

A PROSPECTIVE STUDY OF MANAGEMENT OF MALIGNANT TUMORS OF HYPOPHARYNX IN A TERTIARY HOSPITAL

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ABSTRACT: INTRODUCTION: Malignant growths of Hypo Pharynx are one of the common Head and Neck malignancies in India. Males are commonly affected due to their smoking habit and use of Tobacco products, chewing habits. The combined use of Smoking and alcohol has a synergistic role in causing these malignant tumors. Post cricoid region is commonly involved in the development of malignant growth in females. Iron deficiency plays an important role as an etiologic factor in causing P.V. Syndrome which is a pre malignant condition in women. Malignant growths of hypo pharynx are observed in patients aged above 55 years and rare in age groups below 30 years. Pyriform sinus is the common site of involvement. Squamous cell carcinoma is the common histological finding among these malignancies. It usually presents with the complaints of foreign body sensation on swallowing which is neglected by the patients. This is followed by Hoarseness of voice and Dysphagia. Confirmation is by Direct Laryngoscopy and Biopsy. Multiple modalities of treatment are available now which includes surgery, Radiotherapy and chemotherapy. Nowadays a combination of these modalities is being used frequently to achieve a 5 year survival of more than 60%. The present study is based on chemo radiation in stage III and IV malignant growths of hypo pharynx in a tertiary hospital in Telangana. The study attempts to review the demographic and etiological factors playing a role in the disease process. It also analyses the post therapy effects on normal tissue as well as tumor mass. A 3 year post chemo radiation follow up results are analyzed. **MATERIALS AND METHODS:** The study includes 30 patients attending the OPD of ENT department of GGH, Kurnool, with the complaints of foreign body sensation on swallowing, dysphagia and hoarse voice. Patients are investigated after a thorough history taking. The nature of the growths is confirmed by Biopsy and HPE examination. A treatment protocol consisting of chemo radiation is followed depending on the stage of the lesion. Cisplatin is used as an anchor of chemotherapy prior to radiation. 60 to 66 c Gy cobalt 60 radiations are given over a period of 7 weeks. All the patients are followed up for 3 years. Observed data is analyzed for demographic details and etiological factors are searched for. **OBSERVATIONS:** Complete response at the primary site at the end of 2 weeks is 90%. Complete response to chemo radiation is seen in 90% of the patients with neck metastases after 2 weeks of chemo radiation. At the end of 2 months the overall complete response is 50%, which also remained same at the end of 6 months. Progressive response is seen in 11 patients (36.6%), showing progression of the disease process in spite of therapy. **CONCLUSIONS:** All patients could tolerate the chemo radiotherapy with minimum toxicity due good supportive and nutritional care without a gap in the treatment. In our study group 15 patients shows complete response, 2 patients show partial response, 11 patients show progressive disease, 2 patients show stable disease.

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KEYWORDS: Hypo pharyngeal, Chemo radiation, Carcinoma, Laryngoscopy, C GY, Mucositis, Pyriform sinus, Post cricoid, Marginal zone and Metastases.

