Original Research Article

Comparison of acute toxicities and response of standard chemo radiation versus hyper fractionated radiotherapy in head and neck cancers

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Abstract

Background: Head and neck cancers are the most common malignancy among males in India. Carcinoma of buccal mucosa is the most common cancer among head and neck cancers due to high rate of tobacco chewing habit.

Aim and objectives: To study the comparison of acute toxicities and response of standard chemo radiation versus hyper fractionated radiotherapy in head and neck cancers.

Materials and methods: It was a prospective study of acute toxicity and response in patients diagnosed with head and neck malignancy. Patients with oral cavity site, previously untreated locally advanced III, IV-A and IV -B, age of 20-60 years.

Results: Primary tumor site of the patients included in the both CRT arm and HFRT was not significant (P=0.755). Majority of patients included were T3 (44% in CRT arm and 46.7% in HFRT arm) and T2 (24% in CRT arm and 26.7% in HFRT arm) lesions. The tumors with respect to T stage, the difference between two arms was not statistically significant (P = 0.988). Most of the patients presented with N1 (44% of CRT arm and 40% of HFRT arm) and N2 (28% of CRT arm and 26.7% of HFRT arm) stage. With respect to nodal (N) stage at presentation, CRT arm and HFRT arm were comparable (P=0.987). In HFRT arm, 7 (46.7%) patients were presented in stage III

and 8 (53.3%) patients were in stage IV. With respect to TNM stage, CRT arm and HFRT arm were comparable (P=0.87). Radiotherapy treatment compared in both CRT Arm and HFRT arms was not statistically significant (P=0.493). In CRT arm Grade 2 toxicity: 13/22 (59%) patients developed skin toxicity, 12/22 (55%) patients developed mucous membrane toxicity, 15/22 (68%) patients developed nausea, 8/22 (36%) patients developed vomiting, 10/22 (45%) salivary gland toxicity. Grade 3 toxicity: 2/22 (9%) patients developed skin toxicity, 10/22 (45%) patients developed mucous membrane toxicity, 5/22 (23%) patients developed nausea, 6/22 (27%) patients developed vomiting. **Conclusion:** Standard chemo radiation is better than HFRT in Head and Neck (oral cavity) cancers because of less toxicity, less mean overall treatment time, less number of treatment breaks and better response.

Key words

Hyper fractionated radiotherapy, Chemo radiation, Acute toxicities.

Introduction

Head and neck cancers are the most common malignancy among males in India. Carcinoma of buccal mucosa is the most common cancer among head and neck cancers due to high rate of tobacco chewing habit [1]. Head and neck cancer are aggressive tumors. Tumor response is 52-86% [2, 3]. Loco regional control is 22-46% [4, 5] with conventional fractionation. Loco regional recurrence is the most common form of recurrence in the head and neck cancers [6]. To achieve good loco regional control in head and neck cancers, altered fractionations like hyper fractionation, accelerated fractionation etc., concurrent chemo radiation were came into clinical practice [7]. From the experiments it was evident that the benefits of fractionation were due to four factors, which are now popularly known as `4 Rs' of Radiobiology. This refers to the process by which the function of DNA is restored. Evidence for this came from studies of strand breaks in DNA, which disappears during the few hours after irradiation. This is the potential mechanism by which the normal tissue damage that is caused by irradiation is repaired during the course of radiotherapy. There are two types of recovery processes. First one is recovery from sub lethal damage'(SLD) or `Elkind recovery'. The other one is `recovery from potentially lethal damage' (PLD). The radio sensitivity of cells varies considerably as they pass through the cell cycle. 'S' phase is the most resistant phase of cell cycle whereas cells which are in 'G-2' phase during irradiation are more radiosensitive. Cells that survive a first dose of radiation will trend to be in a resistant phase of cell cycle and within few hours they may progress into a more sensitive phase. This is the factor which increases the radio sensitivity by more cells kill in a fractionated radiotherapy. During an extended course of radiotherapy cells that survive irradiation may proliferate faster and thus increase the number of cells that must be killed. In a tumor, cells that survive a first dose of radiation will tend to be hypoxic but thereafter their oxygen supply may improve leading to an increase in radio sensitivity. There are number of possible processes which contribute to re oxygenation. Tumors, early responding tissues and late responding tissues are having different cell kinetics, so they are affected by these 4 factors in different ways depending upon their kinetics.

