REVIEW ARTICLE

Rationale of Laryngeal Conservation with Induction Chemotherapy followed by Concomitant Chemo Radiotherapy in Resectable Stage III and IV Cancer of Larynx and Hypo pharynx

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INTRODUCTION

Squamous cell carcinoma of head and neck is a common clinical problem in Pakistan. The age standardized incidence rate of laryngeal cancer alone is 9.4 in Karachi. This is the highest rate in Asia and it constitutes 5.8% of all cancers in men. The age standardized incidence rate of pharyngeal cancer is 7.9 and it constitutes 5.0% of all cancers in men[1]. These are comparatively less common in females. Loco regionally advanced presentation is not uncommon in laryngo pharyngeal cancer. Surgical resection in these patients leads to major cosmetic deformities and loss of function of normal speech or swallowing in many. Patients with unresectable disease have poor prognosis. Chemotherapy alone has the potential to induce complete responses in loco regionally advanced disease but it offers little or no chance of cure or long-term control. Standard fractionated radiotherapy and hyper fractionated radiotherapy can achieve a good local control but the cure is infrequently achieved. The optimum methods of utilizing these approaches have not been established.

BACK GROUND AND RATIONALE

In stage III and IV resectable laryngeal and hypo pharyngeal cancer organ preservation is possible and possibly some prolongation of survival can also be achieved by combining induction chemotherapy and radiotherapy.

The first study of induction chemotherapy in head and neck cancer was carried out in 1980s. Two years relapse free survival was seen in 60 % of patients treated with chemotherapy followed by radiotherapy. This study was followed by famous VA Laryngeal study[3]. In VA larynx study stage III and IV laryngeal cancer patients were treated with induction chemotherapy followed by radiotherapy, with surgery reserved for salvage therapy or with standard surgery and radiotherapy. Long-term survival results were reported in 1994[4] .A 53 % survival was noted at 03 years. This was equivalent to the survival seen in patients who failed on chemotherapy and underwent immediate surgery. But the most important thing to note was that the former group of patients remained alive with a functional larynx.

In a similarly structured trial by EORTC 194 pyriform sinus patients were treated with definitive pharyngolaryngectomy plus neck dissection or with induction chemotherapy followed by radiotherapy[5,6]. Median survival was longer in chemotherapy arm, though long-term survival rates were similar in both arms. Like VA study this also showed the ability of organ preservation with induction chemotherapy.

Concomitant chemo radiotherapy has also been studied in this setting. United States Inter Group trial 91-11 studied induction chemotherapy against concomitant chemo radiotherapy, and radiotherapy alone[7]. Two years local control was significantly better for concomitant chemo radiotherapy group (85%) compared to radiotherapy alone (58%) and induction followed by radiotherapy (64%). Overall survival was similar in all these groups. This study indicated better laryngeal preservation with concurrent chemo radiotherapy. However grade 4 mucositis remained a major problem in this study. Others have shown a survival advantage with neoadjuvant or induction chemotherapy in oropharyngeal cancers besides good organ preservation[8].

In all these studies combination of cisplatin on day I with 5 days of 5 -Fluorouracil infusion was used. This combination regimen has been the gold standard of chemotherapy for head and neck cancer for decades. But with the availability of docetaxel, a microtubular stabilizing agent, treatment scenario has changed. This drug has achieved response rates of 21-42 % as a single agent in advanced head and neck cancer and in combination chemotherapy a response rate of 71-100 %. This has led to its

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incorporation with the standard CF protocol in locally advanced head and neck cancer as induction chemotherapy. In one study docetaxel in combination with CF was compared against CF chemo in locally advanced head and neck cancer[9]. Sixty eight percent response rate was seen with docetaxel based therapy vs. 51 % against CF regimen. Progression free survival and overall survival was also significantly better. As response to chemotherapy is predictive of chemo sensitivity[10,11] higher responses with docetaxel based treatment are likely to improve the rate of laryngeal conservation.

With this background it seems appropriate to evaluate the role of docetaxel, cisplatin and 5 fluorouracil induction chemotherapy followed by concomitant cisplatin, 5 fluorouracil chemotherapy and radiotherapy for pre-servation of larynx and pharynx in resectable stage III and IV cancer patients. This combines the two best treatment options together. Further more this approach of induction chemotherapy followed by concurrent chemo radiotherapy has not yet been tested by many.

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