.9), (15.6 ± 6.6), and (16.9 ± 6.1), respectively.Gastro intestinal, respiratory, musclo skeletal system, hematological tests, and eye, ear, mucous membranes were moderately affected systems with the side effects of chemotherapy, and they were also moderately affected systems with combining herbal to conventional chemotherapy (17.3± 3.4), (23.5± 4.9), (24.4 ± 8.3), (25.8 ± 15.6), and (28.0 ± 6.7), respectively.It was also found that, psychological status, nervous system, and skin , hair, and nails were the most affected systems with the side effects of chemotherapy, and they were the least affected systems with combining herbal to conventional chemotherapy (30.3 ± 6.5),(32.5± 10.3), and (33.1 ± 8.9), respectively.On the other hand, for control group, it was also found that, weight changes, reproductive system, liver functions studies , urinary system, and gastro intestinal were the least affected systems with the side effects of chemotherapy, (18.1 ± 12.5), (27.9 ± 5.3), (45.0 ± 15.4) ,(48.3 ± 6.3) and (53.3 ± 7.1), respectively. Nervous system , hematological tests, Skin, hair, and nails, eye, ear, mucous membranes and psychological status were moderately affected systems with the side effects of chemotherapy, (53.8 ± 7.1), (57.3± 12.3), (62.8± 6.9), (64.5 ± 5.6) and (65.0 ± 9.2), respectively. Concerning, respiratory systems, musclo skeletal and renal functions studies were the most affected systems with the side effects of chemotherapy, (65.8 ± 4.8), (68.1 ± 6.0) and (92.5 ± 18.3), respectively.

Table (IV): reveals the effect of herbal and conventional therapy on the side effects of chemotherapy regarding to Health and Life style grades among the study and control groups. Concerning, health grades and life style of the patients, the table revealed that, all the study group have bad and accepted degrees of health grade and life style grades, and all the control group have bad and moderate degrees of health grade and life style grades on the first assessment. In relation to the third assessment post herbal and conventional therapy it was found that the entire study group has good and very good degrees, while all of the control groups have bad and accepted degrees**.**

In relation to significant difference between the three assessments among the study and control groups in relation to health and life style grades. It was found that there was a significant difference between study and control groups in relation to first, second and third assessments P = (0.000).

Table (V): Reveals the effect of herbal and conventional therapy on the side effects of chemotherapy regarding to anthropometric measurements among the study and control groups. Concerning patient's weight, there was an increase in patient's weight of the study group on the third assessment (76.9 ± 11.1), compared with the first assessment of weight (73.6 ±11.0). While there was a decrease in patient's weight of the control group on the third assessment (71.1± 7.8), compared with the first assessment of weight (74.6 ±8.9). There was no statistical significant difference between both groups in relation to assessment of weight in first, second and third assessment P= (0.753, 0.610, 0.063), respectively. The table revealed that, there was statistical significant difference between both groups in relation to assessment of height in first, second and third assessments. P=0.006.

In relation to mid arm circumference, the mean of mid arm circumference in study group was increased in the 2nd and 3rd assessments (31.5± 2.7, 32.1±2.7), respectively, compared with the first assessment of mid arm circumference (31.0± 2.6). While in the control group there was a slightly decrease on the 2nd and 3rd assessments (28.0± 1.8, 27.6±1.8), respectively, compared with the first assessment of mid arm circumference 28.6± 2.0. There was statistical significant difference between both groups in relation to assessment of mid arm circumference on first, second and third assessments P= (0.002, 0.000, 0.000), respectively.

Moreover, the mean of triceps skin fold in study group was increased on the 2nd and 3rd assessments (17.8± 2.1, 18.4±2.2), respectively, compared with the first assessment of triceps skin fold (17.5± 1.9). While in the control group there was a decrease on the 2nd and 3rd assessments (16.5± 1.0, 16.2±1.0), respectively, compared with the first assessment of mid arm circumference (16.8± 1.1). There was no statistical significant difference between both groups in relation to first assessment of triceps skin fold P= (0.137). While on the second and third assessments There was statistical significant difference between both groups P= (0.016, 0.000), respectively.

