

COMPARATIVE STUDY ON EFFICACY AND TOXICITY OF CHEMORADIOTHERAPY AND RADIOTHERAPY IN HEAD, NECK AND CERVIX CANCER PATIENTS

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Summary

To compare the efficacy and toxicity of chemoradiotherapy (CRT) and radiotherapy (RT) in head, neck and cervix cancer patients using cisplatin and radiotherapy. Fifty patients with cervix, head and neck cancer were selected for the study. Among 50 patients, group 1 consists of 25 patients receiving radiation therapy alone for 22 sittings and more than 22 sittings. The remaining 25 patients were selected as group 2 or chemoradiotherapy group receiving both chemotherapy (CT) and radiotherapy for 6 weeks and not less than 22 sittings respectively. The efficacy of the therapy was evaluated by assessing tumour size and the toxicity was evaluated in these patients throughout the course of therapy using the parameters such as nausea, vomiting, alopecia, pigmentation, mucositis and myelosuppression. Out of 25 patients, belonging to radiotherapy group, 13 patients i.e., (52%) achieved complete recovery and 12 patients (48%) achieved partial recovery. Out of 25 patients receiving chemoradiotherapy 17 patients (68%) achieved complete response and 8 patients (32%) achieved partial response, i.e they showed negligible tumour size in C.T scan. Toxicities induced by chemoradiotherapy are more as comparable to radiotherapy throughout the treatment. The chemoradiotherapeutic regimen was found to produce effective tumour response compared with radiotherapy alone receiving group though the toxic effects are more in chemoradiotherapy receiving group.

KEY WORDS: Radiotherapy, Chemoradiotherapy, Cervix, Head and Neck cancer, Cisplatin.

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Introduction

Carcinogenesis is a multistage process comprising of the following steps as promotion, initiation and progression. In the initiation stage, normal cells are exposed to carcinogenic substances producing genetic damage, that if not repaired, results in irreversible cellular mutations. During promotion, the carcinogenic factors alter the environment to favour growth of the mutated cell over normal cells. Progression is the final stage of neoplastic growth involving further genetic damage leading to increased cell proliferation [1, 2, 3].

World wide, cancer of the cervix is one of the most common cancers in women, with more than 80% occurring in developing countries [4]. In developing countries most women present with locally advanced stages compared with developed countries, where most people present with early stage cancer [5]. This could be attributed to a number of factors, including the absence of systematic screening programmes for early detection, inadequate health care facilities, lack of patient awareness and the prevailing poor socioeconomic conditions. Five year disease free survival and overall survival have usually been reported as 50-70% for stage II, 30-50% for stage III and 5-15% for stage IV [6, 7, 8, 9, 10].

To improve the outcome of cancer of the cervix, a number of randomised-controlled trials have aimed to explore the possibility of a survival benefit by incorporating CT as a concomitant agent with RT [11,12,13,14,15]. Concurrent chemotherapy to standard radiotherapy for locoregional treatment has been established to improve overall survival in a variety of solid tumors. The CT regimens in combination with RT are evaluated in randomized controlled clinical trials, platinum containing regimens consistently has shown a survival benefit across tumor types [16]. Cisplatin is used as single chemotherapeutic agent, along with RT. In the present study, the role of platinum based cisplatin as part of concurrent chemoradiotherapy (CRT) and RT is discussed using head, neck, and cervix cancer patients. In clinical practice, number of chemotherapeutic agents have been used in chemoradiotherapy protocols [17]. However, in the current study cisplatin is used as the chemotherapeutic drug. The purpose of the present study is to compare the efficacy and toxicity of CRT and RT in head, neck and cervix cancer patients. More recently, concurrent chemoradiotherapy has been shown to be superior to radiation alone in several randomized phase-III studies as well as in meta-analysis. In a recent randomized intergroup trial, concurrent radiation and cisplatin were superior to standard radiation. Although cisplatin remains the standard drug used in combination with radiation, recent studies incorporating other agents in addition to or instead of cisplatin suggest that might be achievable in most patients with locally advanced head, neck and squamous cell carcinoma (HNSCC). This observation provides evidence that the use of chemoradiotherapy is changing the natural history of locally advanced disease. Ensley, showed that eventhough radiation was generally ineffective in patients with induction failure, the addition of cisplatin to radiation is similarly poor responders seemed to partially overcome radiation resistance. Finally, the Radiation Therapy Oncology Group showed that in patients unresectable disease, the combination of concurrent cisplatin and radiation gave superior results compared with a historical control group that was treated with radiation alone.

Materials and Method

The study was carried out at the Department of Medical Oncology, Meenakshi Mission Hospital and Research center, Madurai between June 2002 to December 2002. 50 patients with head, neck and cervix cancer were selected. 25 patients who received only RT are considered as RT group. Remaining 25 patients who received both RT and Cisplatin are considered as CRT group.

In radiotherapy group, 14 cervix cancer patients and 11 head and neck cancer patients were included. The 11 head and neck cancer patients include, 5 hypopharyngeal, 2 nasopharyngeal, 1 laryngeal and 3 oral cavity cancer. In chemoradiotherapy group, 7 cervix cancer patients and 18 head and neck cancer patients were included. The 18 head and neck cancer patients include 7 hypopharyngeal, 3 nasopharyngeal, 1 laryngeal, 2 oropharyngeal and 5 oral cavity cancer.

The study included patients between the age group of 12-73 years. The radiotherapy group included, 19 females and 6 males. The chemoradiotherapy group included, 11 females and 14 males. The patients included were in the stage-III or stage-IV carcinoma.

In radiotherapy group, 5 patients discontinued therapy after IV cycle and 6 patients discontinued at the end of V cycle, and new cases were not included in the study. There found no dropouts in the CRT group. The study was approved by IEC and the consent was taken.

In CRT group, radiation of 1.5-2.5 Gy/sitting for 5 days in a week and a total of 40-60 Gy was administered for 6 weeks for each patient. On the 6th day of each week 60mg cisplatin was mixed with 20% mannitol injection and administered as infusion. This cycle is repeated for 6 weeks. RT group received 1.5-2.5 Gy/sitting alone of radiation for five days in a week and a total of 40-60 Gy was administered for 6 weeks for each patient. The amount of radiation received by both RT and CRT group is same, with the exception of cisplatin administration at the end of 6th day each week in RT.