Materials and methods

Patients diagnosed with head and neck malignancy from the Out Patient off MNJ IO & RCC were prospectively included in study with prior informed consent from 2013 to 2015.

Inclusion criteria

Patients with oral cavity site, previously untreated locally advanced III, IV-A and IV -B, age of 20-60 years, either males or females, performance status of ECOG 0-1, HPE of

squamous cell carcinoma, life expectancy of at least 6 months, hematological parameters with hemoglobin >9 gm/dl, total leukocyte count >4000 cells/cu. mm, platelet count of >1.5 lakh /cu.mm, renal parameter with serum creatinine <1.5 mg/dl and blood urea <30 mg/dl.

Exclusion criteria

Other sites of head and neck, stage of IV-C, age of younger than 20 years and older than 60 years, performance status of ECOG 2, 3 and 4, HPE of histology other than squamous cell carcinoma, patients treated previously with surgery or radiation, any co-morbid condition or acute infection where treatment is contraindicated, pregnant women, oral sub mucous fibrosis, patients not likely to be available for follow up.

Patient's written consent was taken after explaining the nature of disease, its treatment and side effects in his own vernacular language. Patient were counselled about ill effects of tobacco and alcohol consumption and asked to discontinue the same. Patients were also counselled regarding maintaining good oral hygiene throughout the treatment.

Results

The present study was a prospective randomized study conducted in department of Radiotherapy, MNJIO & RCC, and Hyderabad from 2013 to 2015. The patients were selected according to the inclusion and exclusion criteria as mentioned earlier. A total of 40 patients of head and neck squamous cell cancer (HNSCC) were enrolled in this study and analyzed. All patients underwent baseline evaluation as per protocol. Treatment consisted of either conventional RT (6600 cGy in 33 fractions, 200cGy/day/ fraction over 6.5weeks) with concurrent injection Cisplatin (50 mg/ week) or HFRT (7920 cGy in 66 fraction, 120 cGy / fraction over). During radiation patients were evaluated for acute toxicities. After completion of the treatment, the end response was noted by assessing the primary tumor and node response by RECIST1.1 criteria during first follow up done at two months after treatment.

It was a prospective clinical study with 40 patients of stage III – stage IV B cancers to compare the acute toxicity and tumor response between standard chemo radiation and HFRT. In the study of 40 patients of HNSCC, 1 patient of CRT arm (due to electrolyte imbalance) and 2 patients of HFRT arm (one patient was due to myocardial infarction and another due to pneumonia) expired during the treatment. 3 patients (2 of CRT and 1 patient of HFRT arm) were opted out of the study during the treatment. These 6 patients were excluded from the final analysis of comparison of tumor response between CRT and HFRT, which was the end point of this study.

Age group 40-50 years was most affected group in the study (**Table – 1**).

Primary tumor site of the patients included in the both CRT arm and HFRT was not significant (P=0.755). Majority of patients included were T3 (44% in CRT arm and 46.7% in HFRT arm) and T2 (24% in CRT arm and 26.7% in HFRT arm) lesions. The response with respect to T stage and the difference between two arms was not statistically significant (P = 0.988). Most of the patients presented with N1 (44% of CRT arm and 40% of HFRT arm) and N2 (28% of CRT arm and 26.7% of HFRT arm) stage. With respect to nodal (N) stage at presentation, CRT arm and HFRT arm were comparable (P=0.987). In HFRT arm, 7 (46.7%) patients were presented in stage III and 8 (53.3%) patients were in stage IV. With respect to TNM stage, CRT arm and HFRT arm were comparable (P=0.87) as per **Table - 2**.