INTRODUCTION: Hypo Pharyngeal Cancers of the Head and Neck region are common in India and account for 40-45% of all malignancies. Cancer of the hypo pharynx constitutes 0.2% to 1.3% of all malignancies of the Head and Neck. Pyriform fossa is the commonest site of origin followed by the post cricoid and posterior pharyngeal wall. Carcinoma of hypo pharynx is located in a clinically inaccessible region; the disease is most often diagnosed at relatively advanced stage. Maximum incidence is seen in fifth decade. In India the incidence is 8.4/ 1,00,000 males and 2.7/1,00,000 females. Due to rich lymphatic network in this anatomic region, patients commonly present with regional nodal metastasis. Pyriform sinus is the most common region of origin comprising 65-75%, followed by posterior pharyngeal wall constituting 10-20% and 5-10% originating from postcricoid region. Male to female ratio ranges from 5:1 to 7:1 for pyriform sinus cancer, 3:1 to 4:1 for posterior pharyngeal wall cancer. Postcricoid cancers occur predominantly in women. Prognosis for hypo pharyngeal tumors is poor because of: Extensive loco-regional spread of disease through the sub mucosal route, abundant lymphatic drainage of the region with a greater propensity for distant metastatic spread. These patients present at an advanced stage with frequent association with nutritional depletion. Management of carcinoma of hypo pharynx is a difficult problem due to advanced stage of the disease; the failure is predominantly at local site (21%) and nodal site (39%). Radical surgery such as laryngo-pharyngectomy is often required for hypo pharyngeal cancers. This radical surgery causes increased morbidity and mortality with significant cosmetic and functional changes. Hence definitive radiation therapy (or) chemo radiation is the treatment of choice for locally advanced hypo pharyngeal cancers with preservation of organic function and obtaining local tumor control. Benefits of concurrent chemo-radiotherapy: Local anti-tumor activity of radiotherapy is enhanced by the simultaneous use of chemotherapy as radio sensitizers. The use of concomitant chemo-radiotherapy for loco-regionally advanced unresectable Squamous cell carcinoma of Head and Neck (SCCHN) is further supported by several recent Randomized Controlled Trials (RCTs). Addstein^{1,2,3} et al, olmi et al. Calais⁴ et al reported Randomized Trials comparing conventional doses of radiotherapy with (or) without concomitant chemotherapy; regardless of the specific chemotherapy regimens used, the trials demonstrated a significant and consistent benefit in local control rates. In India poor socio-economic grounds and overall poor results from the multimodality treatment the failure is predominantly at local site (92.1%) and nodal site (39%). Distant metastasis is low⁽⁵⁾ (Biller HF, 1969). Radiation therapy alone has long been the standard non- surgical therapy for the locally advanced disease.

AIMS OF STUDY: The aim of the present Study includes: 1. evaluating the response of concurrent chemo radiotherapy in the early stages and locally advanced carcinoma of hypo pharynx. 2. To determine the toxicity and the compliance of treatment with concurrent chemo radiotherapy. 3. The patient acceptance when compared to surgery for carcinoma hypo pharynx. 4. To evaluates survival and quality of life during a period of 3 years. 5. To review the management of complications during Chemo radiation.

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AIM: The principle objective of concurrent chemo radiotherapy is: To increase local Tumor control, to decrease the distant metastasis, to improve survival and preservation of organ function.

MATERIALS AND METHODS: The present study was carried out in the Department of E.N.T. Government General Hospital attached to Kurnool Medical College, Andhra Pradesh.

INCLUSION CRITERIA: 1. Good general condition with ECOG status 1 or 2. 2. Patients of belonging to both sexes between 18 years to 70 years. 3. Histology showing proven Squamous cell carcinoma. 4. Hemoglobin Level above 10gm%. 5. No prior radiotherapy (or) chemotherapy. 6. Patients with informed and signed. 7. RFT and LFT within normal limits.

EXCLUSION CRITERIA: 1. Poor general condition, ECOG status 3 or 4. 2. Co morbid condition Eg. HTN/DM/COPD/Renal/Liver diseases. 3. Pregnant women. 4. Metastatic disease.

TREATMENT SCHEDULE: All the patients are initially subjected to clinical evaluation consisting of careful history taking, physical examination. Baseline investigations including CBP, RFT and LFT are done. Radiological investigations including X-ray Neck, Chest and pelvis are done. Ultrasound of Abdomen and Pelvis are done. Barium Swallow esophagus is done. CT scan of the neck is included as a part of investigation. Oral hygiene and dental care are undertaken. Biopsy from the primary site is subjected to HPE for confirmation of the diagnosis. After this pre therapeutic work up, the patients are explained about the details of the therapy and their side effects. The patients are admitted in the ward for administration of Cisplatin parenterally 40 Mgs/ml weekly concurrently 1 hour before radiotherapy. The protocol followed in this institute is given below:

Cisplatin is given on Day 1, Day8, Day15, Day22, Day29, Day 36, Day 43, after Complete Blood Picture, Renal Function Test and Weight assessment.

- Inj. Ondonsetron - 16 mg.
- Inj. Decadron - 8 mg. } In 1 bottle of Normal Saline in 1 hour.
- Inj. Rantac-50 mg. }
- Inj. Potassium chloride - 10 Meq + Inj. MgSo4 0.25 mg in 1 bottle of NS.
- Inj. Cisplatinum 40 mg/ml 1 bottle NS, IV slowly over 3 hours.
- Inj. Mannitol - 200 ml stat.
- Inj. Dextrose normal saline 500 ml IV.