Finally the table shows that, there was an increase in study group in relation to body mass index on the 2nd and 3rd assessments (27.8± 3.0, 28.6±3.0), respectively, compared with the first assessment of body mass index (27.3± 3.0). While in the control group there was a decrease on the 2nd and 3rd assessments (25.6± 2.5, 25.0±2.3), respectively, compared with the first assessment of body mass index (26.2±2.7). There was no statistical significant difference between both groups in relation to first assessment of body mass index P= (0.199). While in the second and third assessments There was statistical significant difference between both groups P= (0.020, 0.000), respectively.

Table (VI): shows the relation between age and chemotherapeutic side effects of all body systems among breast cancer women post herbal and conventional therapy.This table revealed that, the chemotherapeutic side effects of all body systems for the study group by its age categories were decreased on the 2nd and 3rd assessment (29.3± 4.3, 22.8±3.6), respectively, compared with the first assessment (42.8±2.7) for the age group 27-38.while for the control the side effects of chemotherapy were increased on the 2nd and 3rd assessments (42.4± 11.4, 53.3±6.2), respectively, compared with the first assessment (36.9±10.3) for the same age group.There was no significant difference between age and all the side effects of chemotherapy among the three assessments of the study group P= (0.700, 0.573, 0.790) respectively. And also for the control group P= (0.443, 0.422, 0.425), respectively.

Table (VII): shows the relation between occupation and chemotherapeutic side effects of all body systems among breast cancer women post herbal and conventional therapy**.**It was found that, the chemotherapeutic side effects of all body systems of the study group was slightly increased between the working group (43.2),compared with the non - working group (43.0) on their first assessment. This result was changed on the third assessment, working group (22.9) and non - working (23.2), while in the control group it was a decrease between the working groups (34.0) compared with the non - working group (39.2) on their first assessment. This result wasn't changed on the third assessment, working group (34.0) and non - working (55.5).The table also revealed that, for non- working group of the study group, the chemotherapeutic side effects of all body systems were decreased on the second and third assessments (30.8±4.4), (23.2± 3.5), respectively, compared with the first assessment (43.0± 5.7). While for the control group, there was an increasing in the chemotherapeutic side effects of all body systems on the second, and third assessments (45.7±4.6), (55.5± 2.9), respectively, compared with first the assessment (39.2± 4.6).

There was no significant difference between occupation and all the side effects of chemotherapy among the three assessments of the study group P= (0.971, 0.977, 0.935), respectively. While for the

control group there was a significant difference between occupation and all the side effects of chemotherapy among the three assessments of the control group P= (0.021, 0.026, 0.030), respectively.

Table(VIII): shows the relation between type and frequency of breast feeding and chemotherapeutic side effects of all body systems among breast cancer women post herbal and conventional therapy. This table illustrated that, the chemotherapeutic side effects of all body systems of the study group was slightly increased between the patients have a history of natural breast feeding for three times and more (43.2±6.9), (43.2±6.8), respectively, compared with patients who have history of bottle feeding for less than three times (42.6±2.7), (42.7± 3.0), respectively on their first assessment. This result was changed on the third assessment; patients have a history of natural breast feeding for three times and more (22.8± 3.5), (23.1 ± 3.3), respectively and patients who have history of bottle feeding for less than three times (23.7±3.3), (23.3± 3.7), respectively.

Concerning, the relation between the type of breast feeding it was found that, the chemotherapeutic side effects of all body systems was decreased on the second , and third assessment (t=0.37), (t=0.58), respectively, compared with the first assessment (t=0.24). While for the control group, there was an increasing in the chemotherapeutic side effects of all body systems on the second, and third assessment (t=0.38), (t=0.43), respectively, compared with first the assessment (t=0.39). On the other hand, for the control group, there was an increasing in the chemotherapeutic side effects of all body systems on the second, and third assessment (t=0.38), (t=0.43), respectively, compared with the first assessment (t=0.39).There was no significant difference between type of breast feeding and all the side effects of chemotherapy among the three assessment of the study group P= (0.812, 0.714, 0.567), respectively. Also for the control group P= (0.705, 0.705, 0.669), respectively.

Regarding, significant difference between frequency of breast feeding and all the side effects of chemotherapy, it was found that, there was no significant difference among the three assessment of the study group P= (0.84, 0.28, 0.96), respectively. Also for the control group P= (0, 41, 0.77, 0.31), respectively.

DISCUSSION:

The use of complementary and alternative medicine using herbals and their natural products for the prophylaxis, protection, and treatment of various diseases has become more popular in recent years than ever before. Surveys indicate that 64% of cancer patients use alternative medicine, either for treating cancer or relieving symptoms that are associated with different cancer treatments [(123)].

