

## ***Original Article***

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# **Induction chemotherapy followed by radiation versus concurrent chemoradiation in laryngeal cancer**

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### **Abstract:**

*Objective: This study was done to evaluate the effectiveness of concurrent chemo-radiotherapy than induction chemotherapy followed by radiotherapy in the loco-regional control of laryngeal cancers.*

*Methods: This experimental study was done at Radiotherapy Department of Dhaka Medical College Hospital and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from June 2004 to July 2005. Fifty three patients were selected purposively with biopsy proven squamous cell carcinoma of laryngeal region. Among the 53 patients 27 patients were treated concurrent chemo-radiation therapy and 26 patients were treated with induction chemotherapy followed by radiation. All patients were evaluated 6 weeks after completion of treatment.*

*Results: After giving concurrent chemo-radiation complete response occurred in 74% and partial response occurred in 26% patients but after giving induction chemotherapy followed by radiotherapy, complete response occurred in 23% and partial response occurred in 77% patients.*

*Conclusion: Concurrent chemo-radiation is more effective than induction chemotherapy followed by radiotherapy.*

**Key words:** Laryngeal cancer, radiotherapy, chemotherapy.

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### **Introduction:**

Cancer is a growing problem globally. At present about 10 million cases have been diagnosed as cancer annually with 6 million deaths. Head and neck cancer remains a significant international health problem with more than 42000 new cases diagnosed annually in the USA and more than 500,000 cases diagnose annually worldwide.<sup>1</sup> The vast majority of head and neck neoplasm arise from surface epithelium and are therefore squamous cell carcinomas (90%) or one of its variants including lymphoepithelioma, spindle cell sarcoma and undifferentiated

carcinoma. Few are adeno-carcinoma of salivary and minor submucous gland.<sup>1</sup> A wide variety of non-epithelial malignancy can also arise in the head and neck region, including lymphoma, plasmacytoma, melanoma and soft tissue sarcoma.<sup>2</sup>

Laryngeal cancer accounts for 0.9% of all cancers and 0.6% of cancer deaths.<sup>1</sup> The yearly incidence is about 4 per 10,000 in the UK.<sup>2</sup> The goals of treatment are mainly based on an appraisal of the patients' tumor. Large primary lesion (T3 and T4) or involvement of cervical lymphatic may require a planned combined approach. The sequential chemotherapy followed by radiotherapy, which has been studied for several decades, remains quite popular in many regions. Use of chemotherapy as an adjuvant to radiation therapy may offer improved survival. The high response rate achieved with induction chemotherapy before loco-regional therapy in patients with locally advanced squamous cell carcinoma of larynx lead to high expectation among oncologists that this approach would be beneficial. However, numerous randomized trials and subsequent meta analysis have demonstrated improved loco-regional control and survival with concurrent chemo-radiation but not with subsequent chemo radiation. Induction chemotherapy also became part of organ preservation protocols. The recently reported organ preservation trials have now demonstrated that concurrent chemo radiation is superior to the strategy of induction chemotherapy followed by radiation. So this study was done to evaluate the effectiveness of concurrent chemo-radiotherapy than induction chemotherapy followed by radiotherapy in the loco-regional control of laryngeal cancers.

#### **Methods:**

This experimental study was done at Radiotherapy Department of Dhaka Medical College Hospital and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka,

from June 2004 to July 2005. Fifty three patients were selected purposively with biopsy proven squamous cell carcinoma of laryngeal region. Among the 53 patients of squamous cell carcinoma of laryngeal region (stage I, II, III and IV) 27 patients (group 1) received induction chemotherapy with Inj. Cisplatin IV 20 mg/m<sup>2</sup> and Inj. 5-FU 500 mg/m<sup>2</sup> IV infusion from day 1 to day 5 along with 50 to 60 Gray in 25 to 30 fractions of 2 Gray daily of external beam irradiation using Cobalt-60. All patients received in every week up to the end of treatment. After completion of treatment patients were advised to attend follow-up examination after six weeks. Another 26 patients (group 2) received induction chemotherapy with injection Cisplatin IV 20 mg/m<sup>2</sup> and Inj. 5-FU 500 mg/m<sup>2</sup> IV infusion from day 1 to day 5, followed by 50 to 60 Gray in 25 to 30 fraction of 2 Gray daily of external beam irradiation using cobalt-60. This group was also evaluated every week and 6 weeks after completion of treatment. Socio demographic and other disease related information was collected from the patient. Clinical examination was conducted to find out clinical feature of laryngeal carcinoma if any. Relevant biochemical tests were carried out. Data were recorded in a pre-designed data collection sheet. Permission was taken from the department concerned for this study. Patients were informed about the nature of the study and agreed to participate in this study. Data were analyzed with the help of SPSS (Statistical Package for Social Science) version 12.0.