The patients were examined physically and then subjected to various medical examinations like pap smear, biopsy, CT scan. If patients experienced more toxicity, few days of rest was given. Toxicity was assessed by using various parameters such as nausea, vomiting, alopecia, pigmentation, mucositis, myelosuppression each week.

Patients with the head and neck cancer came with the complaint of tumour, dysphagia, odynophagia, sore throat, pain in the throat, oral cavity and tongue, vague discomfort in the throat, hoarseness of voice, nasal stiffness, nasal discharge, loss of weight. The cervix cancer patients came with the complaint of tumour, pain in the lower abdomen, leucorrhoea, post coital bleeding and continuous bleeding.

Results

Assessment of tumour response

In RT group, 13 patients achieved (52%) complete response and 12 patients achieved (48%) partial response. The results are shown in fig-1.

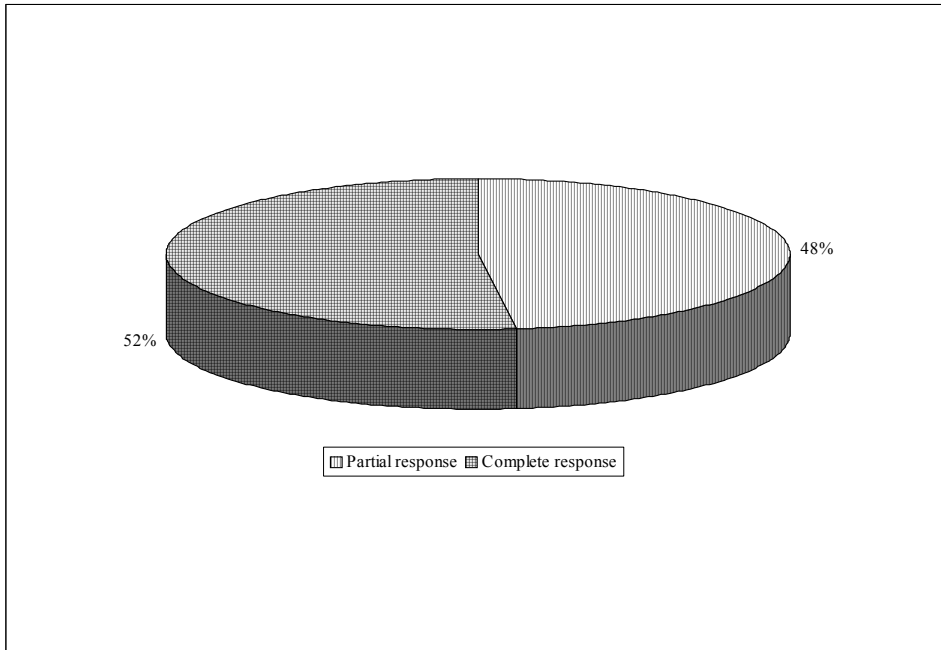


Fig.1: Tumour response in radiotherapy group

In CRT group, 17 patients achieved (68%) complete response and 8 patients achieved (32%) partial response. The results are shown in fig-2.

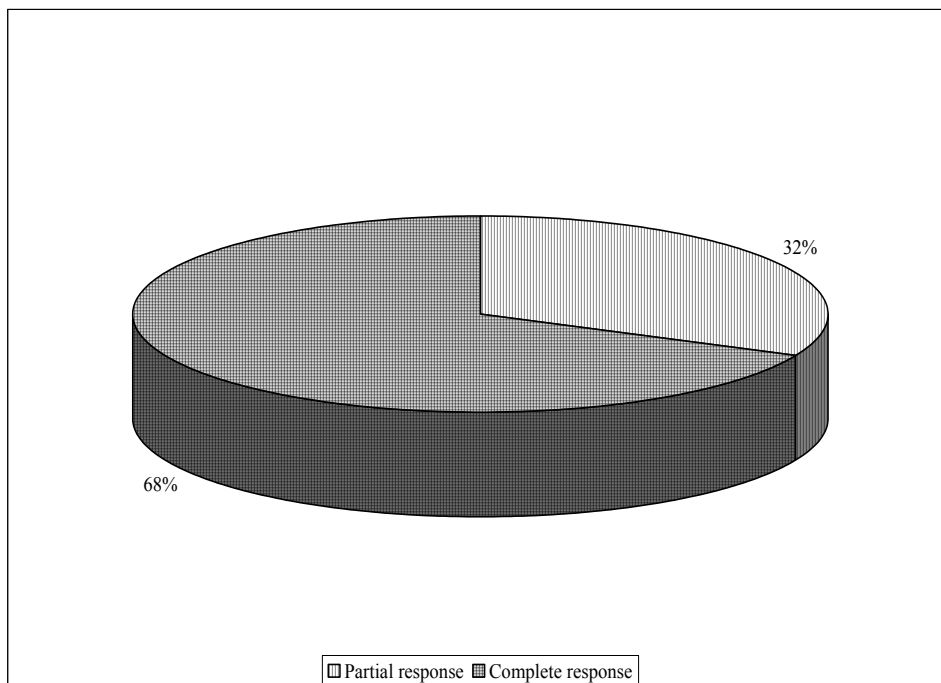


Fig.2: Tumour response in chemoradiotherapy group

Although toxicity is more in case of CRT group, tumour response is better in case of CRT group compared with that of RT group. The toxicity experienced by the patients are assessed using the toxicity chart followed in the hospital, which is given in Table 1.

Table-1 Toxicity Chart

TOXICITY	Grade I	Grade II	Grade III	Grade IV
GASTROINTESTINAL				
Nausea	Reduced but reasonable intake	Intake significantly decreased but still can eat	No significant intake	-
Vomiting	One episode in 24 hr	Two to five episodes in 24 hr	Six to ten episodes in 24 hr	> 10 episodes in 24 hr, or requires parenteral support
Stomatitis	Painless ulcers, erythema or mild soreness	Painful ulcers, erythema, or edema, but still can eat	Painful ulcers, erythema, or edema, and cannot eat	Requires enteral or parenteral support
DERMATOLOGIC				
Alopecia	Mild hair loss	Pronounced or total hair loss	-	-
Pigmentation	Mild discolouration of skin and nails	Moderate discolouration of skin and nails	Severe discolouration of skin and nails	-
HEMATOLOGIC				
White blood cells	3000-4000/ μ l	2000-3000/ μ l	1000-2000/ μ l	<1000/ μ l
Neutrophils	1500-2000/ μ l	1000-1500/ μ l	500-1000/ μ l	<500/ μ l
Hemoglobin	10.0-N/dl	8.0-10.0/dl	6.5-7.9/dl	<6.5g/dl
Platelets	75,000-1,50,000/ μ l	50,000-<75,000/ μ l	2,500-<50,000/ μ l	<25,000/ μ l

