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Effects of Hypofractionated Radiotherapy in Advanced Stage of Non-Small Cell Type Bronchogenic Carcinoma

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Abstract **Original Research Article**

Introduction: Bronchogenic carcinoma accounts for about one-third of all cancer deaths among males. The inclination is such among females as well. This disease is more communal in males than females. Decreasing the number of fractions required for palliative care should be of understandable advantage for both individual patients and the usage of radiotherapy resources. ***Methods:*** This prospective study was carried out in Sylhet MAG Osmani Medical College & Hospital from 1st July 2020 to 30th June 2021 to determine the effects of hypofractionated radiotherapy in an advanced stage of bronchogenic carcinoma. Completed data forms were reviewed, edited, and processed for computer data entry. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0. ***Result:*** The age of the patients ranged from 41-70 years and the maximum prevalence of the disease was seen above the 50s. The male- to-female ratio was 6:1 in the intervention arm and 14:1 in the control arm. The male gender is predominant. All the male patients were tobacco smokers and the females were passive smokers. Lung cancer was found most in cultivators in this study. Cough, chest pain, dyspnoea and haemoptysis were considered as parameters of symptoms. Most of the patients presented with cough, chest pain, dyspnoea and some with haemoptysis. In Arm A, 67% of patients got relief from all the symptoms during treatment time. In the rest 33%, early side effects were developed and treated accordingly. Ultimately 87% of patients got relief from all the symptoms within 2 weeks of completion of treatment. In 13% of cases, there was no relief. In Arm B, 74% of cases got relief from all the symptoms during treatment time. In the rest 26% of cases, adverse reactions developed. These subsided automatically in some cases and others, supportive treatment was required. Finally, 83.33% of cases became free of symptoms and 16.67% of cases were having no symptomatic relief. ***Conclusion:*** Patients can get respite of symptoms for smaller periods by hypofractionation in the radical stage of bronchogenic carcinoma (Non-Small Cell Type) provided the early side effects are managed properly. Hypofractionation is one of the newer concepts of radiotherapy particularly in Bangladesh. So, further study on this matter should be done with interest.

Keywords: Radiotherapy, Treatment, Symptoms, etc.

INTRODUCTION

In Bangladesh, the most common cancers in males are larynx (15.05%), lungs (13.33%) and oral cavity (12%) and in females, breast (25.58%), cervix (23.84%) and oral cavity (8.95%) [1]. Bronchogenic carcinoma accounts for about one-third of all cancer deaths among males [2]. The trend is such among females as well. This disease is four times more common in males than females. However, due to increased smoking habits, the incidence of this disease is increasing among females [3]. Bronchogenic carcinoma is a disease in the older age group and is rarely found in persons below 40 years of age (<1%). It is extremely uncommon in children [4]. Causative factors include most importantly tobacco smoking and depend on frequency, duration and type of smoking; passive smoking may also cause lung cancer [3]. Other factors are asbestos, arsenic, chromium, etc. A significant portion of patients attends oncologists at such an advanced stage where curative treatment is not possible anymore. Only palliative radiotherapy can be given in most cases by conventional fractionation (200 cGy in daily single fraction as 100 cGy, anterior and 100 cGy, posterior fields, 5 days in a week for 5 weeks) [5, 6]. Despite the increasing use of radical radiotherapy schedules, either alone or in combination with

chemotherapy, the majority of patients who present with either locally advanced or metastatic non-small cell lung cancer still have a poor life expectancy. In such cases where patients have other co-morbidities as well, the sole purpose of treatment is to provide effective relief of sufferings with no expectations of improvement of overall survival. Radiotherapy is delivered in a small number of high dose fractions (360 cGy per day, 180 cGy in the anterior field, 180 cGy in the posterior field, 5 days a week for 2.5 weeks, a total of 4320 cGy) may be as effective as more prolonged schedules without increasing morbidity [7, 8]. Technological developments such as radiation therapy, and the support of most treatment regimens, may enable more potent and effective therapies [9]. Reducing the number of fractions required for palliative care should be of obvious advantage for both individual patients and the use of radiotherapy resources. It is of demand that studies should be conducted to see whether the increasing dose of radiation per day and reducing the number of treatment days cause a reduction in morbidity and benefits the patient financially. This study was done to observe the effects of hypofractionated radiotherapy in NSCLC.

