

Efficacy of Complementary Alternative Medicine (Ayurveda) In Combating Adverse Effects Associated With Chemo-Radiation

A Ananya¹, T Pranaya Ravali¹, S Ramesh², D Sudheer kumar³, P Kishore^{1*}

¹Department of Pharmacy Practice, Care College of Pharmacy, Warangal, Telangana, India

²MD (Panchagavya), Maharshi Gowshala, Hanamkonda

³Department of Pharmaceutics, Care College of Pharmacy, Warangal, Telangana, India

Corresponding Author: Dr P Kishore, Department of Pharmacy Practice, Care College of Pharmacy, Oglapur (v), Damera (m), Warangal (rural), Telangana, India

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Abstract

Uncontrolled proliferation of cells and metastasis are the main characteristics of cancerous cell. Surgery, chemotherapy and radiation therapy are the three modalities used in treatment of cancer alone or in combination. In spite of the advances in oncology, outcome of the treatment still remain unsatisfactory. Due to partial response of the conventional treatment and morbidity of the cancer patients, researchers and medical professionals seeking knowledge about alternative medicine in cancer treatment. Alternative medicine such as ayurveda has a potential role in preventing adverse effects. This article aims to provide a brief information about the use of complementary alternative medicine in cancer patients and its role in reducing side effects of chemo-radiation and to improve the effectiveness of conventional therapies. There was a significant reduction in adverse effects such as nausea- vomiting, nephrotoxicity, cardiotoxicity, alopecia and anemia in treatment group as compared to controls throughout chemo-radiation. Clinical pharmacist assists in patient's

safety, prevention of adverse effects and to improve health care by interacting with medical professionals in appropriate medication decision.

Keywords: Chemotherapy, Chemo- Radiation side effects, Complementary Alternative Medicine

Introduction

Cancer is a major illness and a leading cause of death, causing suffering of large population and economic loss worldwide (1). According to 2018 statistics about 18.1 million new cancer cases and 9.6 million cancer deaths were reported (2). Although there has been tremendous advancement in the treatment of cancer, possibly 20 % are cured and an additional 20 % may experience significant prolongation of life. The remaining 60 % have minimal or no benefit from cytostatic treatment and suffer from its toxic adverse effects. Thereby, Complementary alternative medicine have attracted attention.

Chemo-Radiation Side Effects in Cancer Patients

The side-effects and long-term sequelae of anti-cancer treatment (Chemotherapy, Radiation therapy) remain a major source of concern for both patients and clinicians

despite the improved efficacy offered by modern treatments. Common side effects of chemotherapy are nausea, vomiting, diarrhea, mucositis, alopecia, weight loss, hypersensitivity, constipation etc., whereas radiation therapy though administered locally, can produce systemic side effects such as fatigue, anorexia, nausea, vomiting, alteration in the taste, sleep disturbances, headache, anemia, dry skin, constipation etc. Late complications of these therapies include pharyngitis, esophagitis, laryngitis, persistent dysphagia, fatigue, hepatotoxicity, nephrotoxicity, cardiotoxicity, neuropathy, infertility and cognitive deficits (3).

Nausea / Vomiting: Approximately one half of cancer patients will experience nausea or vomiting during the course of their disease either because of the cancer itself or because of the treatment (4). In spite of use of anti-emetic drugs, 70 % of patients show persistent symptoms.

Alopecia: Alopecia is a common adverse cutaneous event in oncology patients receiving antineoplastic therapy. Hair loss occurred in 99.9 % of patients. The mean time from chemotherapy until hair loss was 18.0 days. Regrowth of scalp hair occurred in 98 % of patients. Alopecia is majorly observed in breast cancer patients receiving taxanes and or hormonal therapy (5).

Anemia: Anemia is another common condition in cancer patients receiving chemotherapy. It significantly hampers the quality of life and is an important cause for blood transfusion in cancer patients. Anemia is a frequent finding in cancer patients, occurring in >40 % of cases. It may rise to 90 % treated with chemotherapy (6).

Cardiotoxicity: Several anti neoplastic drugs in clinical use are known to induce cardiac side effects (cardiomyopathy, myocarditis, acute coronary syndrome, arrhythmias, congestive heart failure). The incidence of congestive heart failure (CHF) with doxorubicin was 4–7

% in patients receiving 400 to 550 mg/m², 18 % in those receiving 551 to 700 mg/m², and 30 % at doses above 701 mg/m² (7).