Incidence of nausea and the percentage of patients affected in different cycles of RT and CRT

In radiotherapy group, 5 patients showed grade-I (20%) toxicity and 3 patients showed grade-II (12%) toxicity in the 1st cycle; 11 patients showed grade-I (44%) toxicity and 3 patients showed grade-II (12%) toxicity in the 2nd cycle; 9 patients showed grade –I (36%) toxicity and 4 patients showed grade-II (16%) toxicity in the 3rd cycle; 8 patients showed grade-I (32%) toxicity and 3 patients showed grade-II (12%) toxicity in the 4th cycle; out of 20 patients (why the number has been reduced from 25 to 20, 25 to 14 in subsequent cycles , were there any dropouts) 3

patients showed grade-I (15%) toxicity and 3 patients showed grade-II (15%) toxicity in the 5th cycle; out of 14 patients, 4 patients showed grade-I (28%) toxicity and 2 patients showed grade-II (14%) toxicity in the 6th cycle. In the CRT group, 7 patients showed grade-I (28%) toxicity and 5 patients showed grade-II (20%) (this has been shown as 12% in figure 1) toxicity in the 1st cycle; 13 patients showed grade-I (52%) toxicity and 4 patients showed grade-II (16%) toxicity in the 2nd cycle; 13 patients showed grade-I (52%) toxicity and 6 patients showed grade-II (24%) toxicity in the 3rd cycle; 11 patients showed grade-I (40%) toxicity and 7 patients showed grade-II (28%) toxicity in the 4th cycle; 11 patients showed grade-I (40%) toxicity and 8 patients showed grade-II (32%) toxicity in the 5th cycle; 12 patients showed grade-I (40%) toxicity and 7 patients showed grade-II (28%) toxicity in the 6th cycle. The incidence of nausea and the percentage of patients affected in different cycles of RT and CRT is shown in figure 3.

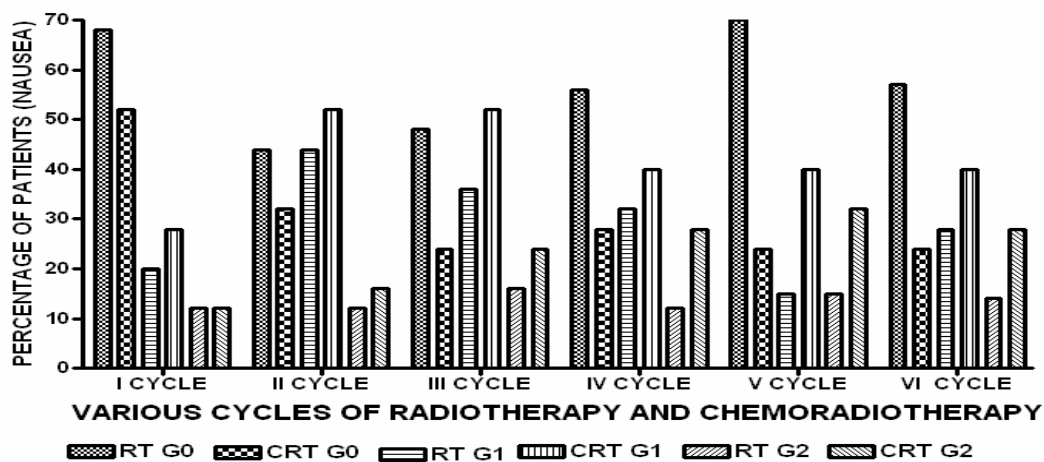


Fig.3 Percentage of patients affected with nausea in different cycles of radiotherapy and chemoradiotherapy

Incidence of vomiting and the percentage of patients affected in different cycles of RT and CRT

In RT group, 3 patients showed grade-I (12%) toxicity, 4 patients showed grade-II (16%) toxicity, 3 patients showed grade-III (12%) toxicity in the 1st cycle; 4 patients showed grade-I (16%) toxicity, 5 patients showed grade-II (20%) toxicity, 1 patients showed grade-III (4%) toxicity in the 2nd cycle; 1 patient showed grade-I (4%) toxicity, 6 patients showed grade-II (24%) toxicity and 2 patients showed grade-III (8%) toxicity in the 3rd cycle; 2 patients showed grade-I (8%) toxicity and 3 patients showed grade-II (12%) toxicity, 2 patients showed grade-III (8%) toxicity in the 4th cycle; out of 20 patients, 1 patient showed grade-I (5%) toxicity, 5 patients showed grade-II (5%) toxicity and 1 patients showed grade-III (5%) toxicity in the 5th cycle; Out of 14 patients, 2 patients showed grade-I (14%) toxicity, 5 patients showed grade-II (35%) toxicity, and 1 patient showed grade-III (7%) toxicity in the 6th cycle. In CRT group, 2 patients showed grade-I (8%) toxicity, 4 patients showed grade-II (16%) toxicity, and 3 patients showed grade-III (12%) toxicity in the 1st cycle; 3 patients showed grade-I (12%) toxicity, 7

patients showed grade – II (28%) toxicity and 2 patients showed grade –III (8%) toxicity in the 2nd cycle; 2 patients showed grade – I (8%) toxicity, 8 patients showed grade – II (32%) toxicity, 3 patients showed grade –III (12%) toxicity and 2 patients showed grade IV (8%) toxicity in the 3rd cycle; 1 patient showed grade – I (4%) toxicity, 6 patients showed grade – II (24%) toxicity, 2 patients showed grade – III (8%) toxicity and 2 patients showed grade IV (8%) toxicity in the 4th cycle; 3 patients showed grade – I (12%) toxicity, 7 patients showed grade – II (28%) toxicity and 2 patients showed grade III (8%) toxicity in the 5th cycle; 2 patients showed grade – I (8%) toxicity, 7 patients showed grade – II (28%) toxicity, and 2 patients showed grade – III (8%) toxicity in the 6th cycle. The incidence of vomiting and the percentage of patients affected in different cycle of RT and CRT is shown in fig 4.

