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Original Article

Oncology Section

Comparison of Conventional Palliative Radiotherapy Fractionation Schedule with Quad Shot Regimen in Locally Advanced Head and Neck Cancer Patients: A Randomised Clinical Trial

SRISHTI PURAIYA[1], JITENDRA KUMAR[2], ARUN KUMAR YADAV[3], AFROZ KAHKASHAN ZAIDI[4], RAJENDRA KUMAR[5], GEETA SINGH[6]

ABSTRACT

Introduction: Head and Neck Cancer (HNC) accounts for 14.3% of all cancers in India and 4.8% of all cancers worldwide. In India, the most common sites are the lip and oral cavity (>80%), which are more prevalent in men than in women. Histologically, most cases are Squamous Cell Carcinomas (SCC). The majority of patients present with locally advanced stages, where surgery and definitive chemoradiation therapy are not possible and palliative Radiotherapy (RT) is considered a treatment option for better symptomatic relief and improved Quality of Life (QoL). The Quad Shot (QS) palliative regimen has shortened treatment time, reduced toxicity and increased compliance.

Aim: To compare the QS regimen administered over two consecutive days versus the Conventional Palliative Regimen in the treatment of locally advanced HNC, in terms of treatment response, acute toxicities and QoL.

Materials and Methods: In this prospective randomised clinical trial conducted from May 2023 to July 2024 in the Department of Radiation Oncology at King George's Medical University (KGMU), Lucknow, Uttar Pradesh, India, patients with biopsy-proven locally advanced carcinoma of the head and neck were recruited, with a sample size of 50 in each of the study Group B and control Group A arms. Patients in the control arm received 30 Gray (Gy) in 10 fractions, 5 fractions per week over two weeks (Conventional palliative arm). In the study arm, patients received 14 Gy in 4 fractions delivered in two daily sessions, six to eight hours apart, for two consecutive days over three cycles (QS arm). The Response Evaluation Criteria in Solid Tumours (RECIST) Criteria 1.1 was used to assess the tumour response objectively three months post-RT. Health-related QoL was assessed using questionnaires developed by the European Organisation for Research and Treatment of Cancer (EORTC), specifically the EORTC Quality of Life Questionnaire (QLQ). Continuous data were compared using the t-test for nominal data and the Mann-Whitney U test was used otherwise.

Results: The mean age was 39.66±12.05 years in Group A and 42.76±11.65 years in Group B. The QS and conventional palliative arms each had 47 and 49 patients recruited, respectively. The QS arm exhibited fewer instances of skin toxicity, with 25 (53.2%) experiencing Grade I and 7 (14.9%) experiencing Grade II toxicity, compared to the conventional palliative arm, where 30 (61.2%) had Grade I and 12 (24.5%) had Grade II toxicity. Mucositis in the QS arm included 22 (46.9%) cases, with 14 (29.7%) classified as Grade I and Grade II, whereas the conventional arm had 12 (24.5%) Grade I cases, 29 (59.5%) Grade II cases and 3 (6.1%) Grade III cases. The treatment response, in terms of partial and stable disease combined, was observed in 61.2% of the conventional arm compared to 78.7% in the QS arm. QoL was reported to be better in the QS regimen post-treatment.

Conclusion: Given the total number of patients recruited, the QS arm, with its shorter treatment time, demonstrated better benefits in terms of reduced toxicities and improved treatment response, as well as enhanced QoL compared to the conventional palliative arm.

Keywords: Hypofractionation, Malignancy, Oral Cavity, Oropharynx, Palliation or Palliative Radiotherapy

INTRODUCTION

A collection of physiologically related tumours that begin in the upper aerodigestive tract is collectively referred to as carcinomas of the head and neck. With an expected 888,000 new cases and 453,000 deaths in 2018, Head and Neck Cancers (HNC) rank seventh globally in terms of cancer incidence (the fifth most frequent disease in males and the twelfth most prevalent in females) [1]. Tumours of the nasopharynx, oropharynx, hypopharynx and larynx are all included in Head and Neck Squamous Cell Carcinoma (HNSCC) [2-4].