#### **Results:**

Among 53 patients with laryngeal carcinoma there was male predominance; male female ratio was 4.8:1. Age of the study patients ranges from 30-70 years. Tumour category, node category, disease stage and histopathological differentiation of tumor were summarized in Table-I. Majority of the patients in both groups presented with neck node and hoarseness of voice Table-II.

**Table-I**

*Tumor category, node category, disease stage, and histopathological differentiation of study patients*

Characteristics of laryngeal carcinoma		Concurrent chemo radiation Group 1 (n=27)	Induction chemotherapy followed by radiation Group 2 (n=26)
Tumor category:	T <sub>1</sub>	01	01
	T <sub>2</sub>	01	01
	T <sub>3</sub>	11	11
	T <sub>4</sub>	14	13
Node category	N <sub>0</sub>	07	06
	N <sub>1</sub>	12	16
	N <sub>2</sub>	08	04
Disease stage:	I	01	01
	II	01	01
	III	10	12
	IV	15	12
Histopathological differentiation	Well	07	06
	Moderate	07	09
	Poor	13	11

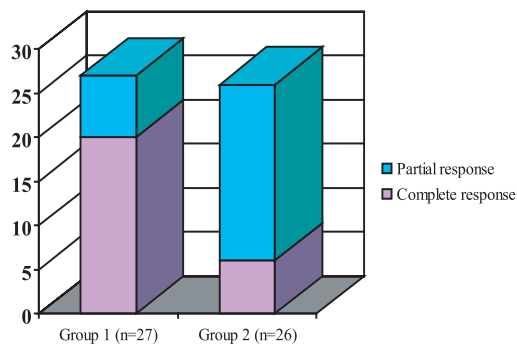
**Table-II**

*Distribution of patients according to major complaints.*

Presenting Complains	Group 1 (n=27)	Group 2 (n=26)
Neck node	20	20
Hoarseness of voice	26	24
Dysphagia	2	1
Referred otalgia	0	1
Others	0	2

After giving concurrent chemo-radiation in 27 patients, complete response occurred in 20 (74%) and partial response occurred in 07(26%) patients. After giving induction chemotherapy followed by radiotherapy in 26 patients, complete response occurred in 06 (23%) and partial response occurred in 20 (77%) patients. Clinical improvement was significantly more (p<0.0002) in concurrent

chemo-radiation therapy (Figure 1). Patients with stage III and IV diseases also showed better response who were treated with concurrent chemo-radiation ( Group 1) than who were treated with induction chemotherapy followed by radiotherapy ( Table-III).



**Fig.-1:** *Clinical response to concurrent chemo radiation (Group1) and Induction chemotherapy followed by radiotherapy (group 2).*

**Table-III**

*Comparison of clinical response to concurrent chemo radiation (Group 1) and induction chemotherapy followed by radiotherapy (group 2) between stage III and stage IV patients.*

Treatment Group	Stage	Complete Response No (%)	Partial Response No (%)	$\chi^2$ value (After Yates Correction)	P value
Group 1 (n=10)	III	8 (81.8)	2 (18.18)	9.96	0.05
Group 2 (n=12)		2 (15.38)	10 (84.62)		
Group 1 (n=15)	IV	11 (75)	4 (25)	3.76	0.03
Group 2 (n=12)		4 (38.40)	8 (61.6)		

**Discussion:**

The objectives of this study were to determine and compare the effects of concurrent chemo-radiation and induction chemotherapy followed by radiotherapy alone in locally advanced laryngeal cancer. Study was also done to assess response rates, clinical outcome, organ and function preservation and to determine the immediate and early toxicities.