Treatment response was assessed by using RECIST 1.1 at 2 months after completion of treatment. In CRT arm, 1 patient expired and 2 patients did not receive complete treatment. In HFRT arm, 2 patients expired and 1 patient did not receive complete treatment. These 6 patients were excluded in response assessment.

Table - 1: Patient characteristics.

Patient characteristics		**CRT (25)**	**HFRT (15)**
Gender	Males	13 (52%)	8 (53.3%)
	Females	12 (48%)	7 (46.7%)
Primary site	B Mucosa	10 (40%)	6 (40%)
	Tongue	10 (40%)	6 (40%)
	Other site	5 (20%)	3 (20%)
Age distribution (years)	20-30	3 (12%)	2 (13.3%)
	30-40	7 (28%)	4 (26.7%)
	40-50	9 (36%)	5 (33.3%)
	50-60	6 (24%)	4 (26.7%)
	Mean age	42.64	44.87
	Standard deviation	8.906	8.399

Table - 2: Site of primary tumor in CRT and HFRT arms, tumor stage distribution, nodal stage distribution.

Site	**N=40**		X^2	**P**
	CRT	**HFRT**		
Buccal Mucosa	10 (40%)	6 (40%)		
Tongue	10 (40%)	6 (40%)	6.679	0.755
Other sites	5 (20%)	3 (20%)		
Total	25	15		
T stage				
T1	4(16%)	2(13.3%)		
T2	6 (24%)	4 (26.7%)		
T3	11 (44%)	7 (46.7%)	0.130	0.988
T4	4 (16%)	2 (13.3%)		
Total	25 (100%)	15 (100%)		
N stage				
N0	4 (16%)	3 (20%)		
N1	11 (44%)	6 (40%)		
N2	7 (28%)	4 (26.7%)	0.140	0.987
N3	3 (12%)	2 (13.3%)		
Total	15 (100%)	35 (100%)		
TNM stage				
III	11 (44%)			0.87
IV	14 (56%)	8 (53.3%)		
Total	25 (100%)	15 (100%)		
Overall treatment time (Days)	49.09	54.75	21.010	0.10

Radiotherapy treatment compared in both CRT Arm and HFRT arms was not statistically significant (P=0.493). In CRT arm Grade 2 toxicity: 13/22 (59%) patients developed skin toxicity, 12/22 (55%) patients developed mucous membrane toxicity, 15/22 (68%) patients developed nausea, 8/22 (36%) patients developed vomiting, 10/22 (45%) salivary gland toxicity. Grade 3 toxicity: 2/22 (9%) patients developed skin toxicity, 10/22 (45%) patients developed mucous membrane toxicity, 5/22 (23%) patients developed nausea, 6/22

(27%) patients developed vomiting as per **Table - 3**.

Acute toxicity was graded by using RTOG acute toxicity criteria. Grade 1, 2, 3 and 4 or more toxicity of skin, mucous membrane, nausea, vomiting, salivary gland, pharyngeal and hematological toxicities were assessed in both CRT arm and HFRT arm. Dead patients and opted out patients were excluded from the study.

Table - 3: Acute toxicity after treatment in the study.

Toxicity	CRT ARM				HFRT ARM				χ^2	p
	G1	G2	G3	G4	G1	G2	G3	G4		
Skin	4(18%)	13(59%)	2(09%)	-	2(17%)	6(50%)	3(25%)	-	1.65	0.65
Mucous membrane	-	12(55%)	10(45%)	-	-	3(25%)	9(75%)	-	0.45	0.83
Nausea	2(09%)	15(68%)	5(23%)	-	4(33%)	3(25%)	1(08%)	-	13.57	0.004
Vomiting	8(36%)	8(36%)	6(27%)	-	2(17%)	2(17%)	-	-	19.99	0.001
Salivary gland	12(55%)	10(45%)	-	-	4(33%)	8(67%)	-	-	1.40	0.24
Pharynx	-	12(55%)	10(45%)	-	-	4(33%)	8(67%)	-	0.47	0.49
Hematology	7(31%)	5(23%)	-	-	3(25%)	-	-	-	4.06	0.13
Kidney	2(09%)	2(09%)	1(4.5%)		1(08%)	1(08%)	-	-	0.59	0.90