The Radiation Therapy Oncology Group (RTOG) 8502 was the first to investigate "QS," a cyclical hypofractionated palliative radiation therapy regimen, for advanced pelvic cancers in a prospective manner. This treatment plan included four twice-daily fractions of 14.0 Gy (3.5 Gy each) spread over two days, with cycles administered every three weeks, usually for a maximum of three cycles. Subsequently, QS was investigated for HNC; the findings indicated that, without causing appreciable toxicity, it may be able to relieve symptoms and aid in local management. With a median duration of fewer than six months for both local control and overall survival, QS radiation alone may not be adequate for long-term disease management [5].

Palliative treatment aims to reduce cancer-related symptoms while causing the fewest side-effects and possible toxicities [6]. Additionally, shorter palliative RT regimens are well-suited for settings in developing countries due to resource limitations, lengthy RT waiting lists and the low socioeconomic status of patients [7].

To strike a balance between speedy and effective palliation and limiting treatment-related toxicity, hypofractionated RT (high-dose per fraction) may be pursued in this group of patients. Perhaps

this is the first study of its kind where these regimens have been compared. Therefore, the present study aimed to compare the outcomes of a conventional palliative RT fractionation schedule with those of a QS regimen in patients with locally advanced HNC.

The primary endpoint of the study was to compare and evaluate the efficacy, tolerability and toxicity of two schedules of palliative RT; 30 Gray in 10 fractions over two weeks versus a QS regimen (14 Gray in 4 fractions administered twice daily, 6-8 hours apart, for two consecutive days), with three cycles each 3-4 weeks apart, in patients with locally advanced HNC. The secondary endpoint was to assess the quality of life (QoL) of patients with locally advanced HNC.

MATERIALS AND METHODS

The present prospective randomised clinical trial was conducted from May 2023 to July 2024 in the Department of Radiation Oncology at KGMU, Lucknow, Uttar Pradesh, India and was approved by the Institutional Ethics Board (Registration No.: ECR/262/Inst/UP/2013/Rr-19, approval reference code: XVI-PGTSC-IIA/P27, on 19/06/2023). The study was conducted according to the international guidelines for Good Clinical Practice and conformed to the ethical standards set by the Declaration of Helsinki. Written informed consent was obtained from all eligible patients before enrollment in the study.

Inclusion and Exclusion criteria: Eligible patients had previously untreated, inoperable squamous cell carcinoma (SCC) of the head and neck region with clinical stages IV and III according to the American Joint Committee on Cancer (AJCC 8th edition) [8], an Eastern Cooperative Oncology Group (ECOG) performance score [9] of two or more and fit for receiving RT. The exclusion criteria included distant metastases, a history of prior malignancy and prior RT to the head and neck.

Sample size calculation: The sample size for the proposed study was calculated in consultation with a statistician at the study Institute. The sample size was calculated by following formula:

$$n = \frac{Z^2 \times P \times (1-P)}{(e)^2}$$

Where, n= the required sample size $Z^2=(1.96)^2$ for 95% confidence

P= prevalence (based on hospital records)

e= maximum tolerable error

$$= \frac{(1.96)^2 \times 0.0215 \times 1-0.0215}{(0.05)^2}$$

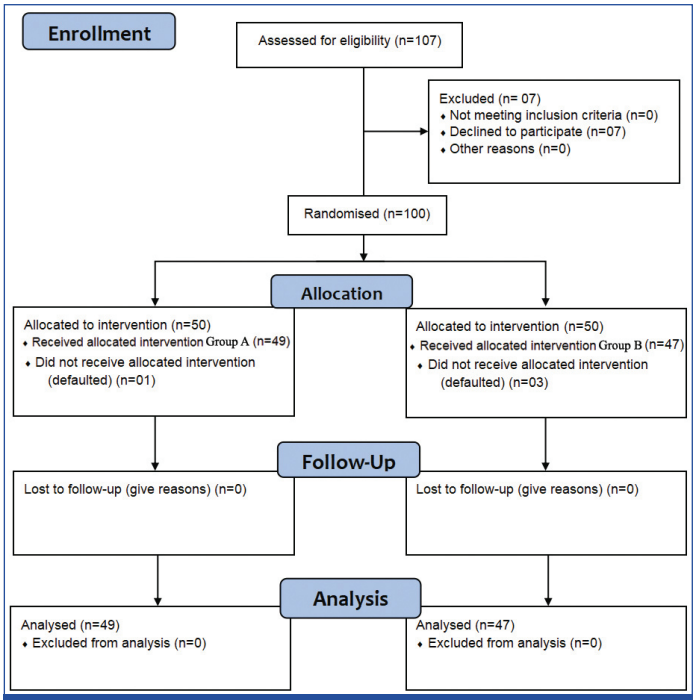
$$= \frac{(1.96)^2 \times 0.0215 \times 0.9785}{(0.05)^2} = 32.327$$