- Inj. Xofer-16 mg } IV at night
- Inj. Rantac-50g }

Before giving Inj. Cisplatin, patient was adequately hydrated giving at least 1000 ml of DNS along with anti emetics and KCL + MgSO₄ to counter emetogenic and electrolyte imbalance caused by inj. Cisplatin. Dose of Cisplatinum is calculated 40 mg/m² and administered in 500 ml

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of NS over a period of 3 hours. After administration of Cisplatin. Mannitol 200 mg is given fast over a period of 15-20 minutes for forced diuresis. The administration of drug is given over a period of 10-12 hours. After giving Cisplatin, the patient is given radiotherapy within 1 hour, 200cGy/day for five days a week.

Radiation Therapy: The radiation treatment is carried as follows:

EQUIPMENT: All patients are given external beam ionizing radiation on a cobalt-60 unit at 80 Cms SSD.

RADIATION PLANNING: Patient position is done by making the patient lie on supine position on the treatment couch. Immobilization is done by Orfit/ plastic Mask. Under simulation planning is done to include the upper cervical esophagus. The lung on involved side is shielded. 46 c Gy dose is delivered by AP/PA fields. Spinal cord is spared and remaining 2 c Gy is given by oblique fields; 2 c Gy/day five day a week over a period of 6-7 weeks. Treatment Prescription: Total dose delivered to the tumor is 66 Gy in 33 fractions, over a period of 6-7 weeks. Radio therapy is given five days in a week, 2 c Gy/day. Cisplatin is given at the beginning of the treatment at a dose of 40 mg/m² and repeated every week i.e. On Monday.

MONITORING DURING TREATMENT: During therapy, patients are closely monitored and supportive care treatment initiated if necessary. CBP and RFT are done before administration of Cisplatin. Maintenance of adequate intake and nutrition, Oro-dental hygiene and adequate hydration were taken care. Acute mucosal reactions were managed by gentian violet for local application, viscous lignocaine gel and mucaïne gel for local pain & pain control according to guidelines (IAPC). Febrile episodes were controlled with appropriate antipyretics. Nasogastric feeding was done whenever indicated due to severe odynophagia. Antifungal nystatin or miconazole was used for fungal infections. During treatment frequent counseling and constant moral support was given keeping a close monitoring on acute reaction and nutritional status.

Follow-up Protocol: During the first 6 months the patients are followed once in 2 months. During the next 6 months, once in 3 months. Initial 6 months the follow up consisted of a detailed history taking and Nutritional status assessment. Clinical Examination and Endoscopic examination including ENT Examination during first 2 months, then once in 6 months is done. CT scan at first follow – up and then after 6 months is done. Responses are usually classified by the new Response Evaluation Criteria In Solid Tumors (RECIST) methodology published in the Journal of the National Cancer Institute in 2000 (thereasse et al. 2000). Baseline lesions are characterized as "measurable" (20 mm or more in longest diameter with conventional spiral computed tomography scan) or a) "non-measurable (smaller lesions and truly non-measurable lesions). To assess response, all measurable lesions up to a maximum of five per organ and ten in total are designated as "target" lesions and measured at baseline. Only the longest diameter of each lesion is measured. The sum of the baseline and longest diameter are taken. There are a variety of lesions in cancer that cannot be measured. These include many metastatic lesions to the bone, effusions, lymphangitic disease of the lung or skin, and lesions that have necrotic or cystic centers.

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b) Response categories are based on measurement of target lesions: 1. complete response is the disappearance of all target lesions. 2. Partial response is a disease of at least 30% in the sum of the longest diameters of target lesions, using as reference to the baseline sum longest diameter. Progressive disease is an increase of 20% or more in sum of the longest diameters of target lesions, taking as reference since the start of the treatment. Stable disease is when neither there is sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease.

Incidence & statistics in E.N.T. dept. of Govt. General hospital: Total number of cases attended to OPD: 31,608. Admissions in the ward in the year 2009 are 1392. Cancer of Hypo pharynx cases is 72. Among these 30 patients are included in the present study and followed up for formulation of thesis for a period of 3 years. It accounts to 5.12% of cases in total admitted patients and 0.22% of cases in OPD attending patients.