METHODS

This study was carried out in the Department of Radiotherapy, Sylhet MAG Osmani Medical College & Hospital Study design was a prospective observational study. The study period was from July 2020 to June 2021. Participants were selected by selection criteria; already diagnosed and confirmed cases of bronchogenic carcinoma were taken as respondents. The total number of participants was 60; 30 cases were selected for hypofractionated radiotherapy (Intervention group: Arm A) and the remaining 30 cases were taken as control (Control group: Arm B). Written informed consent was taken from the participants. Their history and clinical findings were taken in an approved prescribed form. Each participant was interviewed and their history was documented according to the form. Then local and general clinical examination was done. Relevant investigations were conducted. Histological records were collected and documented. Tumour staging was done according to TNM classification. All patients were treated by a cobalt 60 teletherapy machine. The proposed schedule for the bronchogenic carcinoma patients, as control was 5000 cGy in 25 daily single fractions, (100 cGy anterior fields and 100 cGy posterior fields). This schedule was applied as a conventional fractionation method, e.g., 5 days a week for 5 weeks. For the intervention group, the hypofractionated regime was applied: 4320 cGy in 12 fractions, 360 cGy per fraction; 180 cGy in the anterior field and another 180 cGy in the posterior field, 5 days a week for 2.5weeks.

Symptomatic treatment was done at weekly intervals up to the completion of treatment. Then, the patients were advised to follow up after 2 weeks of completion and then once a month. Chest X-rays were done on every follow-up visit to view the effects of radiation. Every participant has managed accordingly for any adverse reactions and supportive treatment was provided where necessary. Four major complaints which are cough, haemoptysis, chest pain and dyspnoea were considered as parameters of symptoms.

Inclusion Criteria

- Clinically diagnosed and histologically confirmed NSCLC.
- Both males and females.
- Patients aged below 70 years.
- Patients have not been treated before.
- Patients were not suitable for radical surgery.

Exclusion Criteria

- Karnofsky's performance status is below 80.
- Patients with Superior Vena Caval Obstruction.
- Patients with distant metastasis.
- Patients with involvement of phrenic or recurrent laryngeal nerve.
- Patients with signs of CNS involvement

Data Analysis

The study coordinators performed random checks to verify data collection processes. Completed data forms were reviewed, edited, and processed for computer data entry. Frequencies, percentages, and cross-tabulations were used for descriptive analysis. χ 2 test was used to analyze statistical significance. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0. The significance level of 0.05 was considered for all tests.

RESULTS

Among the study population (N=60), Arm A or the intervention group had 30 patients, and the maximum was aged 51-60 years (66.67%). Arm A had 93.33% male patients and Arm B had 86.67% males. The male-female ratio was 6:1 in Arm A and 14:1 in Arm B. In Arm A, most patients were cultivators (50%), followed by businessmen (16.67%), whereas in Arm B, the commonest profession was cultivation (60%) followed by service (16.67%) (Table 1). Figure 1 showed the major symptoms of the patients. Cough was present in all the respondents in both arms. Haemoptysis was present in 18 (60%) of patients in Arm A and 16 (53%) of patients in Arm B. Chest pain was evident in 24 (80%) of patients in arm A and 28 (93%) patients in Arm B. Dyspnoea was found in 26 (86%) respondents in Arm A and 28 (93%) in Arm B. The adverse reactions occurred after therapy in patients of the Intervention group (Arm A). It is evident that nausea occurred in most of the patients, that is 22 (73.33%) followed by vomiting, that is 12 (40%). The

rest of the side effects were less prevalent (Table 2a). The adverse reactions in the Control group (Arm B). It is seen that nausea is the commonest side effect that is 18 patients (60%) suffered from it. Then vomiting was common, that is 10 (33.33%) participants. The other side effects were less frequent (Table 2b). the comparison of responses between the hypofractionated intervention group which is Arm A and a conventional control group which is Arm B. It is seen that, in Arm A, among a total of 30 patients, 24 (80%) respondents had symptoms relieved whereas 6 (20%) of their symptoms were not relieved. In arm B, the majority, which is 23 (76.67%) patients had their symptoms relieved and only 7 (23.33%) had not relieved their symptoms. P value was found to be more than 0.05 which indicates there was no statistically significant difference between the two regimes (Table 3). The comparison of adverse effects between the intervention group and control group. In Arm A, out of 30 cases, 15 (50%) and in Arm B, out of 30, 10 (33.33%) had adverse reactions (Table 4).

The comparison of tumour regression between the intervention arm and control arm. According to Chest X-ray findings, in Arm A, 25 (83.33%) patients had tumours regressed, and 5 (16.67%) had no regression. In Arm B, 22 (73.33%) patients had tumour regressed and the rest, 8 (26.67%) had no regression. P value was found to be more than 0.05 which suggests there was no statistical difference between the two treatment regimens (Table 5).