This study was carried out to show the effect of the combination of herbal mixture to conventional chemotherapy on minimizing the incidence of chemotherapeutic side effects for 2nd stage breast cancer.

Geoff, (2006) illustrated that; integrated medicine is a holistic approach to cancer care. Some herbals showed proven effectiveness as adjuvant to conventional medical treatments [(124)]. Janelle et al, (2007) mentioned that, complementary and alternative medicine is widely used by cancer patients due to largely patient's demands for integration of herbal therapies into cancer treatment [(83)]. This was congruent with the findings of the present study which revealed that, patients with herbal and conventional therapies experienced less chemotherapeutic side effects of all body systems than patients with only conventional therapy.

In the present study, as regards to age, it was found that, the majority of patient's age was ranged from 49-65 years old. This was congruent with the American Cancer Society, (2008), which reported that about 80% of all breast cancers arise in women over age 50 [(125)]. In addition, Winsock (2004) stated that the most important risk factor for development of breast cancer is increasing age. As any woman ages, her risk of breast cancer increases, especially over 50 years [(58)] .Also this is in line with Thom et al, (2006) who indicated that people over the age of 50 years old are more risky for developing breast cancers [(126).] DeMichele et al, (2007) reported that, Breast cancer occurs more often in women over 50 and is less common in premenopausal women. Nearly 80 percent of all newly diagnosed invasive breast cancer cases occur in women aged 50 and older [(127).]

Regarding to educational level, the study illustrated that, the majority of the patients were illiterate this result is similar to Ebrahim's findings, (1999) on his study to identify the preoperative stressors among surgical patients, emphasized that, the majority of the studied subjects were illiterate; he stated that the overwhelming majority of the Egyptian population are illiterate or does not have any formal education [(128).] The present findings may be due to the setting of the study is a free governmental hospital and the majority of patients have a low education and

economical standards. This result is not in agreement with Jan and Sundquist, (2007) who mentioned that, highly educated women run a greater risk of developing breast cancer especially noninvasive breast cancer than women with less education. At the same time, highly educated women have better chances of surviving in various types of cancer than those with a low level of education [(129)]. They said that; it is naturally not education itself that causes breast cancer. It is most likely that highly educated women attend mammography in greater numbers. Such screening is the most reliable way to find the earliest stages of breast cancer [(129)]. Furthermore, the present study revealed that the non working patients formed the greatest proportion of the sample. This may be due to their lower educational level and being females which decrease their chance of getting a job, they were house wives which are the greatest proportions of the Egyptian's females [(131)],also it may be due to the setting of the study does not provide health insurance services and there is other hospital for working patients. This result disagree with Ali and Hussain, (2003) who reported that occupations are increasing the risk of getting cancer especially some types of occupations as , teachers who had the highest rates of having breast cancer, and other three occupational groups had statistically significant for cancer of the ovary as printing machine, launderers, and dry cleaners [(132)] .

In relation to marital status the present study showed that, married represented higher percentage than single and widowed, this is opposite to Hayes, (2005) who concluded that, the risk for breast cancer, treatment recommendations and follow-up should not be altered based on a woman's marital status [(133)] .

In agreement with the present study, Frank (2005) mentioned that, current chemotherapeutic techniques have a range of side effects mainly affecting the fast-dividing cells of the body. These side-effects can be reduced by several agents and therapeutic modalities [(138)]. One of these managements which reduce these side effects is the using of herbal medicine as a complementary therapy to eliminate the side effects of cancer therapy [(138)]. This is in line with the present findings, that the herbal components of the study are composed of *nigella sativa*, ginger curcuma, boswella gum, and cardamom. These components have different actions and properties, the commonest actions of these components are; anti-inflammatory, immunomodulator, anti-oxidant, anti- emetic, anti-arthritics, analgesic. Therefore, the aim of this study is decreasing the side effects of the chemotherapy by using these effects and actions of the herbal components to minimizing these side effects.

Braun and Cohen, (2007) stated that, long term side effects of chemotherapeutic drugs, are due to the formation of free radicals that lead to oxidative organ damage [(139)]. Herbal and its ingredients antioxidants have been investigated in humans and several studies have shown improvement or prevention of some side effects and possibly increased treatment effectiveness [(140. 141)].