Discussion

The present study was a prospective randomized analytical study of patients with histo-pathologically proven squamous cell carcinoma of head and neck region, undertaken at Department of Radiation Oncology, Forty patients who were eligible for this study were planned to receive either standard chemo radiation (RT of 66 Gy in 33 fractions, 2 Gy per fraction, 1 fraction per day, 5 fractions per week along with weekly 50 mg Cisplatin) or HFRT (RT of 79.2 Gy in 66 fractions, 1.2 Gy per fraction, 2 fraction per day with minimum of 6 hours gap, 10 fractions per week) as per protocol.

Age

Age of the patients included in the both CRT arm and HFRT arm were matched to avoid the bias caused by difference in the age. **In CRT arm**: Age distribution was 20-30 years - 3 (12%), 30-40 years - 7 (28%), 40-50 year - 9 (36%), and 50-60 years - 6 (24%). **In HFRT arm**: Age distribution was 20-30 years – 2 (13.3%), 30-40 years – 4 (26.7%), 40-50 year - 5 (33.3%) and 50-60 years - 4 (26.7%). Mean age of presentation in CRT arm was 42.64 yrs with standard deviation of 8.906 and mean age at presentation in HFRT arm was 44.87 yrs with standard deviation of 8.399.With respect to age, CRT arm and HFRT arm were comparable.

Gender

Gender of the patients included in the both CRT arm and HFRT arm were matched to avoid the bias caused by difference in the gender. In CRT arm, there were 25 patients, out of which 13 (52%) were males and 12 (48%) were females. In HFRT arm, there were 15 patients out of which 8 (53.3%) were male and 7 (46.7%) were female. In both CRT arm and HFRT arm, males and females were almost equal in percentage. The difference in the gender was not statistically significant. (P = 0.935).

Primary tumor site

Primary tumor site of the patients included in the both CRT arm and HFRT arm were matched to avoid the bias caused by difference in primary tumor site. The site of primary tumor was mainly divided as buccal mucosa, tongue and other sites of oral cavity. In CRT arm, 40% (10/25) of patients had buccal mucosa cancer,

40% (10/25) of patients had tongue cancer and 20% (5/25) patients had cancer of other sites of oral cavity. In HFRT arm, 40% (6/15) of patients had buccal mucosa cancer, 40% (6/15) of patients had tongue cancer and 20% (3/15) patients had cancer of other sites of oral cavity. The difference with respect to primary site was not significant (P=0.755).

Tumor stage

In CRT arm, 16% (4/25) of T1, 24% (6/25) of T2, 44% (11/25) of T3 and 16% (4/25) of T4 patients were included. In HFRT arm, 13.3% (2/15) of T1, 26.7% (4/15) of T2, 46.7% (17/15) of T3 and 13.3% (2/15) of T4 patients were included. Majority of patients included were T3 (44% in CRT arm and 46.7% in HFRT arm) and T2 (24% in CRT arm and 26.7% in HFRT arm) lesions. The response with respect to T stage, the difference between two arms was not statistically significant (P = 0.988).

Nodal Stage: In CRT arm, 4/25(16%) of patients were node negative and in HFRT arm 3/15(20%) were node negative. In CRT arm, 11/25(44%) patients presented with N1 stage, 7/25(28%) with N2 stage and 3/25(12%) with N3 stage. In HFRT arm, 6/15 (40%) patients were presented in N1, 4/15 (26.7%) were in N2 and 2/15 (13.3%) were in N3. Most of the patients presented with N1 (44% of CRT arm and 40% of HFRT arm) and N2 (28% of CRT arm and 26.7% of HFRT arm) stage. With respect to nodal (N) stage at presentation, CRT arm and HFRT arm were comparable (P=0.987).