Table 1: Table showing socio-demographic characteristics of the respondents (n=60)

Characteristics	Arm A (Intervention Group) n=30		Arm B (Control Group) n=30	
	N	%	N	%
Sex				
Male	26	86.67	28	93.33
Female	4	13.33	2	6.67
Male:female ratio	6:1		14:1	
Age				
Maximum respondents	51-60 yrs (20)	66.67	61-70 yrs	60
Range	41-70		41-70	
Occupation				
Cultivators	15	50	18	60
Businessmen	5	16.67	4	13.33
Service holder	4	13.33	5	16.67
Housewife	4	13.33	2	6.62
Teacher	2	6.67	1	3.33

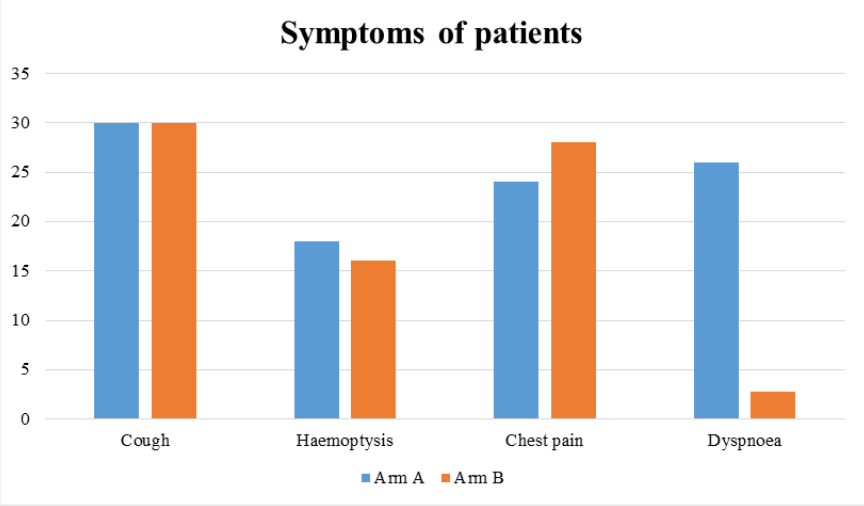

Table 2A: Table showing adverse reactions in Arm A (n=30)

Total cases	Early side effects	No. of patients (n, %)
30	Nausea	22 (73.33%)
	Vomiting	12 (40%)
	Pneumonitis	6 (20%)
	Tracheitis	5 (16.67%)
	Oesophagitis	2 (6.67%)

Table 2b: Table showing adverse reactions in Arm B (n=30)

Total cases	Early side effects	No. of patients (n, %)
30	Nausea	18 (60%)
	Vomiting	10 (33.33%)
	Pneumonitis	5 (16.67%)
	Tracheitis	4 (13.33%)
	Oesophagitis	4 (13.33%)

Table 3: Comparison of responses between Arm A and Arm B (n=60)

Treatment group	Symptoms relieved	Symptoms not relieved	Total
Arm A	24 (80%)	6 (20%)	30
Arm B	23 (76.67%)	7 (23.33%)	30
Total	47	13	60

P value >0.05 (No significant difference between two regimes)

Table 4: Comparison of adverse reactions between Arm A and Arm B (n=60)

Treatment group	No. of cases	Adverse reactions
Arm A	30	15 (50%)
Arm B	30	10 (33.33%)

Table 5: Table showing a comparison of tumor regression (Chest X-ray findings) in Arm A and Arm B

Treatment schedule	Tumor regression	No regression	Total
Arm A	25 (83.33%)	5 (16.67%)	30
Arm B	22 (73.33%)	8 (26.67%)	30
Total	47	13	60

P value >0.05 (No significant difference between two regimes)

DISCUSSION

This prospective study was carried out to determine the effects of hypofractionated radiotherapy and its side effects in advanced-stage bronchogenic carcinoma patients.

