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Study of hypofractionated radiotherapy regime octashots in advanced head and neck cancer patients

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Abstract

Background: Head and neck cancers are the most common type of malignancy in both Developing and developed countries and cause of significant mortality and morbidity with most cases presenting in advanced stages. Even at the first presentation many patients had metastatic and inoperable disease. These patients are not fit for the definitive radio therapy and are treated by palliative radio therapy. This study was performed to evaluate the effect of an accelerated hypo fractionated 4 days schedule octashots in providing palliation to such advanced cases of head and neck cancer.

Materials and methods: A randomized prospective study was done at ATRCTRI Bikaner in which fifty patients with locally advanced squamous cell carcinoma (stage IVA-IVC) were included in the study. All these patients were planned for radiotherapy at cobalt unit with schedule of 3.5Gy/fraction, 2 fractions/day with 6 hr interval between two fractions, for four days (28Gy/ 8fractions/ 4days). Patients were assessed at 2weeks, 1month, 2month, 3month and 6 months to assess for treatment response, any symptomatic relief, dermal and mucosal toxicities (RTOG criteria).

Results: After the completion of radiotherapy, first response evaluation was done at 15 th which showed 54% objective response in 27 patients. At 1 month this response increases to 76% in 38 patients and reaches to 80% at 3 rd. month in 40 patients. At 6 months treatment response is 70% in 35 patients. Only 2% patients had grade III mucositis, 10% patients had grade II mucositis and dermal reactions and remaining patients had grade 0 mucositis. Improvement in symptoms was reported with respect to pain and dysphagia by patients subjectively.

Conclusion: The study concludes that "octashots" is an effective alternative of palliative Radiotherapy in advanced head and neck cancer. It is also convenient for outpatients due to the decreased hospital stay.

Keywords: celebrated hypo fractionation, advanced stage, head and neck cancer, octa shot, palliative.

Introduction

Head and neck cancer is one of the highly prevalent cancers in developing countries like India. It is now the fourth most common malignant disease in world with more than 70% cases occurring in world. Approximately 60,000 patients are diagnosed annually with squamous cell head and neck cancer in United States. Nearly 60%of this population presents with locally advanced but non-metastatic disease. Locoregional failure

constitutes the fatalities result from uncontrolled local and/or regional disease. According to [1] GLOBOCON data Lip, oral cavity followed by cervix uteri, lung and stomach are other higher prevailed cancer types among both genders. Lip and oral cavity is the most common incident cancer in males in India. Oral cancers are the most common amongst all head and neck squamous cell cancer. In Indian females, lip and oral cavity cancer is the fourth most common cancer (Table 1)

Mortality due to head and neck cancer is 15.95% among all the deaths reported due to cancer. Population based cancer registry[2] in India projects that the number of tobacco related cancer and head and neck cancer would be 3,16,734 and 2,18,421 respectively by 2020 . In terms of gender males develop head and neck cancer more frequently, with ratio of almost 3:1 compared to females. Locally advanced head and neck cancer constitutes about 25% of cancer burden in clinical practice in developing countries like India.

Epidemiological studies[3] suggest that the suggest that the risk of developing oral cancer is five to nine times greater for smokers than for non-smokers. International agency for research on cancer classifies the risk factor in cancer development , 64% of laryngeal cancer cases, 37% of pharyngeal cancer cases, 25% of naso pharyngeal cancer cases and 17% of oral cavity cases are caused by smoking[4].

Alcohol drinking is a risk factor for the development of head and neck cancer malignancies, including oral, pharyngeal and laryngeal cancers and coupled with tobacco use , accounts for 75% of oral cancers[5].

Highest risk is observed for hypo pharyngeal cancer followed by oropharyngeal and laryngeal cancer. Patients with HPV positive HNSCC are often diagnosed at a late stage with large cystic lymph nodes in the neck[6].

Patients with advanced squamous cell carcinoma of head and neck region clinically presents with various distressing symptoms and signs, but the most common cause of hospital visit is cervical lymph node enlargement. These patients are found unfit for radical surgical treatment or combined modality due to poor nutritional status .Palliation[7] of distressing presenting symptoms like painful ulcer, throat pain, swallowing difficulty and breathing difficulty is main objective of treatment .Instead of increasing the life expectancy, improvement of quality of life and cost benefit issues are most important in our setting. In India most of the tertiary cancer centers like that of ours are overloaded with patients. In order to strike a balance between radio biologically effective dose and overall treatment duration the present dose fractionation was select Total dose selected was based on randomized study of palliative radiotherapy in advanced head and neck cancer. The twice weekly treatment was designed to reduce the number of hospital attendance as suggested by “hypo trial”[8] The scheme had a high patient compliance rate. It also had the advantage of less opportunity of tumor repopulation. Current evidence seems to favour short course palliative radio therapy[9] schedule than single fraction or protracted course of radiation. Patients treated with palliative intent decision on dose and fractionation is often based on feasibility, quality of life, and palliation rather than on survival or radio biological consideration. Curative radiotherapy of head and neck cancer is a time consuming and intensive treatment, associated with significant morbidity, both in acute and late setting. Palliative radiotherapy is reasonable treatment option in patients

with primary metastatic disease or when treatment of locally advanced disease with curative intent is not possible due to comorbidity or poor performance status.

Materials and Methods

This was a prospective study conducted at Acharya Tulsi Regional Cancer Treatment And Research Institute, Sardar Patel Medical College and associated group of hospitals, Bikaner. The study protocol includes 50 patients of locally advanced head and neck, histologically proven squamous cell carcinoma, who were enrolled from May 2020 to May 2021. The Inclusion criteria were histo logically squamous cell carcinoma of head and neck, Stage IVA, IVB and IVC and or /N3 (American Joint Committee on Cancer Seventh Edition Staging System) inoperable or unfit for surgery, unfit for Radical Radiotherapy Treatment. Patients who had prior history of Radiotherapy at same site or who had severe haematological abnormalities were excluded from the study. All patients were properly informed and consent was taken for treatment. All these patients were planned for Octashot schedule, ,28Gy/8 fractions/4 days in which 3.5

Gy per fraction was delivered, two such fractions were delivered in a day. 6 hour interval gap was given between two fractions. Treatment volume were included primary tumor plus involved node region with an additional margin of 2cm all around . External Beam Radiotherapy was given with radiation therapy parameters on Cobalt -60 machines The ratron 780E/ 780C/ Bhabha Tron II with photon energies of 1.25 Mev. Minimum treatment distance was 80cm SSD.