So, minimum sample size for the study was 33 per arm. Calculating for a 10% dropout rate, approximately 37 patients per arm was required.

Study Procedure

Patients were enrolled consecutively and treatment decisions were made at the Multidisciplinary Team (MDT) meeting. Surgical inoperability was defined in consultation with a surgical oncologist when complete oncological clearance with negative margins was not possible due to the extent of the primary disease or co-existing nodal disease in the neck. The absolute signs of inoperability included adherence to the prevertebral fascia, involvement of the skull base and encasement of the internal carotid artery [10].

Treatment arms and randomisation: Patients were randomly allocated to two groups using a simple 1:1 randomisation based on their seriality. Patients were informed in detail about the treatment plan at the time of allocation and provided written consent. The conventional palliative arm comprised 30 Gy delivered in 10 daily fractions over two weeks (Group A) [11] and a QS regimen of 14 Gy in 4 fractions administered twice daily, 6-8 hours apart, for two consecutive days, repeated for three cycles with a three-week gap (Group B) [Table/Fig-1] [12].



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) 2010 flow diagram [12].

Treatment procedure: Patients were evaluated at baseline during a mandatory MDT meeting. For treatment planning, patients were immobilised in the supine position using custom-made thermoplastic shells as headrests. RT was delivered using a Telecobalt unit, employing parallel-opposed bilateral or, rarely, unilateral fields to target the primary and involved nodal regions with adequate margins to account for set-up errors, internal motion and penumbra. The prescription point of the dose was considered the midpoint of the lateral separation for a bilaterally paired field. Patient treatment was performed daily from Monday to Friday.

The RECIST Criteria 1.1 were used to assess tumour response objectively three months post-RT [13]. Thereafter, the patient was maintained on metronomic therapy with a weekly injection of methotrexate (15 mg/m^2), Tab Gefitinib 250 mg once daily and Tab Celecoxib 200 mg twice daily until the patient developed intolerable side-effects or further progression of the disease. Acute toxicities, in terms of skin and mucosal reactions, were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, as recommended by the National Cancer Institute (NCI), USA [14].

Quality of Life (QoL) assessment: Health-related QoL was assessed using questionnaires developed by the EORTC, specifically the EORTC QLQ. The EORTC QLQ-C30 reports on global health status, functional status (including physical, role, emotional, cognitive and social dimensions) and symptom scores. The EORTC QLQ-C30 consists of 30 questions, including five functional scales: physical functioning, role functioning, emotional functioning, cognitive functioning and social functioning; three symptom scales: fatigue, nausea and vomiting and pain; one global health status scale; five single items: dyspnoea, insomnia, appetite loss, constipation, diarrhoea; and one financial difficulties scale.

It uses a four-point response format for most questions and a seven-point format for the global health status scale. Scores are linearly transformed to a range of 0 to 100. Higher scores on the functioning and global health status scales indicate better health, while higher scores on the symptom scales indicate more symptoms. However, some authors may reverse the symptom scores for consistency. The questionnaire has been translated and validated in over 120 languages and used in more than 5,000 studies worldwide [15].

The QLQ-H&N35 module assesses the symptom scores of patients with head and neck cancer (HNC). The EORTC QLQ-H&N35

questionnaire consists of 35 questions and is used to measure QoL in patients with HNC. The QLQ-H&N35 incorporates seven multi-item scales that assess swallowing, pain, speech, senses (taste and smell), social eating, social contact and sexuality. In addition, it includes 11 single items that assess problems with teeth, opening the mouth, dry mouth, sticky saliva, coughing, feeling ill, use of painkillers, nutritional supplements, or a feeding tube, as well as weight loss and weight gain.