Already diagnosed cases of Non-Small Cell Type of bronchogenic carcinoma patients were included in this study and patients were selected as per the inclusion criteria. 30 cases were taken in the intervention group or Arm A and the rest 30 were in the control group or Arm B. In Arm A, the age of the patients ranged from 41-70 years and maximum prevalence was seen above 50 years of age. In a previous study, Van *et al.,* revealed that the age of the patients ranged from 37 to 57 years and maximum prevalence was seen above 40 years of age [10]. It is a disease of those aged above the 50s and is rarely considered in the differential diagnosis of lung lesions in those aged less than 40 years [11]. Males showed greater preponderance over the females giving the ratio of 6:1 in Arm A and 14:1 in Arm B. As per the observation of another study, it is four times commoner in men than in women [12]. Another study had taken 454 participants and the male-female ratio was 4.6:1 [10]. Regarding occupation in this study, bronchogenic carcinoma was more common in cultivators, i.e., 15 (50%) in Arm A and 18 (60%) in Arm B. In this study, most of the patients presented with complaints of cough, chest pain, dyspnoea which is shortness of breath and haemoptysis meaning blood with cough. These four symptoms were taken as a parameter of complaints. Here, in the control group, the cough was present in 30 (100%) cases, chest pain in 24 (80%) cases, dyspnoea in 26 (86%) and haemoptysis in 18 (60%) cases. These presenting features had concordance with the findings of another similar study. In control arm, cough was present in 30 (100%), chest pain in 28 (93%), dyspnoea in 28 (83%) and haemoptysis in 16 (53%) cases [13]. In a hypofractionated schedule, out of 30 patients, haemoptysis was existent in 89% cases, dyspnoea in 77%, and chest pain in 84% and cough in 67% cases. 20 (67%) patients out of 30 got relief from all symptoms during treatment time for which they had come to hospitals. Rest 10 (33%) presented with a cough only. These patients were treated accordingly with antibiotics, steroids, I/V fluids, analgesics, antiemetics etc. Among these 10 (33%) patients, 6 (20%) got relief from cough within 2 weeks after completion of treatment. There was an association between radiation pneumonitis, tracheitis and oesophagitis. In 4 (13.33%) cases there was no symptomatic relief at all. Clinical trials on altered fractionation that is hypofractionation, and advanced bronchogenic carcinoma by A. Timothy Guy's and St. Thomas' NHS Hospital, showed a significant role of hypofractionated radiotherapy in lung cancer [14]. The author's opinion is that "Several randomized clinical trials have now been completed which show that radiotherapy delivered in a small number of high-dose fractions may be as effective as

more protracted schedules without increasing morbidity. Reducing the number of fractions required for palliation will have obvious advantages both for the individual patient and for the use of radiotherapy resources." In a nutshell, if we conclude the treatment schedule, we can comment that hypofractionated radiotherapy in lung cancer can relieve symptoms in 87% of cases within 2 weeks of completion of treatment [14]. Among the control group, the conventional fractionation schedule resulted in relief of all symptoms in about 22 (74%) cases out of 30 patients during treatment time. Rest 8 (26%) cases presented with a persistent cough. These patients needed supportive treatment and 3 (10%) cases got relief from the symptoms finally at the end of the next 2 weeks after completion of treatment. 5 (16.67%) patients were having no symptomatic relief at all. In this comparative study between the two schedules, the P value > 0.05 meaning there is no significant difference between hypofractionation and the conventional method of relieving symptoms. In chest X-rays taken 1 month after, tumour regression was observed in 25 (83.33%) cases in Arm A and 22 (73.33%) cases in Arm B. In another comparative study, it is reflected that there is a correlation between tumour regression and relief of symptoms. P value > 0.05 meaning there is no significant difference between the 2 regimes of treatment. In other words, for tumour regression, a similar result is obtained in both schedules. During hypofractionated radiotherapy, in Arm A, early side effects developed e.g., nausea in 22 (73.33%), vomiting in 12 (40%), radiation pneumonitis in 6 (20%), tracheitis in 5 (16.67%) and oesophagitis in 2 (6.67%) cases among a total of 30 patients. But this subsided quickly as supportive treatment was given in necessary cases. In the control group, treated with conventional radiotherapy, nausea developed in 18 (60%), vomiting in 10 (33.33%), radiation pneumonitis in 5 (16.67%), tracheitis in 4 (13.33%) and oesophagitis in 4 (13.33%) cases out of 30 patients. These adverse effects subsided automatically in some cases and the rest of the cases, supportive treatment were needed.

In a comparative study, it was seen that there is no significant difference between the 2 regimes in symptom relief and tumour regression. Radiation therapy is reasonable and well-tolerated management for patient's weith locally advanced NSCLS [15]. Survival was statistically superior for the patients receiving chemotherapy and radiation vs the two arms of the study [16].

CONCLUSION

Patients can get relief of symptoms for shorter periods by hypofractionation in an advanced stage of bronchogenic carcinoma (Non-Small Cell Type) provided the early side effects are managed properly. If we can start this regime properly in the hospitals, we will be able to treat more patients in speculated time and give financial benefit to the patients. Reducing the number of fractions will have obvious advantages for both individual patients and the use of equipment. Hypofractionation is one of the newer concepts of radiotherapy particularly in Bangladesh. So, further study on this matter should be done with interest.

RECOMMENDATIONS

There is a necessity for setting a screening docket to cover all age groups for early detection and treatment of cases. Furthermore, strategies should be implemented to accelerate government programs. The burden of long-term morbidity due to Bronchogenic Carcinoma should be put to the notice of the concerned authorities. To get robust data, multicenter studies are in great need of policymakers to interpret the demonstrable scenario and to take necessary steps towards mitigating this problem. Further research is also needed to detect the burden of Bronchogenic Carcinoma in an attempt to reduce the disease burden and facilitate the prognosis of such condition.

FUNDING

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CONFLICT OF INTEREST

None declared.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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