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Research Article

Concurrent Chemoradiation is a Better Alternative than Radiotherapy alone in the Treatment of Inoperable Carcinoma Pyriform Fossa-A Multi Centre Clinical Experience in Bangladesh

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Abstract

Background: The present study was aimed at describing a multicentre clinical experience in the treatment of Inoperable carcinoma pyrifom fossa. Carcinoma pyriform fossa is the most frequent cancer arising from the hypopharynx, is rarely diagnosed in its early stage and still a leading cause of mortality and morbidity in developing countries. Despite improvement in overall survival for pyriform fossa cancer, the locally advanced cancer remains essentially incurable.

Methods: This prospective observational study was carried out to compare the effects of concurrent chemoradiation and radiotherapy alone in locally advanced carninoma pyriform fossa cancer. The main objectives of this study are to assess the response and early toxicities in both concurrent chemoradiation and radiotherapy alone.

Results: A total number of 90 patients, 45 in each arm having advanced pyriform fossa cancer were included in the study. Highest percentage of the patients was habituated with smoking, betal nut chewing and tobacco leaf user. The most common presenting symptoms were cervical lymphadenopathy, sore throat and hoarseness of voice. Overall response of patients treated with concurrent chemoradiation was better than in comparison to only

radiotherapy. As only a new treatment of locally advanced carcinoma of pyriform fossa concurrent chemoradiation (group-A) represents better symptom improvement, more toxicities and better tumor responses than radiotherapy alone (group-B) regimen.

Conclusion: In the treatment of locally advanced carcinoma pyriform fossa, concurrent chemoradiation with paclitaxel (40mg/m^{2}I/V) weekly, represents better symptom improvement, tumor responses with manageable toxicities than radiotherapy alone.

Keywords: Concurrent chemoradiation (when any chemotherapeutic agents added during radiotherapy); Paclitaxel (chemotherapeutic agents)

1. Introduction

The hypopharynx extends the superior border of the epiglottis and the pharyngoepiglottic folds from the level of the hyoid bone above to the lower border of the cricoid cartilage below. It is divided into three primary anatomic subsites: the pyriform sinuses, the postcricoid area and the posterior pharyngeal wall. Squamous cell carcinoma of the hypopharynx is a relatively rare neoplasm accounting for 5% of all head and neck cancers [1]. Hypopharyngeal cancer remains one of the lethal malignancies of the upper aerodigestive tract [2, 3], with causes of death being locoregional reccurences, distant metastases,second primaries and comorbidities [4]. Squamous cell carcinoma of the pyriform sinus is a highly malignant disease with a generally poor prognosis, accounting for almost 70% of all hypopharyngeal cancers [5]. It arises from the mucosa of the anatomic subsite of the hypopharynx represented as analogous to an inverted pyramid situated leteral and medial walls narrowing inferiorly to form the apex with its tip extending slightly below extending slightly below the cricoid cartilage. The pyriform suinus, lying outside the glottis, is a silent area allowing tumors to grow for a substantial period of time before symptoms occur [6]. The majority of patients with pyriform sinus cancer present with a history of significant tobacco or alchohol use [7].

The pyriform sinus is formed by the intrusion of the larynx in to the anterior aspect of the pharynx, which produces pharyngeal grooves lateral to the larynx. The superior margin of the pyriform sinus is the pharyngoepiglottic fold, which is at the level of the hyoid bone. The pyriform sinus is shaped like an inverted pyramid. The inferior margin is the apex of the pyriform sinus and is at the level of the cricoid cartilage. The pyriform sinus has anterior, lateral, and medial walls, but no posterior wall. The anterior and lateral walls are formed by the thyrohyoid membrane and thyroid ala and the medial wall by the arytenoid cartilage and aryepiglottic fold [7].