OBSERVATIONS: Totally 30 patients are included in the present study. This study is conducted between January 2009 and July 2012.

| Sex | No. of Patients/ Total patients | Percentage |
|--------|------------------------------------|------------|
| Males | 20/30 | 66.7% |
| Female | 10/30 | 33.3% |

Table 1: Showing sex incidence (n=30)

Present study showed a Male to female ratio with a male preponderance of 1.5: 1 (Table 1).

Age Group: The age group of 61-70 years showed an incidence of 43.4%. The youngest patient is 35 years old and the eldest patient is 73 years old (Table 2). The median age is 58 years.

| Age group Years | No. of patients | Percentage |
|--------------------|-----------------|------------|
| 31-40 | 5 | 16.7% |
| 41-50 | 4 | 13.3% |
| 51-60 | 7 | 23.3% |
| 61-70 | 13 | 43.4% |
| 71-80 | 1 | 3.3% |

Table 2: Showing the age incidence (n=30)

Presenting symptoms: In the present study it is noted that patients presenting with mass in the neck are 73.3%, Dysphagia in 66.7%, foreign body sensation in 86.6% and Hoarseness of voice in 60% (Table 3).

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| Presenting Symptom | No. of Patients/ Total patients | Percentage |
|--|------------------------------------|------------|
| Neck mass | 22/30 | 73.3% |
| Dysphagia | 20/30 | 66.7% |
| Pain in ipsilateral ear | 24/30 | 80% |
| weight loss | 18/30 | 60% |
| Hoarseness of voice | 17/30 | 56.7% |
| Sore throat (or) foreign body sensation in throat | 26/30 | 86.6% |

Table 3: Showing the incidence of symptoms (n=30)

Staging: Present study showed 63.3% of the patients presenting at Stage IV of their disease. 26.6% of them in stage III and 10% of them in stage in Stage II (Table 4).

| | No. of Patients/Total patients | Percentage |
|-----------|--------------------------------|------------|
| Stage ii | 3/30 | 10% |
| Stage iii | 8/30 | 26.6% |
| Stage iv | 19/30 | 63.3% |

Table 4: Showing the incidence of Different Stages of the disease (n=30)

Histological grading in squamous cell carcinoma: Moderately differentiated squamous cell carcinoma is seen in 40% of the patients, followed by poorly differentiated in 33.3% and well differentiated in 26.6% of the patients (Table 5).

| | No. of Patients/Total patients | Percentage |
|---------------------------|--------------------------------|------------|
| Well differentiated | 8/30 | 26.6% |
| Moderately differentiated | 12/30 | 40% |
| Poorly differentiated | 10/30 | 33.33% |

Table 5: Showing the incidence of different histological types of the disease (n=30)

TREATMENT DURATION: The duration of radiotherapy using 66c Gy for a period of 7 weeks is recorded in 27(90%) patients and more than 7 weeks in 3 patients (Table 6).

| RT dose | Number of patients | 7 weeks of treatment duration | More than 7 weeks |
|---------|--------------------|----------------------------------|----------------------|
| 66 c Gy | 30 | 27 | 3 |

Table 6: Showing the number of patients undergoing treatment for 7 weeks (n=30)

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TOXICITY: 60% of the patients in this study showed grade II skin changes and 86.6% of the patients showed grade II Mucositis (Table 7). Grade III and IV radiation changes of skin are not noted.

| | Grade – II | Grade – III | Grade – IV |
|-----------|-------------------|--------------------|-------------------|
| Skin | 18/30(60%) | 0/30 | 0/30 |
| Mucositis | 26/30 (86.6%) | 0/30 | 1/30 |

Table 7: Showing the incidence of Mucositis and skin changes (n=30)

Nutritional status: More than 10% Weight loss is seen in 26% of the patients. 10% weight loss in 56.7% of them and less than 10% weight loss in 16.67% of the patients (Table 8).

| | 5% | 10% | More than 10% |
|-------------|------------------|------------------|---------------|
| Weight loss | 5/30 (16.67%) | 17/30 (56.7%) | 8/30 (26%) |

Table 8: Showing the weight loss in the study (n=30)

RESPONSE RATES: Subjective response after completion of Chemotherapy and Radiotherapy showed a response in relief of dysphagia is seen in 60% of the patients (Table 9).

| Mode of therapy | No. of patients relived Dysphagia | No. of patients presented with dysphagia |
|------------------------|--|---|
| CT + RT | 18/30 60% | 12/30 40% |

