Concurrent Chemoradiation in Locally Advanced Head and Neck Cancers: A Comparative Study of Weekly Paclitaxel Versus Cisplatin-Based Regimen

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ABSTRACT

Background: Concurrent chemoradiotherapy is the standard of care for patients with unresectable locally advanced squamous cell carcinoma of head and neck (LA-SCCHN). The optimal chemotherapy agents and their dose schedules have yet to be defined. Cisplatin improves the anti-tumour efficacy of radiation therapy (RT) with 5-year loco-regional control rates between 35-70%. The last decade witnessed the introduction of new chemotherapeutic agents. Among these, taxane-based chemotherapies emerged as one of the most powerful compounds that might improve loco-regional control. The aim of this study was to compare the outcome and toxicity of weekly paclitaxel with weekly cisplatin-based concurrent chemoradiation in LA-SCCHN.

Patients and Methods: Fifty two untreated patients with LA-SCCHN were enrolled in a chemoradiation feasibility study in the Oncology Department, Assuit University Hospital, between the time period from November 2006 to September 2008 of whom forty one patients were eligible for the study. The patients were randomized into 2 groups; group I (21 patients) who received paclitaxel 30mg/m² I.V 1 hour infusion weekly and group II (20 patients) received Cisplatin 30mg/m², I.V 2 hours infusion weekly, both during the course of radiation therapy. All patients received 66-70Gy concurrent radiation using a linear accelerator with 6mv photons, at the rate of 2Gy/day, 5 fractions/week, over a period of 6-7 weeks. Response was assessed according to WHO criteria and toxicity according to Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring criteria and NCI-CTC version 2.

Results: Complete response was achieved in 57.1% of patients in group I and 50% of patients in group II while partial response was achieved in 28.6% in group I and 25% in group II. Thus, the objective overall response was 85.7% in group I versus 75% in group II with no statistically significant difference (p=0.3). The median duration of follow-up was 15 months in group I (range 9-28 months) while it was 16.5 months for group II (range 7-29 months). The median progression free survival (PFS) was 26 months for group I and 22 months for group II. The 1-year PFS was 80.7% and 64% for group I and group II while the 2-year PFS were 52.2 and 41.1% for group I and group II respectively with no statistically significant difference (p=0.5). The median survival was 27 and 25 months for group I and II respectively. The 1-year overall survival (OS) was 80.7% and 64.6% for group I and II while the 2-year OS was 58.4 and 46% for group I and group II respectively with no statistically significant difference (p=0.41). Treatment toxicities including skin reactions, mucositis and dysphagia were comparable in both groups and tolerable.

Conclusion: The results of weekly paclitaxel schedule in the treatment of LA-SCCHN were comparable to those of weekly cisplatin schedule with no additional efficacy. So, concurrent chemoradiotherapy with weekly paclitaxel is feasible when contraindication to cisplatin exists as in cases of fear of hearing loss or renal disease.

Key Words: Chemoradiation – Paclitaxel – Cisplatin – Locally advanced head and neck cancers.

INTRODUCTION

Head and neck cancer is the sixth most prevalent cancer in the world, and accounts for 8% of cancers worldwide [1]. The majority of patients with squamous cell carcinoma of the head and neck (SCCHN) presents with loco-regionally advanced disease. For a long time, definitive radiotherapy (RT) has been the standard treatment for locally advanced squamous cell carcinoma of head and neck (LA-SCCHN). High local and regional failure rates typically translated in 3-year survival rates of less than 25% and 5-year survival rates of less than 10%, leaving significant room for improvement [2].
Various strategies to improve outcome by coordinating chemotherapy with radiotherapy have been tried, but the optimal schedule for integrating chemotherapy into the management of this disease has yet to be defined [3]. Multiple chemotherapeutic agents have been investigated in combination with concurrent RT, of which the most commonly used is cisplatin. Cisplatin is a representative cytotoxic chemotherapeutic agent, and it has been known that it acts as a radiation sensitizer and improves the anti-tumour efficacy when combined with RT [4].

