Adherence to Radiotherapy in the Treatment of Cancer Patients: A Tertiary Care Institute Experience at Punjab

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Abstract

Aim: The present study was carried out to analyse the incidence of non-adherence to the radiotherapy treatment and study the factors associated with non-adherence. Patient and methods: The retrospective study was conducted at a tertiary cancer care institute, Punjab. All the patients treated during one year with curative intent with conventional fractionation were included. Incidence of non-adherence was driven and the various parameters like age, gender, site of tumor, stage of disease, intent of treatment, distance from the treating institute, financial constraints were analysed. Results: A total of 660 patients were taken. 6 out of 660 did not come for treatment initiation, hence 654 patients were eligible to be studied. The cumulative incidence of non-adherence was 12.8% (84 out of 654). The majority of patients were of head and neck 31 (36.9%), Elderly >60 years 27 (32.1%), Stage IV 42 (50%), patients residing in more than 50 km from the institute 47 (55.9%), concurrent chemotherapy 71 (84%), the major proportion of patient had more than 1 week gap 54 (64%) with 25 (29%) having more than 2 weeks gap. The factors found to be associated with non-adherence was elderly age (p value 0.06), advanced stage (p value 0.003), use of concurrent chemotherapy (p value 0.001), distance from the institute (p value 0.03), treatment with radical intent (p value < 0.001), patients utilizing various government schemes (p value 0.004). No significant association was found between the gender and site of the tumor (p value 0.17 and 0.14 respectively) with the non-adherence. Conclusions: The factors associated were stage of disease, elderly, concurrent chemotherapy, more distance travelled to reach the institute. Non adherence needs to be addressed by proper counselling of patients at the first visit to hospital itself. After the 3 week of radiotherapy treatment patient needs to be seen and followed more frequently when chances skipping treatment are high.

Keywords: Non-adherence- radiotherapy- non-compliance

Introduction

Cancer treatment is a multimodality approach and radiotherapy plays a vital part, which utilizes ionizing radiation to treat various malignant tumors. It has been used to treat some benign disease and other disorders [1]. Soon after Roentgen’s discovery of X-rays in 1895, ionizing radiation was applied to the treatment of cancer, with remarkable results. Radiation therapy is a time tested treatment modality since ages which has radiobiological principles as its backbone. Withers way back in 1975 define the basis of radiation effects in terms of four principles namely repair of DNA damage, redistribution of cells in the cell cycle, repopulation and reoxygenation of hypoxic tumor cells and later steel added one more factor of radiosensitivity in 1989 [2,3]. Carefully controlled doses of ionizing radiation induce damage to the DNA in cells, with preferential effects on cancer cells compared with normal tissues, providing treatment benefits in most types of cancer and saving lives. They also define the concept of fractionation. The most commonly prescribed conventional fractionation uses 1.8–2.2 Gy per fraction for five fractions in a week for 5-7 consecutive weeks [2,3].

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Over the period of time there are many modifications applied to the conventional radiation therapy schedule. In the current era we have different fractionation schedules which are time tested. Adherence to the cancer treatment is important in terms of outcome, locoregional control and survival. Many times, unplanned interruptions happen either due to technical breakdown of the machine or treatment-related toxicities, sometimes patients do not come for radiotherapy. These interruptions become an important issue and affects the chances of patient getting cured. Different reasons account for this, some of which are social taboos, religious customs, myths about radiotherapy, financial constraints, alternative medicine treatment, etc. This ultimately affects the local control and overall survival [4].

This association between interruptions and treatment outcome has been consistent for several disease sites such as head and neck cancers, lung cancer, cervical cancers, breast cancer and other sites [5]. Delay or prolongation of treatment is associated with relative risk of local recurrence by upto 2% per day for specific malignancies [6]. The previous two decades have experienced remarkable changes in the technology of delivering radiation. The technology has moved from conventional two-dimensional radiotherapy to particle beam therapy [7].