TNM Stage: All patients were staged using the AJCC 7th staging manual and assigned a TNM stage of III to IVB. Stage 0, I, II & IV C patients were not included in this study as per the protocol. In CRT arm, 11 (44%) patients were presented in stage III and 14 (56%) patients were in stage IV. In HFRT arm, 7 (46.7%) patients were presented in stage III and 8 (53.3%) patients were in stage IV. With respect to TNM stage, CRT arm and HFRT arm were comparable (P=0.87).

Radiotherapy treatment: CRT Arm: Patients of CRT arm were planned to give RT of 66 Gy and weekly 40 mg/m^2 of Cisplatin. 22 patients out of 25 (88%) completed the treatment. 3 patients received incomplete treatment <66Gy, out of which 1 patient expired during radiation after receiving only 22 Gy and 2 patients absconded after receiving 38 Gy and 52 Gy respectively.

HFRT arm: Patients of HFRT arm were planned to give RT of 79.2 Gy in two fractions of 1.2 Gy each per day. 12 patients out of 15 (80%) completed the treatment. 3 patients received incomplete treatment < 79.2 Gy, out of which 2 patients expired during radiation after receiving only 22.8 Gy & 55.2 Gy respectively and 1 patient absconded after receiving 32.4 Gy. The difference between two arms was not statistically significant (P=0.493).

Chemotherapy: CRT arm: Patients of CRT arm were planned to give 6 cycles of weekly 40 mg/m^2 of Cisplatin along with RT of 66 Gy. 4/25 (16%) patients received less than 5 cycles, 18/25 (72%) patients received 5 cycles and 3/25 (12%) patients received 6 cycles.

Overall treatment: The mean OTT was 49.09 days in CRT arm and 54.75 days in HFRT arm. There were more treatment breaks in HFRT arm. However, this difference was not statistically significant (P = 0.10).

Acute toxicity: Acute toxicity was graded by using RTOG acute toxicity criteria. Grade 2 and grade 3 more toxicity of skin, mucous membrane, salivary gland, pharyngeal and kidney, hematological toxicities were assessed in both CRT arm and HFRT arm. Dead patients and opted out patients were excluded from the study. CRT arm: Grade 2 toxicity: 13/22(59%) patients developed skin toxicity, 12/22(55%) patients developed mucous membrane toxicity, 15/22(68%) patients developed nausea,

8/22(36%) patients developed vomiting, 10/22(45%) salivary gland toxicity, 12/22 (55%) patients developed pharyngeal toxicity, 5/22(23%) patients developed hematological toxicity and 2/22(9%) patients developed renal toxicity. Grade 3 toxicity: 2/22(9%) patients developed skin toxicity, 10/22(45%) patients developed mucous membrane toxicity, 5/22 (23%) patients developed nausea, 6/22(27%) patients developed vomiting, 10/22(45%) patients developed pharyngeal toxicity, 1/22(4.5%) patients developed renal toxicity and 0/22(0%) patients developed hematological toxicity. In NCOG trial, there was increased acute toxicity with concurrent chemo radiation but radiation was not delayed[8]. In EORTC trial, there was increased acute toxicity with concurrent chemo radiation and radiation was delayed [9].

In Christie Hospital study, mucositis was significantly greater with concurrent chemo radiation [10]. In NCI Canada study, confluent mucositis was more frequent in concurrent chemo radiation arm (32% vs 11%; p = 0.001) [11]. This increase in toxicity did not prolong the delivery of radiation in concurrent chemo radiation.