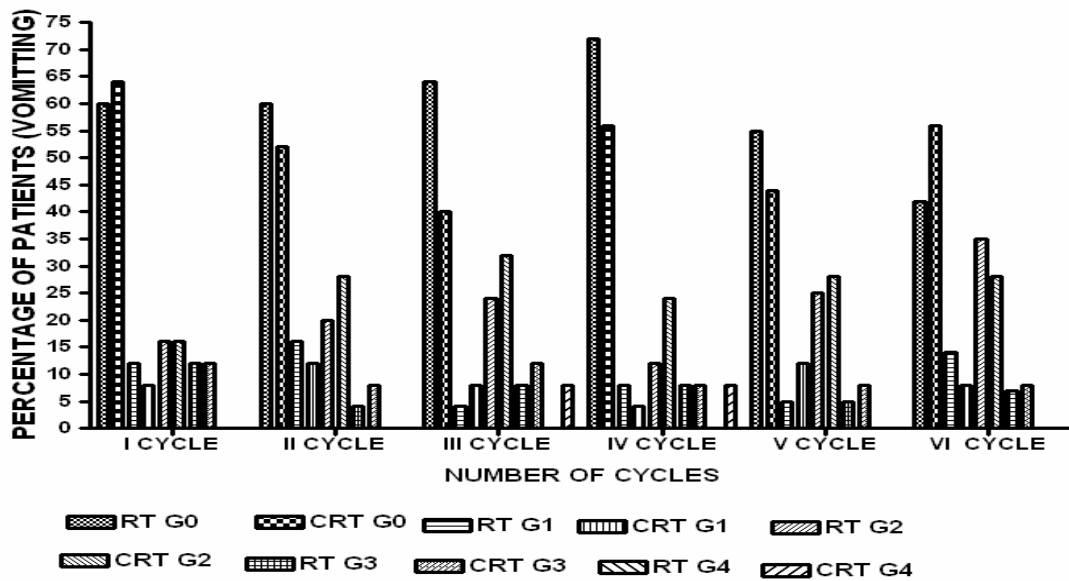


Fig.4 Percentage of patients affected with vomiting in different cycles of radiotherapy and chemoradiotherapy

Incidence of alopecia and the percentage of patients affected in different cycles of RT and CRT

In RT group, all the 25 patients showed grade – 0 (0%) toxicity in the 1st cycle, 14 patients showed grade – I (56%) toxicity in the 2nd cycle; all the 25 patients showed grade – II (100%) toxicity in the 3rd cycle, 20 patients showed grade –I (80%) toxicity and 5 patients showed grade II (20%) toxicity in the 4th cycle; out of 20 patients, 15 patients showed grade – I (75%) toxicity and 5 patients showed grade – II (25%) toxicity in the 5th cycle, out of 14 patients 8 patients showed grade – I (57%) toxicity and 6 patients showed grade – II (42%) toxicity in the 6th cycle. In CRT group all the 25 patients showed 0 (0%) toxicity in the 1st cycle; 18 patients showed grade – I (72%) toxicity in the 2nd cycle; 9 patients showed grade – I (36%) toxicity and 16 patients showed grade – II (64%) toxicity in the 3rd cycle; 8 patients showed (32%) grade – I toxicity and 17

patients showed grade – II (68%) toxicity in the 4th cycle; 5 patients showed grade – I (20%) toxicity and 20 patients showed grade – II (80%) toxicity in the 5th cycle; 3 patients showed grade

– I (12%) toxicity and 22 patients showed grade – II (88%) toxicity in the 6th cycle. The incidence of alopecia and the percentage of patients affected in different cycles of RT and CRT is shown in fig – 5.

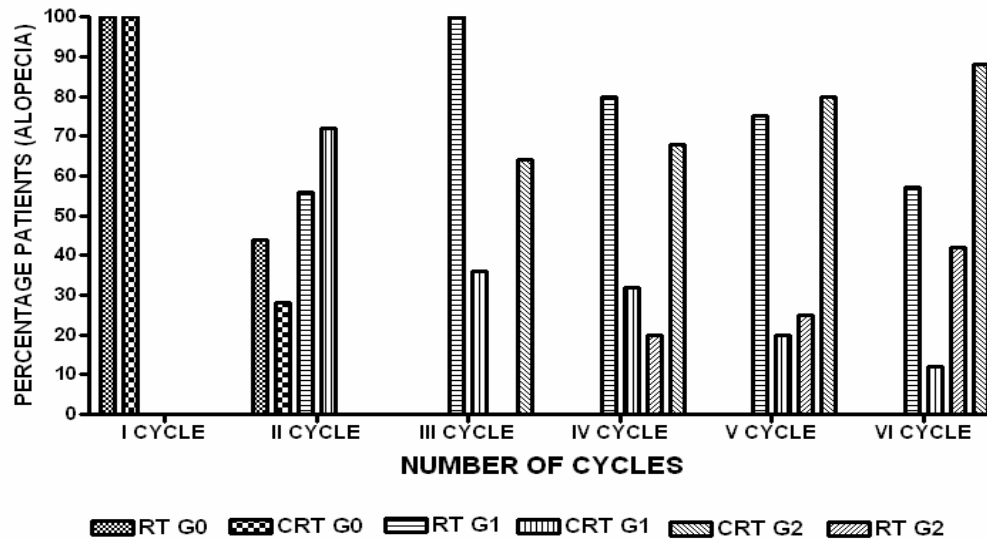


Fig.5: Percentage of patients affected with alopecia in different cycles of radiotherapy and chemoradiotherapy

Incidence of pigmentation and the percentage of patients affected in different cycles of RT and CRT

In RT group, 1 patient showed grade – I (4%) toxicity in the 1st cycle; 2 patients showed grade – I (8%) toxicity and 2 patients showed grade – II (8%) toxicity in the 2nd cycle; 3 patients showed grade – I (12%) and 3 patients showed grade – II (12%) toxicity in the 3rd cycle; 1 patient showed grade – I (4%) toxicity and 6 patients showed grade – II (24%) toxicity and 1 patient showed grade – III (4%) toxicity in the 4th cycle; out of 20 patients, 2 patients showed grade – I (10%) toxicity and 4 patients showed grade – II (20%) toxicity in the 5th cycle ; out of 14 patients, 2 patients showed grade – I (14%) toxicity and 4 patients showed grade – II (28%) toxicity in the 6th cycle. In CRT out of 25 patients, 2 patients showed grade – I (8%) toxicity in the 1st cycle; 5 patients showed grade – I (20%) toxicity 4 patients showed grade – II (16%) toxicity in the 2nd cycle; 5 patients showed grade – I (20%) toxicity and 4 patients showed grade – II (16%) toxicity in the 3rd cycle; 2 patients showed grade – I (8%) toxicity, 9 patients showed grade – II (36%) toxicity and 1 patient showed grade – III (4%) toxicity in the 4th cycle; 2 patients showed grade – I (8%) toxicity, 9 patients showed grade – II (36%) toxicity and 2 patients showed grade – III (8%), toxicity in the 5th cycle; 1 patient showed grade - I (4%) toxicity, 11 patients showed grade – II (44%) toxicity and 2 patients showed grade – III (8%) toxicity in the 6th cycle. The Incidence of pigmentation and the percentage of patients affected in different cycle of RT and CRT is shown in fig – 6.