The questionnaire comprises 35 questions, including 18 symptom-based questions, 12 function-related questions and 5 questions about pain, supplemental feeding and weight. The function scales are scored on a four-point Likert scale from 1 (not at all) to 4 (very much), while the pain, supplemental feeding and weight questions are scored on a dichotomous scale of 0 (no) and 1 (yes). The scales score from 0 to 100, with 100 indicating perfect QoL for function scales and a heavy burden for symptom scales.

The QLQ-H&N35 is a validated and reliable questionnaire that has demonstrated acceptable reliability and construct validity. It is used along with the core questionnaire EORTC QLQ-C30 and is one of the standard instruments for measuring QoL in HNC patients. The EORTC QLQ-C30 version 3.0 and QLQ-H&N35 were administered to the patient at baseline and at the first follow-up visit, which is three months post RT [16].

STATISTICAL ANALYSIS

Analysis was performed according to the intention-to-treat analysis. Categorical variables were compared using Fisher's-exact test (for cell counts less than five) or the Chi-square test for proportions. Continuous data were compared using the t-test for nominal data and the Mann-Whitney U test otherwise. All tests were two-sided, with a significance level set at a p-value of 0.05. Data were analysed using IBM Statistical Package for the Social Sciences (SPSS) Statistics software version 28.0 for Linux (IBM Inc., New York, NY) and R software (www.r-project.org).

RESULTS

A total of 100 patients were included in the study. The demographic profiles indicated that the mean age was 39.66±12.05 years in Group A and 42.76±11.65 years in Group B. Male predominance was evident in both groups, with 34 males (68%) in Group A and 38 males (76%) in Group B. The most common site was the oral cavity, comprising 34 patients (68%) in Group A and 32 patients (64%) in Group B [Table/Fig-2]. Both groups tolerated the treatment well; however, one patient defaulted to conventional palliative care in Group A, whereas two patients defaulted and one died during treatment due to a non oncological cause in the QS arm (Group B), as depicted in [Table/Fig-3]. A total of 49 patients (98%) completed treatment in two weeks in Group A, while 47 patients (94%) finished their treatment in two days in Group B, with each cycle repeated after three weeks for a total of three cycles.

Age group (years)	Group		χ^2 value/ t-value	p-value
	Group-A (n=50)	Group-B (n=50)		
21-30	15 (30.0%)	10 (20.0%)	1.515	0.679
31-40	13 (26.0%)	13 (26.0%)		
41-50	10 (20.0%)	12 (24.0%)		
>50	12 (24.0%)	15 (30.0%)		
Mean age±SD	39.66±12.05	42.76±11.65	-1.308	0.194
	Group			
Gender	Group-A (n=50)	Group-B (n=50)	X^2 value	p-value
Male	34 (68.0%)	38 (76.0%)	0.749	0.504
Female	16 (32.0%)	12 (24.0%)		
	Group			
Stage	Group-A (n=50)	Group-B (n=50)	X^2 value	p-value
3	0 (0.0%)	2 (4.0%)	2.041	0.495
4	50 (100.0%)	48 (96.0%)		
	Group			
ECOG	Group-A (n=50)	Group-B (n=50)	X^2 value	p-value
2	27 (54.0%)	25 (50.0%)	0.160	0.689
3	23 (46.0%)	25 (50.0%)		
	Group			
Involved sites	Group-A (n=50)	Group-B (n=50)	X^2 value	p-value
Oral cavity	34 (68.0%)	32 (64.0%)	0.662	0.882
Oropharynx	8 (16.0%)	9 (18.0%)		
Hypopharynx	4 (8.0%)	6 (12.0%)		
Larynx	4 (8.0%)	3 (6.0%)		

[Table/Fig-2]: Demographic details of the study participants.

Treatment completed	Group	
	Group A (n=50)	Group B (n=50)
Yes	49 (98.0%)	47 (94.0%)
No	1 (2.0%)	3 (6.0%)

[Table/Fig-3]: Treatment completion details of participants.

