

Case Report

A Prospective Phase III Open Label Study Comparing Low Dose Paclitaxel Versus Cisplatin as Weekly Regimen with Concurrent Radiation in Locally Advanced Head and Neck Cancer

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Abstract

A prospective randomized study was done to determine the comparative effectiveness and safety of low dose weekly paclitaxel versus weekly cisplatin with concurrent radiation in the treatment of locally advanced head and neck cancer.

Material and Method: The prospective single centered study was conducted on 122 patients in the department of radiation oncology in a tertiary care hospital from October 2010 to November 2011. All patients were histopathologically proved squamous cell carcinoma. Previously untreated one hundred eight randomly selected and patients were divided into two groups by computer generated programme. The study group received injection Paclitaxel 20 mg/m² while control group received injection Cisplatin 30 mg/m². All patients had received 66-70 Gy concurrent radiation at the rate of 2 Gy/day, 5 #/week, in 6-7 weeks by cobalt-60 Theratron -780 E/780C Teletherapy units.

Result: Out of 122, 112 patients were men and 10 were women with a median age of 51 years range (30 - 65). 63 versus 59 patients were distributed on the basis of computer generated programme in Cisplatin and Paclitaxel arm. There was no statistically significant difference in DFS in CDDP arm and Paclitaxel arm ($\chi^2= 0.072$; p value 0.789) at the 24 months. There was no statistically significant difference in OS in CDDP arm and Paclitaxel arm ($\chi^2= 0.006$; p value: 0.936) at the 24 months. The common adverse effect both in the CDDP arm and Paclitaxel arm was oral mucositis. There was no significant difference in the incidence of mucositis and dermatitis between CDDP and Paclitaxel arm.

Conclusion: Low dose Paclitaxel weekly schedule is comparable to Cisplatin in locally advanced head and neck squamous cell carcinoma both in form of survival and toxicity.

Keywords: Head and neck cancer; Low dose Paclitaxel; Cisplatin

Introduction

Head and neck squamous cell carcinoma is the most common cancer in India [1]. Locally advanced head and neck cancer is a great challenge for oncologists. In India 75% cases presents in advanced stage [2]. These cancers remain confined to the loco-regional site of origin in a significant proportion of patients and the most important cause of death is loco-regional recurrence [3]. Overall, 57.5% of global burden of head and neck cancer contributed by India only, for both sexes. In female accounted for 11-16% while in male accounted for 30% of all sites of cancers [3]. The maximum number of oral cancers among males was seen after the age of 55 years in India. Around 30% of all cancers in India are due to use of tobacco in the form of smoking and chewing. The most aggressive non-surgical treatment is the combination of chemotherapy and radiation [4]. However, advances in radiation therapy as well as combined modality treatment have made local control much more successful, even for

advanced primary site disease. The treatment strategies are numerous for these patients, and advances in organ preservation with attention to quality of life remain the major focus of research investigations. Management of loco-regionally advanced head and neck squamous cell carcinoma (HNSCC) with curative intent has been the subject of intensive investigation during the last three decades and has evolved considerably over time with active research, volumes of literature, large randomized control trials and meta-analyses supporting evidence-based guidelines. Robust and mature data from various randomized studies and meta-analyses have shown the superiority of concurrent chemo-radiation schedules in loco-regional control (LRC) and overall survival [5].

Material and Method

Patients eligibility criteria includes age 18- 65 years, European Co-operative Oncology Group (ECOG) performance status ≤ 2 , histologically proved advanced squamous cell carcinoma of the head

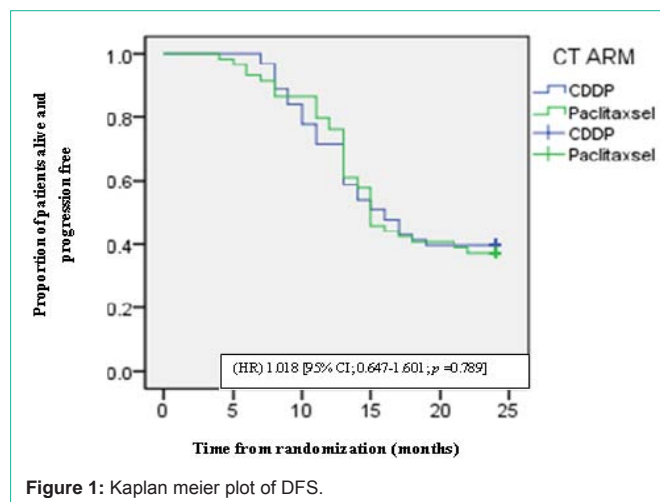
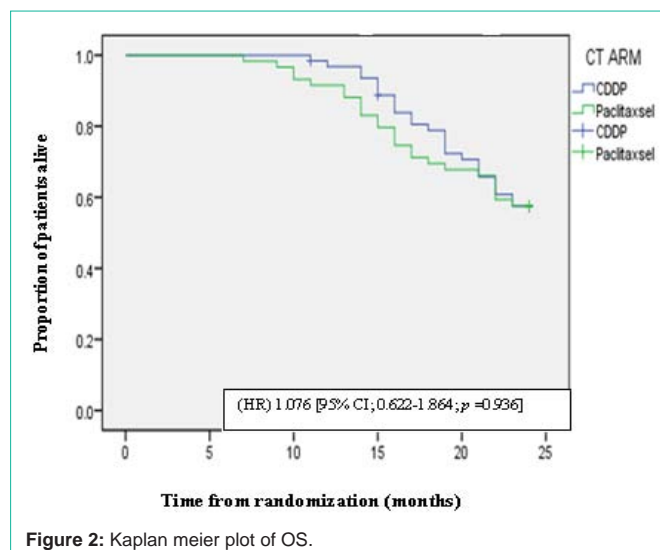
Table 1: Summary of the Patients characteristics.