Since no actual division exists between the pyriform sinus and other parts of the hypopharynx or oropharynx, the tumor spread submucosally, and direct extension can occur to the larynx esophagus,oropharynx and even the nasopharynx. From the apex it can spread to the false cord, aryepiglottic fold, arytenoids, ventricle and the subglottic area. Lymphatic spread is mainly to the jugular group of nodes, commonly to the subdigastric group of nodes and less commonly to the spinal accessory chain [8]. A sore throat that does not go away, ear pain, a lump in the neck, painful of difficulty swallowing, a change in the voice. In retrospective study more than two thirds of patients with pyriform sinus cancer present with in stage III and IV diseases. Both surgery and radiation therapy are the main stays of most curative efforts. In recently year's chemotherapy is added to the treatment modality for advanced pyriform fossa cancer [9].

2. Methodology

This was a prospective observational study. The respondent was selected and categoriesed as per inclusion and exclusion criteria, who were attend in OPD and indoor dept. of BSMMU and DMCH during data collection period. The study was carried out for a period of the 18 months from January 2017 to July 2018. The study was conducted in Department of Oncology BSMMU, NICRH and Radiotherapy Department of Dhaka Medical College Hospital (DMCH). Permission from the concern department were taken properly. Informed consent was taken from each patient before enrolling in the study. 45 patients in each group. Patients suffering from pyriform fossa lesion attending in OPD and indoor department of BSMMU and DMCH were taken as sample. Study population: Histologically confirmed locally advanced pyriform fossa cancer (Stage-Ill & IV (A), Squamous cell carcinoma). Among the registered cases the patients were divided into two groups, Group-A (concurrent chemoradiation) and Group-B (radiotherapy alone) Findings of observation were recorded on a pre-designed structured close-ended interview schedule.

3. Results

A total number of 90 patients 45 in each arm having advanced pyriform fossa cancer were included in the study. Highest percentage of the patients was habituated with smoking, betal nut chewing and tobacco leaf user. The most common presenting symptoms were cervical lymphadenopathy, sore throat and hoarseness of voice. Overall response of patients treated with concurrent chemo-radiation was better than in comparison to only radiotherapy. As only a new treatment of locally advanced carcinoma of pyriform fossa concurrent chemoradiotherapy (Group-A) represents better symptom improvement, more toxicities and better tumor responses than radiotherapy alone (Group-B).

Personal habit	**(n=90)**		**Group A (n=45)**		**Group B (n=45)**		***P*-value**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Smoking habit							
Yes	63	70.00	29	64.44	34	75.55	0.260
No	27	30.00	16	34.78	11	24.44	
Betel nut chewing							
Yes	82	91.11	40	88.89	42	93.33	-
No	508	08.88	05	11.11	03	6.67	
Tobacco leaf							
Yes	81	90.00	39	86.67	42	93.33	-
No	09	10.00	06	13.33	03	6.67	
Alcoholism							
Yes	15	16.67	09	20.00	06	13.33	0.488
No	75	83.33	36	80.00	39	86.67	

Highest percentage of the patients were habituated with smoking (70%), betel nut chewing (91.67%), tobacco leaf (90%), alcoholism (16.67%)

Table 1: Distribution of the subjects by personal habit.

Complaints	**Group A (n=45)**		**Group B (n=45)**		**Total (n=90)**		**P value**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Progressive dysphagia	45	100.00	45	100.00	90	100.00	0.7
Painful Swallowing	42	93.33	44	97.78	86	95.56	
Vomiting	41	91.11	39	86.7	80	88.89	
Weight loss	21	46.67	24	53.3	45	50.00	
On examination							
Palpable lymph node	45	100.00	42	93.33	87	96.67	0.5

All the patients had complaints of dysphagia (100%) followed by painful swallowing (95.56%), vomiting (88.89%), weight loss (50%). However, on examination, 96.67% had palpable lymph node.

Table 2: Distribution of the patients by complaints and finding from clinical examination.

Site of lesion	**Group A (n=45)**		**Group B (n=45)**		**Total (n=90)**		***P* value**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Right	21	46.67	17	37.77	38	42.22	0.153
Left	20	44.44	15	33.33	35	38.89	
Both	04	08.89	13	28.89	17	18.89	
Stages of tumour							
T_4N_1 MO	16	35.56	13	28.89	29	32.22	0.137
T_4N_2 MO	27	60.00	25	44.64	52	57.78	
T_4N_3 MO	02	4.44	07	15.56	09	10.00	

Highest percentage (42.22) of the patients had tumour in right side of the pyriform fossa. Higher percentage (57.78) of patients were in the stage of $T_4N_2M_0$

Table 3: Distribution of the patients by site of lesion and stages of tumour.