Nephrotoxicity: There are numerous systemic adverse effects associated with anti-cancer treatment. Nephrotoxicity remains a significant hurdle limiting the efficacy of therapy additionally deteriorate the level of living. Cisplatin induced nephrotoxicity occurred in more than one-third of patients after the fourth cycle of chemotherapy and worsened after each cycle of chemotherapy (8).

Materials and Methods

Our study was a Prospective dual center study (Cancer Hospital, Maharshi Gowshala) carried out for a period of 6 months after obtaining approval from Institutional Ethics Committee. All the patients diagnosed with cancer (all types), patients receiving chemotherapy and/ or radiation therapy with or without use of alternative medicine were included in our study. Pregnant women were excluded from our study. Patient data was obtained from case sheets and interaction with patients and care givers. Follow up on Weekly basis was done.

Chemo-radiation regimen

All the chemotherapy regimens and radiation dose - number of seatings are given according to standard treatment guidelines.

Breast: cyclophosphamide, paclitaxel, doxorubicin and 25 seatings of radiation

Rectum: 5 fluorouracil, leukovorin and 20 - 25 seatings of radiation

Colon: oxaliplatin, 5 fluorouracil, leukovorin and 20 - 25 seatings of radiation

Ovary: paclitaxel, oxaliplatin and 25 seatings of radiation

Cervix, tongue: cisplatin and 25 seatings of radiation

Complementary Alternative Medicine (CAM) regimen

7 fold filtered cow urine is used as an anticancer liquid refreshment in the morning. Herbs commonly used in the treatment of cancer are holy basil, curcuma longa, neem giloy, periwinkle, cyperus rotundus, indian rosewood, night flowering jasmine, fenugreek and boerhavia diffusa.

Results

Of 400 patients, 200 were unrolled in Complementary Alternative Medicine and 200 patients were on Chemo-radiation and this group was considered as control group. Treatment group is divided into two categories: 75 patients were on Complementary Alternative Medicine alone (CAM) and 125 patients were on both Conventional and Complementary Alternative Medicine (C+C). Of 400 clinically diagnosed cancer patients, highest number of patients had GI cancers and reproductive cancers. Prevalent type of cancer among female and male are reproductive cancers (breast cancer, cervical cancer) and gastrointestinal cancers respectively. It was observed that cancers are highly diagnosed at the age of 41-50 and 51-60 age group. In treatment group, Female (53 %) were predominant. In control group, the male to female ratio was found to be 1: 3.

Nausea- vomiting: Of 200 patients in control group, 192 patients (96 %) presented with nausea and vomiting. Whereas in treatment group of CAM alone (75 patients), more than 50 % patients did not experience nausea / vomiting during and after the treatment. Among 125 patients receiving both C+C, majority of the patients (75 %) did not report Nausea and vomiting.

Nephrotoxicity: Of 75 patients in treatment group of CAM alone, 65 % of the patients reported decreased serum creatinine levels. Of 125 patients receiving both CAM and conventional cancer therapy, 72 % of reported normal Renal Function Test (RFT) during and post

treatment. 169 patients are with increased serum creatinine levels in control group.

Cardiotoxicity: Of 75 patients in treatment group, majority of patients had normal cardiac function. Out of 125 patients, 72 % of cancer patients had normal cardiac functioning. whereas in control group, 47 patients diagnosed with chemotherapy induced diastolic dysfunction.

Anemia: In our study, of 75 patients receiving CAM, more than 50 % patients reported normal blood counts. Of 125 patients receiving both treatments, more than 50 % patients reported normal blood counts. Whereas, in control group, 114 patients (57 %) have low blood counts.

Alopecia: Of 75 patients in treatment group of CAM alone, 23 % patients reported alopecia (Hair loss). Of 125 patients receiving both treatments, majority of the patients (67 %) reported regrowth of hair and no signs of alopecia. Alopecia (hair loss) is observed in 116 patients (58 %) in control group.