Table 9: Showing the response rates following the treatment (n=30)

ENT Findings: Complete response to the treatment is seen after 2 weeks in 90% of the patients. After 2 months the response rate dropped to 56.7% and remained same after 6 months (Table 10).

| | After 2 weeks | 2 months | 6 months |
|---------------------|----------------------|-----------------|-----------------|
| Complete Response | 27/30(90%) | 17/30 (56.7%) | 17/30 (56.7%) |
| Stable Disease | 3/30 (10%) | 3/30 (10%) | 3/30 (10%) |
| Progressive Disease | 0/30 | 10/30 (33.3%) | 10/30 (33.3%) |

Table 10: Showing the response rate over a period of 6 months

Metastatic neck nodes: The neck nodes showed complete response in 90% of the patients after 2 weeks and the response rate fell to 76.78% after 2 months and remained same after 6 months (Table 11).

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| Observation | After 2 weeks | 2 months | 6 months |
|---------------------|---------------|----------------|----------------|
| Complete response | 27/30 (90%) | 23/30 (76.78%) | 23/30 (76.78%) |
| Stable disease | 3/30 (10%) | 3/30 (10%) | 3/30 (10%) |
| Progressive disease | 0/30 | 4/30 (13.3%) | 4/30 (13.35%) |

Table 11: Showing the nodal response to chemo radiation (n=30)

Patterns of failure: Failure of therapy is seen in 43.3% of the patients (Table 12).

| Site of Radiation | Number of patients/Total patients | Percentage |
|-------------------|-----------------------------------|------------|
| Primary site | 13/30 | (43.3%) |
| Nodal metastases | 4/30 | (13.3%) |

Table 12: Showing the failed therapy in percentage (n=30)

Overall Response to Chemo radiation: In the present study is analyzed and found that at the end of 2 months it is 50% complete response, which also remained same at the end of 6 months. Progressive response is seen in 11 patients (36.6%), showing progression of the disease process in spite of therapy (Table 13).

| Observation | 2 months | 6 months |
|----------------------|----------|---------------|
| Complete response | 15/30 | 15/30 (50%) |
| Partial response | 2/30 | 2/30 (6.7%) |
| Stable response | 2/30 | 2/30 (6.7%) |
| Progressive response | 11/30 | 11/30 (36.6%) |

Table 13: Showing the response to overall chemo radiation (n=30)

FOLLOW UP OF PATIENTS: The patients are followed up to 3 years in 60% of the patients. (Table 14)

| | 3 months | 6 months | 9 months | 1 year | 3 years |
|------------------------|----------|----------|----------|--------|---------|
| No. of patients | 30/30 | 27/30 | 22/30 | 20/30 | 18/30 |
| Percentage | 100% | 90.0% | 73.40% | 66% | 60.0% |

Table 14: Showing the period of follow up in the study (n=30)

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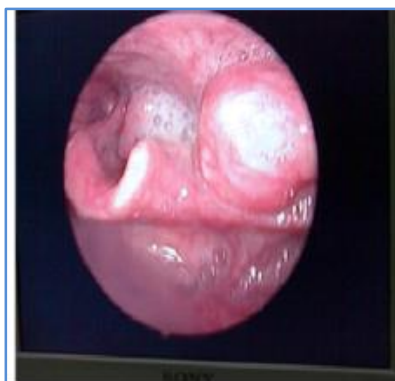