The Biologically equivalent dose (BED) for this Octashot regimen for tumor and late reacting tissue is 37.8 Gy_{10} and 60.6 Gy_3 respectively. The Equivalent dose to 2Gy/ fraction schedule is 31.5 Gy_{10} for tumor and 37.8 Gy_3 for late reacting tissue.

During the treatment patients were assessed for treatment response, control of symptoms and any treatment related morbidity by doing complete blood count , RFT AND LFT, chest X-ray. In case of difficulty in oral intake feeding tube was inserted either through nasal route or endos copically. For patients with severe respiratory distress, tracheostomy was performed before starting radiation.

After the completion of treatment patients were called for review at 15 days, 1month, 2month, 3 month and then 6 month.

The primary end point of the study was the response rate (complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PR). Assessment was done according to WHO criteria. The secondary end point were Acute (within 90 days of radiation) and late toxicity (beyond 90 days after radiation) (graded according to RTOG criteria).

The tumor was measured bidimensional Ly and surface area approximation method was used. In this method the product of longest diameter and greatest perpendicular diameter was taken. These measurements were taken at the beginning of the treatment. The readings after treatment were compared with those before treatment.

Results

In this study, patients were divided into five groups on the basis of age group. 8 (16%) patients were between 30-40 years of age, 11 (22%) patients were between 41-50 years of age, 12 (24%) patients were between 51-60 years of age, 14 (28%) patients were between 61-70 years of age and 5 (10%) were belonging to >70 years of age. Median age was 60 years (Table A.1).

In present study 45 (90%) and 05(10%) of patients were male and female respectively (Table A.2). In our study 32 (64%) and 18 (36%) of patients were Tobacco chewer and non-tobacco chewer respectively. 40(80%) and 10(20%) were smoker and non-smoker respectively (Table A.3). In our study group, 28% patients were presented with well differentiated carcinoma. 50% and 22% patients had moderately differentiated and poorly differentiated histology respectively (Table A.4). 45(90%) Patients were presented with ECOG score 3 and 5 (10%) patients were of ECOG 4 (Table A.5). According to their primary site 26(52%) patients had oral cavity lesions, 12(24%) patients had lesion in oropharynx. 6 (12%) in larynx and 6(12%) had lesion in hypopharynx (Table B.1).

After completion of the "octashots" the patients were called for 1st review at 15th day. Out of 50 patients, 27 (54%) showed partial response, 20 (40%) with stable disease and 3(6%) with progressive disease (Table C.1). While at the end of 1st month, 38 patients (76%) had partial response and 11 patients (22%) came within range of stable disease. 1 patient (02%) was observed to have progressive disease. The patients who responded very well with octashots and had good general condition with improved ECOG score were taken for curative approach and RT was extended to achieve EQD2 66Gy (Table C.2). At the end of 2nd month, 40 patients (80%) had partial response and 06 (12%) patients had stable disease. 04 (8%) patients was observed to have progressive disease (Table C.3). At the end of 3rd month, 38 patients (76%) had partial response and 06 (12%) patients had stable disease. 06(12%) patients had progressive disease (Table C.4). At the end of 6th month, 35 patients (70%) had partial response and 05 patients (10%) had stable disease. 10 patients (20%) had progressive disease (Table C.5).

In terms of toxicities at 15th day , 7 patients (14%) reported grade I mucositis, 23 patients (46%) reported grade II mucositis, 18 patients (36%) had grade III mucositis and only 1 patient (02%) had grade IV mucositis. Patient also presented with dermatitis with 9 patients (18%) showing grade I dermatitis and remaining 23 (46%) and 16 (32%) patients showing grade II and grade III dermatitis respectively. Only 02 patients (04%) presented with grade IV dermatitis. All these patients were managed symptomatically. Despite the high rate of skin and mucosal toxicities, there were no dropouts or treatment breaks more than 7 days due to adequate nutritional and supportive management provided to the patients (Table D.1). On next follow up at 1 month, all these mucosal and skin reactions had reduced effectively. Only 12 patients (24%) presented with Grade I mucositis , 15 patients (30%) presented with grade II mucositis. Only 1 patient presented with grade III and grade IV mucositis. 24% patients and 32% patients presented with Grade I and Grade II dermatitis while 05 (10%) patients presented presented with Grade III dermatitis. All these patients were managed with conservative treatment (Table D.2).

On next follow up at 2nd month, all these mucosal and skin reactions further reduced effectively. Only 07(14%) presented with Grade I mucositis, and 06(12%) presented with Grade II mucositis.

Only 02 (04%) presented with grade III mucositis and no patient presented in Grade IV mucositis. Only 10 (20%) patients had Grade I dermatitis and 10 (20%) patients had Grade II dermatitis while 03 patients (06%) presented with Grade III dermatitis (Table D.3). At 3rd month follow up, mucosal and skin reactions

further reduced more effectively. Only 06 (12%) presented with Grade I mucositis and 02 (04%) presented with Grade II mucositis. 02 (04%) patients presented with Grade III mucositis for which they are managed with symptomatic treatment. None of the patient presented with Grade IV mucositis. Only 04 (08%) patients had Grade I dermatitis and 08 (16%) had Grade II dermatitis. 01 patient had grade III dermatitis. None of the patient presented with Grade IV dermatitis (Table D.4).

The patients were followed for a minimum period of 6 months. Only 03(06%) patients presented with Grade I and Grade II mucositis and one patient had Grade III mucositis .None of the patient had Grade IV mucositis. 05 (10%) Patients had Grade I dermatitis and 02 (04%) patients had Grade II dermatitis. Only 01 (02%) patient had grade III dermatitis. All these patients were managed symptomatically (Table D.5). Of all primaries, the Oral cavity cancer patients had the worst response rates with progressive disease in 20-30% of patients and Laryngeal cancer patients having best response rate.

In addition to the above tumor response and toxicities, symptomatic relief mainly with respective to pain and dysphagia was also observed and subjectively reported by the patients. Before radiation therapy, pain and difficulty in swallowing were the chief complaints in most of the patients. In our study 30 patients reported with complaint of difficulty in swallowing, out of which 07 patients (23%) had Grade I and 12 patients (40%) had Grade II Dysphagia. Only 01 patient (03%) had grade IV dysphagia at end of one month after radiation treatment. At the end of six month, 12 patients (40%) had Grade I and 14 patients (46%) had Grade II dysphagia. only 04 patients (13%) had grade III dysphagia.