Table 1: Distribution based on Nausea/ Vomiting (N / V)

N / V	Number of patients	(%)
Yes	192	96
No	8	4

Table 2: Distribution based on Nephrotoxicity

Nephrotoxicity	Number of patients	(%)
Yes	169	85
No	31	15

Table 3: Distribution based on Diastolic dysfunction

Diastolic dysfunction	Number of patients	(%)
Yes	47	24
No	153	76

Table 4: Distribution based on Anemia

Anemia	Number of patients	(%)
Normal	30	15
Mild	114	57
Severe	56	28

Table 5: Distribution of data based on Hair loss

Hair loss	Number of patients	(%)
Yes	116	58
No	84	42

Discussion

Type of cancer: Conventional (Chemotherapy / Radiation therapy / Chemo-radiation therapy): According to Freddie Bray et al., lung cancer is the most commonly diagnosed cancer (11.6 % of the total cases) closely followed by female breast cancer (11.6 %), prostate cancer (7.1 %), colorectal cancer (6.1 %) and cervical cancer (2). In our study, the most common type of cancer is breast cancer (31 %) followed by cervical cancer (15 %), oral cancers (11 %) which might be due to use of oral contraceptives, hormone replacement therapy and lack of awareness about hygiene.

CAM (Complementary Alternative Medicine): In our study, gastrointestinal cancers (25 %) were predominant followed by reproductive cancers (24 %). In a study conducted by Damery S et al., Patients with breast cancer were most likely to be herbal medicine users, with all other cancer types except female genital cancers having a lower usage (9). Breast, urogenital system, gastrointestinal and soft tissue cancers were predominant which might be due to use of oral contraceptives, poor nutrition, social habits and occupational exposures.

Nausea/vomiting: In a study conducted by Al Qadire M, of 185 cancer patients included in the study, the incidence of nausea and vomiting was high at 71.4 % (10) which is in contrast to our study where 96 % of the cancer patients

reported nausea / vomiting. Patients who are on combination of CAM and conventional therapy, 75 % of the population reported no symptoms of nausea / vomiting which is similar to the study conducted by Yunes Panahi et al., where 78 patients completed the trial (37 in the ginger group and 41 in the control group). Addition of ginger to the standard antiemetic therapy was found to be associated with a significant reduction in the prevalence of nausea and vomiting at 6 to 24 hours post chemotherapy in the ginger group compared with the control group. Scores include no symptoms (48.6 %, 53.7 %), Mild (32.4 %, 31.7 %), Moderate (18.9 %, 14.6 %), Severe (0 %, 0 %) among treatment group and control group respectively (11). Nausea and vomiting are common side effects of chemotherapy. According to Pillai et al., moderate to severe nausea was observed in 93.3 % in the control group and 55.6 % in the experimental group (12) which is similar to our study where nausea was observed in 96 % in the control group and 30 % in treatment group. Herbs like ginger, ginseng, grape seed extract and oil of mentha have anti emetic properties.

Nephrotoxicity: In our study where 85 % of the population reported increased serum creatinine levels indicating nephrotoxicity with conventional cancer therapy, 65 % of the patients receiving only CAM reported decreased serum creatinine levels, 72 % of the patients receiving both CAM and conventional cancer therapy reported normal RFT during and post treatment which is similar to a study conducted by Prasaja Y et al., the prevalence of cisplatin nephrotoxicity was 34.1 % (13) which is contrast to our study, where the prevalence of nephrotoxicity was 85 %. According to Hasanaa Osama et al., a total of 32 patients with cancer were selected to participate in the study. Serum creatinine levels were markedly elevated in the control group treated with

cisplatin only compared to both bee honey and royal jelly groups. Patients on bee honey and royal jelly showed a statistically significant decrease in serum creatinine levels starting from 0.773 +/- 0.3 to 0.71 +/- 0.25 mg/dl in the first cycle and much more lower during the second cycle with a significant difference (14). Medicinal plants used in CAM have anti oxidant properties which halts free radical production thus preventing nephrotoxicity.

