

To Study the Effect of Radiotherapy Induced changes in skin Physiology in Cancer patients

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ABSTRACT

Background: Improvement in loco-regional control with improved 5-year survival rate among cancer patients is seen with the use of concurrent radiation therapy (RT) with cisplatin. In the current project, assessment of dermatitis as acute side effect of 3-dimensional radiotherapy during and immediately after therapy was made among enrolled cancer patients.

Methodology: This study with enrolled patients (106) was carried out after hospital's ethical approval at INMOL Lahore, Pakistan. All patients received radiotherapy according to current treatment protocol. Data was analyzed by applying statistical tests as p-value ≤ 0.05 was taken as significant.

Results: Patients developed different grades of it during treatment till 7 weeks. After one month of post-treatment, improvement in its grades was noted among patients.

Conclusion: The treatment response was good. Patients developed dermatitis of varying grades but post-irradiation period showed improvement in acute side effect so radiation is relatively safe treatment option.

Keywords: Head and Neck Cancer, Acute Side Effects, Dermatitis and 3-D Radiotherapy.

INTRODUCTION

Head and neck cancer has hampered human life badly due to its disfiguring impact both physically and mentally. Nature of disease is versatile as its clinical presentation ranges from hoarseness to neck mass depending on the site involved. Oral cavity, nasopharynx or hypopharynx are commonly target¹. Squamous cell carcinomas constitute majority (90%) of cases.

They are aggressive malignancies with annual incidence of more than 550,000 cases and 300,000 deaths each year². Males suffer more as compared to females with ratio ranges from 2:1 to 4:1. HNSCC is the sixth leading cancer by incidence globally. Mostly, the epithelial lining of mucosal membranes of the upper-aero digestive tract and the oral cavity are involved in their origin. Only 4–5% cases involve salivary glands carcinomas².

There are many factors reported in many previous studies that lead to its emergence. Association between head and neck cancer and other risk factors like human papilloma virus, genetics, environmental influence, occupation and adopted lifestyle (tobacco and alcohol consumption) is very strong. Several countries have documented a downward trend in oral cavity cancer incidence due to less tobacco use. However, it has been reported that an increasing rate of oral cavity cancers occur despite decrease in smoking rates since the 1980s³.

Activation of oncogenes while the inactivation of tumor suppressor genes lead to epithelial carcinogenesis. These alterations produce phenotypic changes⁴. Generally, these changes are grouped into loss of heterozygosity, altered copy number, hyper-methylation, and mutated RNA and DNA molecules. The presence of a tumor suppressor gene is associated with repeated loss of specific chromosomal regions⁵.

Hyper-methylation significantly controls a cell cycle as well as other major events (DNA damage repair, apoptosis, angiogenesis, invasion, and metastasis) leading to carcinoma development. However, gene inactivation can be done by gene silencing rather than somatic mutations and deletions. An early event that causes oral cancer is gene promoter methylation. Generally, down-regulated miRNAs (tumor suppressor genes) while up-regulated miRNAs (oncogenes) are considered for expression in SCC⁶.

They arise usually results from accumulated genetic changes. Changes may be altered DNA sequence, point mutations to deletions, amplifications and translocations⁷. There are eicosanoids which are involved in tumors of head and neck. However, tumour size is inversely related to the capacity of tumour microsomes to synthesize PGs.

Though radiation therapy damages tumor cells maximally but still it is linked with several side effects^{8,9}. In the light of increasing burden and difficulty in treating it due to side effects linked with treatment options, we carried out this study to assess skin changes as acute side effect of 3-dimensional radiotherapy during and immediately after therapy. It helped us in proper management of this side disease by evaluating its side effects in order to reduce the illness.

METHODS

This study was carried out after hospital's ethical approval at INMOL Lahore, Pakistan. All patients received radiotherapy according to current treatment protocol. The calculated sample size was 106 with a confidence level (95%), margin of error (9%), and taking dermatitis with 3D radiotherapy as 33.3%¹⁰. Both male and female patients were enrolled. Patients who did not give informed consent and had any second malignancy or pregnancy were ruled out of the project. Patients were informed with written consent taken. All patients were evaluated during treatment and at one month post-radiation. Data was analyzed by SPSS software, version 20. Age (in years), hemoglobin level and total radiation dose were shown

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as Mean ± S.D. Frequency and percentages were given for gender, site of cancer, cancer stage and ECOG status of enrolled patients. Chi-square and Fisher's exact test was used as p-value ≤ 0.05 was considered significant.

