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Original research article

A prospective randomized study compared the results of 'Christie Regimen' hypo fractionated palliative radiotherapy and standard palliative radiation for head and neck squamous cell carcinoma

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Abstract

Objective: To check the toxicity and efficacy profile of hypo fractionated palliative irradiation (the "Christie Regimen") and standard palliative radiation in patients with HNSCC (head and neck squamous cell carcinoma).

Methods: This was a prospective randomized study carried out at Department of Radiation Oncology, Kamineni Academy of Medical Sciences and Research Centre, L.B. Nagar, Hyderabad, Telangana, India between June 2021 to May 2022. In two arms, approximately 40 cases of locally advanced Head and Neck malignancies were analyzed.

Results: The loco regional control in Arm A and Arm B was characterized by complete response (CR) (50% and 60%), partial response (PR) (40% and 30%), and static response (SD) (10% and 10%), but this difference was not statistically significant (P = 0.220056). In both limbs, there were more Grade II skin reactions. In Arms A and B, grade III skin reactions to radiation were 10% and 10%, respectively. Additionally, arms A and B had a higher incidence of Grade I and Grade II mucosal reactions. Both groups had grade III mucosal responses to radiation, which is statistically insignificant. Frequent Grade III and Grade II reactions occur in the oesophagus, larynx, and salivary ducts of both groups. The patients were observed for a minimum of nine months. The quality of life of Arm A and Arm B had improved in terms of pain, performance status and weight loss after 9 months.

Conclusion: Thus, it may be stated that, despite the fact that Response rates were not significantly different, QOL improvement favored Christie regimen regimens with acceptable toxicities. The hypo fractionated irradiation regimen required less time overall, and this radiobiological superiority is helpful for facilities like ours where the patient load is significantly higher than the radiation facility's capacity. To confirm the long-term effects of this regime, additional research with extended follow-up will be required.

Keywords: Christie regimen, palliative radiotherapy, squamous cell carcinoma

Introduction

Tumors that form in the area below the base of the skull and in the region of the thoracic inlet are frequently referred to as cancers of the head and neck. These diseases are a group, and although they share some epidemiologic, anatomical, and pathologic characteristics, each disease has its own distinct characteristics. In terms of their prognosis, the type of treatment they require, and their natural history, these demonstrate a great degree of variability. Head and neck cancer is a problem that is of major concern to all oncologists and researchers [1, 2]. This is due to the physical and psychological morbidity that is caused by the disease.

More than 25 percent of all cancers, such as head and neck squamous cell carcinoma (HNSCC), are diagnosed in people living in poor countries like India. More than sixty percent of patients have advanced cancer and do not respond favorably to standard treatments such as radiotherapy and surgery [3, 4].

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Because the disease affects a number of vital tissues, including the spinal cord, salivary glands, mandible, nerves, major blood vessels, and the organs in charge of speaking, swallowing, hearing and respiration, head and neck cancers present a significant treatment challenge. Pain, trouble swallowing, odynophagia, otalgia, hoarseness, coughing, and respiratory distress are among the typical symptoms. There is a chance that side effects and treatment toxicity signs and symptoms might frequently and significantly overlap [5, 6].

The development of consensus guidelines and recommendations for the curative intent management of patients with SCCHN that have progressed to a locoregional stage has become more evidence-based as a result of the availability of data from large prospective randomised controlled trials and meta-analyses [7].

Patients with head and neck cancer have a bad prognosis and are more likely to pass away as a result of uncontrolled locoregional sickness [8]. The majority of cases of head and neck cancer are discovered at stage 6, an advanced and incurable stage. Administration that is more advanced locally Because of ongoing research, a plethora of literature, sizeable randomised control trials, and meta-analyses that support evidence-based recommendations, head and neck squamous cell cancer treatment has evolved greatly over the course of time, with the objective of curing the illness. However, a sizeable portion of patients who have head and neck squamous cell carcinoma (HNSCC) are not candidates for aggressive radical surgery or chemotherapy radiation (CRT) as treatments. This could be the outcome of a far-reaching metastatic disease, a very advanced loco regional disease, major co-morbidities, low performance status, or any combination of these things. Patients with this illness have not responded well to rigorous radiation protocols or intense multimodal therapy up until now. This group of patients still needs some sort of therapy in order to control their locoregional disease and treat their bothersome symptoms [9, 10].

It is well knowledge that palliative radiation therapy, also known as PRT, makes a major contribution to cancer care around the world by successfully reducing symptoms and enhancing quality of life (QOL) in patients afflicted with advanced and terminal cancers. However, PRT for malignancies of the head and neck has not received a great deal of attention [11, 12].

