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Original Research Paper

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CONCURRENT CHEMO RADIOTHERAPY WITH WEEKLY CISPLATIN VERSUS WEEKLY CARBOPLATIN IN LOCALLY ADVANCED ORAL CAVITY CANCERS

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KEYWORDS :

INTRODUCTION

Head and neck cancers are among the 10 most common cancers globally and are the most common cancers in developing countries, especially in South East Asia. In India,it accounts for one fourth of male cancers and one tenth of female cancers.Oral cancers are most common amongst all head and neck squamous cell carcinoma(HNSCC). This mainly attributed to tobacco,areca nut, alcohol, etc.[1] According to Cancer statistics of India cancer of oral cavity and lung account for over 25 % of cancer death in male [2]. Concurrent chemoradiation,has become the standard treatment option for locally advanced head and neck squamous cell cancer, since several randomized trials reported a significant survival benefit of adding chemotherapy to radiation over radiation alone [3-6].Cisplatin is among the most common agents used in combination with radiotherapy as well as one of the most studied. It has radiosensitizing properties and it's toxicity does not overlap radiotherapy [4].In an attempt to increase to local control in advanced head and neck cancers chemotherapy has been used before or after surgery and has been associated with good clinical response. Combined chemotherapy and radiation used simultaneously to get synergistic benefit against head and neck cancers has been associated with high level of response in in-operable disease. The most common drugs used are cisplatin, 5-fluorouracil,hydroxyurea and mitomycin [7]. Carboplatin has radiosensitizing properties and has lesser renal and gastrointestinal toxicities than cisplatin and is considered an effective option in National Comprehensive Cancer Network (NCCN) guidelines for patients unfit for cisplatin. Phase II studies of carboplatin based CTRT showed complete response of 65%-70% ,similar to those seen in cisplatin[8].

MATERIAL METHODS

Inclusion Criteria

Biopsy confirmed , locally advanced unresectable , (Stage III and IVa) AJCC 8th , oral cavity cancer , KPS > 70 % , age > 19 years < 70 years ,

Exclusion criteria

Patient not willing to give informed consent , age more than 70 years , histopath inconclusive , metastatic tumors

Study Design

Case control , randomised , prospective carried out at Govt. Mahatma Gandhi Memorial Medical College and Hospital, Indore , Madhya pradesh , India in the year 2018-2019.

Total 60 cases were divided into two groups case (arm 1) and control (arm 2) , first arm received carboplatin (AUC 2 weekly) as concurrent chemotherapy whereas second arm received cisplatin (40 mg per m^2 weekly) . both arms were treated with external beam radiotherapy upto 70 Gy in 35 fractions . 5 fractions per week , 2 Gy per fraction using cone down technique.

Statistics all statistical calculations were done using **SPSS 20 ,** p value < .05 was considered significant **Toxicity assess ment** Toxicity criteria were by RTOG/EORTC.

RESPONSE EVALUATION

Complete response (CR) was defined as the complete absence of disease 6 weeks. Partial response (PR) was defined as a reduction of disease by at least 50% in the sum of all measurable products of the longest perpendicular diameters of measurable tumor masses for at least 6 weeks, with no growth of other lesions or appearance of new lesions. stable diseases (SD)was defined as reduction in lesion by less than 50%, or increase by less than 25%. Progressive disease (PD) was defined as an increase by at least 25% of tumor lesions or appearance of new lesions.

Observation and Results

Total 60 biopsy proven cases of oral cavity cancer were included in the study. Cases were randomly allocated into two groups arm 1 received weekly carboplatin whereas arm 2 received weekly cisplatin . both arms were matched age sex annd stage .

Out of 30 patients in arm 1 , 24 were males and 6 females . 18 cases were stage 3 , 12 belonged to T4a . N1 nodal stage was seen in 10 patients , 14 patients had N2 staging and 6 patients had N3 stage . Buccal mucosa was the most common site observed in our study (n=14) followed by tongue (n=10) , lip (n=4) , GBS and alveolus (n=4).

Arm 2 also comprised of 30 cases , the majority were male (n = 22) and 8 females were included. 13 patients had N1 nodal stage followed by 12 cases having stage N2 and 5 cases N1 stage. Buccal mucosa was the most predominant site involved (n = 16) Tongue , GBS and alveolus were second most common (6 cases each) site involved , 2 cases had carcinoma lip.

