Original Article

Concurrent Chemo Radiation with Carboplatin and Paclitaxel versus Sequential Chemotherapy followed by Radiotherapy in Esophageal Cancer

Atique Anwer Khan, Ahmed Ijaz Masood and Muhammad Arshad

ABSTRACT

Objective: This study was conducted to compare the concurrent chemo radiation with Carboplatin and Paclitaxel and Sequential Chemotherapy followed by Radiotherapy in Esophageal Cancer patients.

Study Design: A randomized control study design

Place and Duration of Study: This study was conducted at the Oncology Department in Nishtar Medical University and Hospital Multan from Feb 2020 to Feb 2021 for a period of one year.

Materials and Methods: Total 60 participants, 30 in each treatment group were included in the study. The Patients aged between 22-75, confirmed cases of esophageal cancer were included in the study. The Patients with organ metastasis, complete obstruction, or tracheoesophageal fistula, and the ones who had lost more than 10% of their body weight or have any other primary cancer or had undergone any defined surgery were excluded from the study. Patients' baseline data related to family history, physical examination, and laboratory work-up were collected. The participants were randomly grouped into two groups Group A and Group B. Group A patients received concurrent chemo radiation therapy. Group B patients received 2 cycles of chemotherapy followed by radiotherapy the tumor response was then evaluated.

Results: Demographic variables of the patients show that the median age of the patients in Group A & B was 58 & 60 years respectively. Among Group A 24 (80%), 4 (13.3%), 1 (3.3%), 1 (3.3%) patients showed complete response, partial response, stable disease & progressive disease respectively. While among Group B patients 12 (40%) showed complete response, 7 (23.3%) showed partial response, 7 (23.3%) showed stable disease and 4 (13.3%) showed progressive disease. The resultant toxicity of treatment was assessed using RTOG scheme. More toxicity was assessed in group A participants who were treated with concurrent chemo radiation.

Conclusion: The study concluded that concurrent chemo radiation with Carboplatin and Paclitaxel provide comparatively better tumor response than sequential chemotherapy followed by Radiotherapy in Esophageal Cancer. However, besides efficacious tumor response, it is also associated with acute and delayed toxicity.

Key Words: Concurrent Chemo radiation, Esophageal cancer, Sequential chemotherapy, Radiotherapy

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INTRODUCTION

Esophageal cancer is characterized as a highly malignant cancer that carries a high potential for metastasis and local recurrence. Although diagnostic and therapeutic sciences have seen significant improvement, the malignancy is still fatal for a large number of patients[1].

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Sequential chemotherapy followed by radiotherapy is a well-established treatment protocol for non-surgery esophageal cancer patients, whereas the intake of 5-fluorouracil (5-FU) with cisplatin is the most followed chemotherapy regimen [2]. However, studies have concluded that 5-year survival rates have been as low as 26% following a definitive chemo radiation treatment. Therefore, less-toxic and more sensitive chemo-therapy regimens are highly needed [3].

Paclitaxel is an effective agent in esophageal malignancy since a response rate of around 32%, when delivered as a single-drug treatment, is seen among metastatic patients. Paclitaxel acts through inhibition of cells during the G2M phase of mitosis, a highly radiosensitive phase, having a 1.48 sensitizing enhancement ratio[4]. Paclitaxel in combination with carboplatin (TC) and concurrent radiotherapy has already been tested in patients with metastasized non-

small-cell lung cancer and the response rate was found to be between 71%-79% [5].

A study conducted phase 2 study of neoadjuvant chemo radiotherapy (nCRT) trial was based on weekly delivery of paclitaxel and carboplatin along with radiotherapy. The treatment regimen resulted in incomplete resection of the tumor with one millimeter of resection margins among the treated patients [6]. Moreover, variable toxicities such as esophagitis, neutropenia, and thrombocytopenia were reported. 96% of the patients had to undergo surgical resection at a later stage. Similarly, other studies have also concluded esophagitis as a major toxic side effect among the patient treated with concurrent radiotherapy regimens. In a study, 10-46% of the treated patients reported grade three or four esophagitis [7].

Therefore besides testing the efficacy of the combined delivery of paclitaxel and carboplatin, it is important to decide the timing of radiotherapy among patients with high-grade esophageal cancer [8]. This study is designed to compare the two chemo-radiotherapy regimens, sequential and concurrent, along with testing of paclitaxel and carboplatin as chemotherapeutic agents for such patients.

MATERIALS AND METHODS

A randomized control study design was used. The study was carried out for one year at the Oncology Department of Nishtar Medical Hospital and University Multan. Written approval was taken from the ethical review board before initiating the study.

Total 60 participants, 30 in each treatment group were included in the study. The Patients aged between 22-75 who were histologically or cytological confirmed cases of esophageal cancer with Eastern Cooperative Oncology Group (ECOG) score 0–2 and locally advanced cases with T2-4NxM0-1a or TxNxM1b were included in the study. The

Patients with organ metastasis, complete obstruction, or tracheoesophageal fistula, and the ones who had lost more than 10% of their body weight or have any other primary cancer or had undergone any defined surgery were excluded from the study. After getting informed consent from the patient's baseline data related to family history, physical examination, and laboratory work-up was collected. The participants were randomly grouped into two groups: concurrent (Group A) and sequential (Group B). In Group A, the patients received 50.4 Gy at 1.8 Gy per fraction for 5.5 weeks along with concurrent infused paclitaxel (50 mg m–2) and carboplatin (AUC=2). In Group B, patients received 2 cycles of chemotherapy, adopting a similar schedule, followed by radiotherapy fractionated in a similar way and at a similar dose. In both the set of patients, chemotherapy was preceded by 25-mg promethazine intramuscular injection at the half-hour, twenty-seven oral doses of dexamethasone (0.75 mg/tablet) at twelve and six hours before the treatment, and 300 mg of intravenous administration of half-hour before paclitaxel treatment. The tumor response was then evaluated.