After 'OCTA SHOT' radiation treatment ,pain was found to be improved in 38 out of 50 patients at the end of six month and 12 had no improvement. Post treatment there was significant mood elevation and decreased anxiety in these patients. None of the patient had worsening of pain or dysphagia, which is commonly associated with radiation induced mucositis. The above data have been shown in form of tables and Histogram.

Discussion

In India, about 70-75% of cases of head and neck cancer presents in locally advanced stage. In most of the cases patients are in their advanced stage with poor general condition and their distressing symptoms calls for palliation with radiotherapy. Improvement in the symptoms along with Quality of life is very significant aspect of palliation. As there is no standard schedule for Palliative radio therapy in LAHNC, various palliative schedules have been tried ranging from 20Gy in 5 fractions to 40-50Gy in 10 to 15 fractions which had variable tumor response and radiation reactions. However Palliative radiation in any advanced head and neck cancer should aim to relieve the symptoms quickly while minimizing the side effects. The treatment should also be delivered in the shortest possible time to the patients and caregivers' convenience.

Appropriate management of previously treated, unresectable, recurrent or metastatic head and neck malignancies remains a clinical challenge. Most of the patients with HNSCC presents in locally Advanced stage which causes symptoms such as pain at local site, difficulty in swallowing, chewing and mouth opening, change in voice, swelling over face and bleeding and airway obstruction. Patients with stage IV disease can

only be treated using single modality due to Low performance status. In these cases surgical resection is not preferred as there are chances of incomplete resection.

In recent years, Short Course hypo fractionated RT has been considered more suitable than protracted, Conventional fractionated RT because it provides equivalent symptomatic improvement, tumor response and survival outcomes while shortening overall treatment time and minimizing effects. Although variety of hypofractionated schemes have been used clinically (from 2.5-8 Gy per fraction, to a total dose of 20-48Gy. Rationale behind using hypofractionated radiotherapy schedule is to reduce overall treatment time which will allow treatment completion before accelerated repopulation and higher dose per fraction gives better control for hypoxic fraction of large Tumors. Furthermore, machine time will be well utilized in the centers where there is excessive workload and is also beneficial for the patients coming from faraway places.

Various palliative regimes[10] have been tried in head and neck cancers like 30Gy in 20 fractions, 20 Gy in 5 fractions, quad shot regime and Christie regime. However objective of all such studies were common to provide symptomatic relief and to improve quality of life in patients with inoperable head and neck cancers. The results of various studies reasoned the palliative radiotherapy and showed that it can achieve 70-80% local tumor control at the end of treatment 20-30% patients with no residual clinical disease with less than 10% severe late radiation reactions at the end of 6 months follow up. Radical treatment in the form of aggressive multimodality approach is not successful in all of these patients because of poor performance status and unrespectability. These advanced and unresectable cases needs palliative treatment.

The table 5.1 shows the various studies which have looked into the outcomes of various hypofractionated studies of palliative radiotherapy for locally advanced Tumors of head and neck. Patients with intermediate prognosis of 4 to 12 months who don't have other treatment options may benefit from a palliative course of octashots (3.5Gy per fraction/8 fractions),

2000cGy in 5 fractions or more protracted course of 5000cGy in 20 fractions. Although QUAD shot[11] and 3000 Gy in 10 fractions can be used for patients whose goals of care align better with such regimens, these regimens are unlikely to provide durable responses in patients with better prognosis and may necessitate additional treatments in future. Although high dose regimens are associated with higher rates of acute toxicity, concerns of late toxicity are important to consider when hypofractionation is used in this subset of patients.

Our study was conducted to determine the efficacy (response rate and symptomatic relief) and toxicities of octashot radiation therapy. Fifty patients with advanced (stage IVA-IVB-IVC) squamous cell carcinoma of head and neck region with ECOG performance status 3 and 4 were enrolled in the study. Palliative radiotherapy was planned with 3.5Gy two fractions per day , 6 hr apart for four days in week for locally advanced head and neck cancers (EQD2 31.5Gy).The tumor response was assessed by using WHO criteria and dermal and mucosal toxicities were assessed using RTOG criteria. All the patients in our study were treated with two dimensional conventional technique using cobalt 60 machine which is most commonly available treatment modality in Indian centers. Use of conformal radiotherapy and Intensity Modulate Radio

therapy Treatment (IMRT) in a palliative setting is resource intensive and is not feasible option in India where machine time and financial constraints are the major limiting factors.

After completion of the "octshot", the patients were called for the first review at 15th day. Out of fifty patients , 27 patients (54%) showed partial response , 20 patients (40%) had stable disease and 3 patients (03%) had progressive disease. While at the end of 1st month, total of 38 (76%) patients accounted to have partial response. At the end of 1st month , 38 (76%) patients had partial response while 11 (22%) patients had stable disease and only 1 (02%) patient had progressive disease. At the end of 2nd month , total of 40 (80%) patients had partial response , 6 (12%) patients had stable disease and 4 (08%) patient had progressive disease At the end of 3rd month 38 (76%) had partial response while 12% patients had stable disease and 6% patients had progressive disease. At the end of 6 months,35 (70%) patients had partial response while 5 (10%) patients had stable disease and 10 (20%) patients had progressive disease.

A "Hypo Trial" conducted by Porceddu et al in which 80% of the patients experienced an overall objective response. They treated 37 patients with incurable head and neck cancer with palliative schedule of 30 Gy in 5 fractions with 2 fractions per week. However, in our study, initially at end of 2 weeks, 27 patients (54%) showed >50% partial response (PR). While at the ends of 1 month, 38 patients (76%) had >70% response and at the end of 3 months, 40 patients (80%) had >75% response. This response rate was 70% in 35 patients at the end of six months.

Ghoshal et al[12] in their study have given two successive "quad shots" to responding patient and have reported partial response in 66.67% patients. They experienced 22 patients with pain and 90% of patients with dysphagia, dysponea and disturbed sleep had greater than 50% relief in symptoms after radiotherapy. Similarly Spartacus et al [13]

experienced improvement of dysphagia in 82% of patients. After four weeks of radiotherapy completion, all patients had pain relief. In another trial Das et al 88% had pain relief in their patients. In our study we achieved pain relief in 76% of patients while dysphagia was relieved in 40% of patients.

In case of effectiveness of this schedule being comparable with that of conventional schedule, this "octashot" may prove to be good option for palliative and outpatients. This will decrease the hospital stay of patients and also hospital workload significantly. With the increase in sample size and proper scailing, more desired results could have been obtained.

However within these given confinement of the investigation, be that as it may, the present examination gives profitable information on the adequacy and wellbeing of this hypofractionated plan for a palliative setting for HNSCC patients who are inadmissible for curative options.