RESULTS

Basic parameters of all enrolled patients like age, hemoglobin level and radiation dose were presented as mean ± S.D (Table 1). Patients distribution in reference to parameters like gender, sites of cancer, stages of cancer and ECOG status was shown in table-2.. Most common cancer stage at time of diagnosis was stage 2 i.e., 46(43.4%) whereas stage 3 was observed in only 19 (17.9%) cases. There were 67 (63.2%) patients with poor ECOG status and good ECOG status was observed in 39 (36.8%) patients. An improvement in its grades appeared among all patients one month post treatment. They showed variation among grades during treatment as observed at weekly intervals (table-3). No significant difference was observed in dermatitis grades among gender at different weeks of treatment as shown in table-4. No significant difference was observed in frequency of dermatitis grades among sites at different weeks of treatment. At 11th week of treatment, frequency of dermatitis grades among sites was also insignificant (table-5). No significant difference was

observed in frequency of dermatitis' grades between poor and good ECOG status patients at 1st, 4th, 7th & 11th week of treatment (table-6).

Table-1: Demographic parameters of enrolled patients (n=106)

	Mean ± S.D	Range
Age (years)	57.8 ± 8.3	39-70
Hemoglobin (g/dl)	10.7 ± 1.24	9.0-13.0
Total radiation dose	62.8 ± 7.4	30-70

Table 2: Enrolled patients with respect to different parameters (n=106)

Variable	Category	Frequency	%age
Gender	Male	44	41.5
	Female	62	58.5
Site	Pharynx	23	21.7
	Hypopharynx	22	20.8
	Larynx	8	7.5
	Nasopharynx	22	20.8
	Oral cavity	31	29.2
Cancer	Stage 1	41	38.7
	Stage 2	46	43.4
	Stage 3	19	17.9
ECOG	Poor	67	63.2
	Good	39	36.8

Table 3: Grade Distribution Of Dermatitis Among Enrolled Patients (n=106)

Week	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
1 st	98(92.5%)	8 (7.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2 nd	67(63.2%)	39(36.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3 rd	8 (7.5%)	90(84.5%)	8 (7.5%)	0 (0%)	0 (0%)	0 (0%)
4 th	0 (0%)	67(63.2%)	31(29.2%)	8 (7.5%)	0 (0%)	0 (0%)
5 th	0 (0%)	14(13.2%)	84(79.2%)	8 (7.5%)	0 (0%)	0 (0%)
6 th	0 (0%)	0 (0%)	51(48.1%)	47(44.3%)	8 (7.5%)	0 (0%)
7 th	0 (0%)	6(5.7%)	8(7.5%)	84(79.2%)	8 (7.5%)	0 (0%)
11 th	0 (0%)	14(13.2%)	53(50%)	39(36.8%)	0 (0%)	0 (0%)

Table 4: Comparison Of Dermatitis Grades Among Enrolled Male And Female Patients

Week	Gender	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	p-value
1 st	Male	40(90.9%)	4(9.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.716
	Female	58(93.5%)	4(6.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
4 th	Male	0 (0%)	26(59.1%)	14(31.8%)	4(9.1%)	0 (0%)	0 (0%)	0.775
	Female	0 (0%)	41(66.1%)	17(27.4%)	4(6.5%)	0 (0%)	0 (0%)	
7 th	Male	0 (0%)	1(2.3%)	4(9.1%)	35(79.5%)	4(9.1%)	0 (0%)	0.625
	Female	0 (0%)	5(8.1%)	4(6.5%)	49(79.0%)	4(6.5%)	0 (0%)	
11 th	Male	0 (0%)	5(11.4%)	21(47.7%)	18(40.9%)	0 (0%)	0 (0%)	0.734
	Female	0 (0%)	9(14.5%)	32(51.6%)	21(33.9%)	0 (0%)	0 (0%)	