Treatment Response	**Group A (n=45)**		**Group B (n=45)**		***P* value**
	No.	**%**	**No.**	**%**	
Partial response	35	77.78	22	48.89	0.089
Stable disease	07	15.56	14	31.11	
Progressive disease	03	6.67	09	20.00	

In group A 77.78% showed partial response where as in group B it was 48.89. Stable and progressive disease is less in group A

Table 4: Distribution of the patient by Treatment Response.

Mucositis	**Group A (n=45)**		**Group B (n=45)**	
	No.	**%**	**No.**	**%**
Pre-treatment				
No	45	100.00	45	100.00
Yes	0	0.00	0	0.0
After 2nd wk				
No	0	0.00	03	6.67
Yes	45	100.00	42	93.33
After 4th wk				
No	0	0.00	02	04.44
Yes	45	100.00	43	95.55
After completion				
No	16	36.67	07	15.56
Yes	29	63.33	38	84.44
1st follow up				
No	21	46.67	16	35.56
Yes	24	53.33	29	64.44
2nd follow up				
No	33	73.33	25	35.56
Yes	12	26.67	20	64.44
3rd follow up				
No	38	83.33	30	55.56
Yes	07	16.67	15	44.44
4th follow up				
No	42	93.33	38	84.44
Yes	03	6.67	507	15.56

During the treatment, the complaints of mucositis increase to nearly 100% both group A and group B patients and then gradually decrease to 6.67% in group A and 15.56% in group B patients, but the difference was not statistically significant

Table 5: Distribution of the subjects by toxicity (mucositis).

Stomatitis	**Group A (n=45)**		**Group B (n=45)**	
	No.	**%**	**No.**	**%**
Pre-treatment				
No	45	100.00	43	95.56
Yes	00	0.00	02	04.44
After 2nd wk				
No	04	08.89	15	33.33
Yes	41	91.11	30	66.67
After 4th wk				
No	04	10.00	12	26.67
Yes	41	90.00	33	73.33
After completion				
No	21	46.67	10	22.22
Yes	24	53.33	35	77.78
1st follow up				
No	36	80.00	24	53.33
Yes	09	20.00	21	46.67
2nd follow up				
No	39	86.67	33	73.33
Yes	06	13.33	12	26.67
3rd follow up				
No	39	86.67	38	84.44
Yes	06	13.33	07	15.56
4th follow up				
No	39	86.67	42	93.33
Yes	06	13.33	03	6.67

Initially one patient had complaint of stomatitis, during treatment increase to 90% in Group A patients and it increased up to 76.67% in Group B patients and then decreased to 13.33% in Group A and 6.67% in Group B, but the difference was not statistically significant

Table 6: Distribution of the subjects by toxicity (Stomatitis).

4. Discussion

Carcinoma of the pyriform fossa is one of the most aggressive tumour of the head & neck region. This tumour is frequently advanced at the time of diagnosis. They have a particularly high propensity for lymphatic spread. Though many treatment options are present but concurrent chemo-

radiotherapy is the best among all of the treatment options [10, 11]. Total 90 patients with advanced squamous cell carcinoma of pyriform fossa were selected randomly according to the selection criteria and treated by organ preserving technique. Patients were followed up for the first time after 4 weeks of the completion of treatment.

In this study the mean age of the patients were 57.2 ± 7.8 years ranging from 40 to 70 years. The mean age of the Group A was 57.3 ± 8.4 years and Group B was 57.0 ± 7.3 years. Highest percentage of the patients were habituated with smoking (70%), betel nut chewing (91.11%), tobacco leaf (90%). All the patients had complaints of dysphagia (100%) followed by painful swallowing (95%), vomiting (88.88%). On examination, majority of the patients had palpable lymph node. Analysis revealed that the severity of pain significantly decrease from initial treatment to final follow up. The mean frequency of vomiting was a little bit increase after 2nd week of treatment and it decrease in subsequent follow up in both groups of patients. Described that pyriform fossa tumors have a rich lymphatic drainage, 55% of patients present with neck nodes of which 16% are bilateral Bomford CK, et al. All the patients described that sore throat is the common presenting symptom of pyriform fossa cancer. The patients in the present study have similar clinical presentation [12, 13].