Fig. 1 & 2: Showing the Malignant growths of Right and Left Aryepiglottic fold

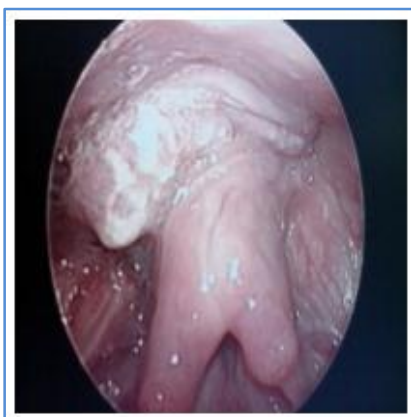


Fig. 3: Malignant growth of post-cricoid region



Fig. 4: Showing Posterior pharyngeal wall tumor

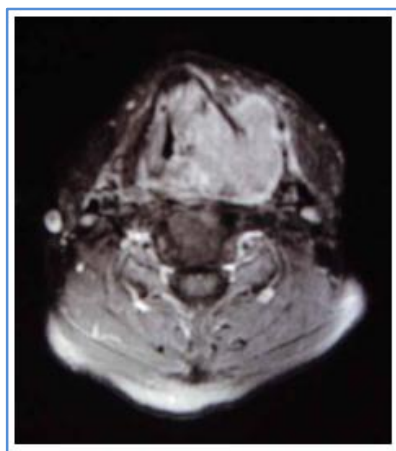


Fig. 5: Showing Ca. Hypo pharynx in CT-Scan before treatment

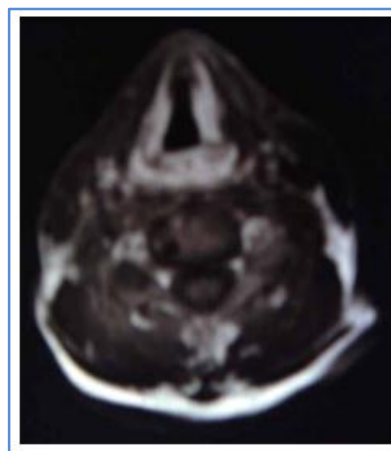


Fig. 6: Showing Ca. Hypo pharynx in CT-Scan after treatment

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Fig. 7 & 8: Showing bilateral neck metastases and fungating ulceration of the neck metastases

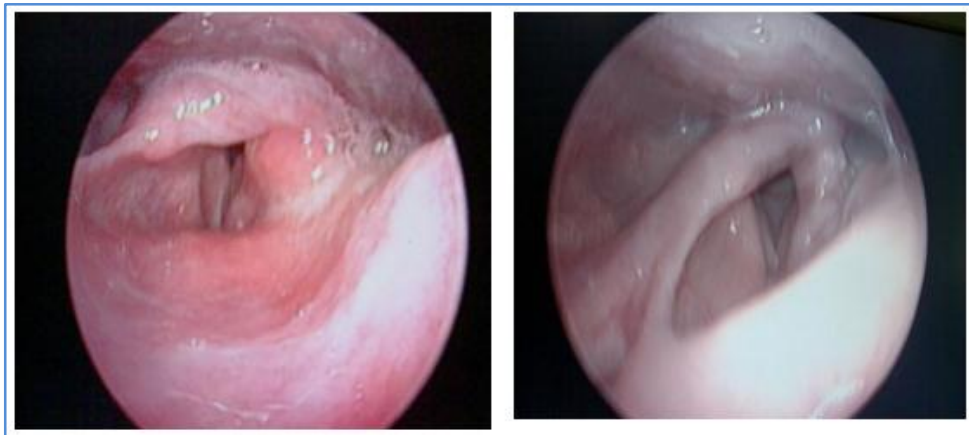


Fig. 9: Showing the tumor before and after completion of therapy



Fig. 10: Showing Post radiation Edema of face on the side of irradiation



Fig. 11: Showing the lesion before Chemo radiation



Fig. 12: Showing after therapy

Mode of action of Cisplatin: Platinum containing compound that exerts anti neoplastic effect by covalently binding to DNA with preferential binding to N-7 position of guanine and adenosine. It can react with two different sites on DNA to cause cross-links. Platinum complex also can bind to nucleus and cytoplasmic protein. A bi functional alkylating agent, once activated to aquated form in cell, binds to DNA, resulting in inter stand cross-linking and denaturation of double helix. Modify dose on basis of Cr Cl. Avoiding the use of Cisplatin, if Creatinine Clearance <60 ml/min.