In Yale University study, hematologic toxicities were more frequently noted in the drug-treated arms, but were acceptable with no drug-related treatment deaths. Non hematologic toxicities were acceptable and not significantly different between the two arms [12]. In GORTEC 94-01 trial, a significant increase in acute mucositis (grade $\geq$ 2) from 39% to 71% (p = .005) [13]. Severe acute cutaneous and hematologic toxicity and worse nutritional status were also significantly more prevalent in the patients who received combined modality therapy. Severe late toxicity, primarily cervical fibrosis, occurred in 27% of the combined modality patients and in 12% of those treated with RT alone (p = .04). Severe dental complications were twice as frequent in the combined modality patients (37% vs. 18%; p = .01). In Intergroup Nasopharynx trial, 48% experienced grade 3, 4, or 5 toxicity. There was one treatment-related death in the CRT arms a result of neutropenia sepsis. There were notably higher incidences of toxicity with CRT. In particular, for non hematologic toxicity, the incidences of oropharyngeal mucositis (48% in CRT v 32% in RT alone, P = .0149), anorexia (22% in CRT v 4% in RT alone, P < .0001), and emesis (5% in CRT v 0% in RT alone, P = .0291) were significantly higher in the CRT arm during the initial phase of treatment. In the case of hematologic toxicity, the incidence of severe neutropenia was significantly higher on CRT than RT alone (14% v 0%, respectively; P = .0001), and it was appreciable in both the initial and adjuvant (33%) phases of chemotherapy. HFRT arm: Grade 2 toxicity: 6/12 (50%) patients developed skin toxicity, 3/12 (25%) patients developed mucous membrane toxicity, 3/12 (25%) patients developed nausea, 2/12 (17%) patients developed vomiting, 8/12 (67%) patients developed salivary gland toxicity, 4/12 (33%) patients developed pharyngeal toxicity, 1/12 (8%) patient developed renal toxicity and 0/12 (0%) patients developed hematological toxicity. Grade 3 toxicity: 3/12 (25%) patients developed skin toxicity, 9/12 (75%) patients developed mucous membrane toxicity, 1/12 (8%) patients developed nausea, 0/12 (0%) patients developed vomiting, 8/12 (67%) patients developed pharyngeal toxicity, 0/12 patient developed renal toxicity and 0/12 (0%) patients developed hematological toxicity. In RTOG 9003 trial [14], acute side effects: the worst grades of acute side effects (Grade 3) during the treatment and up to 2 months after irradiation were most commonly found in the mucous membrane and the pharynx. In comparison with the conventional fractionation group, the altered fractionation groups had slightly worse Grade 2 acute side effects. Grade 3 and 4 acute toxicities were 55% with hyper fractionated radiotherapy. Late side effects: The worst late side effects (Grade 3) were most commonly found in the mucous membrane. There were 9% of late toxicities. In Horiot, et al. [9] study,

there was more acute mucositis with hyper fractionated radiation. There was no difference in the late complication rate.

In Cummings, et al. [15] study, there was more acute mucositis with hyper fractionated radiation. Grade 3-4 late toxicity was 8% vs. 14% (p= 0.31). In Pinto, et al. [16] study, there was early onset of acute reactions with hyper fractionated radiation. No details available about late complication. Toxicities in hyper fractionated radiotherapy arm were similar to that of above mentioned studies. Treatment response: Treatment response was assessed by using RECIST 1.1 at 2 months after completion of treatment. In CRT arm, out of 25patients, 1 patient expired and 2 patients did not receive complete treatment. In HFRT arm, out of 15 patients, 2 patients expired and 1 patient did not receive complete treatment. These 6 patients were excluded in response assessment.

In CRT arm, out of 22 patients, 13 (59.1%) patients had complete response (CR), 6 (27.3%) patients had partial response (PR), 1 (4.5%) patient had stable disease (SD) and 2 (9.1%) patients had progressive disease (PD) with respect to primary tumor and node response.

In meta-analysis of chemotherapy in head and neck cancer (MACH-NC) trial [17], there was absolute benefit of 6.5% of OS with concurrent chemoradiation. In Northern California Oncology Group (NCOG) trial, locoregional control was 35% vs 70% (p = 0.001), disease free survival was 15% vs 31% (p = 0.04), survival was: 24% vs 43% (p = 0.11).