The mean size of lymph nodes was significantly decreased from pre-treatment status to final follow up in both group of patients. It was found that in both group of patients weight was significantly decreases from pre-treatment status to final follow up. In this study in Group- A, partial response and no response were 36 (80.00%) and 03 (06.67%) respectively. In Group-B, partial response and no response were 22 (48.89%) and 9 (20.00%) respectively. The result of the present study is similar to the others study done by number of investigators. It is now established that concurrent chemo- radiation is more effective than radio-therapy alone in locally advanced pyriform fossa cancer. After completion of the treatment, all the patients attended for follow up care. Follow up period was one and a half months to eighteen months and median six months. All patients were evaluated clinically and with haematological and biochemical investigations. The mean size of lymph nodes was significantly decrease from pre-treatment status to final follow up in both group of patients. Analysis revealed that the size of the lymph nodes significantly decrease among the Group A patients compared to Group B patients.

5. Conclusion

In the treatment of locally advanced carcinoma pyriform fossa, concurrent chemo-radiation with low dose paclitaxel (40 mg/m^2 I/V) weekly, showed better symptoms improvement and better tumor responses with manageable toxities than radiotherapy alone. However, further studies are recommended in larger number of patients.

References

1. Hall SF, Groome PA, Irish J, et al. The natural history of patients with squamous cell arcinoma of the hypopharynx. Laryngoscope 118 (2008): 1362-1371.
2. Samant S, Kumar P, Wan J, et al. Concomitant radiation therapy and targeted cisplatin chemotherapy for the treatment of advanced pyriform sinus carcinoma: Disease control and preservation of organ function. Head Neck 21 (1999): 595-601.
3. Prades JM, Schmitt TM, Timoshenko AP, et al. Concomitant chemoradiotherapy in pyriform sinus carcinoma . Arch Otolaryngol Head Neck Surg 128 (2002): 384-388.

4. Lefebvre JL, Chevalier D, Luboinski B, et al. Larynx preservation in pyriform sinus cancer: Preliminary resuts of an Eurpean Organization for Research and Treatment of Cancer phase III Trial. EORTC Head and Neck Cancer Cooperative Group. J Natl Cancer inst 88 (1996): 890-899.
5. Elias MM, F. Hilgers FJM, Keus RB, et al. Cacinoma of the pyriform sinus: A retrospective analysis of treatment results over a 20- year period. Clin Otolaryngol Allied Sci 20 (1995): 249-253.
6. Bomford CK, Kunkler IH. Walter Miller Textbook of Radiotherapy, 6th Edn. Churchil livingstonc (2003): 400-406.
7. Devita VT, Lawrence TS, Rosenberg SA. Cancer, Principles and practice of oncology, 10th edition, Lippincott Willims Wilkins, Chapter 37 (2015): 240-467.
8. Pazdur R, Wagman LD, Camphausen KA, et al. Cancer Management, A multidisciplinary Approach 13th Edn. (2010): 36-42.
9. Sudhindrea S, Nishi S, Prakash M, et al. Cervical node metastasis in Carcinoma of Pyriform Sinus: A prospective analysis of prevalence and distribution. Indian J Otolaryngol Head Neck Surg 53 (2001): 273-276.
10. Ann Barrett, Stephen Morris, Jane Dobbs, et al. Practical Radiotherapy Planning. 4th Edn. Arnold publishers (2009): 165-176.
11. Jones AS, Wilde A, Mcrae RD, et al. The treatment of early squamous cell carcinoma of the piriform fossa, Clin, Otolaryngol 19 (1994): 485-490.
12. Rubin P, Rubin P, Williams JP. Clinical Oncology, A Multidisciplinary Approach for physicians and students 8th Edn. W.B. saunders Company (2001): 686-698.
13. Halperin CE, Perez CA, Brady LW, et al. Radiation Oncology, Lippincott- Williams and Wilkins Philadephia, 6th Edn. (2013): 850-867.