The taxoids represent a new class of agents having both a specific chemical structure and mechanism of action [5]. Paclitaxel is one of the most active agents for SCCHN in the metastatic and recurrent setting and has been shown to be a radiosensitizer for human SCCHN cell lines. It promotes the polymerization and stabilization of microtubules, leading to an accumulation of cells at the G2-M boundary, the most relatively radiosensitive phase of the cell cycle. This suggests an obvious mechanism for radiosensitization, but the reality may be more complex. Paclitaxel has also been shown to improve tumour reoxygenation and to activate apoptosis. It has also been suggested that exposure to subcytotoxic concentrations of paclitaxel may simply suppress tumour repopulation, as during a course of fractionated RT [6]. In recent trials paclitaxel has been studied concurrent with RT, as prolonged infusion, weekly infusion or in combination with different cytotoxic agents, with long-term local control and survival in patients with SCCHN [7].

**Objective:** To compare the efficacy and toxicity of weekly paclitaxel with weekly cisplatin-based concurrent chemoradiation in LA-SCCHN.

**PATIENTS AND METHODS**

This study included fifty two patients with LA-SCCHN presented to the Oncology Department, Assuit University Hospital, during the time period from November 2006 to September 2008 of whom forty one patients were eligible for the study. The patients were randomized into 2 groups; group I (21 patients) and group II (20 patients).

**Eligibility criteria:**

Patient selection: Patients were required to have pathologically proven SCCHN without evidence of distant metastases and had not been previously treated with chemotherapy or RT. Tumour and lymph node classification were assigned according to the American Joint Committee on Cancer staging system [8]. Other requirements for eligibility were: age 18 years, ECOG performance status (P.S) of ≤2, life-expectancy of at least 12 weeks, adequate hematologic (white blood cell ≥3.5 x 10^9/L, platelets ≥100 x 10^9/L, hemoglobin (Hb) ≥9g/dl), renal (serum creatinine <120µmol/L, calculated creatinine clearance >50ml/min) and hepatic (bilirubin <17µmol/L) function. Pregnant or lactating females were excluded. All patients provided full, written informed consent.

**Treatment plan:**

Staging procedures included clinical examination, chest radiograph, endoscopy and computerized tomographic scan (CT scan), and/or magnetic resonance imaging (MRI) of the neck. All patients underwent a pretreatment dental evaluation with appropriate preventative care and audiogram.

**Chemotherapy:**

The patients were randomized into 2 groups; group I (21 patients) who received paclitaxel 30mg/m^2 I.V 1 hour infusion weekly and group II (20 patients) who received Cisplatin 30mg/m^2, I.V 2 hours infusion weekly both during the course of RT. Standard anti-emetic prophylaxis was given. It consisted of 16mg of ondansetron and 16mg of dexamethasone given as intravenous bolus as pre-medication, 30 minutes prior to chemotherapy. Anti-emetic prophylaxis was continued with ondansetron and metoclopramide orally 2-3 days after each cycle of weekly cisplatin chemotherapy.

**External beam radiotherapy:**

All patients were treated with conventional once daily radiotherapy using a linear accelerator with 6mV photons. The simulator was used for planning and immobilizing masks were used for reproducibility of the sittings. Two parallel opposing neck fields including the tumour and the surrounding tissues and the draining lymphatics were defined in most of the cases. After a tumour dose of 45 gray (Gy), the posterior
margin of the lateral border was brought ante-
riorly excluding the spinal cord and then the
rest of the dose of radiotherapy was given. In
case of clinically positive lymph nodes, an
electron beam (9-12MeV) was used to increase
the dose to the posterior cervical nodes after
45Gy without allowing further dose to the spinal
cord. Treatment of the primary tumour and gross
nodal disease continued via shrinking fields to
a total dose of 66-70Gy. The lower neck (usually
below the level of the thyroid notch) was treated
with an anterior portal delivering 50Gy given
dose. If no palpable lymph nodes are present
at or near the midline, a 5 half-value layer 1.5
to 2cm wide midline block was used to shield
the larynx and spinal cord. This block was not
used in cases of laryngeal and hypopharyngeal
tumours.

Fractionation: Two Gy were given per frac-
tion. One fraction per day and five fractions
per week had been the applied fractionation
scheme.

