



## Comparative Analysis of Weekly Cisplatin Versus Weekly Paclitaxel with Radiotherapy in Locally Advanced Head and Neck Cancer

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### Abstract

**Introduction:** Globally head and neck cancer is 7<sup>th</sup> most common cancer with more than 66,000 new cases and about 50% deaths annually. In India, head and neck cancer incidence is higher as compared to western world due to risk factors like oral tobacco, betel nut chewing, Pan masala, poor oral hygiene, and smoking habits.

**Material and Method:** We included 120 Patients. All patients were treated with radical intent. All the patients were histologically proven advanced head and neck carcinoma from stage II, III & IV in 8-month duration from – Sept 22 to April 23, patients were divided into two arms.

**Conclusion:** Weekly paclitaxel with the dose of 75 mg/nm<sup>2</sup> with radiotherapy can be considered as a promising and feasible alternative for the treatment of locally advanced Head and Neck Carcinoma.

Haematological toxicities mucositis and skin reaction was higher but manageable. xerostomia and the loss of taste was reported more in cisplatin arm.

**Keywords:** Head and Neck Carcinoma; Oral Cancer; Chemoradiotherapy

### Introduction

Globally head and neck cancer is 7<sup>th</sup> most common cancer with more than 66,000 new cases and about 50% deaths annually [1,2]. In India, head and neck cancer incidence is higher as compared to western world due to risk factors like oral tobacco, betel nut chewing, Pan masala, poor oral hygiene, and smoking habits [3].

About more than half million cases of head and neck cancer diagnosed annually. Common cancer is oral cancer pharyngeal and laryngeal squamous cell carcinoma. Contributed more than 90% of cases, Surgery, Radiotherapy or both modalities have been used for past few decades [4,5].

Multimodality treatment can be considered in locally advanced head and neck cancer like surgery radiotherapy and chemothera-

py. Sequence of these modalities are customized according to site of tumor, histology, and patients' conditions. Respectability and functional outcome of treatment general condition of patients should also be considered before taking any decision for treatment [6,7].

### Material and Methods

We included 120 Patients. All patients were treated with radical intent. All the patients were histologically proven advanced head and neck carcinoma from stage II, III and IV in 8-month duration from – Sept 22 to April 23, patients were divided into two arms.

Arm A- 60 Patients included and treated with concurrent chemoradiotherapy. Patients Inj Cisplatin 400mg/m<sup>2</sup> weekly with radiotherapy.

Arm B- 60 Patients included in this arm treated with concurrent chemoradiation Inj paclitaxel 75mg/m<sup>2</sup> given Weekly with radiotherapy.

**Inclusion criteria**

- Age < 70 Years
- Stage II to IV Proven Disease Histologically
- Routine Blood Investigation Should be normal
- Hb > 10 g/dl
- TLC > 3300 m/dl
- DC > 8000/DC
- LFT and KFT should be with in Normal Limit.

**Exclusion criteria**

- Patients with Metastatic disease.
- Patients with prior history of chemotherapy or radiotherapy.
- Patients with recurrent cancer.
- Pre-treatment workup in terms of history complete local examination, Physical examinations, Blood Test CCBC, RFT, LFT.
- Chest X ray, CECT, cardiology examination, Ultrasound abdomen Dental Check have been done.

**Radiation**

All the patients were treated with intensity modulated radiotherapy with linear accelerated 6 mU photon energy. Target volume included primary tumor with regional lymph node microscopic disease with two apprising field 200 cGy Per fraction per day up to 66-70 Gy 5 fraction per week for 6-7 week with concurrent chemoradiation.

**Response assessment**

Response was assessed by using RECIST criteria version 5.0 (Complete response Partial response stable Disease).