Non adherence to treatment issue has often been ignored and consequences of non compliance never been addressed. A clinical audit performed to provide key information associated with radiotherapy process. Some of the key factors that have been assessed compliance to radiotherapy, waiting time to radiation therapy, intention of treatment, effect on overall treatment time, and integration with allied treatment modalities [8]. Non compliance to the planned treatment course is one of the major reasons for the treatment failure. In this study we tried to analyse the factors and reasons behind not following the treatment recommended for their treatment.

Materials and Methods

We retrospectively evaluated the radiotherapy records of those patients who were treated in the radiotherapy department at the Institute. A total of 660 patients were found eligible. 6 out of 660 patients did not came for treatment even when their plans were ready to execute. Hence 654 patients were eligible for the study. Their records were analysed for compliance to the treatment protocol. Compliance was defined as completion of prescribed dose of radiation during the prescribed time frame. Noncompliance was defined as the premature termination of the planned treatment by the patient without consultation or recommendation from the treating clinician. Majority of the patients were of head and neck, gynaecologic, breast and oesophagus diagnosis. The usual dose prescription was 66–70 Gy @2 Gy per fraction for head-and-neck cancer, 50 Gy @2Gy per fraction for breast cancer, 50 Gy @2Gy per fraction of external beam radiation for cervical cancer, 50.4Gy @1.8Gy per fraction for GI tumors. Dose was delivered with 2 Gy per fraction for five fractions in a week over a period of 6-7 weeks. Compliance was found to be associated with various factors such as age, gender, site of primary disease, distance patients had to travel to receive treatment, administration of concurrent chemotherapy, and financial expenses of the treatment.

Results

The characteristics of the patients included in the study has been given in Table 1. Out of 660 patients, 6 patients did not come to start their treatment, hence the evaluable patients were 654.

Among the 654 patients, 315 (48.1%) were males and 339 (51.8%) were females. Head and neck (26%), breast (18%), gynaecologic (20.6%) accounts for the major proportion of malignancies. The cumulative incidence of non-adherence was 12.8% (84 out of 654 patients). Various factors associated with non-adherence is given in Table 2. The most common cause of non-adherence is the development of radiation induced toxicities. These side effects generally develop in the second week of treatment with varying degree of severity. The head and neck patients develop dysphagia as result of mucositis and desquamation of skin in the irradiated areas. Chemotherapy given concurrently increases the side effects. Patients receiving pelvic radiation develop GI toxicities in form of diarrhea and patients with breast conservation surgery followed by radiotherapy develop skin reactions in the inframammary region. Among the non-adherence patients, 47 (55.9%) used to come from a distance within 50 km from the institute. Majority of them were receiving concurrent chemotherapy 71 (84%) and all were treated with radical intent. 71 (84%) patients in the non-adherence group were getting some financial aids from the various government schemes. A major proportion of them were in stage IV cancers 42 (50%). A comparable number of patients took gap of 1 week and between 1-2 week (35%).

Discussion

Radiation treatment is a time tested modality in multimodality approach to cancer especially solid tumors. Radiation therapy is used to cure cancers that are localized; it can also provide local control in form of complete response with no evidence of recurrence in the treated area (curative) or symptom relief in cancers that are locally advanced or disseminated (palliative). It is frequently used in combination with surgery, either preoperatively or postoperatively, as well as in combination with systemic chemotherapy before, during, or subsequent to the course of Radiotherapy. Conventional fractionation was defined as delivering 1.8-2 Gy over 5 days a week over 6-7 weeks. It was proposed to achieve an acceptable therapeutic ratio- defined as probability of tumor control versus the probability of unacceptable toxicity. These radiobiology concepts have been thoroughly inspected and with the help of advanced and sophisticated equipments, altered fractionation schedules were explored to keep
Hansen et al. have shown that prolongation of the overall treatment time only leads to reduced locoregional control in well-to-moderately differentiated SCC of the head and neck [12]. Overgaard et al. have shown the importance of overall treatment time for the response to radiotherapy in patients with SCC of the head and neck [13, 14]. They concluded that the locoregional control rate, the disease-specific survival, and overall survival have significant dependency on the overall treatment time. The most beneficial results are achieved when this is short.