Altman and Marcussen, (2001) high lights the study findings regard to musclo skeletal system, which is a moderately affected system by the combining herbal to conventional therapy, the result illustrated that, there was no significant difference between study and control groups in relation to first assessment. While, in the second and third assessments there was a statistically significant difference between the two groups. This may be attributed by the effect of ginger inhibits the production of immune-system components called cytokines. These chemicals are believed to create a long-term tendency toward inflammation. Stated that, Ginger stimulates blood circulation. These effects of ginger are taken advantage in treating a number of disorders marked by swelling and pain, such as arthritis [(95)]. The finding is congruent with Cassiani et al, (2002) who reported that, studies have also shown that ginger can relieve pain without the side effects typically found when using nonsteroidal anti-inflammatory drugs (NSAIDs) and steroids [(145)].

This view is also supported with Goldberg et al, (2000) who mentioned that ginger can decrease inflammation. In fact, many health care professionals today use ginger to help treat health problems associated with inflammation, such as arthritis and muscle stiffness. In a study of 261 people with osteoarthritis of the knee, those who received a ginger extract twice daily experienced less pain and required fewer pain-killing medications compared to those who received placebo [(146)]. Davis et al, (2007) reported that, Boswella can reduce painful symptoms of arthritis on dozens of patients, who received the herb and showed better movement and less pain and stiffness [(98)].

Moreover, the study also revealed that, there was a significant difference between study and control groups in relation to first, second and third assessments of the nervous system, This result were supported by Fahs and Kinny, (2005) who reported that the main effect of curcuma, in which curcumin is the main constituent, is to protect against free radical damage because it is a strong antioxidant, and reduces inflammation. It accomplishes this by reducing histamine levels and

possibly by increasing production of natural cortisone by the adrenal glands by these mechanisms curcumin can inhibits headache, and suppress the unpleasant effects of the nervous system [147,148].

As regard to respiratory systems it was found that, there is no significant difference between study and control groups in relation to first assessment. While in the second and third assessments there was a significant difference between the two groups. This result was supported by Vanbree et al (2002). Who noted that boswellia was believed to support the respiratory and immune systems during respiratory attacks as flu, bronchitis, coughs and decreasing restlessness [149]. It is also in line with Hadidy et al, (2003) who noted that Cardamom used to sooth the respiratory tract, and it is used also for asthma, cold, cough, bronchitis [150].

Recent studies as indicated by Ashraf and Ali, (2005) who support the action of fixed and essential oils of the *nigella sativa* seeds which has anti-inflammatory, an immunomodular activity, and analgesic effects [151]. So; the present findings is due to the combined effects of boswellia and cardamom as well as *nigella sativa* seeds.

Furthermore, the current study also revealed that , there is a significant difference between study and control groups in relation to first , second and third assessments of the reproductive and psychological status. This result is congruent with Basil, (2007) who reported that, due to the analgesic effect and / or the pain reliving properties of ginger; it can reduce discomfort associated with breast cancer. Also added that, ginger also helps control inflammation, due to the presence of gingerols, which is the main constant of ginger, which work like the older anti-inflammatory drugs, such as aspirin. Ginger unlike aspirin, has a calming effect on the intestinal tract [152]. Gingerols prevent the aggregation of platelets, as well as reducing inflammation; they can help to minimizing platelets aggregation. [152].

This was congruent with the present findings, especially related to a menorrhea and decreasing breast and vaginal discharge which may be due to inflammatory effects. Ahmed et al, (2003) added that, in addition to these benefits; Ginger can decrease the risk of heart disease by "platelet inhibition" and by lowering cholesterol. It is a strong antioxidant and can inhibit certain bowel infections (Salmonella) and it can be effective against vaginal Trichomonas infections, which is the commonest cause of vaginal discharge [153].

Jane et al, (2004) mentioned that, ginger has a long history of use for treating anxiety and depression [154]. Heller et al, (2001) recommended the use of ginger as anti depressant and for managing or treating insomnia, especially before the bed time [155]. Emphasized that, ginger works in a similar way to some prescription antidepressants by increasing the brain chemical serotonin, involved in controlling mood.

Adesson, (2007) patients are more concerned about the occurrence and management of side effects than the actions of particular chemotherapeutic agents. Identifying the side effects or patient's problems, will assist in achieving the desired outcome. As well as the time sequence in which side effects generally occur may allay patient anxiety and will assist nurses in selecting the appropriate interventions [156].

