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Original Research Paper

Oncology

CLINICAL OUTCOME AND TOXICITIES AFTER CONCURRENT CHEMORADIATION IN ADVANCED HEAD AND NECK CANCER PATIENTS WITH WEEKLY PACLITAXEL VERSUS CISPLATIN: A COMPARATIVE STUDY

Dr. Jyoti Dane	Resident, Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Ramesh Arya	Professor Cum Superintendent, Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Prabhakar Gupta	Resident, Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Preety Jain*	Asso. Professor Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India. *Corresponding Author
Dr. Om Prakash Gurjar	Asso. Professor Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Manish Verma	Asstt. Professor Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Ayush Naik	Asstt. Professor Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Abhishek Pratap Singh	Resident, Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Ashish Malviya	Resident, Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Priyanka Raj Ahirwar	Resident, Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India
Dr. Vipin Kumar Dubey	Resident, Government Cancer Hospital, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh – 452001, India

ABSTRACT

OBJECTIVE: To compare the effect and toxicity of paclitaxel to cisplatin as a concurrent chemoradiation agent in locally advanced squamous cell carcinoma of head and neck (H&N) region. **MATERIALS AND METHODS:** Hundred patients diagnosed with stage III and Stage IVA locally advanced H&N squamous cell carcinoma were taken in this study. 50 patients in study arm and 50 patients in control arm were administered with paclitaxel 30 mg/m^{2}and cisplatin 40 mg/m^{2}respectively with one hour infusion four hour before radiation, repeated weekly for 7 cycles. Patients of both the arms received a total dose of 70 gray (Gy) by external beam radiotherapy in 7 weeks at the rate of 200 cGy/fraction, 5 fractions/week. **RESULT:** Acute higher grade renal toxicity and nausea were reported more in number of cases in control arm in comparison to study arm. There was no significant difference observed in both the arms in terms of treatment response and failure pattern. On follow-up, up to 6 weeks, 54% of cases are disease free in the study arm and 50% of cases in the control arm. **CONCLUSION:** Weekly paclitaxel concurrent with external beam radiation therapy is comparable to concurrent cisplatin in locally advanced H&N squamous cell carcinoma in terms of efficacy. There is lower incidence of severe renal toxicity and vomiting with concurrent paclitaxel than with cisplatin.

KEYWORDS : Concurrent chemotherapy; external beam radiotherapy; head and neck cancer

INTRODUCTION

The treatment of patients with locally advanced and unresectable, head-and-neck squamous cell carcinoma (HNSCC) are very challenging. The rates of locoregional tumor control and overall survival are poor when radiotherapy (RT) alone is used.[1]

Studies on different concurrent chemoradiotherapy schedules have been done to enhance the results. Trials evaluating concurrent chemoradiotherapy have utilized radiosensitizing agents, such as hydroxyurea, cisplatin, carboplatin and taxane.[2-7]

Phase II studies from the Radiation Therapy Oncology Group (RTOG) and the Eastern Cooperative Oncology Group (ECOG) utilizing high-dose cisplatin regimens showed good response and better survival rates of patients.[8,9]

A follow-up phase III Intergroup study showed improvement in overall survival of patient with concurrent RT and high dose cisplatin in comparison to RT alone.[10] Newer agents such as the taxane have demonstrated antitumor activity in H&N cancer.[11,12]

Paclitaxel promotes microtubular assembly and prevents microtubular depolymerization, thereby synchronizing cells at G2/M phase of the cell cycle during which cells are most susceptible to radiation.[7,13]

Improved cell sensitisation have been observed by using

taxane along with concurrent RT in advanced HNSCC have been presented by some studies.[14]

Weekly dosing allowed frequent exposure of the tumor to 2 highly active radiosensitizers during the course of RT. In addition, the use of paclitaxel was expected to have a less toxicity of mucositis, nephrotoxicity, neurotoxicity, and nausea/vomiting when compared with standard cisplatin and 5-fluorouracil.

This prospective study has been carried out with the objective of evaluating the response rate, locoregional control, disease free as well as overall survival in this setting.