DISCUSSION: An Overview: The preferred method of hypo pharyngeal carcinoma management remains controversial, with a wide variety of techniques reported throughout the literature. The approach to management requires consideration of the tumor's natural history, the patient's performance status, the extent of disease, and the presence and extent of lymph node metastasis. The traditional goal of hypo pharyngeal cancer management is to achieve the highest loco-regional control with the least functional injury, preserving respiratory function, deglutition, and phonation. Surgery and irradiation, either alone or in combination, are the standard therapeutic modalities. Induction and concurrent chemotherapy with radiotherapy have been recently used to prolong survival and to preserve organ function. Despite these new treatment modalities, an optimal treatment strategy for head and neck cancers, including hypo pharyngeal cancers, is difficult to determine because no randomized study comparing outcomes following surgery with outcomes following radiation or chemo radiation has been completed.⁶⁻¹⁵ Radiation therapy is the treatment for locally advanced non-resectable head and Neck cancers. Concurrent chemo- radiation has reported better loco-regional control and an overall 80% improvement in 5 year survival compared to treatment with Radiotherapy alone. The ultimate goal in concurrent chemo-radiation is to improve therapeutic ratio, which is to enhance the anti-tumor effect, while minimizing the toxicity of the treatment to normal tissue. Steel and Peck had defined four principles by which therapeutic ratios of combined treatments can be improved; spatial

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cooperation, independence of toxicity, enhancement of tumor response and protection of normal tissue. Most randomized clinical trials show the superiority of combined radio therapy and chemo therapy to RT alone for the treatment of locally advanced, non- metastatic squamous cell carcinoma of the Head and Neck. A Meta-analysis of response to chemo radiation therapy demonstrated that, the majority of benefit resulted from the use of concurrent chemotherapy a 19% reduction in the risk of death, and an overall 8% improvement in 5 year survival compared to treatment with RT alone (P<.0001). According to the EORTC study, in late stage disease surgery with postoperative radiotherapy appears to offer survival results that are equivalent to those of chemo radiation regimens, nonsurgical regimens offer patients the opportunity to preserve their larynx. The difficulty is that a preserved larynx does not necessarily equate to a functioning larynx. Long term dysphagia and the need for a tracheostomy negatively affect quality of life, as doe's loss of a laryngeal voice following surgery. For this reason, many centers tend to favor chemo radiation for advanced lesions that still have reasonably good function. The Radiation Therapy Oncology group (RTOG) conducted a three arm trial of radiation alone versus radiation and concurrent Cisplatin versus. Induction Cisplatin followed by irradiation in larynx carcinoma ^(16, 17). Concurrent therapy clearly constituted the most effective means of larynx preservation and provided the best disease control. One can infer from these studies that concurrent chemo-radiation has significant improvement in loco-regional control, organ preservation and overall improvement in survival.

Comparisons with the literature: The Hypo pharyngeal Cancer Care Evaluation reported by Hoffman⁸ et al is the largest study in the literature on carcinoma of hypo pharynx. Data were obtained by a survey of 1,800 acute care hospitals across America on patients from 1980-1985 and 1990-1992. The second largest study was recently (2005) published by Sewnaik¹⁸ et al, this is a population based study of 893 cases in Holland. Eckel¹⁷ et al reported a series of 228 consecutive cases treated a single institution in Germany. According to these studies the mean age was 65.8, 62.2, and 53 years respectively, in our study group 30 patients the mean age was 57years, which was comparable to Sewnaik et al, and Eckel et al study groups.^{17,18} 75%, 80% are males in their study groups, and 67% are males in our study. In our study patients present 67% with dysphagia, 73% neck mass, 86% sore throat, and 57% were had hoarseness, which were comparable to Hoffman et al, study, the most common symptoms in their study were dysphagia, neck mass, sore throat, and hoarseness. Patients with cancer of the hypo pharynx are the poorest of all cancer patients, it is known that (SES) socio economic status as measured by (MHI) median house hold income tends to be lower in patients with head and neck cancers than other cancers¹⁹ and that SES is associated with survival. 86% of our study patients were had low socio economic status. Groome²⁰ et al recently published a study on the impact of SES on outcome in laryngeal and hypo pharyngeal cancer, they found that 51% of patients with supra glottic cancer & 54% of the hypo pharynx cancer patients were from the MHI lowest 2 quintiles. According to Hoffman et al, over 90% had smoked and over 50% responding patients drank more than 10 drinks per day, in our study group (26 out of 30) 86% had smoking and/or alcohol more than 20years in their life. Garden²¹ AS, study says 65% - 85% of hypo pharyngeal cancers involve the pyriform sinus,10% -20% involve the posterior pharyngeal wall, and 5%-15% involve the post