Related to the hematological studies, renal, and liver and endocrine studies, the study illustrated that, these systems are the latest affected systems with the side effects of chemotherapy. And they are the most affected systems by the combining herbal to conventional chemotherapy as well as there is a significant difference between the study and control groups in relation to first assessment except for renal functions. While in relation to second and third assessment there was a significant difference between the tow groups. This result was congruent with Elassafy, (2001) who mentioned that; cancer patient should continue the intake of *nigella sativa* during chemotherapy. This can be effective way of limiting the side effects of chemotherapy, because *nigella sativa* supports maintenance of trileaneal erythropoiesis (red blood cells, white blood cells and platelets). The guiding principles is the adherence to 6 sessions of chemotherapy which usually are the hemoglobin level, the white cell count, the platelet count with administering of *nigella sativa* help in maintaining these normal levels during chemotherapy [157].

Nagi et al, (2008) concluded that, *nigella sativa seeds* are effective in protecting against hypertension and renal damage especially serum creatinine level possibly via its antioxidant activity of thymoquinone (TQ), the main constituent of the volatile oil of *nigella sativa* seeds [158]. Also it is in line with Elkahtany et al, (2007) who added that, ginger has been used to reduce the toxic side effects of some chemotherapeutic drugs, as showed in protective effects against nephrotoxicity induced by chemotherapeutic agents[159].Ahmed et al, (2006) reported that, there is a significantly reduction in the elevated levels of blood glucose, lipids, plasma insulin

and improved altered levels of lipid peroxidation products and antioxidant enzymes which minimizing the harmful effects of the liver and kidney [160]. These results confirm the antidiabetic activity of *nigella sativa* seeds extract and suggest that because of its antioxidant effects its administration may be useful in controlling the diabetic complications [160].

Block & Mead, (2003) added that, curcumin and boswella, combination have been used in cancer therapy, not only to reduce the associated side effects but also to enhance the effectiveness of chemotherapy [161]. On a systematic review of these herbals for chemotherapy induced side-effects in cancer patients, Taixiang et al, (2005), analyzed the results of four trials that used a formulation containing Curcumin can stimulate immuno-competent cells and decrease side effects in patients treated with chemotherapy. [162]

One of the more problematic side effects of chemotherapy is the incidental damage to normal tissues and all body systems. This damage to normal tissues of the body systems, in some patients, can be sufficiently severe to stop chemotherapy. Ginger and *nigella sativa* have a powerful anti inflammatory effects and immunomodulatory effects; so they can reduce these side effects [93, 95].

It is imperative to assess accurately the patient's physical and emotional status before therapy is initiated. This information assists the health-care team to identify risk factors that could contribute to the occurrence or severity of side effects. Other factors that may affect the patient's response to therapy are age, general condition, coexisting illnesses, and nutritional status [163].

Concerning to health and life style grades, it was found that there was a significant difference between study and control groups in relation to first, second and third assessments. This result is opposite to Ganz, (2004) who mentioned that, patients survivors older than the age of 65, less educated individuals and people living in urban areas were less likely to make or maintain healthy lifestyle changes after awarning they had cancer [164]. While it is in line with Petter, (2006) who concluded that, being diagnosed with cancer can be a "teachable moment," when people are very open to suggestions about eating better, exercising and other healthy habits. So, in the present study, when the patients had low chemotherapeutic side effects of all body systems, they became more healthy and their life style became better [165].

In relation to body mass index (BMI), there was no statistical significant difference between study and control groups in relation to first assessment. While in the second and third assessment there was significant difference between both groups. This result is congruent with Massimo, (2005) who indicated that, when nausea and vomiting decreased; body weight and body mass index eventually can be also increased. He also added that, high BMI has been considered as a prognostic indicator for managing cancer patients [166] .This findings are not in agreement with to Kifeli, (2005) who mentioned that, high BMI is known as an important risk factor for development of breast cancer this is at the pre diseased period [167] .But, in the present study, the patients are already cancer patients so; high BMI has considered as a prognostic indicator for managing cancer.

Concerning to the relation between age and all the side effects of chemotherapy, there is no significant difference among the three assessments of the study and also for the control group. It is observed that, breast cancer's women of the study group at the age of (49-65) experienced minimal side effects than other age groups. This result is congruent with Lancet, (2001) who reported that, the effects of chemotherapy are more pronounced in younger women than elders, emphasized this by younger women who are likely to need chemotherapy because their cancer often has a worse prognosis, and she experienced a severe degree of the chemotherapeutic side effects [168].