In European Organization for the Research and Treatment of Cancer (EORTC) [9] trial, disease free survival was 22% vs 23% (not significant), survival was 23% vs 22% (not significant). In Christie Hospital trial, locoregional control was 50% vs 70% (p = 0.02), survival was 37% vs 47% (p = 0.07) [10].

In National Cancer Institute (NCI) Canada trial, disease free survival was 30% vs 50% (p=0.06), survival was 50% vs 63% (p=0.08) [11].

In Yale University study, locoregional control was 54% vs 76% (p = 0.003), survival was 42% vs 48% (not significant) [12]. In National Institute for Cancer Research (NICR) Italy study, locoregional control was 32% vs 64% (p = 0.04), disease free survival was 9% vs 21% (p = 0.008), survival was 10% 24% (p = 0.01) [13]. In GORTEC 94-01 trial, locoregional control was 25% vs 48% (p = 0.002), disease free survival was 15% vs 27% (p = 0.01), survival was 16% vs 23% (p = 0.05) [14]. In Intergroup Nasopharynx trial, disease free survival was 24% vs 69% (p = <0.001), survival was 47% vs 78% (p = 0.005).

In HFRT arm, out of 12 patients, 5 (41.6%) patients had CR, 3 (25%) patients had PR, 2 (16.7%) patient had SD and 2 (16.7%) patient had PD. In Radiation therapy Oncology Group (RTOG) 9003 trial, locoregional control was 54%, disease free survival was 38%, and survival was 54% with hyper fractionated radiotherapy [14]. In European organization for research and treatment of cancer (EORTC) 22791 trial, 5 year locoregional control was 40% vs 59% (p = 0.02), there was improved local control of T3 tumors [9]. In Pinto, et al. [16] study, tumor response was 64% vs 84% (p = 0.02), 3.5 year overall survival was 8% vs 27% (p = 0.03). In Cummings, et al. [15] study, 5 year locoregional control was 37% vs 45% (p = 0.01), 5 year overall survival: 30% vs 40% (p = 0.01). In Mach Meta-Analysis, there was 6.4% of locoregional control with altered fractionation, 8% of 5 year overall survival with hyper fractionated radiotherapy [17]. The overall locoregional response rates at the end of 2 months were 59.1% in CRT arm and 41.6% in HFRT arm (P = 0.54). The locoregional failure rates at the end of 2 months were 40.9% (PR of 27.3% + SD of 4.5% + PD of 9.1%) in CRT arm and 58.4% (PR of 25% + SD 16.7% + PD of 16.7%) in HFRT arm (P = 0.43). So, the tumor

response was better with standard chemoradiation than hyper fractionated radiotherapy. However this was not statistically significant.

Conclusion

Grade 2 toxicity of skin, mucous membrane, nausea, vomiting, salivary gland pharynx and hematology is more in CRT arm. Out of these, toxicities of mucous membrane, nausea, vomiting and of pharynx were statically significant. Grade 3 toxicity of nausea and vomiting was more in CRT arm whereas Grade 3 toxicity of skin, mucous membrane and pharynx were more in HFRT arm. All these toxicities were statistically significant. The mean duration of overall treatment time was 49.09 days in CRT arm whereas the mean duration of overall treatment time was 54.75 days in HFRT arm. However, this difference was not statistically significant. The overall locoregional response rates at the end of treatment were 59.1% in CRT arm and 41.6% in HFRT arm. However, this difference was not statically significant (P = 0.54). The locoregional failures at the end of treatment were 40.9% in CRT arm and 58.4% in HFRT arm. However, this difference was not statistically significant (P = 0.43). Statically significance could not be reached on response rates and locoregional failures as the sample size was insufficient.

A larger study with greater sample size needs to be undertaken to prove the therapeutic advantage of HFRT. The conclusion is standard chemoradiation is better than HFRT in Head and Neck (oral cavity) cancers because of less toxicity, less mean overall treatment time, less number of treatment breaks and better response.

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