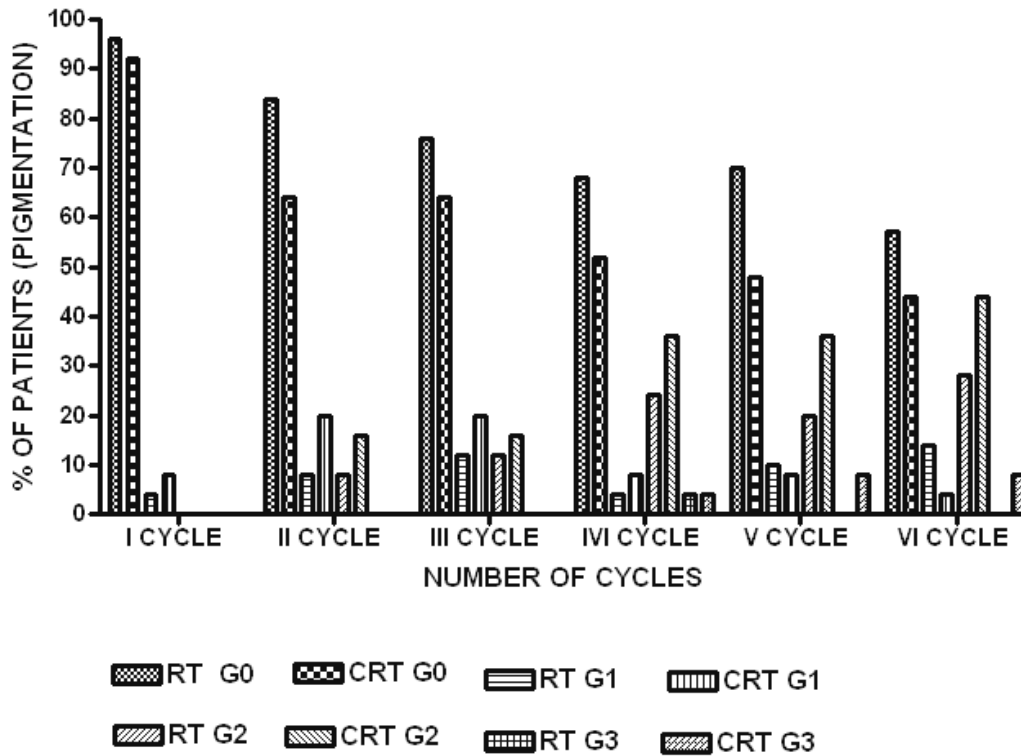


Fig.6: Percentage of patients affected with alopecia in different cycles of radiotherapy and chemoradiotherapy

Incidence of mucositis and the percentage of patients affected in different cycles of RT and CRT

In RT group, 10 patients showed grade – I (40%) toxicity and 4 patients showed grade – II (16%) toxicity in the 1st cycle; 10 patients showed grade– I (40%) toxicity and 4 patients showed grade – II (16%) toxicity in the 2nd cycle ; 8 patients showed grade – I (32%) toxicity and 4 patients showed grade – II (16%) toxicity in the 3rd cycle; 7 patients showed grade – I (28%) toxicity and 4 patients showed grade – II (16%) toxicity in the 4th cycle; out of 20 patients, 6 patients showed grade – I (30%) toxicity and 2 patients showed grade – II (10%) toxicity in the 5th cycle ; out of 14 patients, 6 patients showed grade – I (42%) toxicity and 2 patients showed grade – II (14.2%) toxicity in the 6th cycle. In CRT group out of 25 patients, 3 patients showed grade – I (12%) toxicity and the 13 patients showed grade – II (52%) toxicity in the 1st cycle; 3 patients showed grade – I (12%) toxicity and 13 patients showed grade – II (52%) toxicity in the 2nd cycle; 9 patients showed grade – I (36%) toxicity and 8 patients showed grade – II (32%) toxicity in the 3rd cycle; 15 patients showed grade – I (60%) toxicity and 4 patients showed grade – II (16%) toxicity in the 4th cycle; 16 patients showed grade – I (64%) toxicity and 3 patients showed grade – II (12%) toxicity in the 5th cycle; 19 patients showed grade - I (76%) toxicity and 1 patient showed grade – II (4%) toxicity in the 6th cycle. The incidence of mucositis and the percentage of patients affected in different cycles of RT and CRT is shown in fig – 7.

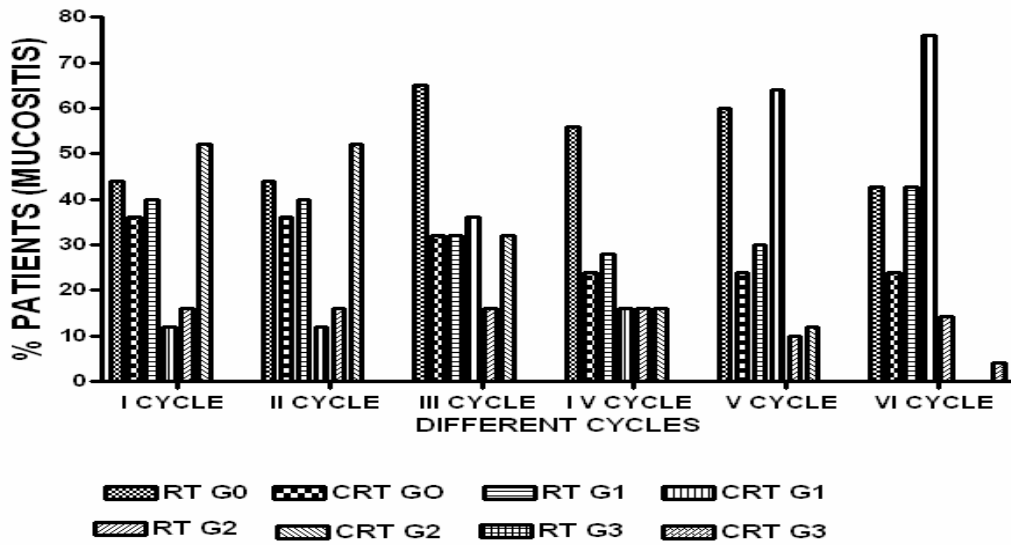


Fig.7: Percentage of patients affected with mucositis in different cycles of radiotherapy and chemoradiotherapy