Furthermore, from radio biological, financial and calculated perspectives, hypo fractionated schedule would be the most reasonable alternative. Firstly, the treatment is finished before quickened repopulation turns into a critical radiobiologic factor.

Secondly, the decrease in the number of portions likewise permits an increasingly proficient utilization of resources, which can help evade long waiting time for other patients and finally, taking into account that this group of patients are usually of old age and frequently have poor performance status just as critical comorbidities, it is

practically compulsory to keep the overall treatment time as short as could reasonably be expected.

Limitations

For the evaluation of symptomatic parameters, proper scaling needs to be added in the study.

A longer follow up is desired to study for disease progression and patients' survival data. In addition, it is a single armed study, which demands for studies comparing it with conventional schedules of radiation. A randomised trial with bigger/larger sample size should be conducted to confirm the "octashot" trial efficacy.

Conclusion

Head and neck cancer patients having limited life expectancy and not suitable for curative treatment, the octashot palliative Radiotherapy regimen offers good palliative response rate and is well tolerated. Patients responding well to octashot regimen can be further taken up for dose escalation.

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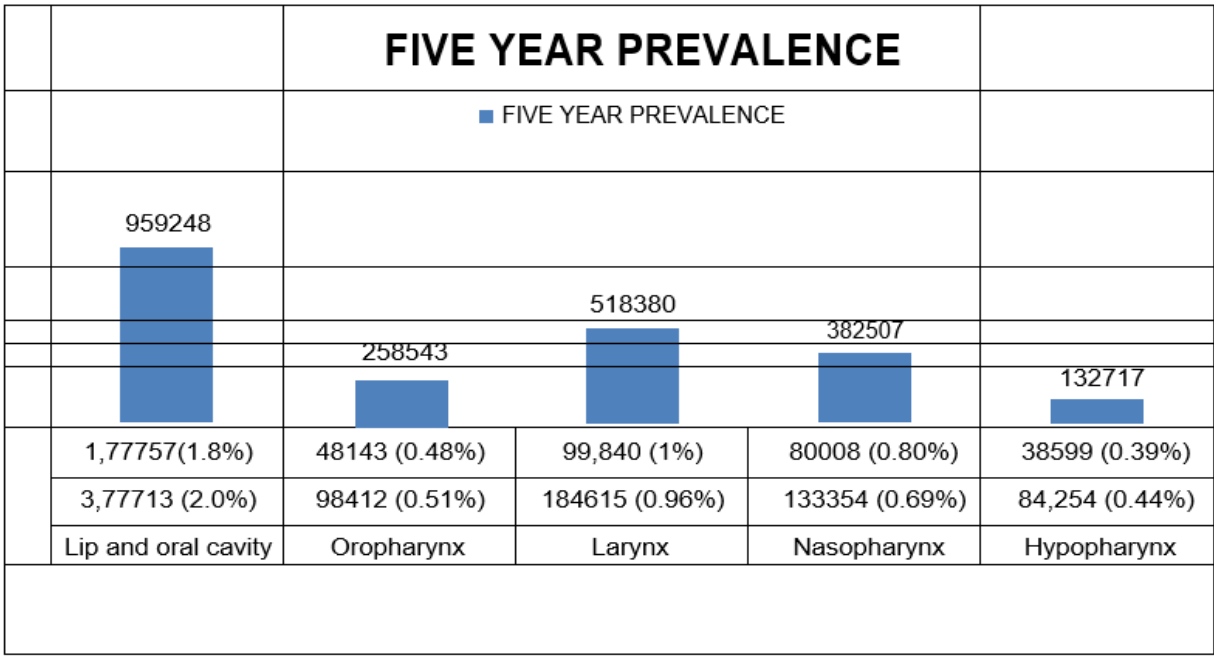
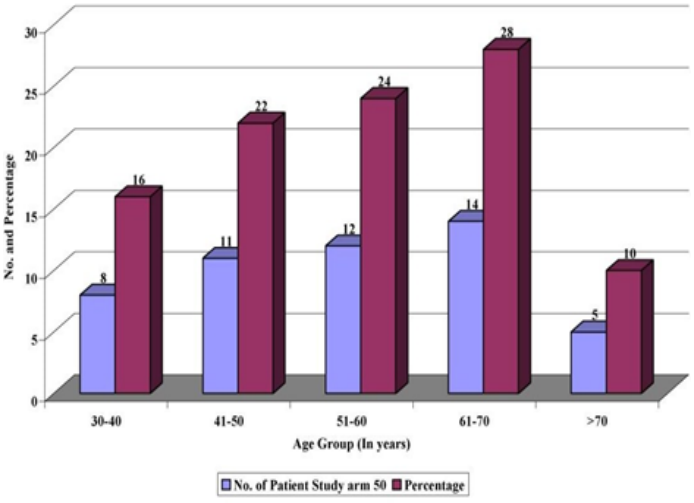
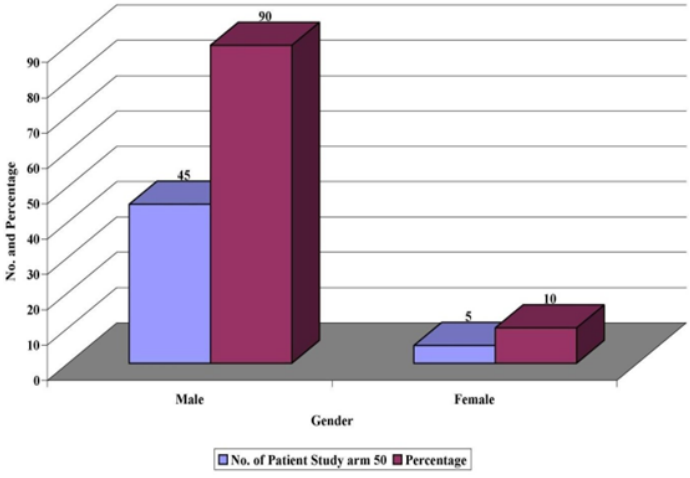


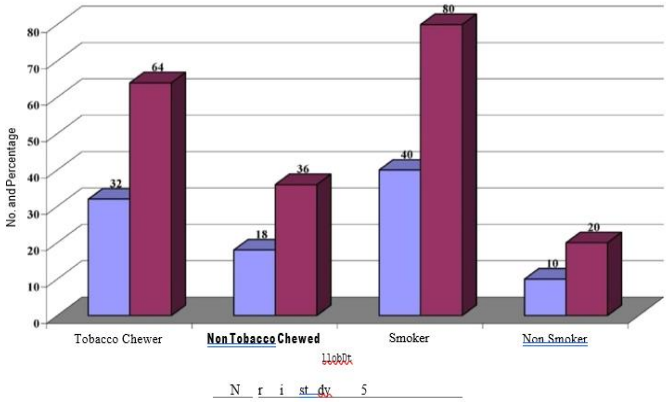
Graph 1: Age wise Distribution of Patients