Various trials are going on to analyse the effects of hypo fractionated radiotherapy in cancers of different sites like breast, prostate, brain, and head and neck, cervix. With such short course of treatment, it has also been noticed that the compliance rate of patients to the radiotherapy has increased [15,16]. Squamous cell carcinoma (SCC) of the head and neck is a locoregional disease with comparatively less prone to develop metastasis. Radiotherapy and the overall treatment time short, like in continuous hyper fractionated accelerated radiotherapy for lung cancer and stereotactic body radiotherapy for tumors of central nervous system and lung [9]. This lesson we have learned in recent and ongoing COVID -19 era, during which it is worthwhile to keep the hospital visits to minimal.

Compliance to the treatment is unresolving issue in oncology management. The extended time gap intervals alter the aim of cure. Sub curative doses accelerates repopulation of tumor cells and makes the re treatment challenging. Different studies have suggested altered fractionation in head-and-neck cancer patients.

Patient education through interactive programmes can enhance the overall awareness about radiotherapy [10]. In addition to educational and counselling sessions, understanding and responding to patient’s emotional issues is imperative to reduce the anxiety and increased preparedness to radiotherapy treatment [11].

| Parameter          | Total number n (654) (%) | Adherence 570 (%) | Non adherence 84 (%) |
|--------------------|--------------------------|-------------------|----------------------|
| Gender             |                          |                   |                      |
| Male               | 315 (48.1)               | 273 (47.8)        | 42 (13.3)            |
| female             | 339 (51.8)               | 297 (52.1)        | 42 (12.3)            |
| Age                |                          |                   |                      |
| <20 years          | 3 (0.4)                  | 3 (0.52)          | 0                    |
| 21-30 yrs          | 16 (2.4)                 | 12 (2.1)          | 4 (4.7)              |
| 31-40 yrs          | 77 (11.7)                | 70 (12.2)         | 7 (8.3)              |
| 41-50 yrs          | 157 (24)                 | 140 (24.5)        | 17 (20.2)            |
| 51-60 yrs          | 192 (29)                 | 167 (29.2)        | 25 (29.7)            |
| 61-70 yrs          | 154 (23)                 | 127 (47)          | 27 (32.1)            |
| 71-80 yrs          | 43 (6.5)                 | 42 (7.3)          | 1 (1.1)              |
| >80 yrs            | 12 (1.8)                 | 9 (1.5)           | 3 (29.7)             |
| Site of tumor      |                          |                   |                      |
| Head and neck      | 172 (26.2)               | 141 (24.7)        | 31 (36.9)            |
| Breast             | 118 (18)                 | 110 (19.2)        | 8 (9.5)              |
| Gynec              | 135 (20.6)               | 119 (20.8)        | 16 (19)              |
| Thoracic           | 25 (3.8)                 | 24 (4.2)          | 1 (1.19)             |
| CNS                | 23 (3.5)                 | 19 (3.3)          | 4 (4.7)              |
| GI                 | 89 (13)                  | 71 (12.4)         | 18 (21.4)            |
| GU                 | 50 (7.6)                 | 45 (7.8)          | 5 (5.9)              |
| Bone and soft tissue | 6 (0.9)               | 5 (0.8)           | 1 (1.19)             |
| other              | 36 (5.5)                 | 36 (6.3)          | 0                    |
| Intent             |                          |                   |                      |
| Radical            | 622 (95)                 | 538 (94.3)        | 84 (100)             |
| palliative         | 32 (4)                   | 32 (5.)           | 0                    |
| Chemotherapy       |                          |                   |                      |
| Yes                | 441 ( 67)                | 379 (66.4)        | 62 (73.8)            |
| no                 | 213 (32)                 | 191 (33.5)        | 22 (26.1)            |
| Stage of tumor     |                          |                   |                      |
| Stage I/II         | 76 (11.6)                | 67 (11.1)         | 3 (3.5)              |
| Stage III          | 403 (61.2)               | 357 (62.6)        | 39 (46.4)            |
| Stage IV           | 175 (26.7)               | 146 (25.6)        | 42 (50)              |