Patients in Group A achieved a Biologically Effective Dose (BED) of 39 Gy to the tumour, while those in Group B received a cumulative dose of 56.7 Gy to the tumour over three cycles. Grade III mucosal toxicity was observed in 3 patients (6.1%) in Group B, with no patients experiencing this toxicity in Group A. Similarly, 12 patients (24.5%) in Group A and 7 patients (14.9%) in Group B experienced Grade 1 skin toxicity. During treatment, no Grade IV mucosal or Grade 3 or 4 skin toxicities were observed in either group. None of the patients died from acute toxicity. Significantly less toxicity was observed in Group B compared to Group A (p=0.004) [Table/Fig-4].

Toxicities	Group		χ^2 value	p-value
Skin toxicity grade	Group-A (n=49)	Group-B (n=47)		
0	7 (14.3%)	15 (31.9%)	4.640	0.098
1	30 (61.2%)	25 (53.2%)		
2	12 (24.5%)	7 (14.9%)		
	Group			
Mucositis grade	Group-A (n=49)	Group-B (n=47)	X^2 value	p-value
0	5 (10.2%)	11 (23.4%)	12.388	0.004
1	12 (24.5%)	22 (46.9%)		
2	29 (59.2%)	14 (29.7%)		
3	3 (6.1%)	0 (0.0%)		

[Table/Fig-4]: Participants' toxicities post-RT.

One month after treatment completion, an objective response assessment was performed on both the tumour and the node. There was no complete response in either group. However, after three months of follow-up, 20 patients (40.8%) in Group A and 22 patients (46.8%) in Group B achieved a Partial Response (PR). Stable disease was observed in 10 patients (20.4%) in Group A and 15 patients (31.9%) in Group B, while 19 patients (38.8%) in Group A and 10 patients (21.3%) in Group B had progressive disease [Table/Fig-5].

Response	Group		χ^2 value	p-value
	Group-A (n=49)	Group-B (n=47)		
Partial Response (PR)	20 (40.8%)	22 (46.8%)	0.146	0.146
Stable disease	10 (20.4%)	15 (31.9%)		
Progressive disease	19 (38.8%)	10 (21.3%)		

[Table/Fig-5]: Participants' objective responses three months post-RT.

Using the EORTC QLQ-C30 version 3.0 and QLQ-H&N35, the mean±standard deviation before and after three months of

treatment completion in both arms were assessed. On intragroup comparison, no significant change was observed in any of the QoL subgroups [Table/Fig-6]. However, significant improvements in pain, swallowing, coughing, sticky saliva, weight gain and mouth opening were noted during the inter group comparison of QoL, with patients in Group B showing better QoL after RT [Table/Fig-7].