Data analysis: The primary effect of tumor response was evaluated by following the "Response Evaluation Criteria in Solid Tumors (RECIST) guideline" (version 1.1). Radiation-associated toxicity was weekly assessed through the "Radiation Therapy Oncology Group (RTOG) radiation morbidity scheme". Acute and delayed toxicity was considered as an outcome of radiation therapy. SPSS (version 25) was used for data analysis. Fisher's exact probability test and chi-square test were used. P-value <0.05 was considered significant.

RESULTS

Among 60 participants, 30 were included in each group randomly. Group A was treated with concurrent chemo radiation and Group B was treated with sequential chemotherapy followed by radiotherapy. Demographic variables of the patients show that the median age of the patients in Group A & B was 58 & 60 years respectively. Group A was comprised of 18 (60%) males and 12 (40%) females while 17 (56.6%) males and 13 (43.3%) females were included in Group B. No significant difference was observed in ECOG status, Cancer stage, and dysphagia among both groups (Table I).

Laboratory and radiological findings were considered to assess tumor response in both groups by using RECIST criteria. Among Group A 24 (80%), 4 (13.3%), 1 (3.3%), 1 (3.3%) patients showed complete response, partial response, stable disease & progressive disease respectively. While among Group B patients 12 (40%) showed complete response, 7 (23.3%) showed partial response, 7 (23.3%) showed stable disease and 4 (13.3%) showed progressive disease (Table II). The p-value for difference in tumor response was statistically significant among both groups (<0.05).

The resultant toxicity of treatment was assessed using the RTOG scheme. The profile was prepared by considering a combination of Grade 0 & I and Grade II & III. Statistically, a significant difference was seen in terms of acute toxicity of Skin, GIT, Kidney, Lung, and resultant neutropenia among group A & B participants. More toxicity was assessed in group A participants who were treated with concurrent chemo radiation. On follow-up, relapse was reported in more patients from Group A however the difference among the number of relapses reported among the two groups was not significant (p>0.05).

DISCUSSION

Many research studies based on randomized clinical trials have revealed that sequential chemotherapy is a better treatment option in comparison to concurrent

chemo radiation [9]. In terms of prevalence, about 6% of gastrointestinal malignancies are Esophageal carcinoma [10]. More males than females are likely to get affected with esophageal cancer. The typical and most frequently seen symptom of this condition is Dysphagia [11]. We also report the presence of dysphagia in the current study group. The treatment for esophageal cancer is chosen based on the prognosis. Nonsurgical is more often selected for patients with bad prognosis for example the ones presenting with metastasized tumors. Chemo radiation is mostly the procedure of choice in patients with contraindication for chemotherapy [3]. Moreover, with advances, hyper-fractionated radiotherapy which offers better results is being used over conventional one [12].

One of the previous studies with the "ECOG EST-1282 trial" showed that combination (modality) therapy is more effective than only radiotherapy however that trial had an element of surgery in it. Besides this, no significant improvement was achieved in terms of survival rate [13]. In another study, the clinical trial was designed to compare concurrent chemo radiation with systemic chemotherapy. The results showed a better median survival rate in patients who received concurrent chemo radiation [14]. Likewise, in a study conducted by "The German Esophageal Cancer Study Group," a comparison was made "between preoperative chemo radiation followed by surgery versus chemo radiation alone". The follow-up of 10 years showed no significant difference in survival rate among the two groups [15]. Despite these results, it is important to explore different treatment modalities in combination and alone in order to assess both efficacy and toxicity [16]. Our study results indicate a significantly efficacious response rate towards patients treated with concurrent chemo radiation therapy showing complete response (effectively killing and reducing tumor cells) in 24 (80%). A longitudinal study was done at Department of Oncology of Jinnah Postgraduate Medical College. "A partial clinical response was acheived in majority of the patients following concurrent chemoradiation therapy (CCRT) (55.7%). However, 14 patients achieved complete response, 10 patients showed stable disease, 6 patients expired and only one patient showed disease progression with metastases" [17]. Studies also show that concurrent chemo radiation therapy also reduces symptoms of dysphagia in patients with esophageal cancer. However concurrent chemo radiation therapy is also linked with enhanced toxicity profile. Several studies have concluded that higher incidence of Grade 3 and Grade 4 toxicities are more associated with chemo radiation than radiotherapy only.

CONCLUSION

The study concluded that concurrent chemo radiation with Carboplatin and Paclitaxel provide comparatively better tumor response than sequential chemotherapy followed by Radiotherapy in Esophageal Cancer. However, besides efficacious tumor response, it is also associated with acute and delayed toxicity.

Author's Contribution:

Concept & Design of Study:	Atique Anwer Khan
Drafting:	Ahmed Ijaz Masood
Data Analysis:	Muhammad Arshad
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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