Darry, (2002) mentioned that, cancer patients who continue to work are as productive on the job as other workers. Most cancer patients who are physically able to work do go back to their jobs. Returning to work can help them feel they are getting back to the life they had before being diagnosed with cancer [169]. This is in line with the study findings regarded to the relation between occupation and all the side effects of chemotherapy, it was found that there is no significant difference among the three assessments of the study while for the control group there was a significant difference among the three assessments. This result was opposite to Ashing, (2004) findings who documented that breast cancer and it's treatment have varying effects on women employment, several women choose to change jobs or stop working, others lost their function and experience serious job disruptions [170].

Recent studies revealed that herbal components, the subject of the current study, have anti inflammatory, anti oxidant and immunomodulator effects, which support the present findings in decreasing and minimizing the side effects of conventional chemotherapy. Robbson, (2006) stated

that, oncology nurses are engaged in a collaborative practice with all members of the care team to provide optimal management of patients with cancer. Their professional practice requires detailed knowledge of the biologic and psychosocial dimensions of the cancer problem. They have key roles not only as caregivers but in patient and family education and clinical cancer research. Oncology nurses also are continuously involved in the enhancement of nursing practice through research, continuing education, and advanced education [(171)].

Also it was concluded that, when patients integrate these complementary therapies as herbals into their medical and surgical care, they are creating a more comprehensive treatment plan and helping their own bodies to regain health and vitality [(22)]. Therefore, minimizing of the chemotherapeutic side effects requires skillful nursing interventions as well as collaborative work between oncologist, pharmacologist, nutritional therapy, laboratory technicians, and oncology

This study aims at declaring the effect of the herbal combination of herbal mixture to conventional chemotherapy on minimizing the incidence of chemotherapeutic side effects for 2nd stage breast cancer patients. Based on the results of this study, it can be concluded that:

The risk of breast cancer was found to be highly among women with age group (49 – 65) years, and common among breastfeeding women who lactated for three times and more through their life.

Patients with herbal and conventional therapies experienced less chemotherapeutic side effects of all body systems than patients with only conventional therapy. It was also concluded that, liver functions and endocrine studies, renal functions, reproductive system, urinary system, and weight changes were The least affected systems with chemotherapeutic side effects and were also the most affected systems when combined herbal to conventional therapy

Gastro intestinal, respiratory, musclo skeletal systems and hematological studies, as well as eye, ear, mucous membranes were moderately affected systems with the side effects of chemotherapy, and also with combining herbal to conventional chemotherapy. While Psychological status, nervous system, and skin, hair, and nails were the most affected systems with the side effects of chemotherapy, and they were the least affected systems with combining herbal to conventional chemotherapy.

Patients with combining herbal and conventional therapy group have good and very good degrees of health grades and life style, after three months of treatment by herbal and conventional therapy combination. While patients with only conventional therapy, have bad and moderate degrees.

Patients with herbal and conventional therapy have increased body mass index, after three months of treating with herbal and conventional therapy. While patients with only conventional therapy, have decreased their body mass index.

It was found that, there was no relation between chemotherapeutic side effects with age, occupation, type and frequency of breast feeding.

The present findings declare that herbal combination of the study has a great action on attenuating, decreasing, minimizing and protecting the body from the usual side effects appears during conventional chemotherapy.

Recommendations

Based on the findings of the present study, the following recommendations are derived and suggested:-

A- Recommendations for oncology team:

1. Herbal education should be introduced in nursing and medical curriculum as well as health awareness about herbals with proven efficacy, and its health effects should be increased.

2. It is essential to increase the level of awareness among public, patients and health care providers regarding the efficacy and toxicity of these medicinal herbals, through mass media.

B- Recommendations for further researchers:

1. Further researches are needed for these herbal components to measure its efficacy on minimizing the side effects of chemotherapy for breast cancer and / or other types of cancer.

2. Clinical studies to identify the effect of these herbals on different cancer therapies, different chemotherapeutic protocols, as well as specifically pre or post mastectomy.

3. Further research also needed for larger number of sample, as well as long period of study time to confirm the effect of these herbals on minimizing the chemotherapeutic side effects.

4. Investigate the relation between awareness of educated patients towards herbal medicine and their compliance.
5. Collaboration, guidance and support for relevant research in herbal medicines to test its safety and efficacy for managing other diseases.

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