Parameters	Group-A (30 Gy/10#) (n=49)			Group-B {Quad Shot (QS)} (n=47)		
	Before RT	After RT	p-value	Before RT	After RT	p-value
Global health scale/QOL						
Global health status/QoL (revised)	41.26±22.96	43.89±24.52	0.75	40.63±19.29	42.86±20.65	0.79
Functional scale						
Physical functioning (revised)	55.04±12.30	58.45±13.44	0.57	53.63±14.87	56.28±15.64	0.49
Role functioning (revised)	48.25±9.76	49.10±15.16	0.51	47.14±10.30	47.30±14.144	0.79
Emotional functioning	64.28±19.33	61.89±15.67	0.49	66.61±18.10	61.20±20.38	0.81
Cognitive functioning	58.37±15.13	60.24±12.35	0.81	59.39±13.69	60.16±11.17	0.89
Social functioning	71.74±16.39	74.52±15.56	0.57	70.43±18.41	72.02±17.72	0.35
Symptom scale/items HN30						
Fatigue	70.74±15.58	72.78±18.87	0.67	72.98±22.89	74.06±17.31	0.77
Nausea and vomiting	28.09±5.43	27.28±7.35	0.11	26.37±7.90	27.86±9.45	0.79
Pain general	80.15±30.88	68.02±18.77	0.63	78.57±27.48	70.10±23.37	0.77
Dyspnoea	17.13±4.74	17.74±4.98	0.29	18.08±4.41	17.22±4.03	0.43
Insomnia	41.78±8.67	41.78±9.50	0.19	49.20±6.62	44.04±8.48	0.31
Appetite loss	66.89±9.34	61.65±12.84	0.77	67.39±10.65	64.90±10.32	0.15
Constipation	26.35±5.67	27.80±7.36	0.27	27.63±7.22	28.16±8.80	0.91
Diarrheoa	16.72±4.33	17.69±5.48	0.04	14.26±4.90	16.12±6.10	0.06
Financial difficulties	54.17±20.77	63.52±20.35	0.57	56.49±22.50	76.96±17.53	0.49
Symptoms HN35						
Pain (head and neck)	58.24±15.72	47.50±13.74	0.13	57.67±11.88	50.20±10.76	0.43
Swallowing	36.41±6.83	34.28±7.32	0.81	38.16±6.37	36.88±6.80	0.77
Teeth	76.08±22.38	69.39±12.33	0.11	73.32±14.58	71.04±15.78	0.17
Opening mouth	53.80±11.32	50.74±10.74	0.19	56.61±8.47	55.12±9.72	0.63
Dry mouth	18.15±7.43	16.13±10.38	0.31	20.04±10.68	18.59±8.98	0.21
Sticky saliva	14.19±5.30	16.96±6.09	0.71	16.80±6.61	17.12±7.03	0.41
Senses	20.80±5.12	23.65±7.33	0.91	19.18±4.73	21.12±6.40	0.71
Coughing	20.11±3.64	17.24±4.58	0.31	27.41±6.07	26.10±7.38	0.17
Felt ill	64.67±17.33	60.33±19.52	0.81	63.77±23.45	60.18±20.87	0.79
Speech	32.82±7.11	35.80±12.15	0.43	36.26±9.92	37.24±10.33	0.31
Social eating	47.37±10.53	44.85±13.50	0.81	48.31±12.83	46.29±10.49	0.57
Social contact	30.67±6.98	27.28±8.24	0.17	32.98±8.30	30.57±10.43	0.07
Sexuality	17.45±4.52	15.63±4.02	0.13	16.02±4.33	15.08±3.87	0.21
Pain killers	80.43±16.40	73.91±18.46	0.33	85.71±13.30	80.61±15.70	0.06
Nutritional supplements	89.13±22.26	94.56±23.67	0.15	91.80±25.77	92.86±20.55	0.17
Feeding tube	40.22±8.34	43.48±12.57	0.11	42.86±7.20	43.88±10.54	0.47
Weight loss	55.43±13.72	52.17±17.20	0.87	57.14±16.50	55.10±20.43	0.45
Weight gain	8.69±2.10	9.78±3.34	0.19	7.14±2.38	8.16±2.20	0.13

[Table/Fig-6]: Intragroup comparison of Quality of Life (QoL) in both the groups.

Parameters	Before RT			After RT		
	Group-A	Group-B	p-value	Group-A	Group-B	p-value
Global health scale/QOL						
Global health status/QoL (revised)	41.26±22.96	40.63±19.29	0.88	43.89±24.52	42.86±20.65	0.82
Functional scale						
Physical functioning (revised)	55.04±12.30	53.63±14.87	0.62	58.45±13.44	56.28±15.64	0.47
Role functioning (revised)	48.25±9.76	47.14±10.30	0.59	49.10±15.16	47.30±14.144	0.55
Emotional functioning	64.28±19.33	66.61±18.10	0.55	61.89±15.67	61.20±20.38	0.85
Cognitive functioning	58.37±15.13	59.39±13.69	0.73	60.24±12.35	60.16±11.17	0.97
Social functioning	71.74±16.39	70.43±18.41	0.69	74.52±15.56	72.02±17.72	0.47
Symptoms scale/items HN30						
Fatigue	70.74±15.58	72.98±22.89	0.61	72.78±18.87	74.06±17.31	0.73
Nausea and vomiting	28.09±5.43	26.37±7.90	0.22	27.28±7.35	27.86±9.45	0.74