Evaluation:

Follow-up: Patients were evaluated weekly
by history, physical examination, documentation
of P.S and toxicity evaluation. Laboratory testing
(complete blood cell count, differential leuco-
cytic and platelet count, and renal and hepatic
functions) was carried out at least every other
week and more often as indicated. The response
evaluation was performed 4-6 weeks after the
completion of concurrent chemoradiotherapy.
For the evaluation of tumour response, physical
examination and endoscopy, when it was indi-
cated, were performed, as well as CT and/or
MRI for objective evaluation. Endoscopy and
biopsy were performed if there was clinical
evidence of residual tumour. Patients were not
routinely biopsied to confirm the absence of
tumour. Subsequent clinical follow-up was 3
monthly in the first 2 years, then 6 monthly
afterwards. CT scan and endoscopy with biopsy
were performed whenever persistent disease or
local recurrence was suspected during the fol-
low-up period. Chest X-ray was annually per-
formed or when it was clinically indicated.

Tumour response: The primary end point of
our study was response rate. For the evaluation
of the response to concurrent chemoradiother-
apy, tumour response criteria of the World
Health Organization (WHO) [9] was applied.
Complete response (CR) was defined as disap-
pearance of all objective evidence of disease
confirmed by physical examination, endoscopy
and imaging. Partial response (PR) was defined
as a decrease of the sum of the products of
longest and its perpendicular diameter in all
measurable lesions by at least 50%. Progressive
disease (PD) was defined as the appearance of
new lesion or an increase of the sum of the
products of the longest and its perpendicular
diameter in all measurable lesions by more than
25%, and stable disease (SD) was all cases who
did not belong to the above mentioned 3 cate-
gories.

Survival: The secondary end point was pro-
gression-free survival and overall survival. The
progression-free survival was defined as the
time from the initiation of treatment to the date
of first observation of progressive disease.
Overall survival (OS) was defined as the date
from initiation of treatment to death due to any
cause.

Toxicity evaluation: Toxicities were evalu-
ated by history, physical examination and lab-
oratory blood cell counts and serum tests. Lab-
oratory and clinical toxicities were considered
acute if discovered during the first 12 weeks
after the initiation of therapy. The grading sys-
tem was based on the Radiation Therapy On-
cology Group (RTOG) acute radiation morbidity
scoring criteria for the following in-field toxic-
ities [10]: Dysphagia, fibrosis, hearing loss,
mucositis, osteoradionecrosis, skin toxicity and
xerostomia. The remaining systemic toxicities
were graded according to the National Cancer
Institute Common Toxicity Criteria, version 2.0
(NCI-CTC) [11]. Patients were monitored weekly
during their treatment in an effort to manage
treatment-induced adverse effects, particularly
mucositis and myelosuppression. Neutropenia
with fever necessitated hospitalization and ap-
propriate antibiotic therapy. Hospitalization was
also required when mucosal injury precluded
an adequate oral intake. Percutaneous endoscop-
ic gastrostomy feeding tubes or nasogastric
feeding tubes were placed as needed. Tracheo-
stomy was performed in patients with signif-
cantly compromised airways, either at presen-
tation or, if required, during the course of their
treatment.
Statistical analysis:

Data were recorded on specialized forms and all statistical tests were performed using SPSS version 16 for windows (SPSS Inc, Chicago, IL, USA) and Microsoft Excel (Realmond, W.A, USA) software. Descriptive analysis (e.g., mean, standard deviation, frequencies, percentage) were calculated and analysis was performed using the student’s t-test and Fisher Exact t-Test. p value <0.05 was considered significant. The survival curves were made using the Kaplan-Meier method and comparison was with the log rank test.

RESULTS

Patient characteristics: Table (1).

The mean age for group I was 55.1 ± SD 8.18 years, while it was 55.7 ± SD 12.02 for group II. The majority of patients were males comprising 15 patients (71.4%) in group I and 18 patients (90%) in group II. Most of the patients had ECOG P.S of ≤1; 19 patients (90.4%) in group I and 19 patients (95%) in group II. Smoking was the main special habit in 13 patients (61.9%) in group I and 18 patients (90%) in group II. The most common primary site was hypopharynx in group I seen in 9 patients (42.9%) while it was the supraglottic in group II constituting (7 patients, 35%). The majority of patients in both groups had stage IV disease, constituting 14 patients (66.7%) in group I and 15 patients (75%) in group II. Table (2), shows the TNM classification of both groups.