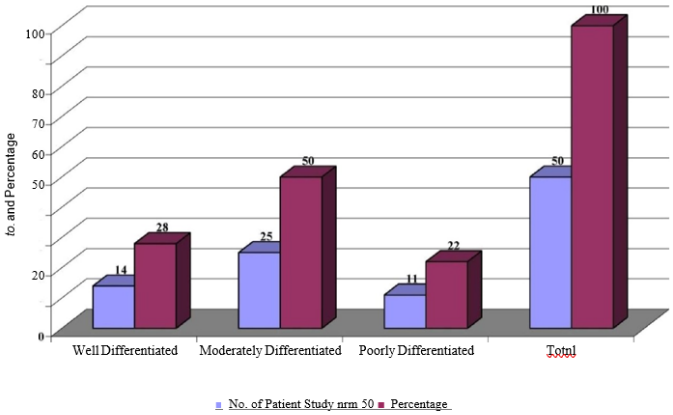
Graph 2: Gender wise Distribution of Patients



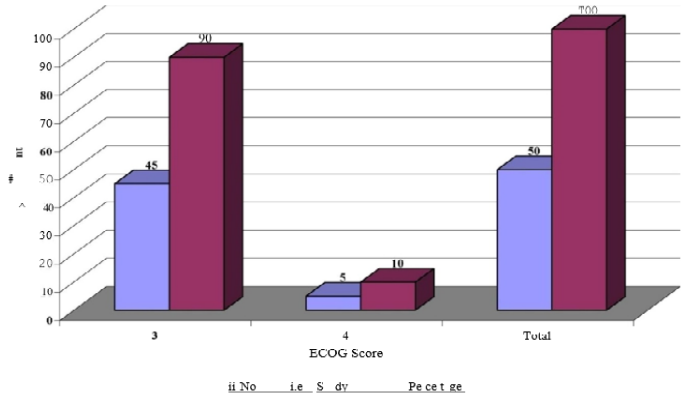
Graph 3: Patients Charncteristics - Habit



Graph 5: Histological Differentiation of Tumor



Graph 6: Patients with ECOG Score



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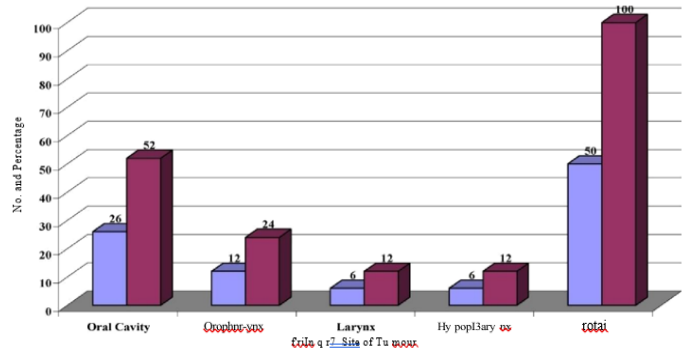
Graph 7: Patients According to Primary site of Tumour



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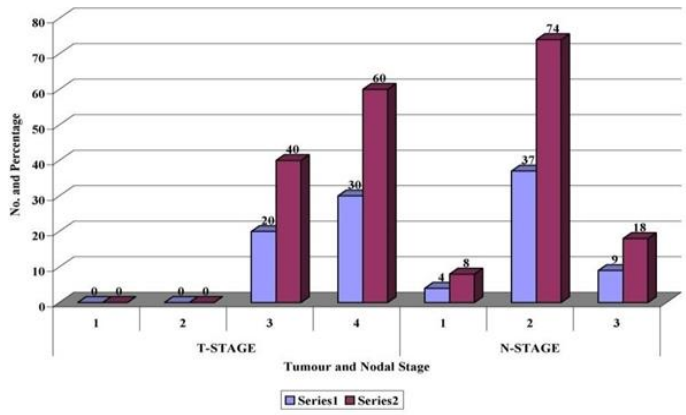
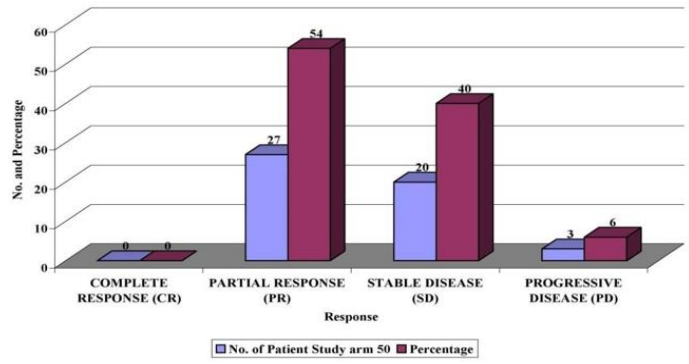
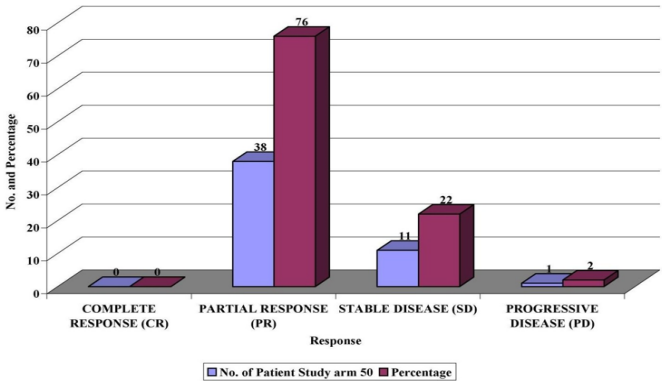
Graph 8: Tumour and Nodal Stage