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cricoid region, in our study group (30 patients) 70% (20 patients) involve the pyriform sinus, 20% (7 patients) postcricoid, and 10%(3 patients) involve the posterior pharyngeal wall which was comparable. In our study group 10% were stage ii, 27% stage iii, 63% stage iv, this was comparable to Hoffman et al study group, in which the TNM stage distribution was 10.5%, 12%, 23%, and 53.66% for stage 1 to 4 respectively, and also comparable to Sewnaik et al study group, in which 4.2%, 9.9%, 17.3%, and 68.5% for stage 1 to 4 respectively. According to National Cancer Data Base reports (November 6, 2005), majority of the institutions worldwide treating the patients of the advanced carcinoma of hypo pharynx by chemo radiation methods. Several randomized phase iii trials and meta-analysis have documented a survival and/or organ preservation benefit from the addition of chemotherapy to radiation as primary therapy for locally advanced SCCHN.²² Multiple chemotherapeutic agents have been investigated in combination with concurrent radiation. The most commonly used of which is Cisplatin; in patients with unresectable, locally advanced SCCHN, a subset of patients with a particularly poor outlook, a phase iii trial showed that radiotherapy with Cisplatin was superior to radiotherapy alone the 3 year survival improved from 23% to 37%. In the same three arm study however, a regimen of concurrent radiation, Cisplatin and 5-Flurouracil with optional surgical salvage failed to show superiority over radiotherapy alone. Garden et al (RTOG) phase ii trials that included Cisplatin based combinations and radiation have shown promising results.²¹ Whether two drug combinations offer an advantage over mono therapy in the setting of concurrent chemo radiotherapy for SCCHN remains uncertain. In our study 30 patients were given weekly Cisplatin chemotherapy 1hour before radiotherapy dose. This approach has been superior to radiation alone in terms of loco-regional control, organ preservation and/or overall survival and has been widely accepted as the standard nonsurgical therapy of locally advanced SCCHN⁶. A phase iii Head and Neck intergroup study in unresectable SCCHN, a population similar to our study, has reported results with a median follow-up of 41months. In this study by Adelstein² et al. patients treated with radiation plus high dose Cisplatin had a 3year overall survival of 37%, and also the complete response(CR) rate of 40-49% seen in two chemo radiotherapy arms in the study by Adelstein³ et al. is comparable to the CR rate in our study we observed 50%. 27 Of 30 assessable patients (90%) had an objective response, with a complete response rate of 56.7% with median follow up of 1year for surviving patients. The concurrent chemo radiotherapy regimen with weekly Cisplatin we employed after proper hydration and pre-medication with normal hemogram and renal function test. Patients were assessed periodically for toxicity and nutritional status. Most patients experienced grade I and II Mucositis after 3 weeks. These patients are managed conservatively. The patients tolerated this therapy well and there are low potential for toxicity resulting in nausea, vomiting and Mucositis. Only 3(10%) of the patients experienced a treatment delay or interruption. Grade1-2 Mucositis/ Stomatitis were observed in 86.6% of our study patients which was low incidence compared with a 90% incidence of grade 3-4 Mucositis that Chougule¹⁴ et al. observed Only 1 patient we had to give colony stimulating factor and 2 patients had to receive blood transfusions. Among all the patients 22 patients underwent elective tracheostomy during the period of treatment. Even though most of the patients were with ECOG performance status 1 to 2, this concurrent chemo radiotherapy was well tolerated with manageable side effects and with complete response significant improvement in quality of life.

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CONCLUSION: In our study 30 patients with locally advanced carcinoma of hypopharynx were treated with concomitant chemotherapy and radiotherapy. All patients were given weekly Cisplatin 40mg/m², 1/2 an hour to 1 hour before Radiotherapy. Radiotherapy was given 6600cGy in 6-7 weeks. All patients could tolerate the chemo radiotherapy with minimum toxicity due to good supportive and nutritional care without a gap in the treatment. In our study group 15 patients show complete response, 2 patients show partial response, 11 patients show progressive disease, 2 patients show stable disease. Pyriform sinus cancers respond well to treatment than post cricoid and posterior pharyngeal wall Tumors. The response of the tumor and nodal disease was significantly better with concomitant chemo radiotherapy with acceptable toxicity. There is significant improvement in disease free survival (DFS) overall survival (OS) and quality of life. A randomized trial with good number of patients to show advantage in overall survival compared to Radiotherapy alone (or) neo adjuvant chemotherapy + radiotherapy is the need of the hour to gain confidence in the management of advanced malignant Tumors of head and Neck.

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