MATERIALS AND METHODS

Prospective comparative study has been carried out in hundred newly diagnosed and biopsy proven patients with locally advanced, nonmetastatic (stage III–IVa, according to AJCC 8th edition) HNSCC, and with Karnofsky performance status of >70 in the year 2020-21. Patients were required to have measurable or evaluable disease, absolute neutrophil count of at least 1800/mm^3, serum creatinine less than 1.6 mg%, haemoglobin > 9g%, platelet count >1 lack. All the patients gave informed consent and their age range between 19 to 70. Patient not willing to give consent, age more than 70 years, and metastatic tumour were not included in study.

These 100 patients were divided into 2 groups, study arm and control arm. Study arm received paclitaxel (30 mg /m^2 weekly) as concurrent chemotherapy whereas control arm receive cisplatin (40 mg/m^2 weekly), both arm treated with external beam radiotherapy up to 70 gray (Gy) in 35 fraction and 5 fraction per week using reducing field technique by Theratron 780C (Theratronics, Canada). Patient details have been given in table 1.

Table 1: Patients characteristic

	Study arm	Control arm
Total Patient	50	50
Male	37	35
Female	13	15
Stage (T) Stage		
T3	30	32
T4a	20	18
N(Node)		
N1	18	20
N2	27	25
N3	5	5
Location		
Buccal mucosa	28	30
Tongue	7	6
Lip	7	4
GBS and Alveolus	8	10

Assessment of toxicities viz. mucositis, skin reaction, renal toxicity and haematological toxicity were asses according to RTOG/EORTC scale.

Response Evaluation

Complete response (CR) was defined as complete absence of disease for at least 6 weeks after complete treatment. Partial response was defined as a reduction of disease by at least 50% in the sum of all measurable products of the longest perpendicular diameter of measurable tumor masses for at least 6 weeks, with no growth of other lesions or appearance of new lesions. Stable disease (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 if new lesions.

RESULTS

Table 2: Response in the patients treated by paclitaxel+radiotherapy (study arm) and cisplatin+ radiotherapy (control arm)

Response	Study arm	Control arm
Complete response	27	25
partial response	15	15
stable disease	5	7
progressive disease	3	3

Patient (Total =100) with locally advance head and neck cancer (stage 3 and 4) were irradiated with concurrent chemotherapy, 50 were with concurrent paclitaxel and 50 with concurrent cisplatin.

After completion of treatment 54% (27/50) in paclitaxel arm (study) and 50% (25/50) in cisplatin arm (control) show complete response of disease. And partial response was seen in 30% (15/50) in both case and control arm. Disease was stable in 10% (5/50) in case and 14 % (7/50) in control arm. Disease was progress in 3 patients in both the arm. The response of all the patients has been given in table 2. Figure 1 is of one of the patient diagnosed with ulceroproliferative growth in right buccal mucosa with level-II nodes treated with concurrent paclitaxel with radiotherapy, and the figure 2 is of one of the patient diagnosed with ulceroinfiltrative left lateral border of the tongue involving the floor of mouth and associated with involvement of ipsilateral side of neck nodes level II and III treated with concurrent cisplatin with radiotherapy.

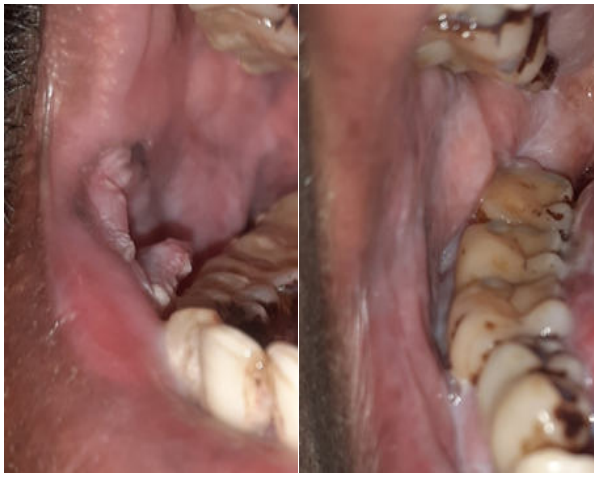

Figure 1: One of the patient diagnosed with ulceroproliferative growth in right buccal mucosa with level-II nodes treated with concurrent paclitaxel with radiotherapy (a) with disease before treatment and (b) disease free after treatment

