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Response of Paclitaxel-Capecitabine Prior Radiotherapy in Locally Advanced Inoperable Oesophageal Carcinoma

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Abstract **Original Research Article**

Introduction: The incidence of oesophageal carcinoma is increasing in the world as well as in Bangladesh. ***Aim of the Study:*** The aim of the present study was to assess the efficacy and safety of paclitaxel-capecitabine based sequential chemoradiotherapy for advanced inoperable oesophageal cancer. ***Material & Methods:*** This prospective analytical study was conducted in the Department of Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh and in the Department of Radiation oncology and Department of Radiotherapy, National Institute of Cancer Research and Hospital, Dhaka, Bangladesh from July 2016 to June 2017. Forty (40) patients with locally advanced carcinoma of the oesophagus (stage IIB – stage IVA) treated with sequential chemo radiation were enrolled in this study. They were treated with Paclitaxel and Capecitabine followed by radiotherapy. ***Results:*** Final follow up was done at 6 month (24 weeks) after completion of treatment and it was observed that 72.5% had clinical response. ***Conclusion:*** Sequential chemo radiation with Paclitaxel-Capecitabine is an effective, tolerable and convenient regime in the treatment of locally advanced carcinoma oesophagus.

Keywords: Advanced carcinoma of the oesophagus, Sequential chemo radiation, Paclitaxel-Capecitabine.

INTRODUCTION

The incidence of oesophageal carcinoma is increasing in the world as well as in Bangladesh. Oesophageal cancer is the sixth most commonly diagnosed cancer, with over 480,000 new cases and more than 400,000 deaths annually in the world [1]. Oesophageal cancer is frequently diagnosed at the advanced stages of disease and the 5-year survival rate of oesophageal cancer is still very low. Locally advanced cancer means that the cancer has spread into the tissues around the oesophagus. As a result, these patients are unable to undergo resection, the gold standard therapy for solid tumor [2]. Indeed, treatment of advanced inoperable locally advanced oesophageal cancer patients involves chemotherapy and radiotherapy. Systemic chemotherapy with local radiation therapy has been developed to control local disease and metastasis and to improve progression-free survival (PFS) in patients with inoperable oesophageal cancer. Different combinations of chemotherapeutic drugs with radiation treatment greatly affect the efficacy and response. Current standard treatment involves Cisplatin and 5-fluorouracil (PF) along with sequential radiation therapy though the toxicity especially gastrointestinal adverse effects significantly limit their use [3]. Over the past decade, there have been advancements in drug development and many alternative chemotherapeutic drugs have been identified. For example, taxane has been successfully used to treat patients with different types of cancer in various settings [4]. In addition to its antitumor activity, taxane can sensitize tumor cells to radiation therapy. Taxane in combination with cisplatin has also been used to treat esophageal cancer patients, with a response rate of over 50%. Furthermore, sequential chemo radiation with Paclitaxel and platinum has improved the survival of patients with locally advanced oesophageal cancer [5]. Recently, Capecitabine has demonstrated an extended spectrum of antitumor activity and does not have cross-resistance with cisplatin thus it can effectively treat cisplatin-resistant oesophageal cancer [6]. In addition, it was found that carboplatin and Paclitaxel treatment improved the survival of inoperable oesophageal cancer when compared with Cisplatin-5F.U. treatment [7]. However, more studies are needed to provide medical evidence for the treatment of advanced inoperable esophageal cancer with Paclitaxel-Capecitabine based sequential chemoradiotherapy.

OBJECTIVES

To describe efficacy and safety profiles of paclitaxel-capecitabine based sequential chemoradiotherapy for advanced inoperable oesophageal cancer.