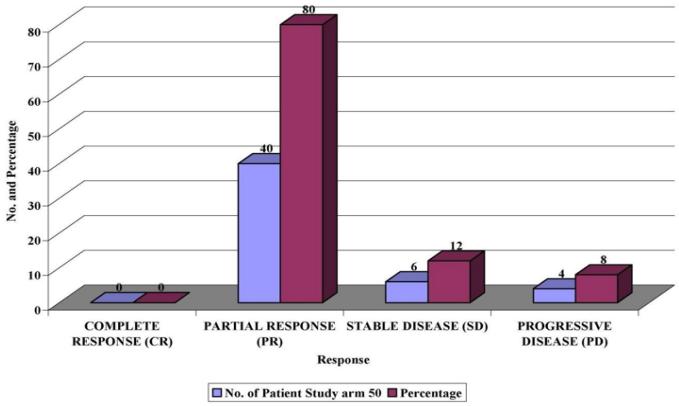
Graph 9: Disease Response (By WHO Criteria)
(I) Treatment Response at 15th Day



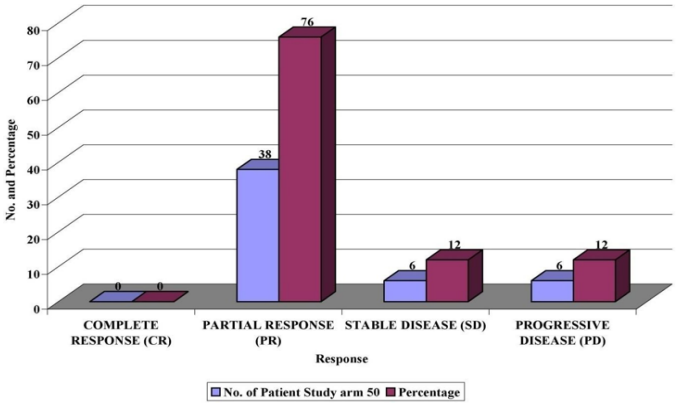
Graph 10: (II) Treatment Response at 1 Month



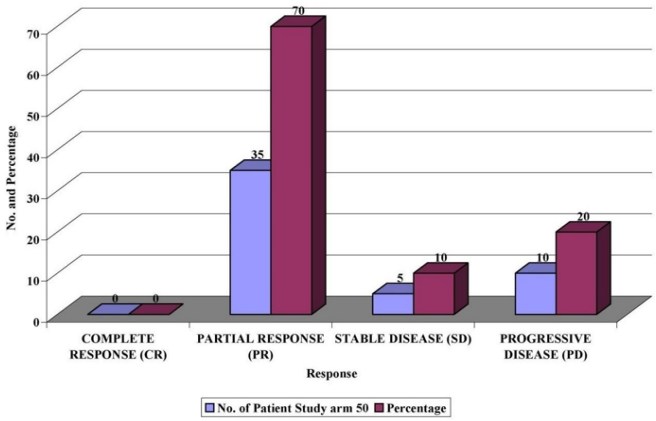
Graph 11: (III) Treatment Response at 2ndMonth



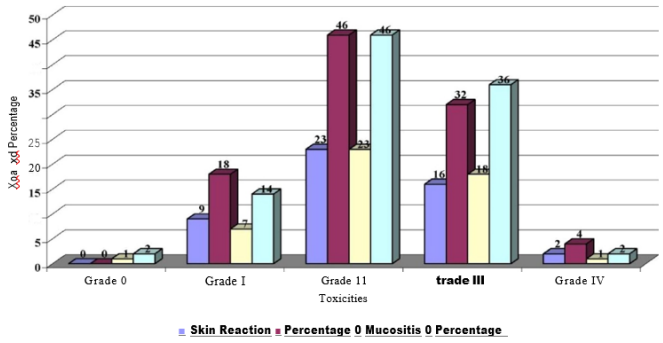
Graph 12: (IV) Treatment Response at 3rdMonth



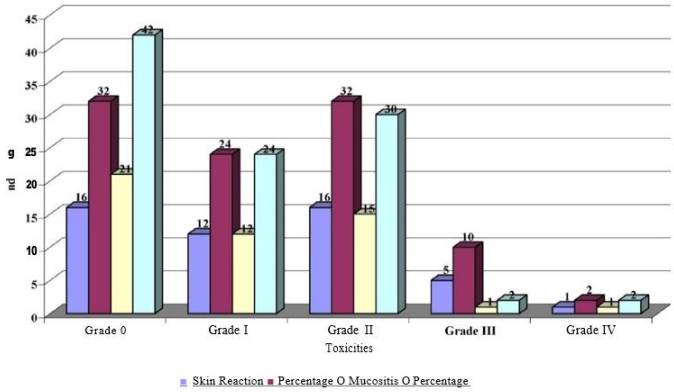
Graph 13: (V) Treatment Response at 6thMonth



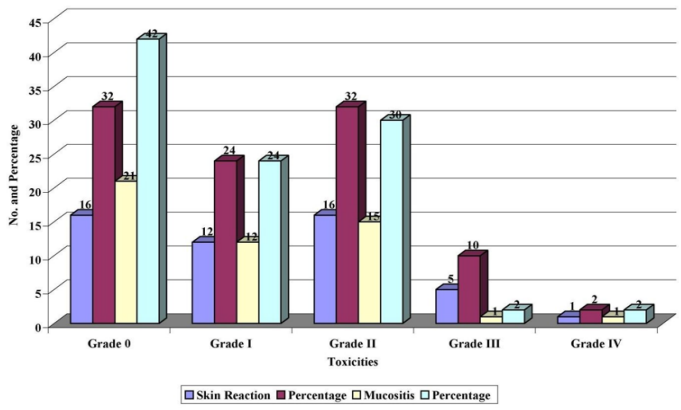
Graph 14: Toxicities after treatment by RTOG Criteria
Toxicities at l5th Day



