Chapter III

Research Methodology
RESEARCH METHODOLOGY

This chapter describes the methodology adopted to gather valid and reliable data for the study. It deals with a brief description of research approach, research design, the setting, the population, sample and sampling technique, development and description of tools, data collection procedure and the plan for data analysis.

Research Approach

The research approach covers the basic procedure for conducting research. The present study aimed to find out whether breast cancer patients undergoing radiation therapy suffer from cancer related fatigue and if so, whether there is a difference in the level of cancer related fatigue between patients who perform pranayama and who do not perform pranayama during the course of radiation therapy. The study also attempted to find out the difference in the level of few enzymatic and non–enzymatic antioxidants between these two groups of patients and whether the levels of antioxidants have any relationship with the development of cancer related fatigue. Thus, an evaluative approach was found to be appropriate for the study.

Research Approach: Evaluative approach
Research Design

Randomized Controlled Trial

Fig 2: Consort Flow Chart of Randomized Controlled Trial
### Groups and Frequency of Measurements

<table>
<thead>
<tr>
<th>Groups</th>
<th>Frequency of Measurements</th>
<th>Week1 (At the beginning of Radiation Therapy)</th>
<th>Week2</th>
<th>Week3</th>
<th>Week4</th>
<th>Week5</th>
<th>Week6 (At the completion of Radiation Therapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td></td>
<td>AF</td>
<td>P</td>
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<tr>
<td>Control</td>
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<td>BP</td>
</tr>
</tbody>
</table>

**Fig3: Diagrammatic Representation of Study Design**

**Key:**
- AF - assessment of fatigue
- P - Pranayama daily for 5 days a week for six weeks
- BP: Biochemical Parameters.

**Variables**

**Dependent Variable:** Cancer related fatigue, selected biochemical parameters

**Independent Variable:** Pranayama

**Research Setting**

The present study was conducted at Shirdi Sai Baba Cancer Hospital & Research Centre, Kasturba hospital, Manipal. Kasturba Hospital is a 2200 bedded multi-specialty hospital. Shirdi Sai Baba Cancer Hospital & Research Centre is a part of Kasturba Hospital with facilities for surgical oncology, radiation therapy and chemotherapy. It is a tertiary care cancer hospital with an average new admission of 1100 to 1200 cancer patients per year. Out of these, around 450 to 500 are female patients with different types of cancers.
Kasturba medical college has a well-established biochemistry laboratory with equipment like spectrophotometer and refrigerator centrifuge. The biochemical parameters of the present study (enzymatic and non-enzymatic antioxidants) were done in this laboratory.

**Population**

The population for the present study included breast cancer patients undergoing radiation therapy in Shirdi Sai Baba Cancer Hospital & Research Centre, Kasturba hospital, Manipal.

**Sample**

Sample size was calculated based on the following assumptions (Hypothesis testing for two means)

- The outcome variable is continuous
- The sampling distribution of the sample mean is approximately normal
- The observations are independent
- The variances in the two groups are similar

**Sample size Formula**

\[
 n = \frac{2s_p^2 \left[ z_{1-\alpha/2} + z_{1-\beta} \right]^2}{\mu_d^2} \\
 S_p^2 = \frac{S_1^2 + S_2^2}{2}
\]

Where,

- \( S_1^2 \): Standard deviation in the first group
- \( S_2^2 \): Standard deviation in the second group
\[ \mu_d^2 : \text{Mean difference between the samples} \]

\[ \alpha : \text{Significance level} \]

\[ \beta : \text{Power} \]

\[ n = 2 \times 400 \left[1.96 + 1.282\right]^2 \]

\[ = \frac{8408.4512}{324} \]

\[ = 26 \text{ in each group} \]

The cancer fatigue scale had 18, eleven point scales. The minimum score was zero and the maximum score was 180. The questionnaire was administered to twenty patients and the mean fatigue score was 53 and the standard deviation was 20. The value of standard deviation applied in the above formula is based on this data. Since there are 18, eleven point scales in the questionnaire, an average minimum decrease of 18 units in the total fatigue scores after Pranayama was anticipated. The value of “Mean difference between the samples” applied in the above formula is based on this assumption.

The sample size required for a ‘t’ test (26) is computed initially and 15\% (26 + 4 = 30) is added in each group to make it possible even to apply non-parametric tests. 10\% more (30 + 3 = 33) is added to the sample size anticipating a drop-out rate of ten percent. A sample size of 66 was found to be adequate for the study. But, it was decided to include the maximum number of patients recruited during the data collection period as per the doctoral committee’s advice. Thus a total of 160 patients were included as study participants. The patients were randomized into control group (80) and experimental group (80) based on block randomization.
Inclusion Criteria

- Women with breast cancer, undergoing daily adjuvant radiation for 6 weeks in the Department of Radiotherapy and Oncology at Shirdi Sai Baba Cancer Hospital & Research Centre, Kasturba hospital, Manipal
- Age 18 years of age or older.
- Able to read and speak Kannada, Malayalam or English
- Patients who are willing to participate in the study