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Table 2. Factors Affecting Compliance

| Factors                  | Non adherence (%) |
|--------------------------|-------------------|
| Distance from the institute |                  |
| <50 km                  | 47 (55.9)         |
| 50-100 km               | 25 (29.7)         |
| >100 km                 | 12 (14.2)         |
| Chemotherapy            |                   |
| Yes                     | 71 (84)           |
| No                      | 13 (15)           |
| Intent of treatment     |                   |
| Radical                 | 84 (100)          |
| Palliative              | none              |
| Financial support       |                   |
| Govt Scheme             | 71 (84.5)         |
| Paid                    | 13 (15)           |
| Stage of disease        |                   |
| Stage I/II              | 3 (3.5)           |
| Stage III               | 39 (46)           |
| Stage IV                | 42 (50)           |
| Time gap                |                   |
| 1 week                  | 30 (35)           |
| 1-2 week                | 29 (34)           |
| >2 week                 | 25 (29)           |
| Age                     |                   |
| 21-30 yrs               | 4 (4.7)           |
| 31-40 yrs               | 7 (8.3)           |
| 41-50 yrs               | 17 (20.2)         |
| 51-60 yrs               | 25 (29.7)         |
| 61-70 yrs               | 27 (32.1)         |
| 71-80 yrs               | 1 (1.1)           |
| >80 yrs                 | 3 (29.7)          |

Adherence to radiotherapy is an important aspect to consider in the management of cancer patients. Various factors can influence a patient's adherence to radiotherapy, including age, stage of disease, intent of treatment, financial support, and distance from the treatment center. For instance, elderly patients, those with advanced stage disease, those receiving palliative care, those who are not financially supported, and those living far from the treatment center are more likely to default. Certain interventions such as counseling, simplifying treatment schedules, and providing support can help improve adherence. For example, in a study by Palwe V et al., 105 (6.7%)/1,548 patients were defaulters. They analysed that elderly patients, head and neck cancers sites (52%), advanced stage and patients receiving concurrent chemotherapy are more likely defaulters. Patients receiving intensity modulated radiotherapy had low rates of nonadherence. Only 5% of defaulters had planned IMRT which causes less toxicities and thus increases chances of adherence. Distance from residence to hospital strongly influence the adherence of planned treatment due to logistic issues. Patients with Good socioeconomic background are more likely to complete their treatment. Non – adherence to planned treatment plan is common among patients who are referred for radiotherapy only from other institutes. This emphasis the fact that all treatment modalities should be made available at a single centre.

In case of cervical cancer, the American Brachytherapy Society recommends keeping the total treatment duration to < 8 weeks i.e 56 days. Chumworathayi et al. have found 100% completion of chemotherapy but with delay in 30.3% cycles in the 3 weekly group and 12.9% cycles delay in the weekly group, which was not significant.

Palwe et al in their study cited certain interventions to improve the adherence to radiation therapy treatment. Since elderly patients are more prone to default, they should be given priority. Patients should be counselled regarding various aspects like nature of treatment,
possible toxicities. Intervention should be made as early as possible to limit the side effects with close monitoring. Patients should be assessed nutrition and nasogastric tube / feeding gastrostomy should be done as and when required. Accommodation facility should be provided to the patients travelling long distance. Radiation oncologist along with psycho-oncologists or counsellors should understand the their fear and remove the misconceptions. Waiting time in the radiotherapy department should be kept minimal. Patients should be seen more frequently after the third week of radiotherapy treatment [22].

In conclusions, interruptions in the radiotherapy treatment adversely affects the outcome of disease. Non adherence to treatment is a major concern. The various parameters have been studied which can affect the treatment gaps. The factors suggested are age, gender, distance from the treating centre, financial constraints, toxicities of radiotherapy, advanced stage of disease. Counselling and addressing the various emotional issues and fear associated with radiation treatment can increase the chances of adherence to the treatment. The retrospective nature and limited number of patients are the limitations of the study.

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