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Analysis of 80 Cases of Nasopharyngeal Carcinoma Treated by Intracavitary Brachytherapy Using A New-Type Applicator

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OBJECTIVE To evaluate the results and complications associated with nasopharyngeal carcinoma (NPC) treated with combined external-beam radiotherapy (EBR) and intracavitary brachytherapy (IB) using a new-type applicator.

METHODS Eighty patients with untreated NPC were divided into two groups based on therapy methods. An experimental group was treated with EBR plus IB and a control group was treated only with EBR. IB was given to the patients of the experimental group when the external radiotherapy dose amounted to more than 60~65 Gy. The total dose of IB was 6~20 Gy and the total dose of EBR of the control group was 70~75 Gy.

RESULTS Follow-up was conducted for 97.5% of the patients with results as follows: the overall response rates (ORR) for the experimental and the control groups were 92.5% and 75.3% respectively ($P<0.05$); the 3 and 5-year survival rates for the experimental group were 87.5% and 74.2% and for the control group, 65.0% and 55.6% ($P<0.05$); for the experimental group, the 3 and 5-year disease-free survival rates were 72.5% and 64.5% and for the control group, 60.0% and 52.8% ($P>0.05$).Some complications following radiotherapy showed a significant difference.

CONCLUSION External irradiation plus intracavitary brachytherapy using a new-type applicator may improve the ORR and survival rates, reduce radiation complications and increase the quality of life.

KEYWORDS: nasopharyngeal carcinoma, external-beam radiotherapy, intracavitary brachytherapy, applicator.

INTRODUCTION

A high-dose-rate intracavitary brachytherapy is one of the modalities for the treatment of nasopharyngeal carcinoma (NPC). Most clinical studies have shown that external beam radiotherapy (EBR) plus intracavitary brachytherapy (IB) will improve the local tumor control rate and reduce radiotherapy complications. However, it is unknown whether or not this therapy will increase patient survival as well as reduce local recurrence and metastasis[1-3]. Based on the anatomic structure of the nasopharyngeal cavitary, our department developed and manufactured a new-type radiotherapy applicator. To evaluate the results and complications of treating NPC by a combination of EBR and IB using the new-type applicator, we compared the results of therapy of NPC by EBR plus IB with that using only EBR.

MATERIALS AND METHODS

Patients

Eighty in-patients with untreated NPC were divided into experimental and control groups according to the therapy methods. The experimental group was treated with EBR plus IB and the control group received only EBR. All patient tumors were confirmed by pathologic examination. Pretreatment evaluations consisted of a complete history and physical, direct nasopharyngeal endoscopy coupled with a biopsy of the nasopharynx, computed tomography (CT) and magnetic resonance imaging (MRI) of the nasopharynx and neck. Their tumors were staged according to the Fuzhou Cancer Staging Standard. The patients' baseline characteristics are listed in Table 1.

Methods

The course of treatment for the experimental group typically began with the standard lateral opposed field of the nasopharynx plus tangential field of the neck and supraclavicular fossae. A dose of 2.0 Gy/fraction/day was applied for 5 days/week using 6-MV photons. The primary tumor received a total dose of 60~65 Gy. A total dose of 50 Gy to clinically uninvolved areas of the neck, including the supraclavicular fossae was delivered, and the dose of any involved nodes was boosted with electrons to 70 Gy. The dosage to the spinal cord was limited to $<$40 Gy. The new-type applicator designed by our department was used to administer intracavitary brachytherapy (Fig.1). Before the applicator was inserted into the nasopharyngeal cavity, the patient's nasal cavity, nasopharynx, and oropharynx were anesthetized using 4% lidocaine spray. Then two catheters were inserted through the bilateral nasal cavities for localization and treatment planning. The catheter placements were thus verified under a simulator. An orthogonal pair of treatment planning films were used for simulation. The dwell positions of the primary cancer corresponding to the radiopaque markers on the catheters were noted with the length usually being 2~4 cm. Computerized treatment planning was performed to conform the isodose line to the target volume. Normally the minimal peripheral dose, typically 3.0~4.0 Gy per fraction, twice per day or 5.0~6.0 Gy per fraction, once per day, was prescribed within 1.0~1.3 cm of the catheters. The total dosage of IB was 6~20 Gy with a median of 12 Gy.

The method of EBR of the control group was similar to that of the experimental group. However, for the control group, the primary tumor received a total dose of 70~75 Gy.