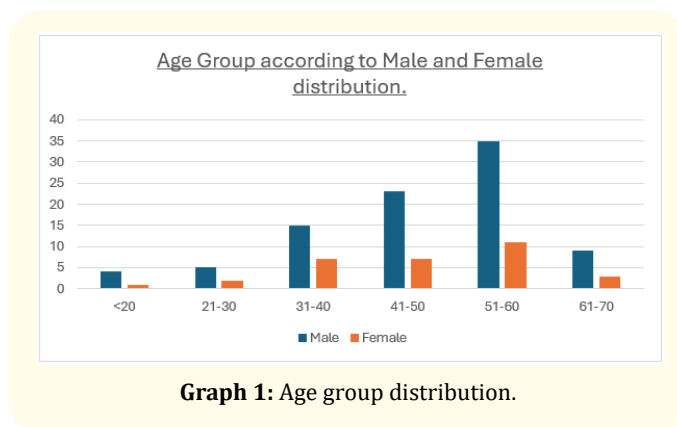
Toxicities was asserted and categorized according to CT CAE Version 5.0. Patients were evaluated weekly for toxicity and advised treatment accordingly.

**Results**

**Table 1:** Age Group according to Male and Female.

| Age Group | Male | Female |
|-----------|------|--------|
| <20       | 4    | 1      |
| 21-30     | 5    | 2      |
| 31-40     | 15   | 7      |
| 41-50     | 23   | 7      |
| 51-60     | 35   | 11     |
| 61-70     | 9    | 3      |
| Total     | 89   | 31     |

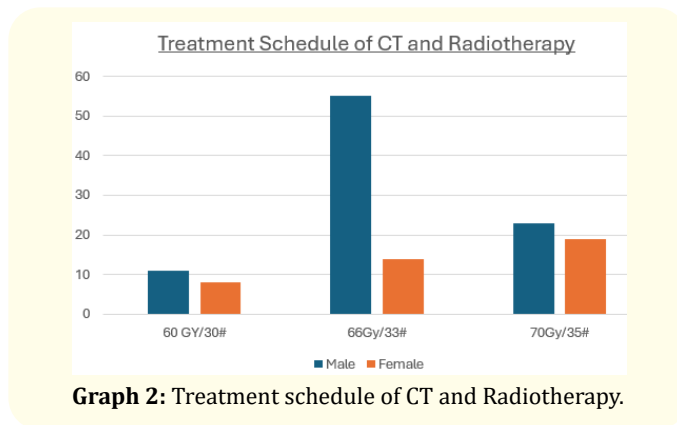
Total No. of Patients = 120



**Graph 1:** Age group distribution.

**Table 2:** Treatment Schedule of CT and Radiotherapy.

| Schedule  | Male | Female |
|-----------|------|--------|
| 60 GY/30# | 11   | 8      |
| 66Gy/33#  | 55   | 14     |
| 70Gy/35#  | 23   | 19     |
| Total     | 89   | 31     |



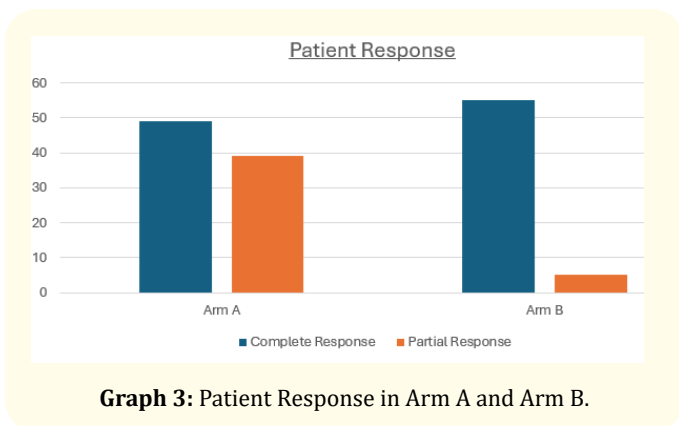
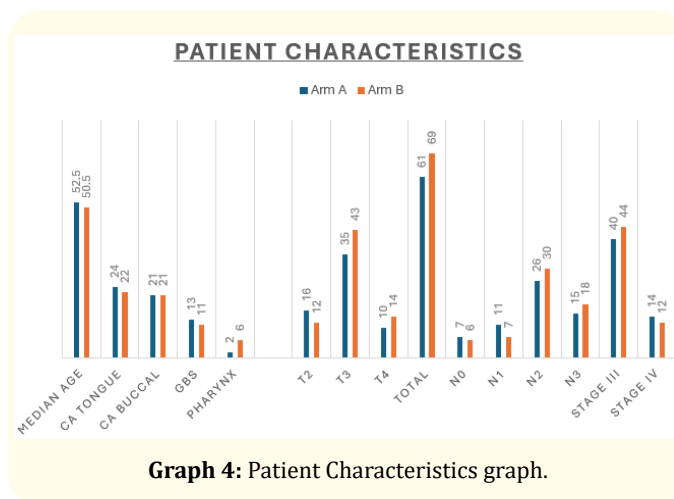
**Graph 2:** Treatment schedule of CT and Radiotherapy.