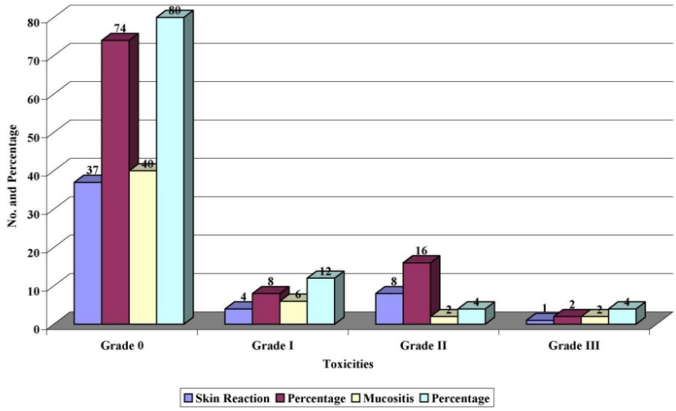
GfiRQh 15: (II) Toxicities at 1 Month



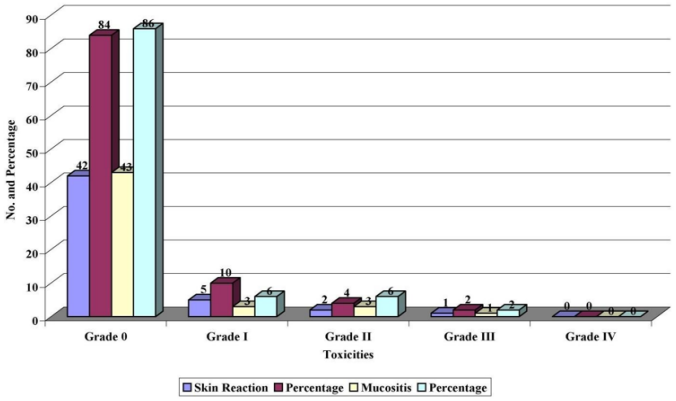
Graph 16: (III) Toxicities at 2ndMonth



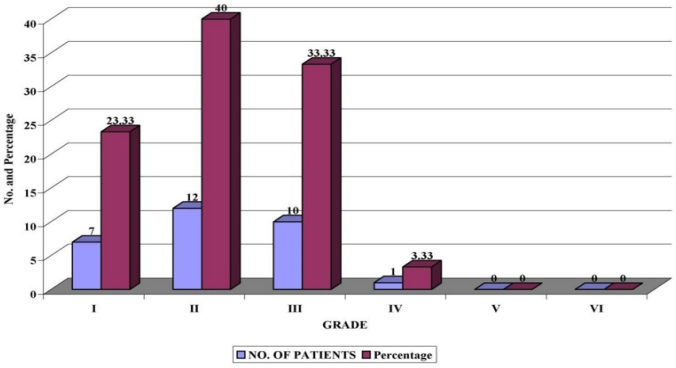
Graph 17: (IV) Toxicities at 3rd Month



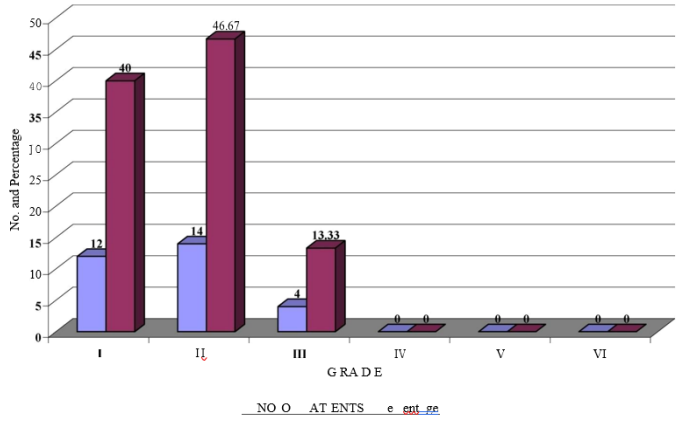
Graph 18: (V) Toxicities at 6th Month



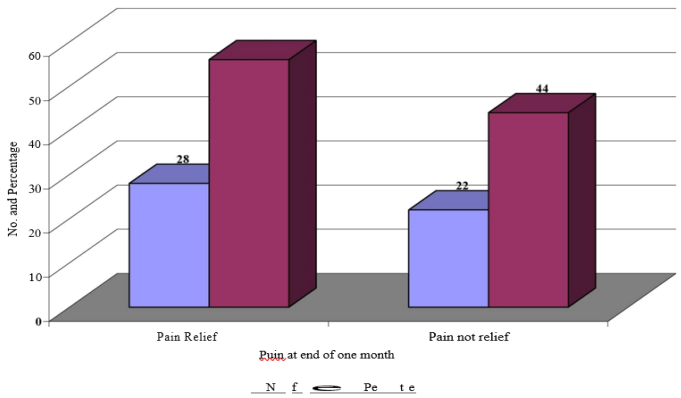
Graph 19: (I)Dysphagia At end of One Month



Graph 20: (II) Dysphagia At the end of six month



Graph 21: (III) Pain at end of one month



Graph 22: (IV) Pain at end of six month

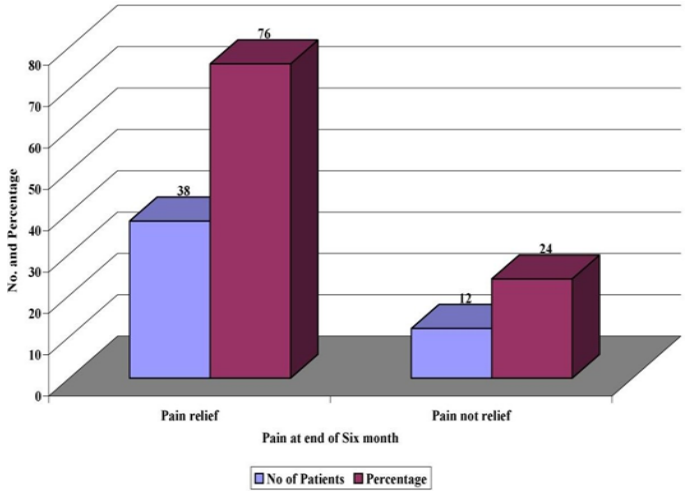


Table 1: Globo can 2020 head and neck cancer statistics.

Type of hnc	Incidence of new cases	Number of deaths	Five-year prevalence
Lip and oral cavity	3, 77713 (2.0%)	1,77757(1.8%)	959248
Oropharynx	98412 (0.51%)	48143 (0.48%)	258543
Larynx	184615 (0.96%)	99,840 (1%)	518380
Nasopharynx	133354 (0.69%)	80008 (0.80%)	382507
Hypopharynx	84,254 (0.44%)	38599 (0.39%)	132717

Table A 1: Age wise distribution of patients.

Sn.	Age Group	No. of Patients Study arm 50	Percentage (%)
1.	30-40	8	16%
2.	41-50	11	22%
3.	51-60	12	24%
4.	61-70	14	28%
5.	>70	5	10%

Table A 2: gender wise distribution of patients.

Sn.	Gender	No. of Patients study arm 50	Percentage (%)
1.	Male	45	90
2.	Female	5	10

Table A 3: patient's characteristics-habits.

Patients Characteristics	Habit	No. of Patients study arm 50	Percentage (%)
Tobacco Chewing	Tobacco Chewer	32	64
	Non-Tobacco Chewer	18	36
Smoking	Smoker	40	80
	Non-Smoker	10	20

Table A 4: histological differentiation of tumour.