METHODOLOGY AND MATERIALS

From July 2016 to June 2017 this prospective analytical study was conducted at the Department of Oncology in Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh and at the Department of Radiation oncology and Department of Radiotherapy in National Institute of Cancer Research and Hospital, Dhaka, Bangladesh. All the patients included in this study were informed about the nature, risk and benefit of the study. Proper permission was taken from the department and institution concerned for this study. Inclusion Criteria for the study included histopathological diagnosed case of carcinoma of oesophagus (stage IIB to IVA). Patients were excluded if they had History of prior chemotherapy, radiotherapy or surgery, patients with ECOG performance status more than 2, patients with obstructive feature, serious concomitant medical illness and age more than 70 years. A total of 40 patients with above mentioned criteria were selected by purposive sampling. The aims and objectives of the study, risks and benefits of this study were explained to the patient's in easily understandable local language and then an informed written consent was taken from each of them. Patients were assured that all information and records would be kept confidential. Data was collected in a pre-designed structured data collection sheet. On admission, the particulars of the patients including socio-demographic status, detailed history, presenting complaints and findings of relevant investigations were recorded. The findings of detail clinical examination and clinical staging were recorded. Selected patients received chemotherapy with Paclitaxel 80 mg/m2 I.V on day 1 and day 8 and Capecitabine 900mg/m2 orally from day 1-14. They received this regime three weekly for a total of six cycles. Proper hydration and premedication were maintained. All the patients received radiation treatment with a total dose of 44 Gy in 22 daily fractions at 2 Gy per fraction with Telecobalt machine 3 weeks after receiving the chemotherapy.

Tumour response was evaluated after completion of 6th cycle of chemotherapy and at week 6 (1st follow up) and 12 (2nd follow up) after completion of radiotherapy but symptomatic responses and toxicities were assessed after completion of each cycle of chemotherapy and in every week during radiotherapy and at week 6 (1st follow up) and 12 (2nd follow up) after completion of treatment.

Tumour response was evaluated according to the WHO criteria issued in 1979 WHO 1979. To assess the tumor response to the treatment WHO criteria was followed which is attached in appendix. Tumour responses were categorized as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). The final response was assessed after clinical examination including upper GIT endoscopy which was done at twelve weeks after completion of all therapy.

To assess toxicity, the national cancer institute "Common terminology criteria for adverse events, v. 4.0 published on June 14, 2010" was used. Any development of toxicity during treatment was managed appropriately.

RESULTS

Completed response were seen in 17.5%. Partial response was found in 55.0%. Stable disease was in 6 patients (15.0%). Progressive response was in 5 patients (12.5%). Mean age of patients was 47.1 ± 12.0 years. Distribution of patients according to gender showed males were predominant than female. Tumor site of the patients -maximum tumors were in distal esophagus. Maximum tumors (75%) were > 5cm long. Histology of the tumors showed predominance of adenocarcinoma (57.3%). Toxicity was observed in 25.0%. Hematological toxicity was in 2 (5.0%). Non hematological toxicity was in 8 (20.0%). Progressive dysphagia in 29 (72.5%). Painful swallowing was complained by 5 (12.5%). Completed response was in 7 (17.5%). Partial response was in 22 (55.0%) patients. Stable disease was 6 (15.0%). Progressive response was in 5 (12.5%). Final follow up was done at 6 month (24 weeks) after completion of treatment and it was observed that total 72.5% had clinical response.

Table-1: Clinical and Demographic Characteristic of patients (n=40)

Years	**Characteristic**	
	Distribution By Age	
	N	%
≤31	5	12.5
31 - 40	6	15
41 - 50	4	10
51 - 60	24	60
>60	1	13.8
Mean ± SD	49.9 ± 8.6	47.1 ± 12.0
Gender Distribution		
	N=	%
Male	29	72.5
Female	11	27.5
TMN Stage		
	N=	%
T1	1	2.5
T2	3	7.5
T3	14	35
T4	22	55
N1	28	70

Tumour Site		
Esophagus	N=	%
Upper	11	27.5
Mid	5	12.5
Distal	21	52.5
GEJ	3	27.5
Tumour Length (CM)		
	N=	%
≤ 5	10	25
> 5	30	75
Histology		
	N=	%
SCC	17	4.5
AC	23	57.5

Table-2: Distribution of patients according to toxicity (n=80)

Toxicity	**N**	**%**
Toxicity	10	25
Hematological	2	5
Febrile Leucopenia	2	5
Thrombocytopenia	2	5
Bleeding	2	5
Anaemia	2	5
Non hematological	8	20
Nausea/vomiting	0	0
Fatigue	0	0
Diarrhea	1	2.5
Mucositis	2	5
Others	5	12.5