**Table 3:** Patient Characteristics.

|                   | Arm A | Arm B |
|-------------------|-------|-------|
| Median Age        | 52.5  | 50.5  |
| Ca Tongue         | 24    | 22    |
| Ca Buccal         | 21    | 21    |
| GBS               | 13    | 11    |
| Pharynx           | 2     | 6     |
| Staging           |       |       |
| T2                | 16    | 12    |
| T3                | 35    | 43    |
| T4                | 10    | 14    |
| Total             | 61    | 69    |
| N0                | 7     | 6     |
| N1                | 11    | 7     |
| N2                | 26    | 30    |
| N3                | 15    | 18    |
| Stage III         | 40    | 44    |
| Stage IV          | 14    | 12    |
| Response          |       |       |
| Complete Response | 49    | 55    |
| Partial Response  | 39    | 5     |

**Table 4:** Response.

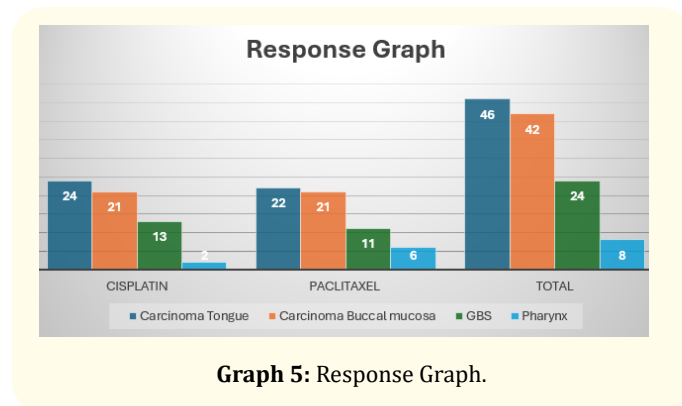
| Site                    | Cisplatin | Paclitaxel | Total |
|-------------------------|-----------|------------|-------|
| Carcinoma Tongue        | 24        | 22         | 46    |
| Carcinoma Buccal mucosa | 21        | 21         | 42    |
| GBS                     | 13        | 11         | 24    |
| Pharynx                 | 2         | 6          | 8     |
| Total                   | 60        | 60         | 120   |



**Table 5:** Distribution according to Toxicity Profile.

|                  |           | Completion | Cisplatin | Paclitaxel |
|------------------|-----------|------------|-----------|------------|
| Haematological   | Grade I   | 5          | 3         |            |
|                  | Grade II  | 10         | 14        |            |
| Neutropenia      | Grade I   | 12         | 18        |            |
|                  | Grade II  | 4          | 4         |            |
| Thrombocytopenia | Grade I   | 11         | 13        |            |
|                  | Grade II  | 9          | 8         |            |
| Mucositis        | Grade I   | 20         | 16        |            |
|                  | Grade II  | 22         | 20        |            |
|                  | Grade III | 18         | 24        |            |
| Xerostomia       | Grade I   | 38         | 35        |            |
|                  | Grade II  | 10         | 9         |            |
|                  | Grade III |            |           |            |

|                            |       |     |    |    |
|----------------------------|-------|-----|----|----|
| Taste Sensations dysgeusia | Grade | I   | 46 | 42 |
|                            | Grade | II  | 10 | 9  |
| Weight Loss                | Grade | I   | 35 | 42 |
|                            | Grade | II  | 10 | 7  |
| Dysphagia                  | Grade | I   | 11 | 12 |
|                            | Grade | II  | 5  | 8  |
|                            | Grade | III | 15 | 13 |



Graph 5: Response Graph.