Statistical analysis

Statistical analysis was carried out using SPSS13.0 and Kaplan-Meier survival curves were produced for selected variables. Log-rank tests were performed for statistical differences and other data were examined by χ^2 tests.

RESULTS

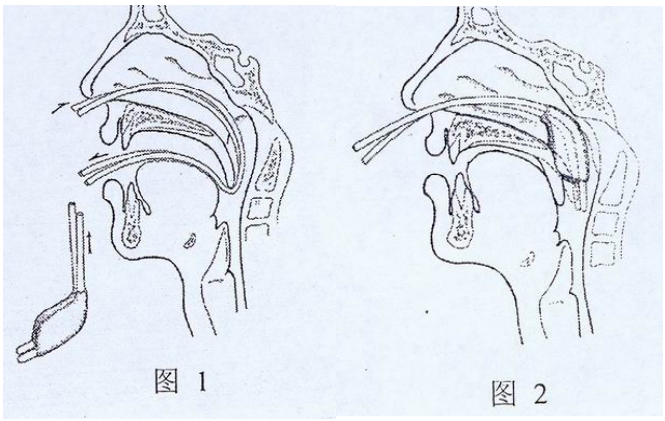
Local control, overall and disease-free survival

All patients were treated from August 1997 to July 2002. A total of 97.5% patients were followed-up by May 2006. The rates of local control (LC) of the experimental and control groups were 92.5% and 75.3%

Table 1. Patient and treatment characteristics.

	EG	CG	χ^2	*P*
Sex				
Male	29	25	0.912	0.340
Female	11	15		
Median age (year)	48	48		
Pathology				
Poorly differentiated squamous carcinoma	29	21	3.710	0.054
Vesicular nucleus cell carcinoma	7	12		
Well differentiated squamous carcinoma	4	7		
Clinical stages				
Stages I+II	13	12	0.058	0.809
Stages III+IVa	27	28		
T stages				
T1+T2	25	24	0.053	0.818
T3+T4	15	16		

EG, Experimental group; CG, control group



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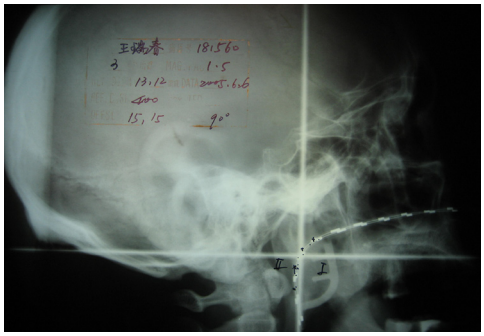

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Fig.1. A: Placement of the new-type nasopharyngeal applicator. B: Sagittal plane for placement of the applicator in th enasopharyngeal cavity.

respectively (P<0.05). Kaplan-Meier survival curves are shown in Fig.2. Log-rank tests revealed that the differences in survival rates for the two groups were statistically significant (P=0.008). The 3- and 5-year overall survival (OS) and disease-free survival (DFS) are shown in Table 2.

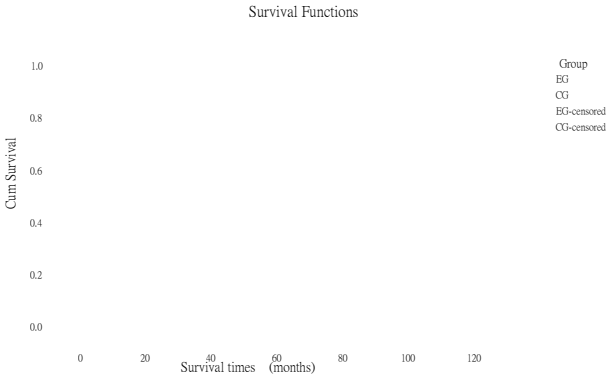

Fig.2. Overall survival rates of the two groups.

Table 2. 3- and 5-year OS and DFS of the two groups.

	EG	CG	χ^2	P
3-year OS	87.5%	65.0%	5.591	0.018
3-year DFS	72.5%	60.0%	1.398	0.237
5-year OS	74.2%	55.6%	2.517	0.113
5-year DFS	64.5%	52.8%	0.943	0.331

OS, overall survival; DFS, disease-free survival

Regional and distant control

Eight patients in the experimental group developed distant metastases. The number of patients and metastatic sites were as follows: six in the liver; four had multiple skeletal metastases; three in the lungs; one in the brain, stomach, retroperitoneum, base of the skull and chest wall (one patient had multiple metastases), two had a nasopharyngeal regional recurrence and three had metastases of the cervical lymph nodes. Among the thirteen patients with local and distant failure, six died, the median survival time being 58 months.