Outcome:

Response: Table (3).

Comparing the results of the two groups CR was achieved in 12 patients (57.1%) in group I and 10 patients (50%) in group II, while PR was achieved in 6 patients (28.6%) in group I and 5 patients 25% in group II. Thus, the clinical overall response was 85.7% in group I and 75% in group II with no significant statistical difference (p=0.3). Three patients (13.3%) in group I had no response of whom 2 patients had PD and one patient had SD while 5 patients (25%) in group II had no response of whom 3 (15%) had PD and 2 patients had SD (10%) with no significant statistical difference (p=0.3).

Survival:

For surviving patients in group I, the median duration of follow-up was 15 months (range 9-28 months) while it was 16.5 months (range 7-29 months) in group II. The median progression free survival was 26 months for group I while it was 22 months for group II. The 1 and 2 year PFS were 80.7% and 52.2% for group I while they were 64% and 41.1% for group II with no significant statistical difference (p=0.5), (Fig. 1).

The median overall survival was 27 months for group I and 25 months for group II. The 1 and 2-year OS was 80.7% and 58.4% for group I and 64.6% and 46% for group II with no significant statistical difference (p=0.41), (Fig. 2).

Toxicity:

Acute toxicities were considered tolerable in both groups, (Fig. 3). The most common acute toxic effects were skin reactions, mucositis and dysphagia, (Table 4). Most of them were grade I and 2 and were treated on an out patient basis. Pharyngo-oesophgitis occuring in some patients induced anorexia, nausea, and vomiting which lead to weight reduction and deterioration of P.S.

Late toxic effects recorded were xerostomia, hypothyroidism and hearing impairment. Six patients (28.6%) in group I and 4 patients (20%) in group II developed xerostomia. One patient in group I (4.8%) had hypothyroidism and 2 patients (10%) in group II experienced hearing impairment.

Pattern of failure:

In group I, 10 patients (47.6%) had experienced disease recurrence; 6 patients (28.6%) had loco-regional failure and 4 patients (19%) had distant recurrence of whom one patient had both locoregional and distant recurrence and all of them had pulmonary metastasis. In group II, 11 patients (55%) had experienced disease recurrence with no significant statistical difference from group I (p=0.7). Seven patients (35%) in group II had loco-regional failure while 4 (20%) had distant recurrence of whom one patient had bone metastasis and the other 3 patients had pulmonary metastasis.
Table (1): Characteristics of the 41 LA-SCCHN patients.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55.10±8.18</td>
<td>55.7±12.02</td>
<td>0.8**</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15 (71.4%)</td>
<td>18 (90%)</td>
<td>0.13*</td>
</tr>
<tr>
<td>Female</td>
<td>6 (28.6%)</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (61.9%)</td>
<td>18 (90%)</td>
<td>0.07*</td>
</tr>
<tr>
<td>No</td>
<td>8 (38.1%)</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>ECOG (P.S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>4 (19%)</td>
<td>6 (30%)</td>
<td>0.65*</td>
</tr>
<tr>
<td>T1</td>
<td>15 (71.4%)</td>
<td>13 (65%)</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>2 (9.5%)</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supraglottic</td>
<td>7 (33.3%)</td>
<td>7 (35%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Glottic</td>
<td>5 (23.8%)</td>
<td>3 (15%)</td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0 (0%)</td>
<td>4 (20%)</td>
<td></td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>9 (42.9%)</td>
<td>6 (30.0%)</td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>7 (33.3%)</td>
<td>5 (25%)</td>
<td>0.35*</td>
</tr>
<tr>
<td>Stage 4</td>
<td>14 (66.7%)</td>
<td>15 (75%)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher exact test,
** Independent t test.
LA-SCCHN= Locally advanced squamous cell carcinoma of head and neck.

Table (2): Staging of primary tumours of the 41 LA-SCCHN patients.