**Discussion**

The treatment of locally advanced Head and Neck is a challenge for Oncologists. Chemotherapy and Radiotherapy is the commonest prescribed treatment for locally advanced Head and Neck Cancer [8]. Studies suggested that paclitaxel causes cell cycle arrest at G2 phase to mitosis (M) phase. By this activity it acts as a radiosensitizer in head and neck carcinoma. It also increases oxygen supply [9-11] to tumor which increases radiation effect to tumor [12]. The study conducted by Hamad RH [13] shown 60% patients achieved complete response with paclitaxel and 53.8% patients with cisplatin in advanced Head and Neck Cancers. 73% patients reported complete response with paclitaxel and 64% with cisplatin in a study done by R K Jain, *et al.* [14] Hoffman, *et al.* [15] shown result of 18 patients received increasing dose of paclitaxel from 10 mg/nm<sup>2</sup> to dose of 30 mg/nm<sup>2</sup> with radiation shown high incidence of mucositis. The study done by Steinberg, *et al.* [16] shown result of 24 patients with the dose Paclitaxel From 75 to 105 mg/nm<sup>2</sup> 24 hour infusion and achieved 75% complete response. Maximum delayed dose was determined less than 75 mg/nm<sup>2</sup>.

Incidence of Fabrile granulocytopenia was > 50% and more number of patients reported slow reaction and mucositis. Study done by Madhavan, *et al.* [17] shown 70% complete response by

using paclitaxel 30 mg/nm<sup>2</sup> and 30% partial response. In oropharyngeal and retropharyngeal cancer reported much better with 86.6% and 73.3% complete response in cisplatin arm. Lovey, *et al.* [18] reported the result of low dose paclitaxel in 26 patients 2 mg/m<sup>2</sup> three times a week . Response rate 65% and 46% 2 years survival rate. The study done by Tishler, *et al.* [19] shown the result of 14 patients of locally advanced head and neck cancer with paclitaxel and radiotherapy with the dose of 100 mg/nm<sup>2</sup> every 3 weeks interval have shown 92% complete response. Major toxicities reported mucositis. Study done by Milas, *et al.* [12] shown Radiation sensitization effects on the normal tissue was less as compared to tumor.

In our study mucositis skin reaction was more in paclitaxel arm as compared to cisplatin arm. Haematological toxicity was more in paclitaxel arm than the cisplatin arm. Another study shown the result of using Paclitaxel 75 mg/nm<sup>2</sup> with the radiotherapy in 24 patients with the high grade of mucositis and febrile neutropenia [18]. Study done by Madhavan, *et al.* shown higher incidence of skin reaction mucositis, swallowing difficulty. In paclitaxel arm as compared to the cisplatin arm [20]. Concurrent chemoradiotherapy acts as a synergetic effect and enhanced the therapeutic ratio without prolonging overall treatment time.

In our study we used paclitaxel 75 mg/nm<sup>2</sup> weekly with radiotherapy of 66-74 mg/nm<sup>2</sup> in 6-7 weeks' time and cisplatin 40 mg/nm<sup>2</sup> weekly with 66-74 gy in 6-7 weeks' time. The paclitaxel arm shown 88% complete response and 12% partial response at completion of treatment. While in cisplatin arm shown 73% complete response and 27% partial response at the completion of treatment. The commonest age group in our study was 50-60 years (48.3%) most common site was carcinoma tongue (38%) followed by carcinoma buccal mucosa (35%) 10% patient in paclitaxel arm required nutritional support during treatment due to skin reaction and mucositis. The loss of taste and dysphagia was higher in cisplatin arm as compared to the paclitaxel arm. Haematological toxicity was reported higher in paclitaxel arm as compared to the cisplatin arm.

Xerostomia was higher in cisplatin arm as compared to the paclitaxel arm. Mucositis was higher in paclitaxel arm as compared to the cisplatin arm. 5 patients in paclitaxel arm required blood transfusion during the treatment.

Patient with partial response were adjusted for palliative chemotherapy.

### Conclusion

Weekly paclitaxel with the dose of 75 mg/nm<sup>2</sup> with radiotherapy can be considered as a promising and feasible alternative for the treatment of locally advanced Head and Neck Carcinoma.

Haematological toxicities mucositis and skin reaction was higher but manageable. xerostomia and the loss of taste was reported more in cisplatin arm.

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