Cardiotoxicity: In our study, 24 % of our study population treated with chemotherapy alone had diastolic dysfunction which is slightly in contrast to the study conducted by Hyun Ju Yoon et al, where 11.4 % had chemotherapy induced diastolic dysfunction (15) which might be due to adverse effects of anthracycline and non-anthracycline chemotherapy regimens. As per Bei-Yu Wu et al., 2015, 18-year-old adolescent male with refractory acute lymphoblastic leukemia (ALL) had experienced anthracycline- induced congestive heart failure (CHF) for 3 weeks. Patient was treated with modified Zhi Gan Cao Tang (ZGCT), three times a day for 2 months. After 6 days of CHM treatment, the patient could tolerate daily activity without supplemental oxygen. After 2 months of CHM treatment, follow-up chest X-ray showed great improvements in pulmonary edema and cardiomegaly with normal cardiac functioning (16). In our study 72 % of the population reported normal cardiac functioning during and post treatment with CAM. In our study 72 % of the study population reported normal cardiac functioning.

Anemia: According to M. Dicato et al., Anemia is a frequent finding in cancer patients, occurring in >40 % of cases. In patients treated with chemotherapy, the incidence of anemia may rise to 90 % (6). Cancer induced anemia results from disruption in the equilibrium of pro- and anti apoptotic factors inducing a fine-tuned selective

differentiation of the trilineage committed hematopoietic stem cell. In our study, among 200 cancer patients, 57 % and 28 % of the total population treated with only chemotherapy had mild anemia and severe anemia respectively. According to Shi Guang Li et al., there is decrease of hemoglobin at the toxicity grade of I-IV in patients with CHM therapy was significant reduced (17). In a study conducted by Samuels et al., a randomized, placebo-controlled, double blinded trial found a significant reduction in chemotherapy-induced hematological toxicities in patients with breast cancer receiving adjunct treatment with LCS101. These patients significantly reported less severe anemia, leucopenia and neutropenia when compared to controls. In our study, of 75 patients receiving CAM 61 %, 14 %, 22 % reported normal blood counts, mild anemia and severe anemia respectively. Of 125 patients receiving both conventional cancer therapy and CAM, 56 %, 22 %, and 22 % reported normal blood picture, mild anemia and severe anemia respectively. CAM suppress cancer related symptoms without affecting functioning of normal cells. Thus cancer patients respond better to cancer therapy and maintain regularity in chemotherapy cycles.

Alopecia: According to Trueb RM, the incidence of alopecia in chemotherapy treated cancer patients was found to be 65 % (18) which is similar to our study where of 200 patients, 58 % of total cancer patients reported alopecia. Abha saxena et al., stated that at the end of chemotherapy, 38.8 % and 32.1 % patients from Maharishi Amrit Kalash (MAK) and control groups reported minimal alopecia. Complete alopecia was observed in 20.4 % and 26.8 % in MAK and control group respectively (19) which is contrast to our study where 87 % and 67 % of the sample population reported no

alopecia using CAM alone and both CAM and conventional therapy respectively.

Conclusion

Of all the different types of cancers in our study, majority of cases were reproductive cancers among which breast and cervical are commonly seen. Chemotherapy and radiation therapy used in cancer treatment have high propensity to cause adverse effects during and after treatment. Majority of the stage IV cancer patients opted for alternate treatment. Our observation indicated that use of complementary alternative therapy along with conventional cancer therapy lowers side effect profile associated with the treatment and improves the health status of the patient. In our study, amalgamation of both treatments has shown that side effects like nausea / vomiting, drop in blood counts, nephrotoxicity, cardiac toxicity and hair loss in the treatment group are reduced in frequency compared to control group. Clinical pharmacist in oncology department should create awareness in cancer patients regarding treatment modalities available and side effects of therapy. Pharmacist have a key role in counseling patients and creating positive attitude in them.