Incidence of myelosuppression and the percentage of patients affected in different cycles of RT and CRT

In RT group, all the 25 patients showed grade - 0 (100%) leucopenia, all the 25 patients showed grade - 0 (100%) neutropenia, 22 patients showed grade - I (88%) and 3 patients showed grade - II (12%) haemoglobin count, all the 25 patients showed grade - 0 (100%) platelet count in the 1st cycle; 1 patient showed grade - I (4%) leucopenia, 4 patients showed grade - I (16%) neutropenia, 21 patients showed grade - I (84%) and 4 patients showed grade - II (16%) haemoglobin count, all the 25 patients showed grade - 0 (100%) platelet count in the 2nd cycle; 7 patients showed grade - I (28%) leucopenia, 6 patients showed grade - I (24%) and 2 patients showed grade - II (8%) neutropenia, 18 patients showed grade-I (72%) and 7 patients showed grade - II (28%) haemoglobin count, all the 25 patients showed grade - 0 (100%) platelet count in the 3rd cycle. 11 patients showed grade-I (44%) leucopenia, 4 patients showed grade - I (16%), 3 patients showed grade - II (12%) and 3 patients showed grade - III (12%) neutropenia, 11 patients showed grade - I (44%) and 14 patients showed grade-II (56%) haemoglobin count and all the 25 patients showed grade - 0 (100%) platelet count in the 4th cycle; Out of 20 patients, 5 patients showed grade - I (25%) leucopenia, 3 patients showed grade-I (15%) 5 patients showed grade - II (25%) and 3 patients showed grade III (15%) neutropenia, 11 patients showed grade - I (55%) and 9 patients showed grade - II (45%) haemoglobin count, and all the 20 patients showed grade - 0 (100%) platelet count in the 5th cycle. Out of 14 patients, 2 patients showed grade - I (14.2%) leucopenia, 2 patients showed grade I (14.1%), 3 patients showed grade - II (21.4%), 3 patients showed grade III (21.4%) and 1 patient showed grade - IV (7.14%) neutropenia, 5 patients showed grade - I (35.7%) and 9 patients showed grade - II (64.2%), haemoglobin count and all the 14 patients showed grade - 0 (100%) platelet count in the 6th cycle.

In CRT group, 6 patients showed grade - I (24%) leucopenia, 2 patients showed grade - I (8%) and 1 patient showed grade - II (4%) neutropenia, 5 patients showed grade - I (20%) and 20 patients showed grade - II (80%) haemoglobin count, 7 patients showed grade - I (28%) platelet count in the 1st cycle; 9 patients showed grade - I (36%) leucopenia, 2 patients showed grade - I (8%) neutropenia, 2 patients showed grade I (8%) and 23 patients showed grade - II (92%) haemoglobin count, 5 patients showed grade I (20%) platelet count in the 2nd cycle; 6 patients showed grade - I (24%) and 1 patient showed grade - II (4%) leucopenia, 3 patients showed grade - I (12%) and 2 patients showed grade - II (8%) neutropenia, 2 patients showed grade - I (8%) and 23 patients showed grade II (92%) haemoglobin count, 5 patients showed grade - I (20%) platelet count in the 3rd cycle; 7 patients showed grade-I (28%) leucopenia, 2 patients showed grade-I (8%) and 2 patients showed grade-II (8%) neutropenia, 2 patients showed grade-I (8%) and 23 patients showed grade-II (92%) haemoglobin count, 5 patients showed grade-I (20%) platelet count in the 4th cycle; 4 patients showed grade - I (16%) leucopenia, 3 patients showed grade - I (12%), 3 patients showed grade-II (12%) and 2 patients showed grade-III (8%) neutropenia, 1 patient showed grade-I (4%) and 24 patients showed grade-II (96%) haemoglobin count, 5 patients showed grade-I (20%) platelet count in the 5th cycle; 5 patients showed grade-I (20%) leucopenia, 3 patients showed grade-I (12%), 3 patients showed grade-II (12%) and 4 patients showed grade-III (16%) neutropenia, 3 patients showed grade-I (12%) and 22 patients showed grade-II (88%) haemoglobin count, 5 patients showed grade-I (20%) platelet count in the 6th cycle. The incidence of myelosuppression and the percentage of patients affected in different cycles of RT and CRT is shown in fig – 8,9,10,11.

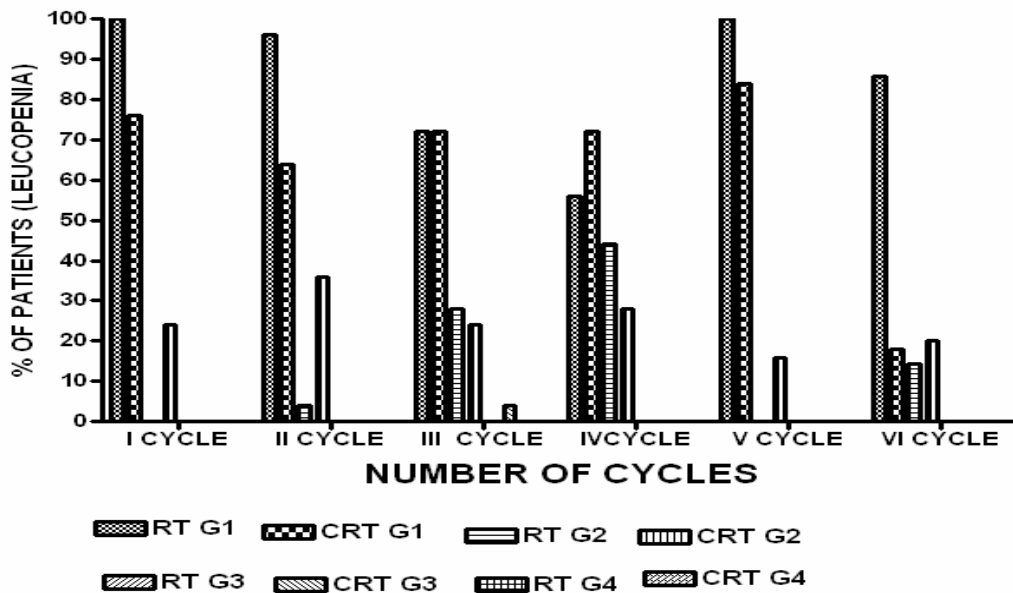


Fig:8: Percentage of patients affected with leucopenia in different cycles of radiotherapy and chemoradiotherapy