Table 5: Comparison of grade of Dermatitis among Different sites

Week	Site	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	p-value
1 st	Pharynx	22(95.7%)	1(4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.704
	Hypopharynx	19(86.4%)	3(13.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	Larynx	8(100.0%)	0(0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	Nasopharynx	21(95.5%)	1(4.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	Oral cavity	28(90.3%)	3(9.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
7 th	Pharynx	0 (0%)	0(0%)	3(13.0%)	19(82.6%)	1(4.3%)	0 (0%)	0.582
	Hypopharynx	0 (0%)	2(9.1%)	1(4.5%)	16(72.7%)	3(13.6%)	0 (0%)	
	Larynx	0 (0%)	0(0%)	1(12.5%)	7(87.5%)	0(0%)	0 (0%)	
	Nasopharynx	0 (0%)	3(13.6%)	0(0%)	18(81.8%)	1(4.5%)	0 (0%)	
	Oral cavity	0 (0%)	1(3.2%)	3(9.7%)	24(77.4%)	3(9.7%)	0 (0%)	
11 th	Pharynx	0 (0%)	3 (13.0%)	11(47.8%)	9(39.1%)	0 (0%)	0 (0%)	0.973
	Hypopharynx	0 (0%)	3(13.6%)	12(54.5%)	7(31.8%)	0 (0%)	0 (0%)	
	Larynx	0 (0%)	1(12.5%)	4(50.0%)	3(37.5%)	0 (0%)	0 (0%)	
	Nasopharynx	0 (0%)	3(13.6%)	13(59.1%)	6(27.3%)	0 (0%)	0 (0%)	
	Oral cavity	0 (0%)	4(12.9%)	13(41.9%)	14(45.2%)	0 (0%)	0 (0%)	

Table 6: Comparison of grade of Dermatitis between ECOG status

Week	ECOG	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	p-value
1 st	Poor	63(94.0%)	4(6.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.462
	Good	35(89.7%)	4(10.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
4 th	Poor	0 (0%)	43 (64.2%)	20(29.9%)	4(6.0%)	0 (0%)	0 (0%)	0.731
	Good	0 (0%)	24(61.5%)	11(28.2%)	4(10.3%)	0 (0%)	0 (0%)	
7 th	Poor	0 (0%)	5(7.5%)	3(4.5%)	55(82.1%)	4(6.0%)	0 (0%)	0.257
	Good	0 (0%)	1(2.6%)	5(12.8%)	29(74.4%)	4(10.3%)	0 (0%)	
11 th	Poor	0 (0%)	8(11.9%)	35(52.2%)	24(35.8%)	0 (0%)	0 (0%)	0.798
	Good	0 (0%)	6(15.4%)	18(46.2%)	15(38.5%)	0 (0%)	0 (0%)	

DISCUSSION

Radiation Therapy (RT) was planned for patients with head and neck carcinoma (HNSCC). The high incidence of this disease has impacted our lives badly among our population but due to limited resources, this health issue remained undiscovered. Thus we examined the safety of RT in non-metastatic, stage I-III cancer patients¹¹.

In our project, dermatitis was evaluated during and one month after post-treatment. There was gradually increase in grades of dermatitis in all patients after treatments till 7th week. At 4th week after treatment, dermatitis of grade 1 and 2 was observed in 98(92.5%) patients and grade 3 was observed in 8(7.5%) patients. Grade 4 and 5 was not observed at 4th week of follow up. At 7th week of treatment, dermatitis of grade 4 was observed in 58 (7%) patients, dermatitis of grade 2 and 3 was observed in 8 (7.5%) and 84(79.2%) patients respectively. Decrease in grades of dermatitis among all patients was observed at one month post-treatment period. Similar results were shown by previous studies of head and neck cancer patients treated with chemo-radiotherapy¹².

Both males and females were recruited in our work as in other previous studies. Females were 58.5% (62) while males were 41.5% (44) (table-2) paradoxically to the fact that male gender (21%) is the major victim of this cancer across Pakistani population respectively as well as globally¹³. Selection of gender among subjects was paradoxical to our study i.e 83% males and 17% females in one Brazilian population¹⁰.

They were given total radiation dose with mean±SD as 62.8 7.4 Gy (70Gy) given in table-1 for 49 days (7weeks). Our work was in lines with many previous studies who prescribed same dose of RT 66-70 Grays to their patients in their studies¹⁴.

In current study, the frequency of dermatitis of varying grades was compared with respect to ECOG status as done in many previous studies. Results showed that there was no significant difference in frequency of dermatitis grades between poor and good ECOG status patients at 1st, 4th, 7th & 11th week of treatment (table-6). Our work was in lines with one previous studies who showed similar results in their study¹⁵.

CONCLUSION

The treatment response was good. Patients developed dermatitis of varying grades but post-irradiation period showed improvement in acute side effect so radiation is relatively safe treatment option.

Limitations: Our study had several limitations like too small sample size, too small study duration, financial constraints, lack of resources and last but not the least only acute side effects were evaluated in present study.

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