Pain general	80.15±30.88	78.57±27.48	0.79	68.02±18.77	70.10±23.37	0.63
Dyspnoea	17.13±4.74	18.08±4.41	0.31	17.74±4.98	17.22±4.03	0.58
Insomnia	41.78±8.67	49.20±6.62	0.29	41.78±9.50	44.04±8.48	0.22
Appetite loss	66.89±9.34	67.39±10.65	0.81	61.65±12.84	64.90±10.32	0.17
Constipation	26.35±5.67	27.63±7.22	0.34	27.80±7.36	28.16±8.80	0.83
Diarrheoa	16.72±4.33	14.26±4.90	0.11	17.69±5.48	16.12±6.10	0.19
Financial difficulties	54.17±20.77	56.49±22.50	0.60	63.52±20.35	76.96±17.53	0.19
Symptoms HN35						
Pain (head and neck)	58.24±15.72	57.67±11.88	0.84	47.50±13.74	50.20±10.76	0.03
Swallowing	36.41±6.83	38.16±6.37	0.21	34.28±7.32	36.88±6.80	0.05
Teeth	76.08±22.38	73.32±14.58	0.47	69.39±12.33	71.04±15.78	0.57
Opening mouth	53.80±11.32	56.61±8.47	0.17	50.74±10.74	55.12±9.72	0.04
Dry mouth	18.15±7.43	20.04±10.68	0.32	16.13±10.38	18.59±8.98	0.22
Sticky saliva	14.19±5.30	16.80±6.61	0.13	16.96±6.09	17.12±7.03	0.02
Senses	20.80±5.12	19.18±4.73	0.11	23.65±7.33	21.12±6.40	0.08
Coughing	20.11±3.64	27.41±6.07	<0.001	17.24±4.58	26.10±7.38	<0.001
Felt ill	64.67±17.33	63.77±23.45	0.83	60.33±19.52	60.18±20.87	0.97
Speech	32.82±7.11	36.26±9.92	0.06	35.80±12.15	37.24±10.33	0.53
Social eating	47.37±10.53	48.31±12.83	0.70	44.85±13.50	46.29±10.49	0.56
Social contact	30.67±6.98	32.98±8.30	0.15	27.28±8.24	30.57±10.43	0.09
Sexuality	17.45±4.52	16.02±4.33	0.12	15.63±4.02	15.08±3.87	0.5
Pain Killers	80.43±16.40	85.71±13.30	0.09	73.91±18.46	80.61±15.70	0.06
Nutritional supplements	89.13±22.26	91.80±25.77	0.59	94.56±23.67	92.86±20.55	0.71
Feeding tube	40.22±8.34	42.86±7.20	0.10	43.48±12.57	43.88±10.54	0.87
Weight loss	55.43±13.72	57.14±16.50	0.59	52.17±17.20	55.10±20.43	0.45
Weight gain	8.69±2.10	7.14±2.38	0.001	9.78±3.34	8.16±2.20	0.01

[Table/Fig-7]: Intergroup comparison of Quality of Life (QoL).

DISCUSSION

The present randomised clinical trial included 100 patients aged 21-64 years. Patients with histologically proven SCC of locally advanced HNCs; ECOG scores of 2-3; Stage III, IVA and IVB; and inoperable locally advanced HNCs that were not considered for definitive chemoradiation were enrolled in this study. Patients with prior treatments in the form of RT or chemoradiation, those who underwent surgery, or defaulters were excluded from the study. The study participants were randomised into two equal groups (Group A and Group B). Soni A et al., Upadhyay R et al., and Choudhary A et al., also employed a similar methodology in their respective studies [17-19]. The participants in this study had a mean age of 39.66 ± 12.05 years in Group A and 42.76±11.65 years in Group B, respectively. Age, sex and religion were comparable between the groups. Soni A et al., Upadhyay R et al., and Choudhary A and Gupta A, also noted a comparable demographic distribution among the groups [17-19].

This study found that more than 65.0% of the cases studied showed oral cavity involvement, followed by the oropharynx (17.0%), hypopharynx (10.0%) and larynx (7.0%). The distribution of the areas involved in both groups was comparable. Head and neck site involvement was also comparable with previous studies conducted by Soni A et al., Upadhyay R et al., and Choudhary A and Gupta A [17-19].

In this study, 98.0% of patients in Group A and 94.0% of patients in Group B completed their treatment regimen. Meyur S et al., reported that this regimen had a 97% treatment completion rate in their study [20]. The overall dose, length of fractionation therapy and comorbid infections all affect the severity of radiation-induced mucositis. The mucositis findings in the present study were in concordance with the pattern of toxicity observed in Chen AM et al., where 9% (n=2/23) of patients reported grade three toxicities in the RTOG 8502 arm [21].