Measuring outcomes in this population is difficult due to low rates of drug adherence, minimal enrollment in prospective studies, and high attrition rates. In addition, the lack of resources in undeveloped nations, particularly in terms of staff and radiation equipment, makes it more difficult to provide prompt PRT treatment to patients who have a reduced life expectancy. An expert panel had previously reached the judgment that there is not enough data to determine the frequency, severity, or duration of symptomatic improvement as a result of PRT for head and neck cancer. This was the prior finding of the panel. There aren't many recommendations for the optimal palliative regimens for these patients in the existing body of research because there isn't enough data on their toxicity, duration, dose, and fractionation, not to mention the concerns that are related to QOL [13, 14].

Material and Methods

This was a prospective randomized study carried out at Department of Radiation Oncology, Kamineni Academy of Medical Sciences and Research Centre, L.B. Nagar, Hyderabad, Telangana, India between June 2021 to May 2022. In two arms, approximately 40 cases of locally advanced Head and Neck malignancies were analyzed.

Inclusion criteria

- Age >65 years; Squamous cell carcinoma of the head and neck confirmed by biopsy; and Stage IV locally advanced tumours that are inoperable.
- Fungating tumours, poor performance status, distant metastases, significant comorbidities, and/or a combination of one or more of the aforementioned criteria.

Exclusion criteria

- Histopathology of Non-Squamous Tumours.
- Nasopharyngeal, nasal, and paranasal sinus tumours.

Prepare the patient

- Due to research showing that smoking during radiation has a negative impact on treatment outcomes, all patients were urged to stop smoking and drinking.
- Suggested to have a soft diet to prevent mucosal damage.
- Regular use of soda water to gargle the mouth.
- Dental care.
- Maintaining good oral hygiene.

Treatment

- All the patients were treated as in patients.

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Chemotherapy

The patients were treated for palliation, with the goals of ideal palliation including optimal symptomatic relief, tumour response, low toxicity, with possibly minimal intervention (typically a single modality), and minimization of the time spent in a healthcare facility or treatment centre. Chemotherapy was not a consideration for the patients who were receiving this palliative radiotherapy regimen protocol as: The majority of patients who received this palliative care were in their twilight years or older. The majority of patients who went through with this palliative operation had both a general state of poor health as well as multiple co-existing medical disorders.

In order to get permission from the institution's ethical committee before beginning the study, we first got authorization from them.

The regions of discomfort, appearance, movement, leisure, chewing, speech, shoulder, taste, saliva, mood, and anxiety are the ones that are of concern. In addition, the scores for the physical domain, the social domain, the health-related quality of life over the preceding week, and the total quality of life were computed. It was determined that translating the questions into the patient's native tongue would make them easier to understand. The quality of life was assessed both at the beginning of therapy and again one month after the treatment had been completed as per the treatment plan [15-17].

The outcomes of the study were recorded, and they included information regarding effective completion of prescribed treatment, treatment interruptions, toxicity, local control rates, and illness state at the time of the most recent follow-up in each group.

Results

Study based on population

The procedure included the recruitment of 40 patients who met the eligibility requirements.

They were randomly assigned as Arm A- 20 patients using the basic randomization approach. 20 patients in Arm B.

Arm A (Control arm): 30 Gy in 10#, 300cGy 2 weeks/once day

Arm B (Study arm): 50 Gy in 16#, 3.125cGy/#/3.1 weeks/once day

Table 1: Distribution of patient Age wise

Age (In years)	A Arm	B Arm
51-60	4 (20%)	4(20%)
61-70	12(60%)	14(70%)
>71	4 (20%)	2(10%)

Table 2: Distribution of patient Sex wise

Sex	A Arm	B Arm
Male	16(80%)	18(90%)
Female	4(20%)	2(10%)

Table 3: Distribution of patient Side wise

Site	A Arm	B Arm
Oral cavity	10(50%)	14(70%)
Oropharynx	4 (20%)	4 (20%)
Hypo pharynx	3 (15%)	1 (10%)
Larynx	3 (15%)	1 (10%)

Table 4: Distribution of patient based on Smoking

Smoking	A Arm	B Arm
Yes	16(80%)	18(90%)
No	4 (20%)	2 (10%)

Table 5: Distribution of patient based on Tobacco chewing

Tobacco	A Arm	B Arm
Yes	16(80%)	18(90%)
No	4 (20%)	2(10%)

Table 6: Distribution of patient based on Tumor Grade

Grade	A Arm	B Arm
Strong Differentiated	1 (5%)	2 (10%)
Moderate Differentiated	16 (80%)	14 (70%)
Poor Differentiated	2 (10%)	2 (10%)
Non differentiated	1 (5%)	2 (10%)

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Table 7: Distribution of patient Stage wise

Stage	Arm A	Arm B
III	4 (20%)	6 (20%)
IV	16 (80%)	24 (80%)

Analysis: At the conclusion of the study, toxicities, QOL, and response were evaluated.