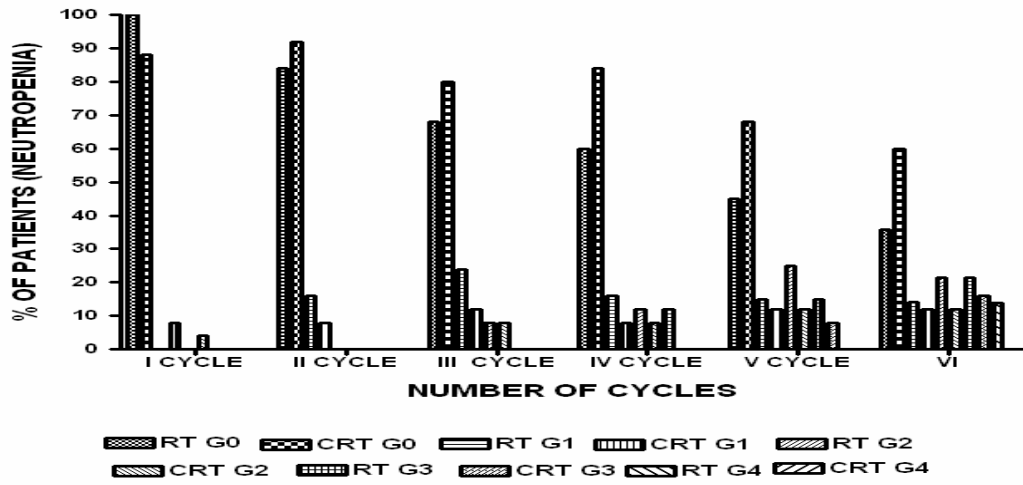


Fig.9: Percentage of patients affected with neutropenia in different cycles of radiotherapy and chemoradiotherapy

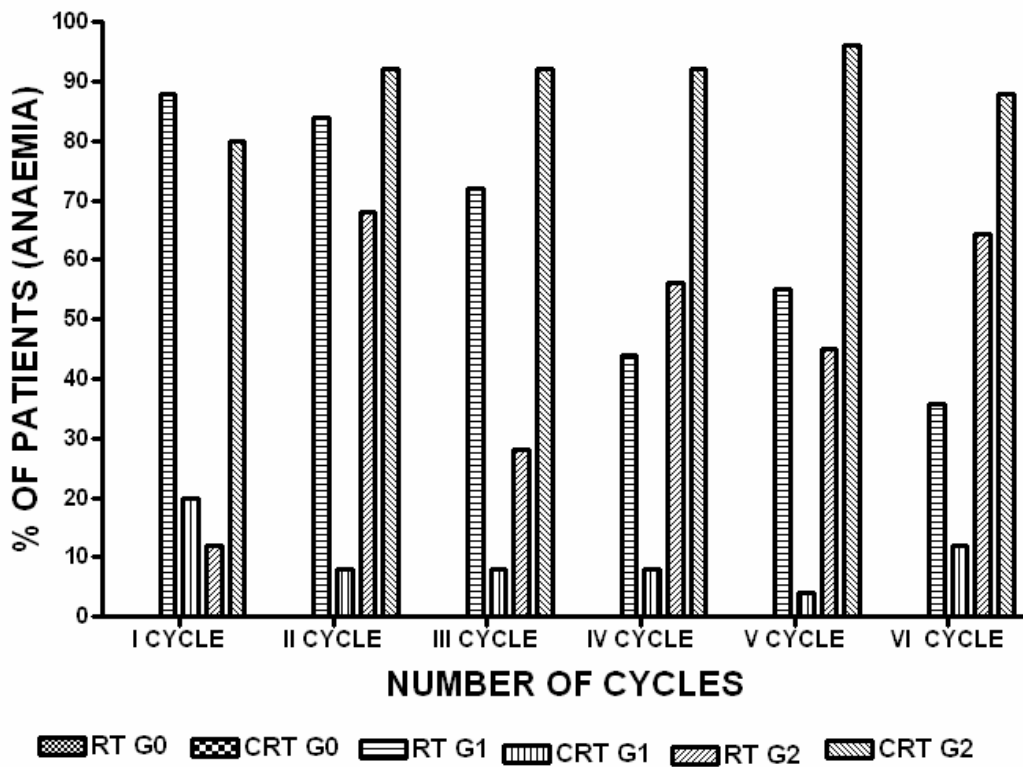


Fig.10: Percentage of patients affected with anaemia in different cycles of radiotherapy and chemoradiotherapy

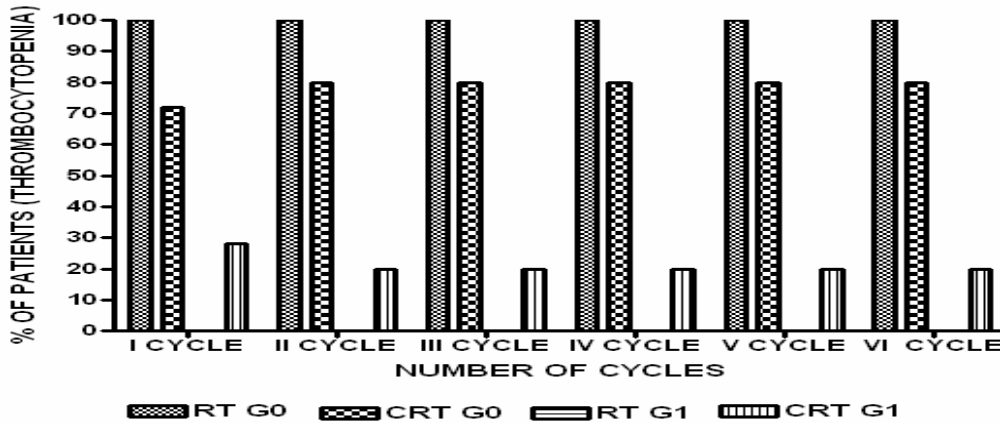


Fig.11: Percentage of patients affected with thrombocytopenia in different cycles of radiotherapy and chemoradiotherapy