The present study noted that the post-RT response rates- Partial Response (PR), stable disease and progressive disease- after three months of follow-up in Group B were better than those in Group A. In Group A, 40.8% of patients showed a PR, followed by progressive disease in 38.8% and stable disease in 20.4% of patients. In Group B, 46.8% of the patients showed a PR, followed by stable disease in 31.9% and progressive disease in 21.3%. Meyur S et al., reported that the objective response rate in their study was 66.7% (p=0.001), with a further 16.7% of patients having stable disease [20]. Dubey M et al., reported that at the end of treatment, the complete tumour response (CR) in Group I was better than in Group II (40% vs. 36.7%) in their study [22]. Murthy V et al., reported that overall response rates were 42% for primary disease and 55% for nodal disease [23]. Meanwhile, Paliwal R et al., reported a PR in the majority of patients (92%), with no patients experiencing progressive or stable disease [24].

Ghoshal S et al., evaluated symptom relief and QOL in patients with Locally Advanced Head and Neck Cancer (LAHNC) using the Quality of Survival (QS) schedule [25]. The UWQOL questionnaire was used to assess QOL before and after radiation. After the first course, all patients experienced good symptom relief and improvement in QOL; 86.7% of patients had more than 50% objective response at one month post-treatment. Furthermore, 100% of patients with pain and over 90% of patients with dysphagia, dyspnoea and insomnia experienced more than 50% symptom relief. Cough was relieved in 60% of the patients [25]. Mohanti BK et al., treated 127 patients with stage IV LAHNC with a uniform dose of 20 Gy in 5 fractions over one week. Good symptom relief (≥ 50%) was observed for pain, dysphagia, hoarseness, otalgia, respiratory distress and cough [26]. Corry J et al., attempted the QS, yielding a 53% objective response. In 67% of the patients, the performance status stabilised or improved. The treatment was well tolerated, with an overall improvement in QOL in 44% of patients. Treatment was deemed worthwhile in 43%, 58% and 63% of patients after the first, second and third courses of cyclical radiation, respectively [27]. Al-mamgani A et al., using the Christie schedule, achieved excellent palliation, resulting in acceptable

response rates, excellent symptom control, an acceptable toxicity profile and good QOL for patients [28]. The results of these studies were comparable to those of the present study, with patients in the QS regimen showing better QOL after RT.

Limitation(s)

The present study was conducted with a limited number of patients at a single centre. The findings should be validated in larger sample sizes and multicentre randomised clinical trials. In the present study, patients were treated using two-dimensional techniques with telecobalt radiation. However, using advanced RT techniques like three-dimensional or intensity-modulated radiotherapy may have been more effective in reducing side-effects by better protecting normal tissues. The patients were prescribed palliative RT (lower dose) instead of high-dose radical radiotherapy, which could have greatly enhanced their QoL.

CONCLUSION(S)

The present study highlights the role of a small but frequent palliative RT regimen, i.e., QS, which contributes to similar local control and comparatively less acute mucosal toxicity when compared to conventional palliative RT in advanced HNSCC. Additionally, the QoL of patients in the QS regimen was better than that of the conventional regimen after RT. Furthermore, the QS regimen promises minimal visits to the hospital, reducing the burden on working days and overall making it cost-effective. Developing nations like India will benefit the most, where patient load, lack of manpower and limited treatment centres pose significant challenges.

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PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Radiation Oncology, King George's Medical University, Lucknow, Uttar Pradesh, India.
2. Consultant, Department of Radiation Oncology, Mahatma Gandhi Institute of Medical Sciences, Hisar, Haryana, India.
3. Assistant Professor, Department of Radiation Oncology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, Uttar Pradesh, India.
4. Senior Resident, Department of Medical Oncology, Asian Institute of Medical Sciences, Asian Institute of Medical Sciences, Faridabad, Haryana, India.
5. Professor, Department of Radiation Oncology, King George's Medical University, Lucknow, Uttar Pradesh, India.
6. Senior Resident, Department of Radiation Oncology, King George's Medical University, Lucknow, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Arun Kumar Yadav,
Flat No. 1103, Tower 1, Bhagirathi Enclave, Awadh Vihar Yojana-226002,
Lucknow, Uttar Pradesh, India.
E-mail: aruny8732@gmail.com

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