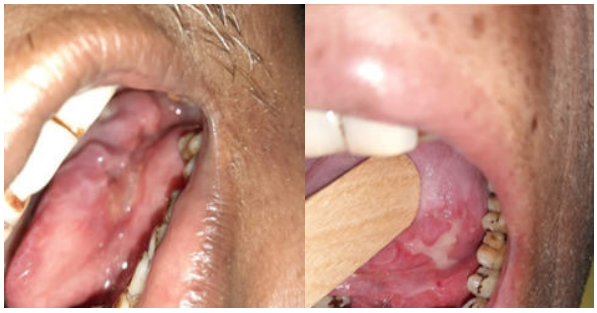

Figure 2: One of the patient diagnosed with ulceroinfiltrative left lateral border of the tongue involving the floor of mouth and associated with involvement of ipsilateral side of neck nodes level II and III treated with concurrent cisplatin with radiotherapy (a) with disease before treatment and (b) disease free after treatment

Table 3: Acute toxicities in the patients treated by paclitaxel+radiotherapy (study arm) and cisplatin+ radiotherapy (control arm)

Toxicity	Study arm	Control arm
HEMATOLOGICAL		
≤Grade2	42	44
>Grade2	8	6
ORAL MUCOSITIS		
≤Grade2	35	32
>Grade2	15	18
Nausea		
≤Grade2	43	33
>Grade2	7	17
Renaldysfunction		
Grade1 OR more	17	33

In comparison of toxicity result in both group hematological toxicity ≤Grade2 in 84% (42/50) and 88% (44/50) and >Grade2 toxicity 16 % (8/50) and 12% (6/50) in respectively study and control group.

Oral mucositis toxicity ≤Grade2 in 70% (35/50)and 64% (32/50) and >Grade2 toxicity 30 % (15/50) and 36% (18/50) in respectively study and control group.

Nausea was seen more with cisplatin arm (control), nausea ≤Grade2 in 86% (43/50) and 66% (33/50) and >Grade2 toxicity 14 % (7/50) and 34% (17/50) in respectively study and control group.

Renal toxicity was also higher with cisplatin arm (control), renal toxicity Grade1 OR more in 34% (17/50) and 66% (33/50) in respectively in study and control group. Detailed results have been presented in table 3.

DISCUSSION

In this study 50 patients in study group (paclitaxel+radiotherapy) and 50 patients in control group (cisplatin+radiotherapy) were taken for the comparison of clinical outcome. 74% male patients and 26% female patients were in study group and 70% male and 30% female patients were in control group.

On follow-up it has been found that the cases with disease free are better in study arm by 4%, opposite to it the cases of stable disease are less by 4% in study arm as compared to that in control arm. While the cases with partial response and persistent disease are similar in both the arms. These results are in concurrence with the results published by Essa *et al*.[15]

In our study a regimen of concurrently administered injection paclitaxel combined with conventionally fractionated radiation therapythis combination may provide an acceptable disease control with no enhancement of toxicities in comparison to concurrent cisplatin. The rationale for using low-dose weekly paclitaxel is based on preclinical and clinical data that suggest the direct antitumor activity and radiosensitization effect of paclitaxel.[16]

Hematological and mucositis toxicity are higher seen in with the paclitaxel arm (study) due to taxane have more toxic effect on marrow than platin. Hematological toxicity can be manage with hematinics and colony stimulating growth factor and mucositis can be manage with hydration, local analgesic and maintaining the oral hygiene. Although renal toxicity and nausea were higher with cisplatin arm (control arm) because of platinum compound are nephrotoxic, ototoxic and emetogenic. These toxicities can be managed with supportive treatment hydration and antiemetic agents.

Acute higher grade of renal toxicity and nausea were reported higher in control group in comparison to study group, because of cisplatin are more nephrotoxic and emetogenic.[17,18]

CONCLUSION

Paclitaxel can be used as a safer alternative as concurrent chemotherapy agent with radiation without compromising result in locally advanced cancer of head-and-neck (H&N) cancer. Nephrotoxicity was lesser with paclitaxel arm while there was an increase hematological toxicity, which can be managed with hematinics and growth factors.

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