Characteristic	CDDP (n=63) No.of patients	%	Paclitaxsel (n=59) No.of patients	%
Male	47	74.6	49	83.0
Female	16	25.4	10	17.0
Age Mean	43.8		47.3	
Age Range	21-65		30-65	
ECOG				
0-1	42	66.6	46	77.9
2	21	33.4	13	22.1
Site of lesion				
Oral Cavity	27	42.8	23	38.9
Oro-Pharynx	26	41.2	28	47.4
Hypo-Pharynx	10	16.0	8	13.7
T stage				
T1	-	-	-	-
T2	28	44.4	31	52.5
T3	20	31.7	19	32.2
T4	15	23.8	9	15.2
N stage				
N0	9	14.2	5	8.5
N1	28	44.4	32	54.2
N2a	26	41.4	22	37.3
N3	-	-	-	-
TNM Stage				
III	34	54.0	35	59.3
IVA	29	46.0	24	40.7

and neck (Stage III /IV) and have not received prior malignancy oriented treatment (Table 1) [6]. The patients who gave informed patients consent and fully cooperative during study process were considered in study. The patients with distant metastases, concurrent malignancies, pregnant and lactating woman, associated severe co morbidities and history of previous treatment with any of the following modalities-surgery, radiotherapy, chemotherapy were excluded from study. One hundred eight randomly selected patients were divided into two groups study and control of patients each [7]. The criteria for putting a patient in group was done by computer generated programme and no particular patient is given a priority bias. The study group received injection Paclitaxel 20 mg/m² while control group received injection Cisplatin 30 mg/m². All patients were received 66-70 Gy concurrent radiation at the rate of 2 Gy/day, 5 #/week, in 6-7 weeks by cobalt-60 Theratron -780 E/780C Teletherapy units.

Result

Out of 122, 112 patients were men and 10 were women with a median age of 51 years range (21 - 65). The distribution of the disease according to the primary site was on follows Oral cavity (40.98%), Oropharynx (44.26%), Hypopharynx (14.76%). The commonest histopathology was moderately differentiated squamous cell carcinoma. 63 versus 59 patients were distributed on the basis

**Figure 1:** Kaplan meier plot of DFS.**Figure 2:** Kaplan meier plot of OS.

of computer generated programme in Cisplatin and Paclitaxsel arm. At 24 months, in CDDP arm disease free survival (DFS) was 39.69% while 37.29% in Paclitaxsel arm. The median DFS was 16.80 [95% CI; 15.276-18.406] months for CDDP arm versus 16.66 months [95% CI; 15.186-18.441] for Paclitaxsel arm respectively, with a hazard ratio (HR) 1.018 [95% CI; 0.647-1.601]. There was no statistically significant difference in DFS in CDDP arm and Paclitaxsel arm ($\chi^2 = 0.072$; p value 0.789) at the 24 months (Figure 1). At 24 months, in CDDP arm overall survival (OS) was 58.74% while 57.63% in Paclitaxsel arm. The OS throughout study was 21.40 months [95% CI; 20.526-22.364] for CDDP and 20.50 months [95% CI; 19.277-21.808] for Paclitaxsel arm, with a HR 1.076 [95% CI; 0.622-1.864]. There was no statistically significant difference in OS in CDDP arm and Paclitaxsel arm ($\chi^2 = 0.006$; p value: 0.936) at the 24 months (Figure 2). The common adverse effect both in the CDDP arm and Paclitaxsel arm was oral mucositis. There was no significant difference in the incidence of mucositis between CDDP and Paclitaxsel arm [$\chi^2 = 0.72$; p value = 0.39]. Most of patients developing grade II or III mucositis needed dietary modification in the form of liquid diet. Most of patients developing severe mucositis were managed with intravenous fluids, steroids and analgesics with Ryles tube insertion.

There was no significant dermatitis between CDDP and Paclitaxel arm [$\chi^2=0.60$ p value = 0.43]. Bone marrow toxicity was rare, as only one patient in the control group developed grade II anemia for which blood transfusion was administered.

Discussion

Ideal management giving results in the shape of long disease free survival of cancer patients is the ultimate dream of an oncologist. Efforts are on to achieve as high as possible survival rates. It is realized that, there is no unique modality of treatment, which helps in achieving this objective. However multimodality treatment takes us a step of two closer to our target. This study intended to compare concomitant chemo- radiation using newer active agent Paclitaxel in low dose weekly schedule with Cisplatin added to conventional radiation in locally advanced head and neck cancer. Although some patients in the Paclitaxel arm sustained local toxicity, Mucositis with dysphagia, this was acceptable and comparable to the use of concurrent Cisplatin. No dose limiting systemic toxicity was encountered in this study. There was no statistically significant difference in DFS in CDDP arm and Paclitaxel arm ($\chi^2= 0.072$; p value 0.789) and OS in CDDP arm and Paclitaxel arm ($\chi^2= 0.006$; p value: 0.936) at the 24 months.

Comparing these results the Paclitaxel dose of 20mg/m²/wk was well tolerated with none of the patients requiring percutaneous gastrostomy. The mucosal toxicity observed during radiotherapy

subsided with symptomatic treatment in the form of IV steroids and intravenous fluids. Looking at the results of these studies it can be concluded that the weekly administered of paclitaxel concurrent with radiation in carcinoma of head & neck is associated with an acceptable therapeutic profile and can be investigated further.

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