The standard management of a laryngeal cancer has been controversial. There were proponents combining surgery and radiotherapy, while others preferred radiotherapy with surgery reserved as salvage treatment.<sup>3</sup> Actually it was well established that standard therapy is with radiotherapy, surgery or the combination. Cure rates of less than 40% in-patient is with loco-regionally advanced head and neck cancer.<sup>4</sup>

The role of induction chemotherapy in laryngeal cancer, not all early promises have been fulfilled,<sup>5</sup> while randomized studies of

concurrent chemo-radiotherapy have demonstrated the superiority of this modality over radiotherapy alone.<sup>6</sup> Though the acute and perhaps chronic toxicities may be greater with chemo-radiation than with radiotherapy alone, survival seems to be increased and organ preservation is made possible.

However it is better to integrate early systemic therapy into the overall management plan of the patient and to use it in the context of concurrent chemo-radiotherapy. It is likely that its effects on the control of micro-metastatic disease and increasing survival rates will become more easily measurable.<sup>5</sup>

In this study 53 patients of squamous cell carcinoma of laryngeal region (stage I, II, III and IV) in which 27 patients received concurrent chemo-radiation, another group of 26 patients received induction chemotherapy followed by radiation. Complete responses were observed in 20 (74%) out of 27 patients who were treated with concurrent chemo-

radiation. In contrary complete response occurred in only 6 (26%) who were treated with induction chemotherapy followed by radiation. Local effects of radiation were observed in all 53 patients in both groups, acute reaction was more in concurrent chemo-radiation group but majority of the patients were well spontaneously after 6 weeks. Patients with stage III and IV diseases also showed better response in concurrent chemo-radiation group.

Observing the survival rate may support the significant loco-regional tumor control in squamous cell carcinomas of larynx with induction chemotherapy followed by concurrent chemo-radiation. In a study, it was found. In a study, significant survival rate was found with concurrent chemo-radiation significant survival rates with concurrent chemo radiation.<sup>6,7</sup> But in this study survival rate was not observed due to shorter duration of study. But this series revealed better improvement of signs & symptoms with concurrent chemo-radiation for laryngeal cancer patients. So in conclusion, induction chemotherapy followed by radiotherapy and concurrent chemo-radiotherapy program has been found effective with acceptable toxicity, but concurrent chemo radiation is more effective than induction chemotherapy followed by radiotherapy.

#### References:

1. Bomford CK, Kunkler IH, Sheriff SB, Miller H. Text book of Radiotherapy, Radiation Physics, Therapy and Oncology, 6<sup>th</sup> edition. Edinburgh. Churchill Livingstone; 2003; 512 – 25.
2. Cortan RS, Kumar V, Robbin SI. Robins pathological basis of disease, 6<sup>th</sup> edition. Philadelphia. WB Saunders; 1999; 760 – 67.
3. Sweeney PJ, Haraf DJ, Vode EE. Radiation therapy in head and neck cancer: Indications and limitations. *Semin Oncology* 1994; 296-306.
4. Harrison LB, Sessions RB, Forastiere AA. Tumor of the larynx and hypopharynx. In: Devita JVT, Hellman S, Rosenberg SA (eds). *Principle and Practice of Oncology*, 5<sup>th</sup> edition. Philadelphia. Lippincott Raven; 1997; 8025-29.
5. Vokes EE, Schilsky RL, Weichselbaum RR. Induction chemotherapy with cisplatin, flurouracil and high dose leukoverin regime for locally advanced head and neck cancer: a clinical and pharmacological analysis. *J Clin Oncol* 1990; 8: 241-43.
6. Vokes EE, Kies M, Harraf DJ, Mick R, Moran WJ, Kozloff M, Mittal B. Inducion chemotherapy followed by concomitant chemoradiotherapy for advanced head and neck cancer: impact on the natural history of the disease. *J Clin oncol* 1995; 13(4): 876-83.
7. Kies MS, Haraf DJ, Athanasiadis I. Inducion chemotherapy followed by concomitant chemoradiotherapy for advanced head and neck cancer: Improved disease control and survival. *J Clin Oncol* 1998; 16: 2715-21.