Patient Characteristics (Table 1)

	Arm 1 (case)	**Arm 2 (control)**
Total Patients	30	30
Male	24	22
Female	6	8
Stage (T) Tumor		
T3	18	19
T4a	12	11
N (Node)		
N1	10	13
N2	14	12
N3	6	5
Location		
Buccal Mucosa	14	16
Tongue	8	6
Lip	4	2
GBS and Alveolus	4	6

RESPONSE

In the present study disease assessment after CRT complete response in Arm 1 were 66.66% and in Arm 2 63.33%, partial response were 20% in both the arm.Progressive disease were same in both arm 3.33%.Stable disease in Arm1 and Arm 2,10% and 13.33% respectively.

Table2

Response	Arm 1 (case) (n= 30)	Arm 2 (control) (n= 30)	P value
CR	20	19	0.79
PR	6	6	1
SD	3	4	0.69
PD	1	1	1

Toxicity

The comparison of both the regimens revealed that carboplatin was associated with higher rate of haematological toxicity. Mucositis grade 3 higher on Arm2 whereas grade 4 toxicity more in Arm1. Grade 3 Skin reactions were higher in Arm 2. Renal toxicity both grade 1 were higher in Arm 2.

Table 3

Toxicity	**Arm 1 (case)**	**Arm 2 (control)**	**P Value**
Hematological Toxicity			0.16
Grade 3	26	22	
Grade 4	2	1	
Mucositis			0.78
Grade 3	23	25	
Grade 4	7	4	
Skin reaction			0.76
Grade 3	24	26	
Grade 4	2	1	
Renal toxicity			0.65
Grade 1	11	18	

DISCUSSION

Definitive concurrent chemoradiotherapy is considered standard of care for inoperable locoregionally advanced head and neck squamous cell carcinoma.Cisplatin is the most common chemotherapeutic agent used in combination with radiotherapy[9]. In the present study the arms had almost similar disease response and the p value was not significant.Brainslav et al. In a three arm study compared concurrent CTRT daily low- dose cisplatin 6mg/m2, CTRT carboplatin 25mg/m2 and radical radiotherapy alone in locally advanced head and neck cancers. They found overall similar response rate in both the arm compared to radiotherapy alone arm. Non hematological toxicities were similar in all three arm.But haematological toxicities similar in both the CTRT arm but higher than the radiotherapy alone arm [10].

Chitapanarux et al. showed that in nasopharyngeal cancer, treatment completion rates were 59% versus 73%, respectively, in cisplatin versus carboplatin arm of concurrent CTRT, showed that carboplatin is better tolerated than cisplatin[11].Dutta et al.compared carboplatin AUC 6 every 3 weeks and cisplatin 100 mg/m 2 every 3 weekly, both given concurrently with radiotherapy, in locally advanced unresectable head and neck cancers excluding nasopharynx and oral cavity cancers. They reported response rates (CR plus partial response) of 76.9% and 63.6% in carboplatin and cisplatin arms, respectively. They reported significantly higher rates of nausea, vomiting, dermatological toxicity, and mucositis in cisplatin than in carboplatin arm. Hematological toxicities were higher in carboplatin than in cisplatin arm [12]. In the present study complete response 66.66% vs 63.33% in Arm1 and Arm 2 respectively. Skin toxicity observed as follows grade3,Arm 1 80% and Arm 2,86.66%, and grade 4 in Arm 1 6.66% and Arm2 3.33%. The difference were however statistically insignificant.

During RT 76.66% patient had grade 3 mucositis and 23.33% patient had grade 4 mucositis in Arm1 while 83.33% patients had grade 3, 13.33% patients had 4 mucositis in Arm2. Overall incidence of mucositis was higher in arm1 but it couldn't reach significant level.

In the current study 86.66% patients in Arm 1 and 73.33% patients in Arm 2 had grade 3 haematological toxicities and grade 4 haematological toxicities were 6.66% and 3.33% in Arm 1 and Arm 2 respectively.

Hematological toxicities though higher in arm1 , were manageable with hematinics. Our results were comparable to other similar studies.

In the present study, nephrotoxicity grade 1 was higher in Arm 2, (60%) while in Arm 2,grade 1 nephro toxicity was (36.66 %.) it was statistically insignificant .

CONCLUSION

Carboplatin can be used as safer alternative as concurrent chemotherapy along with radiation without compromising outcome in locally advanced oral cavity cancer patients. Nephrotoxicity was lesser in carboplatin arm while there was an increase in hematological toxicity which was manageable with hematinics however it was not significant (p value >0.05). Carboplatin is a safer alternative to cisplatin in patients whose renal function is compromised and in elderly patients.

Limitation small sample size and limited follow up are major limitations of the study.

Conflict of interest - There was no conflict of interest.

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