<table>
<thead>
<tr>
<th></th>
<th>Group I = 21 patients</th>
<th>Group II = 20 patients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1 T2 T3 T4 Total</td>
<td>T1 T2 T3 T4 Total</td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>0 0 3 2 5</td>
<td>0 0 2 1 3</td>
<td>0.8</td>
</tr>
<tr>
<td>N1</td>
<td>0 1 3 1 5</td>
<td>0 0 3 2 5</td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td>0 1 3 2 6</td>
<td>0 2 4 2 8</td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td>0 1 2 2 5</td>
<td>0 2 1 1 4</td>
<td></td>
</tr>
</tbody>
</table>

Total 0 3 11 7 21 0 4 10 6 20

There was no significant difference in T and N stages between the 2 groups.
T: Tumour, N: Nodal.
p value ≤0.05 is significant.

Table (3): Response rate during chemoradiation of 2 groups of 41 LA-SCCHN patients.

<table>
<thead>
<tr>
<th>Response</th>
<th>Group I</th>
<th>Group II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>12 (57.1%)</td>
<td>10 (50%)</td>
<td>0.3</td>
</tr>
<tr>
<td>PR</td>
<td>6 (28.6%)</td>
<td>5 (25%)</td>
<td></td>
</tr>
<tr>
<td>Overall response</td>
<td>18 (85.7%)</td>
<td>15 (75%)</td>
<td></td>
</tr>
</tbody>
</table>

No response 3 (14.3%) 5 (25%)

There was no significant difference in response rate between LA-SCCHN patients treated with paclitaxel (group I) and patients who received cisplatin (group II).

CR = Complete response,
PR = Partial response.
p value ≤0.05 is significant.

Table (4): Acute toxicity during chemoradiation of the 41 LA-SCCHN patients.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Group I</th>
<th>Group II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 + Grade 2</td>
<td>17 (81%)</td>
<td>18 (90%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Grade 3 + Grade 4</td>
<td>4 (19%)</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Mucositis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 + Grade 2</td>
<td>11 (52.4%)</td>
<td>15 (75%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Grade 3 + Grade 4</td>
<td>10 (47.6%)</td>
<td>5 (25%)</td>
<td></td>
</tr>
<tr>
<td>Dysphagia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 + Grade 2</td>
<td>15 (71.4%)</td>
<td>16 (80%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Grade 3 + Grade 4</td>
<td>6 (28.6%)</td>
<td>4 (20%)</td>
<td></td>
</tr>
</tbody>
</table>

No significant difference in acute toxicity between LA-SCCHN patients treated with paclitaxel (group I) and patients who received cisplatin (group II).
p value ≤0.05 is significant.
Combined treatment approaches have become standard for patients with LA-SCCHN. Several randomized phase III trials and meta-analysis documented a survival and/or organ preservation benefit from the addition of chemotherapy to RT as primary therapy [12]. Multiple chemotherapeutic agents had been investigated, of which cisplatin was the most extensively used and was considered as the standard of care for patients with LA-SCCHN. Taxane based chemotherapies might improve locoregional control as had been shown in phase I and II trials [13]. This study was intended to compare the newer agent paclitaxel with the most extensively used cisplatin as a chemoradiotherapy schedule.

**DISCUSSION**

Kaplan-Meier curves showing a non-significant difference in progression free survival between LA-SCCHN patients treated with paclitaxel (group I) and patients who received cisplatin (group II) \( p=0.5 \).

Kaplan-Meier curves showing a non-significant difference in the overall survival between LA-SCCHN patients treated with paclitaxel (group I) and patients who received cisplatin (group II) \( p=0.41 \).

The most common acute toxic effects were skin reactions, mucositis and dysphagia and most of them were grade 1 and 2.

Fig. (1): Progression-free survival of the 41 LA-SCCHN patients.

Fig. (2): Overall survival of the 41 LA-SCCHN patients.

Fig. (3): Acute toxicity during chemoradiation of the 41 LA-SCCHN patients.
In this study, the 57.1% CR in the paclitaxel group and the 50% in cisplatin group were inferior to those reported by Jain et al., [14] where CR was achieved in 73% of patients of paclitaxel group and 64% of patients who received cisplatin concurrently with radiotherapy. The inferior results of this study might be due to the observation that the majority of our patients were stage IV, while in Jain's et al., study the majority were stage III, but the difference between the two groups was insignificant in both studies.