Table-3: Distribution of the patients by symptomatic response during 1st follow-up

Systematic Response	**N**	**%**
Progressive dysphagia	29	72.5
Painful swallowing	5	12.5
Vomiting	*10*	*25*
Cough	7	17.5
Loss of appetite	10	25
Hoarseness of voice	1	2.5

Table-4: Assessment of treatment response (n=40):1st follow up

	N	**%**
Completed response	7	17.5
Partial response	22	55
Stable disease	6	15
Progressive response	5	12.5

Table-5: Assessment of treatment response (n=40): follow up

Treatment response	**N**	**%**
(Follow up-1st)		
Yes	29	73
No	11	28
(Follow up-2nd)		
Yes	29	73
No	11	28
Final follow up(24 weeks)		
Yes	29	73
No	11	28

DISCUSSION

In this study, mean age were 47.1 ± 12.0 years. Age was comparatively higher in another study [7]. Males were predominant than female. Male predominance was also observed in another study [7].Regarding tumor site, 27.5% was in the upper, 12.5% was in the mid, 52.5% was in the distal esophagus and 7.5% was in GEJ. Maximum tumors were > 5cm long (75.0%). Similar findings were also seen in one study [7]. Toxicity was low (25.0%). Hematological toxicity was in 2 patients (5.0%). Febrile leucopenia occurred in 2 patients (5.0%), thrombocytopenia in 2 patients (5.0%), bleeding was in 2 patients (5.0%) and anemia was in 2 patients (5.0%). Non hematological toxicity occurs in 8 (20.0%) patients- diarrhoea in 1 (2.5%), mucositis in 2 (5.0%) and other non-hematological toxicity in 5 (12.5%). In this study, completed response was 17.5% patients after 1st follow up. Partial response was 55.0. Stable disease was in 6 patients (15.0%). Progressive response was seen 5 patients (12.5%). Clinical Response was seen in total 72.5% patients.

LIMITATIONS OF THE STUDY

Small sample size was a major limitation to have an accurate clinical outcome. Some of the relevant investigations could not be done due to financial constrain.

CONCLUSION AND RECOMMENDATIONS

Sequential chemo radiation with Paclitaxel-Capecitabine is effective, tolerable, convenient and less toxic regime in the treatment of locally advanced carcinoma oesophagus. Further study involving multiple centers with a larger sample size should be carried out to see overall survival and late toxicities of this treatment regime.

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REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. International journal of cancer. 2010 Dec 15; 127(12):2893-917.
2. Lu XJ, Chen ZF, Guo CL, Li SS, Bai WL, Jin GL, Wang YX, Meng FS, Gao F, Hou J. Endoscopic survey of esophageal cancer in a high-risk area of China. World journal of gastroenterology: WJG. 2004 Oct 15;10(20):2931.
3. Cho SH, Shim HJ, Lee S, Ahn JS. Concurrent chemoradiotherapy with S-l and cisplatin in advanced esophageal cancer. Dis Esophagus, 2008; 21, 697-703.

4. Yamazaki S, Sekine I, Saijo N. Paclitaxel (taxol): a review of its antitumor activity and toxicity in clinical studies. Gan to kagaku ryoho. Cancer & chemotherapy. 1998 Mar;25(4):605-15.
5. Zhang P, Xie CY, Wu SX. Concurrent chemoradiation with paclitaxel and platinum for locally advanced esophageal cancer. Zhonghua zhong liu za zhi [Chinese journal of oncology]. 2007 Oct;29(10):773-7.
6. Wheate NJ, Walker S, Craig GE, Oun R. The status of platinum anticancer drugs in the clinic and in clinical trials. Dalton transactions. 2010;39(35):8113-27.
7. Honing J, Smit JK, Muijs CT, Burgerhof JG, de Groot JW, Paardekooper G, Muller K, Woutersen D, Legdeur MJ, Fiets WE, Slot A. A comparison of carboplatin and paclitaxel with cisplatinum and 5-fluorouracil in definitive chemoradiation in esophageal cancer patients. Annals of oncology. 2014 Mar 1;25(3):638-43.