Table 8: Complete/Overall response rates

	Arm A	Arm B	P-value
Complete Response (CR)	10 (50%)	12(60%)	
Partial Response (PR)	08 (40%)	06(30%)	
Static Disease (SD)	02(10%)	02 (10%)	
			0.220056

Following completion of the duration of treatment, the loco regional controls in Arm A and Arm B showed complete responses (CR) of 50% and 60%, partial responses (PR) of 40% and 30%, and static responses (SD) of 10% and 10%, however this was not statistically significant (P = 0.220056).

More Grade II skin reactions were observed in both arms, with the percentage of Grade II reactions being higher in Arm A than in Arm B. In Arms A and B, the incidence of skin reactions caused by grade III radiation was 10% and 10%, respectively. In addition, there were a greater number of Grade I and Grade II mucosal reactions in Arms A and B in comparison to Arms B. The incidence of grade III radiation mucosal reactions was the same in both groups (10%), which is statistically insignificant. The oesophagus, larynx, and salivary glands are common sites for both Grade III and Grade II reactions in both populations.

The patients were observed for duration of at least 6-9 months. At the end of the first half of the study, the quality of life in Arms A and B had improved by 40% and 50% respectively in terms of performance status, 40% and 50% respectively in terms of discomfort, and 10% and 10% respectively in terms of weight loss.

EORTC H&N35 QoL questionnaires were given to patients who were seen for follow-up at 9 months in order to do a retrospective evaluation of their quality of life (QoL). The questionnaires were only completed and returned by 20 patients in Arm A and 20 patients in Arm B, respectively. The symptoms with the highest H&N-35 module scores in this group of patients included sticky saliva and dry mouth. The symptom that scored second highest was trouble swallowing. The Christie ratings for Arm B have significantly improved as compared to Arm A in the areas of pain, appearance, exercise, recreation, swallowing, mood, and the social domain. Saliva production and taste ratings have both dramatically decreased when compared to Arm A.

Discussion

In this study, two different palliative radiotherapy treatment plans for locally advanced head and neck cancers (LAHNC) are compared and contrasted. This is a study that is prospective and randomised. Surgery without adjuvant radiation therapy is associated with very poor odds of success in curing LAHNC. The addition of adjuvant radiotherapy to surgery alone resulted in an increase in cancer-specific survival and overall survival rates of approximately 10%. Due to the fact that chemotherapy cannot be curative on its own, it is commonly coupled with radiation therapy. Whether or not radiotherapy is used with chemotherapy, the primary mode of treatment for LAHNC is still considered to be radiotherapy. In spite of developments in therapeutic approaches for the management of LAHNC, local failure rates are still as high as 40-50% due to the advanced state of the disease when it is presented for treatment. For the palliative care of LAHNC, there is no standard dose fractionation schedule of radiation that can be used. A number of authors have tried out various treatment plans with regard to both the overall dose and the number of irradiation fractions in an effort to reduce the symptoms of LAHNC [18, 19].

Even if the therapy is palliative and only aims to control the patient's locoregional disease and diminish their painful symptoms, patients who have been deemed inoperable and unfit to handle the burden of chemotherapy radiotherapy (ChemoRT) still need to get care. This is true even if the therapy is only designed to regulate the patient's locoregional disease. The ideal palliative radiotherapy schedule is one that would result in a worthwhile regression of the tumour and local symptoms over the course of a condensed overall treatment time with the least amount of toxicity, despite the fact that there is a paucity of information regarding the best hypo fractionated palliative regimen for incurable HNSCC. This is because there is a paucity of information regarding the best hypo fractionated palliative regimen for incurable HNSCC. The treatment is concluded before the rate of repopulation becomes a significant radiobiological influence. Because this population of patients is typically older, and because they frequently have a low performance status in addition to major co-morbidities, it is virtually essential to keep the OTT as brief as is practically possible. Second, the decrease in the total number of fractions

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makes it possible to make better use of the available resources, which in turn helps to reduce the likelihood that other patients may have to endure severely protracted wait periods [20, 21].