In the control group eight patients developed distant metastases as follows: four in the liver; four had multiple skeletal metastases; three in the lungs; one in the brain, pelvis and spinal cord, four had a nasopharyngeal regional recurrence and two had metastases in the cervical lymph nodes. Of the fourteen patients with local and distant failure, eleven died with a median survival time of 54 months.

Radiotherapy complications

Five patients in the experimental group experienced xerostomia, but in the control group, thirteen patients had this complication (χ^2=4.588, P=0.032). In addition, auditory deficits were found in two patients in the experimental group and in one patient in the experimental group, radiation myelitis and cervical dermatofibrosis were noted.

In the control group, auditory deficits occurred in three patients and two patients lost a tooth. In one patient, cervical dermatofibrosis, nasopharyngeal necrosis and dysphagia were noted.

DISCUSSION

Radiotherapy currently is the standard care in treating patients with primary nonmetastatic NPC. After conventional high-dose EBR, the local recurrence rates and distant metastasis rates may reach 30% to 39%. Moreover, with tumors in later stages and with large primary tumor volumes, the local recurrence rates and distant metastasis rates may be even higher[4]. Local relapses and metastases are the main

reasons for inadequate treatment of NPC by EBR[5]. However, with the development of remote afterloading high-dose-rate (HDR) systems, IB can boost the total dose to the tumor volume in patients with primary NPC. According to a number of reports addressing the use of adjuvant IB in primary NPC, we know that EBR with IB can result in better results compared to treatment by only EBR[6-9].

A new-type applicator for treating NPC designed by our department was used for IB after EBR, and our study showed that the results from the experimental group receiving IB was better than that of the control group without IB ($P<0.05$). Moreover, IB-boosting treatment also improved local control rates of local residuals, local recurrences and tumors insensitive to EBR.

There have been inconsistencies in the medical literature regarding the effect on the survival rates with different schedules using brachytherapy. Our study indicated that the 3- and 5-year survival rates of the experimental group were better than that of the control group, reaching statistical significance. We also found that most of the deceased patients in the control group died within 3 years following treatment with most of them dying of dyscrasia and cardiorespiratory failure. In addition, although the distant metastasis rates in the two groups were similar, most patients in the experimental group suffered from simple organic metastases, such as bone or lung metastases etc. These patients tend to live longer lives with cancer, while most patients in the control group developed multiple organic metastases, and most died of dyscrasia in a relatively short time. For example, thirteen patients in the experimental group developed a local recurrence, cervical lymph node metastasis and distant metastasis, and seven remained alive with cancer, but in the control group, only three patients survived with cancer. It is probable that this phenomenon may be related to the lower local control rates and the bigger residual tumors in the control group, which easily could result in a local recurrence and distant metastasis.

The incidence of oropharynx-xerosis in the experimental group was significantly less than that of the control group, and may be related to the lower total dose of EBR used for the experimental group. The other complications showed no statistical difference. Some studies have indicated that IB treatment for NPC had given rise to some unfortunate complications, such as perforation of the hard or soft palate, nasal cavity sequestration and so on. However, these complications did not occur with our treatment using the new-type applicator designed by our department. Its stabilizing contour conforms to the anatomic structure of the nasopharyngeal cavitary, and it can be placed so as to fill the cavitary. Two brachytherapy catheters inserted through the bilateral nostrils lie between the stabilizing device and nasopharyngeal mucosa. This method optimizes the therapeutic ratio by taking full advantage of the rapid dose fall-off with distance associated with the brachytherapy source. In addition, the ventral aspect of the device pushes the soft palate down, so the normal tissues are protected during the treatment[10].

In summary, local recurrences and distant metastases are still the main reasons for inadequate treatment of NPC. Therefore, many effective therapy methods should be studied to reduce local recurrences and distant metastases. We all know that locoregional control of NPC is an independent prognostic factor in predicting the development of metastatic disease and overall survival. Treatments using conventional EBR, with or without IB, intensity-modulated radiation therapy, stereotactic radiotherapy and chemotherapy should be studied in detail in the future.

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