Exclusion Criteria

- Patients who have any diagnosed psychiatric disorder.
- Patients who have not undergone any surgical treatment and adjuvant chemotherapy for their breast cancer will be excluded to ensure a more homogeneous sample.
- Patients with extreme mobility issues (e.g., unable to get in and out of a chair unassisted)
- Patients who have practiced yoga or taken yoga classes prior to diagnosis.
- Patients diagnosed with lymphedema at baseline
- Patients with recurrent breast cancer
- Patients with metastases

Data collection instruments

- Demographic Proforma
- Cancer Fatigue Scale
Biochemical Parameters: Biochemical parameters were standardized using serial concentrations of known standards. Precision was tested by repeated measures of the same sample. Tests were done in the biochemistry department of Kasturba medical college.

**Description of the tool**

Assessment of fatigue was done using the Cancer fatigue scale. Cancer fatigue scale was prepared after referring to the guidelines given by National Cancer Institute, ICD -10 and NCCN (National Comprehensive Cancer network) on cancer related fatigue. The Cancer fatigue scale had 18, eleven point scales to measure fatigue in physical and functional aspects, affective and cognitive areas.

Scoring of Cancer fatigue scale:

0 - : No fatigue
1 - 54 : Mild fatigue
55 - 108 : Moderate fatigue
109 - 180 : Severe fatigue

This scoring is done based on the NCCN guidelines for age>12 years, fatigue will be measured on a 0 – 10 scale, and can be classified as:

None to mild : 0 - 3
Moderate fatigue : 4 - 6
Severe fatigue : 7 - 10^7
Content validity of the tool

Content validity of the tool was done by giving it to three experts in the field of radiation oncology, one expert in the field of psychiatry, one expert in the field of clinical psychology and two experts in the field of nursing. All the items had 100% agreement and no items from the cancer fatigue scale were deleted. The tool was translated into Kannada and Malayalam and was re translated to English by language experts.

Pretesting

Pretesting of the tools was done on five breast cancer patients and the average time taken to complete the questionnaires was found to be twelve minutes.

Reliability

Reliability was done on twenty breast cancer patients each undergoing radiation therapy in Shirdi Sai Baba Cancer Hospital & Research Centre, Kasturba hospital, Manipal and reliability for the Kannada tool was found to be 0.82 and for the Malayalam tool was 0.80. Reliability was calculated using Cronbach’s alpha for both the tools.

Pilot study

Pilot study was conducted on 20 patients at Shirdi Sai Baba Cancer Hospital & Research Centre, Kasturba hospital, Manipal. Patients who met the inclusion criteria and gave informed consent were randomized into control group and experimental group. Experimental group of patients performed Pranayama (Brahmari, Seethali and Nadisodhana), morning and evening, five days a week for six weeks along with radiation therapy whereas control group of patients received radiation therapy alone. Patients were
allocated to different groups using block randomization. Two blocks of ten patients were included for pilot study. Pilot study was done to assess the feasibility of the study and to decide on the statistical analysis to be used. Pilot study was conducted during the period January to June 2009.

During the inception of the study, it was planned to assess the cancer related fatigue from breast cancer patients every week during radiation therapy. But after the pilot study, it was decided to assess the cancer related fatigue only at the beginning and at the end of six weeks of radiation therapy since there was not much of a difference in the scores of cancer related fatigue between each week for those 20 patients. Initially there was also discussion about recruiting patients based on stratified block randomization based on age. But since most of the patients for pilot study were above 45 years of age, only block randomization was done for the main study excluding stratification.

**Procedure for data collection**

Main study was conducted during the period July 2009 to August 2012. The cancer fatigue scale was administered by the researcher in the radiation oncology wards or in the linear accelerator room when they came for radiation therapy. The time taken by the patients to complete the self-report questionnaire was approximately 10-15 minutes. The initial sessions on Pranayama were given in the Yoga department for one week. Pranayama techniques were taught by yoga experts. The patients performed Pranayama morning and evening daily for the next 5 weeks in a separate room in the hospital under supervision. The patients were very cooperative and were eager to learn and practice the pranayama techniques. The investigator coordinated with the yoga department and the radiation
oncologists to send the patients for pranayama. The blood was collected two times for 80 patients and one time i.e., at the completion of radiation therapy for 160 patients to analyze the enzymatic and non-enzymatic antioxidants. It was collected mostly by the staff nurses along with other routine blood investigations to avoid unnecessary pricks to the patients. The tests were done free of cost as the study was funded by the Indian Council of Medical Research. The details about randomization of patients, pranayama techniques practiced by them, treatments received by these patients, details about assessment of cancer related fatigue and enzymatic and non-enzymatic antioxidants are given below.

**Randomization:** The study was conducted after obtaining institutional ethical committee clearance. The study group consisted of a total of 160 patients which included both the control group (80) and the experimental (80) group. The patients were allocated into experimental group and control group using block randomization procedure (sixteen blocks of ten patients) after getting informed consent. Random sequence generation and concealed allocation was achieved by using concealed and numbered envelopes.