Sn.	Histological Differentiation	No. of Patients study arm 50	Percentage (%)
1.	Well Differentiated	14	28
2.	Moderately Differentiated	25	50
3.	Poorly Differentiated	11	22
	Total	50	100

Table A 5: ecog score

Sn.	ECOG Score	No. of Patient study arm 50	Percentage (%)
1.	3	45	90
2.	4	5	10
	Total	50	100

Table b 1: Distribution according to primary site of tumour

Sn.	Primary Site of Tumour	No. of Patient study arm 50	Percentage (%)
1.	Oral Cavity	26	52
2.	Oropharynx	12	24
3.	Larynx	6	12
4.	Hypopharynx	6	12
	Total	50	100

Table b 2: Tumour and nodal stage

	Tumour and Nodal stage	No. of Patient study arm 50	Percentage (%)
T-stage	1	0	0
	2	0	0
	3	20	40
	4	30	60
N-stage	1	4	08
	2	37	74
	3	9	18
	Total	50	100

Table C 1: Disease response (who criteria) Treatment response at 15th day

S.No.	Response	No. of Patient study arm 50	Percentage (%)
1.	Complete response (cr)	00	00
2.	Partial response (pr)	27	54
3.	Stable disease (SD)	20	40
4.	Progressive disease (pd)	03	06

Table C 2: Treatment Response at 1 Month

S.No.	Response	No. of Patients study arm 50	Percentage (%)
1.	Complete response (cr)	00	00
2.	Partial response (pr)	38	76
3.	Stable disease (SD)	11	22
4.	Progressive disease (pd)	01	02

Table C 3: Treatment Response at 2nd Month

S.No.	Response	No. of Patients study arm	Percentage (%)
1.	Complete response (cr)	00	00
2.	Partial response (pr)	40	80
3.	Stable disease (sd)	6	12
4.	Progressive disease (pd)	4	08

Table C 4: Treatment Response at 3rd Month

S.No.	Response	No. of Patients study arm 50	Percentage (%)
1.	Complete response (cr)	00	00

2.	Partial response (pr)	38	76
3.	Stable disease (SD)	06	12
4.	Progressive disease (pd)	06	12

Table C 5: Treatment Response at 6thMonth

S.No.	Response	No. of Patients study arm 50	Percentage (0%)
1.	Complete response (cr)	00	00
2.	Partial response (pr)	35	70
3.	Stable disease (SD)	05	10
4.	Progressive disease (pd)	10	20

Table D 1: Toxicities after treatment by rtog criteria

(I) Toxicities at 15th Day

Toxicities	Skin Reaction	Percentage (%)	Mucositis	Percentage (%)
Grade 0	00	00	01	02
Grade I	09	18	07	14
Grade II	23	46	23	46
Grade III	16	32	18	36
Grade IV	02	04	01	02

Table D 2: Toxicities at 1 Month

Toxicities	Skin Reaction	Percentage (%)	Mucositis	Percentage (%)
Grade 0	16	32	21	42
Grade I	12	24	12	24
Grade II	16	32	15	30
Grade III	05	10	01	02
Grade IV	01	02	01	02

Table D 3: Toxicities at 2ndMonth

Toxicities	Skin Reaction	Percentage (%)	Mucositis	Percentage (%)
Grade 0	27	54	35	70
Grade I	10	20	07	14
Grade II	10	20	06	12
Grade III	03	06	02	04
Grade IV	00	00	00	00

Table D 4

(II) Toxicities at 3rd Month

Toxicities	Skin Reaction	Percentage (%)	Mucositis	Percentage (%)
Grade 0	37	74	40	80
Grade I	04	08	06	12
Grade II	08	16	02	04
Grade III	01	02	02	04
Grade IV	00	00	00	00

Table D 5: Toxicities at 6th Month

Toxicities	Skin Reaction	Percentage (%)	Mucositis	Percentage (%)
Grade 0	42	84	43	86
Grade I	05	10	03	06
Grade II	02	04	03	06
Grade III	01	02	01	02
Grade IV	00	00	00	00

Table E 1: Dysphagia at the end of 1 month

Grade	No. Of patients	Percentage (%)
I	07	23
II	12	40
III	10	33

IV	01	03
V	00	00
VI	00	00

Table E 2: Dysphagia at the end of six month

Grade	No. Of patients	Percentage (%)
I	12	40
II	14	46
III	04	13
IV	00	00
V	00	00
VI	00	00

Table E 3: Pain at the end of one month

Pain at the end of one month	No. Of patients	Percentage
Pain relief	28	56
Pain not relived	22	44

Table E 4: Pain at the end of six month

Pain relief	38	76%
Pain not relief	12	24%

Table 5 1: A comparative view of studies with different palliative schedule in advanced head and neck cancers.

References	No. of patients	Dose (Gy)	No. of fractions	Schedule	Response	Toxicities
Present Study	50	3.5 BID	8	Daily	76% RR (One month) 70% RR (six month)	02% Grade III mucositis and 10% Grade III dermatitis at the end of 1 month. 02% Grade III mucositis and 02% Grade III dermatitis at the end of 6 month.
Jakhar et al [14]	22	3.5 BID	8	Daily	73% RR (one month)	9% grade 3 mucositis No grade 3 dermatitis
Spartacus etal	98	6.25/week	4	Weekly	93% RR >50% pain Relief (4 week)	29% skin toxicity 27% mucositis
Lok et al	75	3.7 BID	4	Daily	65% RR (4 weeks)	5% acute dermatitis and functional mucositis
Laursen et al	77	4 Gy twice weekly	13-14	Biweekly for 6-7 weeks	45% RR (7 weeks)	25% acutemucositis 15% acute dermatitis

Paris et al[15]	37	3.7 BID	4	Repeated 3 weekly for 3 times	77% RR (8-9 weeks)	No late toxicity
Carrascosa et al[16]	7	3.7 BID	4	Course repeated 4 weekly for 3 times with paclitaxel	5% RR 90% palliation (9 weeks)	10% grade 3 acute No late toxicity
Monnier et al	78	3	8	Day 1 and 3 repeated weeks 1,3,5,7 cisplatin	54% RR (7 weeks)	31% needed break 4% acute grade 3-4 12% late grade 3-4
Das et al	33	4	10	Twice/weekly	88% pain relief 60% improved Ps (5weeks)	Grade 3 mucositis 18% Dermatitis 3%
Mohanti et al	505	4	5	Additional RT for responders	37%RR 47%-59% Symptom relief	Not stated for palliative RT

QoL= quality of life, RR= response rate, PS= performance status, RT= radiotherapy.