From a radiobiological, budgetary, and logistical point of view, a hypo fractionated schedule would be the more optimal option to go with. When compared to conventional radiotherapy, hypo fractionated radiation employs a smaller number of higher-dose fractions. In most cases, the time span in its whole is shorter. These regimens, when used in a therapeutic setting, have more severe long-term effects than the more conventional method of fractionation. The early effects are bearable if the treatment volumes are kept to a minimum; additionally, the tolerance can be raised by finishing the therapy sooner. Patients with a low performance status, the primary treatment goals of which are symptom palliation and minimum side effects, are the best candidates for the kinds of regimens that fall under this category. The prognosis for these people does not appear to be good at all. Hypo fractionated palliative radiation has been studied in several phase I and phase II clinical trials for advanced SCC of the head and neck. The QUAD SHOT27 was created with the intention of delivering brief but powerful radiation doses that were much below the level at which mucositis would be brought on. The 14 Gy is given through a four-part delivery over the course of two days. Responders may undergo this therapy up to a total dose of 42 Gy [22, 23].

Total 10 portions of Gy in total. Objective responses were reached in 53% of cases, and 44% of patients with highly advanced disease and low performance status had improvements in their quality of life. Objective responses were achieved in 80% of cases. Other treatments for palliative purposes include the one that Paris utilized, in which she administered 3.7 Gy twice a day for two days, and then continued to administer it once a month for three months. 80% of cases resulted in responses, despite the fact that 40% of students did not complete the entire course. Patients received treatment on a hypo fractionated schedule two times per week, with each fraction being 6 Gy, for a total dosage ranging from 30–36 Gy. In terms of the effects on tumours and mucosa, this is similar to administering 40 Gy in 2 Gy increments, and it is well tolerated in terms of the acute reactions it causes. It is difficult to compare these techniques with one another because of the many different advanced SCCs that can affect the head and neck, as well as the difficulties involved in determining a patient's quality of life rather than merely whether or not they will live. During World War II, there were not many RT facilities available, thus the Medical Hospital in Manchester developed a regimen of RT that lasted for three weeks [24]. In terms of local control and toxicity, it was found that the results were the same as those obtained with the typical regimens that were used throughout the earlier treatment periods. As a direct consequence of this, Christie Hospital and a number of other cancer institutions in the United Kingdom decided to adopt this programme as their standard RT regimen for early-stage laryngeal cancer. According to a large number of randomized and uncontrolled trials, there is also no difference in terms of the ability to maintain local control between standard and hypo fractionated regimens. It is unexpected, considering the relatively short OTT and the significant percentage dose, that several of these regimens exhibited late normal tissue reactions that were less severe than was predicted. The clinical trial titled "Three weeks RT for T1 glottis cancer: The Government Hospital Experience" looked at a total of 200 patients (100 from each site) who had definitive radiation treatment for T1 glottic invasive squamous cell carcinoma between the years 1989 and 1997. The median age was 65 years old. All of the patients got once-daily fractionation five days a week for a total tumour dose that ranged from 50 to 52.5 Gy in a total of 16 fractions, and the fraction size ranged from 312 to 328 cGy. The follow-up process took an average of five years and ten months to complete. This study has two different goals in mind. The impact of this schedule on the quality of life (QoL) of patients who are still alive one year after the completion of therapy, in addition to the response rates, toxicity, and overall survival of patients who were treated. Oropharyngeal cancer was present in 20% of patients, male patients made up 20% of the total, and stage IV illness affected 80% of patients. A total response rate of 50% was achieved, with 40% of patients exhibiting full responses and 20% of patients exhibiting partial responses; 10% of patients exhibited stable disease and 20% of patients saw progression of their condition during or shortly after the conclusion of treatment. The median amount of time a patient survived after RT was 18 months, and 40 of them, or roughly 40 percent, made it to the one-year mark. At one year and three years, respectively, the actuarial rates for disease-free survival, overall survival, and locoregional control were 40 percent, 22 percent, and 40 percent, respectively. Acute cutaneous toxicity of grade 2 was observed in 40% of patients, while acute mucosal toxicity of grade 2 was observed in 50% of patients. It was claimed that 10% of patients had experienced significant late toxicity. Patients who had survived 1 year after RT and had their charts reviewed retrospectively showed that 50% of them had gained weight, 50% had experienced pain alleviation, 40% had improved performance status and 20% were still dependent on feeding tubes [25].

According to the results of our research [26], the Christie protocol performed significantly better than the typical palliative RT schedule in terms of response rates and quality of life.

Conclusion

Despite the fact that there was no discernible difference in response rates, one would reason that the Christie regimen schedules with manageable toxicities were preferable in terms of improving quality of

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life. This is despite the fact that there was no difference in response rates between the two. This radiobiological advantage is beneficial for facilities such as our hospital, where the number of patients is greater than the capacity of the radiation treatment facilities that are now available. This radiobiological advantage was helpful, since it resulted in a reduction in the overall amount of time needed for the hypo fractionated radiation regimen. To confirm the long-term effects of this regimen, additional research will be required, along with a follow-up period that is significantly longer than what was initially envisioned.

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Conflict of interest: Nil.

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