**Pranayama:** The patients in the experimental group performed pranayama (Sheethali, Brahmari and Nadisodhana Pranayama) along with radiation therapy whereas patients in the control group received radiation therapy only. Experimental group of patients performed Pranayama, morning and evening for 5 days a week for 6 weeks (from the day of starting radiotherapy till the last day of radiotherapy). Patients performed Nadisodhana for approximately 5 minutes (21-25 cycles), Sheethali for approximately 5 minutes (50-60 cycles) and Brahmari for approximately 8 minutes (10 cycles). The initial sessions on Pranayama were given in the Yoga department for one week. The patients performed
Pranayama morning and evening for the next 5 weeks in a separate room in the hospital under supervision. The procedure for different types of pranayama employed for the study is explained in Appendix - I

In **Brahmari Pranayama**, patients were taught to take deep inhalations and deep exhalations with a humming sound.\(^{17}\)

In **Sheethali Pranayama**, patients were taught to draw in air slowly and deeply through a curled tongue which is stretched out of the mouth. After the inspiration, the tongue is withdrawn and the mouth is closed and they were asked to exhale passively through the nose. Those who had difficulty in making a curled tongue were taught to draw in air slowly and deeply through clenched teeth and exhale passively through the nose.\(^{17}\)

In **Nadishodhana Pranayama**, the patients were taught the following procedure. “The right hand was brought to the nostrils. Left nostril was blocked completely with the ring finger and small finger of the right hand without disturbing the septum. Patients were instructed to exhale through the right nostril slowly, steadily and deeply and inhale though the same side in the same way. When the inspiration was completed, the right nostril was blocked with the thumb of the right hand and they were asked to exhale slowly and steadily through the left nostril. Once the exhalation is completed through the left nostril, patients were instructed to inhale slowly and steadily through the same nostril. Again they were asked to slowly and steadily exhale through the right nostril. This completed one cycle of Nadishodhana Pranayama\(^{17}\).
While doing Pranayama, the patients were taught to sit on the floor in Padamasana. Those who had difficulty sitting in Padmasana were sitting in "ardha Padmasana or sitting on a chair with the leg dangling and with the spine straight.

**Treatment received by breast cancer patients:** Patients who were having locally advanced breast cancer and who underwent Modified radical mastectomy or Breast conserving surgery, followed by 8 cycles of chemotherapy [Doxorubicin 60 mg/m² IV d1] Cyclophosphamide 600 mg/m² d1] 3 weekly* 4 cycles Followed by Paclitaxel 175mg/m² IV 3 weekly* 4 cycles] were enrolled in this study. After chemotherapy, patients were given external beam radiation of 50 Gy in divided doses. Patients performed pranayama on same days when they came for radiation therapy.

**Cancer Related Fatigue Assessment**

Cancer related fatigue was assessed at the beginning of radiation therapy and at the completion of radiation therapy from both the groups using cancer fatigue scale. The cancer fatigue scale was administered by the researcher in the radiation oncology wards or in the linear accelerator room when they came for radiation therapy. The time taken by the patients to complete the self-report questionnaire was approximately 10-15 minutes. English, Kannada and Malayalam versions of cancer fatigue scale are given in the Appendix II.

**Assessment of Enzymatic and Non-enzymatic Antioxidants**

Blood was collected in red coloured vacutainers for serum sample and purple vacutainers with EDTA for packed cell, from both the group at the completion of radiation therapy. The samples were analyzed for levels of serum protein thiols and serum glutathione...
S transferases, glutathione peroxidase, glutathione reductase and glutathione (GSH). Pre-test for these antioxidants were done in a sample of 80 patients at the beginning of radiation therapy and post-test was done for 160 patients. The blood was collected two times (at the beginning of radiation therapy and at the completion of radiation therapy) for 80 patients and one time i.e., at the completion of radiation therapy only for 160 patients to analyze the enzymatic and non-enzymatic antioxidants. The detailed procedures for estimation of these enzymes are given in the Appendix III.

Ethical Considerations

Institutional ethical committee clearance was obtained from the ethical committee, Manipal University. Informed consent was obtained from the patients before recruiting them for study.

Communications by the ethical committee, permission to conduct the study from Kasturba hospital, biochemistry department of KMC, subject information sheet and consent forms are attached in the Appendix IV.

Data analysis

Data analysis was planned in consultation with a statistician. SPSS Statistical package 16.0 was used. It was planned to use descriptive and inferential statistics based on the objectives and the hypotheses to be tested.

Summary

This chapter has dealt with the research approach, research design, variables, research setting, sample and sampling technique. Data collection techniques, instruments
used for data collection, validity and reliability testing of the tools, pilot study and procedure for data collection are also described. A randomized controlled design was adopted for the study. The tools used for collecting data were demographic proforma and cancer fatigue scale. Standardized procedures were used for the analysis of antioxidants and antioxidant enzymes. Ethical clearance was taken from the concerned authorities and informed consent was taken from the participants. Descriptive and inferential statistics will be used for data analysis.