Discussion

The primary goal of the present study was to develop a regimen of alternating radiotherapy and chemotherapy that could be given over a condensed period of time without compromising the total dose of radiotherapy. Induction chemotherapy followed by radiation therapy is a common treatment approach for patients with locally advanced inoperable squamous cell carcinoma of the head and neck (SCCHN), although its real advantage over standard radiotherapy is still unknown. A prolonged treatment time might be deleterious for tumour control, and the recruitment of tumour cells into the cell cycle induced by one treatment modality could also improve the anti-tumour efficacy. The concomitant administration of chemotherapy and radiotherapy provides a 5-year survival rate of 32% to 59%, and when chemotherapy is alternated with radiation therapy, the 3 year overall survival rate is 41%. In randomized trials, the addition of chemotherapy to radiotherapy favours the combination over radiotherapy alone. The only prospective randomized study comparing radiation alone with combined treatment was recently reported by the Gynecologic oncology group as demonstrating no survival advantage. Although multiple negative randomized trials appear to have discouraged the use of induction neoadjuvant chemotherapy, about 25% of patients in the current National Survey received chemotherapy concurrent with irradiation. Platinum containing regimens were also used concurrently with irradiation in many of the patients in the 1992-1994 survey. The use of altered fractionation RT was found to be superior to once-a-day RT for SCCHN in a randomized trial of over 1,000 patients conducted by the Radiation Therapy Oncology group. Further improvement in the treatment of SCCHN cancer may be seen with the addition of chemotherapy to RT. Cisplatin remains one of the most effective chemotherapeutic agents with activity against SCCHN. Laboratory and clinical evidence suggests that cisplatin enhances the effects of radiation when given concurrently. Several studies have reported high rates of tumour response, associated organ preservation, and improved survival using cisplatin-based regimens with concurrent standard or altered fractionation RT. The hyperfractionated radiation therapy and cisplatin seem to be associated with improved patient tolerance compared with previously reported chemoradiation experiences.

In order to improve the outcome in locally advanced head and neck cancer, several approaches have been investigated, including altered radiation fractionation regimens, the addition of chemotherapy to radiotherapy.

For many years, the standard treatment for patients with locally advanced carcinoma of the cervix was external beam irradiation to the pelvis and low-dose rate brachytherapy. The standard of care has changed in recent years, thanks to several large, prospective, randomized clinical trials. It has been long recognized that many patients with locally advanced carcinoma of the cervix harbor occult paraaortic metastases [1–7]. Pioneers in the field found that extended field irradiation was associated with greater toxicity, especially gastrointestinal toxicity, than pelvic irradiation [8,9]. However, that may not be so with modern techniques [15–17]. Following the publication of the Rotman *et al.* study, [9] our group began administering extended-field irradiation to patients with locally advanced carcinoma of the cervix. More recently, randomized studies supported the value of cisplatin based chemotherapy for patients with locally advanced carcinoma of the cervix [10–15]. The use of concomitant chemotherapy with pelvic irradiation in locally advanced carcinoma of the cervix has led to a reexamination of the role of extended-field irradiation.

The RTOG has also investigated the addition of drugs, including hypoxic cell sensitizers and cytotoxic chemotherapeutic agents, to conventional fractionated radiotherapy in the treatment of advanced inoperable disease. Phase I-II combined modality studies established the efficacy of concurrent high-dose cisplatin and radiotherapy in the treatment of advanced disease and provided the basis for further testing in Phase III trials for nasopharyngeal carcinoma, larynx preservation, and high-risk advanced operable disease. Preliminary results of the Intergroup Phase III trial for nasopharyngeal cancer showed significantly improved progression-free and overall survival in patients who had Stage III or IV nasopharyngeal cancer treated with combined radiotherapy and chemotherapy compared to radiotherapy alone.

The publication of results of five randomized clinical trials in February 1999 [18,19] resulted in a National Cancer Institute suggestion that platinum-based concurrent chemoradiation should be considered as the current gold standard treatment for women with locally advanced cancer. A large randomized trial by Herod *et al* in 2000 shows comparable overall and disease-free survival to CRT arm. When cisplatin-containing CT regimens were analyzed separately, grade - 3 and grade - 4 acute toxicities showed a similar profile to the combined studies, with a two fold increase in gastrointestinal and hematological toxicities. Long-term toxicity was only described in eight trials of which seven reported no statistical difference in the incidence of long-term side effects [20, 21, 22]. Intensity-modulated radiotherapy (IMRT) is thought to represent an important technological advance. Preliminary studies have shown that IMRT is feasible for treatment of cervical cancer and have suggested a more favourable toxicity profile [23]. Concurrent CT\RT have used nonconventional RT fractionation schedules [24, 25, 26, 27, 28]. One of the most active drugs in cancer is cisplatin, which acts primarily as a radiosensitiser and hypoxic cell sensitiser [29]. Reference to be written as superscript It should therefore be expected to improve the local controls compared with radiotherapy alone.

Conclusion

The main research theme of the cancer institutes currently, is to develop a standard treatment for patients with head and neck cancer and cervix cancer. CT or cytotoxic agents are drugs which interfere with cell division by preventing DNA synthesis and RT involves the use of high energy ionising radiation to cause DNA damage and ultimately cell death. Although it is possible to cure many patients with advanced cervical cancer and head and neck cancer using radiation alone, loco-regional relapse continues to be a component of most recurrences. To improve control rates, clinicians have investigated ways of combining CT and RT. In the present study, although toxicity was more in case of CRT receiving patients, tumour response was better, compared with that of RT alone. Weekly cisplatin-based CRT can be given with acceptable acute toxicity and excellent early control rates. All new trials using CRT should include parallel quality-of-life studies and prospective data collection of both acute and chronic toxicity to inform clinicians and patients of the early effects and late sequelae of treatment. The study may nevertheless be a valuable tool to aid the design of future clinical trials, using cisplatin as the radiosensitizer.

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