The complete response rate in the paclitaxel group was more than that achieved by Hoffmann et al., (36%) [15], yet, it was inferior to that of Steinberg et al., (72%) [16], Tishler et al., (92%) [17] and Sunwoo et al., (70%) [18]. In these studies, paclitaxel was administered as prolonged continuous infusion over 3-24 hours every 3 weeks which was different from our schedule. The rationale for this dosing schedule was based on preclinical and clinical data that suggested that anti direct tumour activity and radiosensitization were more dependent on the duration of paclitaxel exposure than on the peak of serum concentration. The comparison of biologic effectiveness and radiation sensitization of these different schedules was difficult and needs a randomized study.

Also, the complete response rate of our study was comparable to that reported by Chougule et al., (57%) [19]; Wanebo et al., (60%) [20] and Agawala et al., (52%) [21] but inferior to Kies et al., (69%) [22]. In all these studies paclitaxel was administered in combination with other chemotherapeutic agents. In theory, the use of multiple chemotherapeutic agents in combination would seem more attractive than monotherapy. However, the role of multiagent concurrent chemoradiotherapy schedules remains ill defined.

The rate of complete response in the cisplatin group was comparable to Zend et al., (50%) [23] and Kim et al., (54.2%) [4] but it was more than that reported by Adelstein et al., (40.2%) [12]. It was inferior to that of Vokes et al., (67%) [24], Poole et al., (82%) [28] and Hung et al., (77%) [26] but in these studies cisplatin was used in combination with other chemotherapeutic agents.

As regards survival, similar to our approach, two other groups had published their experience in the comparison of paclitaxel and cisplatin with concurrent radiotherapy. The 1-year OS and PFS of this study were better than that reported by Jain et al., [14] where at 3-10 months 59% of patients of paclitaxel group and 42% of patients of cisplatin group were alive and disease free. In Sharma et al., study [13], 2-year PFS was 60% for paclitaxel group and 52% for cisplatin group.

The results of this study compared favorably to other studies of concurrent paclitaxel with radiotherapy. Agarwala et al., [21] reported 3-year OS and PFS of 45% and 36% and Suntharalingam et al., [27] reported both 3 years OS and PFS of 48%. Also, Loveya et al., [28] reported 2-year OS of 46% but they administered low dose paclitaxel to patients of poor general condition.

The survival in the cisplatin group was comparable to other studies, where the 2-year PFS was comparable to the other studies of Jeremic et al., [29] and Ang et al., [30] (46% and 53.5%). Meanwhile, Adelstein et al., [12] reported 3-year OS of 37%.

Studies examining the radiation potentiating activity of taxanes had indicated that the effects on normal tissue were less pronounced than those on tumour [31]. Some patients in the paclitaxel arm had significant local toxicity in the form of skin reactions, mucositis and dysphagia which were acceptable and comparable to those of cisplatin arm and none was dose limiting. The degree of these toxicities was comparable to other studies [14,18,28].

The pattern of failure for patients with SCCNH have changed. Historically, local and/or regional failure have been the major problems in disease control. However, loco-regional control after chemoradiotherapy was excellent, and distant metastasis emerged as the most common cause of treatment failure [32]. In our study, the incidence of distant metastasis remained high in both groups and this might be explained by the fact that the systemic level of the drug, which was usually suboptimal during radiation, was not sufficient to control micrometastatic disease. Improved control of distant disease could be achieved by eradicating micrometa-
static disease through systemic drug delivery by addition of adjuvant or neoadjuvant chemotherapy to chemoradiotherapy. Patient tolerance to adjuvant chemotherapy was limited by the cumulative toxic effects of concurrent chemoradiotherapy [33]. The poor compliance with adjuvant chemotherapy after concurrent chemoradiation could be overcome by the use of neoadjuvant chemotherapy. Neoadjuvant chemotherapy followed by concurrent chemoradiation program was feasible, and improved local and distant disease control [34,35].

The loco-regional control can be improved more in the future with the different boost techniques using brachytherapy, 3D conformal irradiation or IMRT which provides dose escalation with better dose differentiation between tumour and normal tissues.

**Conclusion:** The results of weekly paclitaxel schedule in the treatment of LA-SCCHN were comparable to those of weekly cisplatin schedule with no additional efficacy. So, concurrent chemoradiotherapy with weekly paclitaxel is feasible when contraindication to cisplatin exists as in cases of fear of hearing loss or renal disease.

**REFERENCES**