References

1. Kashinath Metri, Hemant Bhargav, Praerna Chowdhury, Prasad S Koka. "Ayurveda for Chemoradiotherapy Induced Side Effects in Cancer Patients". *Journal of Stem Cells*. 2014 Volume 8, Number 2.
2. Freddie Bray, Jacques Ferlay, Isabelle Soerjomataram, Rebecca L. Siegel, Lindsey A. Torre, Ahmedin Jemal. "Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries". *CA CANCER J CLIN* 2018; 68:394–424
3. Kulmira Nurgali, R. Thomas Jago, Raquel Abalo. "Editorial: Adverse Effects of Cancer Chemotherapy: Anything New to Improve Tolerance and Reduce Sequelae?". *Frontiers in Pharmacology*. March 2018. Volume 9. Article 245
4. D.G. Warr. "Chemotherapy- and cancer-related nausea and vomiting". *CURRENT ONCOLOGY*. Volume 15, Supplement 1
5. Takanori Watanabe, Hiroshi Yagata, Mitsue Saito, Hiroko Okada, Tamiko Yajima et al., "A multicenter survey of temporal changes in chemotherapy-induced hair loss in breast cancer patients". *PLOS ONE*. January 9, 2019
6. M. Dicato, L. Plawny, M. Diederich. "Anemia in cancer". *Annals of Oncology* 21.2010; (Supplement 7): vii167–vii172.
7. Diwakar Jain, Tauseef Ahmad, Mitchel Cairo, Wilbert Aronow. "Cardiotoxicity of cancer chemotherapy: identification, prevention and treatment". *Ann Transl Med* 2017;5(17):348
8. Hasnaa Osama, Aya Abdullah, Bassma Gamal, Dina Emad, Doha Sayed et al., "Effect of Honey and Royal Jelly against Cisplatin Induced Nephrotoxicity in Patients with Cancer". *Journal of the American College of Nutrition*. 28 May 2017
9. S Damery, C Gratus, R Grieve, S Warmington, J Jones, P Routledge, S Greenfield. "The use of herbal medicines by people with cancer: a cross-sectional survey". *Br J Cancer*. 2011 Mar 15; 104(6): 927–933.
10. Al Qadire M. "Chemotherapy-Induced Nausea and Vomiting: Incidence and Management in Jordan". *Clin Nurs Res*. 2018 Jul; 27 (6):730-742.
11. Yunes Panahi, Alireza Saadat, Amirhossein Sahebkar, Farshad Hashemian, Mojgan Taghikhani, Ehsan Abolhasani." Effect of Ginger on Acute and Delayed Chemotherapy-Induced Nausea and Vomiting: A

- Pilot, Randomized, Open-Label Clinical Trial”. Integrative Cancer Therapies. 2012; 11(3) 204–211.
12. Pillai, A.K., Sharma, K.K., Gupta, Y.K., Bakhshi, S. “Anti-Emetic Effect of Ginger Versus Placebo as an Add-On Therapy in Children and Young Adults Receiving High Emetogenic Chemotherapy”. *Pediatr. Blood Cancer*.2011; 56: 234-238.
13. Prasaja Y, Sutandyo N, Andrajati R. “Incidence of cisplatin-induced nephrotoxicity and associated factors among cancer patients in Indonesia”. *Asian Pac J Cancer Prev*. 2015; 16(3):1117-22.
14. Hasanaa Osama, Aya Abdullah et al “Effect of Honey and Royal Jelly against Cisplatin-Induced Nephrotoxicity in Patients with Cancer”. *J Am Coll Nutr*. 2017 Jul; 36(5):342-346.
15. Hyun Ju Yoon, Kye Hun Kim, Jong Yoon Kim, Hyuk Jin Park, Jae Yeong Cho, Young Joon Hong et al. “Chemotherapy-Induced Left Ventricular Dysfunction in Patients with Breast Cancer”. *J Breast Cancer*. 2016 Dec; 19(4): 402–409.
16. Bei- Yu Wu, Chun- Ting Liu, Shih- Yu Chen, Ming- Yen Tsai. “A case of chemotherapy- induced congestive heart failure successfully treated with chinese herbal medicine”. “Complementary Therapies in Medicine. Elsevier”. 12 january 2015
17. Shi Guang Li, Hai Yong Chen, Chen Sheng Ou-Yang, Xi-Xin Wang, Zhen-Jiang Yang, Yao Tong. “The Efficacy of Chinese Herbal Medicine as an Adjunctive Therapy for Advanced Non-small Cell Lung Cancer: A Systematic Review and Meta-analysis”. *PLOS ONE*. February 28, 2013; Volume 8 Issue 2.
18. Trueb RM. “Chemotherapy-induced hair loss”. *Skin Therapy Lett*. 2010 Jul-Aug;15 (7):5-7.
19. Abha Saxena, Smita Dixit, Sandeep Aggarwal, Vuthaluru Seenu, Rajinder Prashad, S.M. Bhushan. “An Ayurvedic Herbal Compound to reduce Toxicity to Cancer chemotherapy: A Randomized Controlled Trial”. *Indian Journal of Medical & Pediatric Oncology*. 2008; Vol. 29 No 2.