Once vs. Twice Daily Thoracic Irradiation in Limited Stage Small Cell Lung Cancer

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Purpose : A retrospective study was conducted comparing single daily fraction (SDF) thoracic radiotherapy (TRT) with twice daily (BID) TRT to determine the potential benefit of BID TRT in limited-stage small cell lung cancer (SCLC). Endpoints of the study were response, survival, pattern of failure, and acute toxicity.

Materials and Methods : Between November 1989 to December 1996, 78 patients with histologically proven limited-stage SCLC were treated at the Department of Therapeutic Radiology, Chungnam National University Hospital. Of these, 9 were irradiated for palliative intent, and 1 had recurrent disease. Remaining 68 patients were enrolled in this study. There were 26 patients with a median age of 58 years, and 22 (85%) ECOG performance score of less than 1 in SDF TRT. There were 42 patients with a median age of 57 years, and 36 (86%) ECOG performance score of less than 1 in BID TRT. By radiation fractionation regimen, there were 26 in SDF TRT and 42 in BID TRT. SDF TRT consisted of 180 cGy, 5 days a week. BID TRT consisted of 150 cGy BID, 5 days a week in 13 of 42 and 120 cGy BID, in 29 of 42. And the twice daily fractions were separated by at least 4 hours. Total radiotherapy doses were between 5040 and 6940 cGy (median, 5040 cGy) in SDF TRT and was between 4320 and 5100 cGy (median, 4560 cGy) in BID TRT. Prophylactic cranial irradiation (PCI) was recommended for patients who achieved a CR. The recommended PCI dose was 2500 cGy/10 fractions. Chemotherapy consisted of CAV (cytoxan 1000 mg/m^2, adriamycin 40 mg/m^2, vincristine 1 mg/m^2) alternating with VPP (cisplatin 60 mg/m^2, etoposide 100 mg/m^2) every 3 weeks in 25 (96%) of SDF TRT and in 40 (95%) of BID TRT. Median cycle of chemotherapy was six in both group. Timing for chemotherapy was sequential in 23 of SDF TRT and in 3 BID TRT, and concurrent in 3 of SDF TRT and in 39 of BID TRT. Follow-up ranged from 2 to 99 months (median, 14 months) in both groups.

Results : Of the 26 SDF TRT, 9 (35%) achieved a complete response (CR) and 14 (54%) experienced a partial response (PR). Of the 42 BID TRT, 18 (43%) achieved a CR and 23 (55%) experienced a PR. There was no significant response difference between the two arms (p=0.119). Overall median

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and 2-year survival were 15 months and 26.8%, respectively. The 2-year survivals were 26.9% and 28% in both arm, respectively (p=0.51). The 2-year survivals were 35% in CR and 24.2% in PR, respectively. The grade 2 to 3 esophageal toxicities and grade 2 to 4 neutropenias were more common in BID TRT (p=0.028, 0.003). There was no difference in locoregional and distant metastasis between the two arms (p=0.125 and 0.335, respectively). The most common site of distant metastasis was the brain.

Conclusion : The median survival and 2-year survival were 17 months and 26.9% in SDF TRT with sequential chemotherapy, and 15 months and 28% in BID TRT with concurrent chemotherapy, respectively. We did not observe a substantial improvement of long-term survival in the BID TRT with concurrent chemotherapy compared with standard schedules of SDF TRT with sequential chemotherapy. The grade 2 to 3 esophageal toxicities and grade 2 to 4 neutropenias were more common in BID TRT with concurrent chemotherapy. Although the acute toxicities were more common in BID TRT with concurrent chemotherapy than SDF TRT with sequential chemotherapy, a concurrent chemotherapy and twice daily TRT was feasible. However further patient accrual and long-term follow up are needed to determine the potential benefits of BID TRT in limited-stage SCLC.

Key Words : Limited stage, Small cell lung cancer, Chemotherapy, Radiotherapy, BID

INTRODUCTION

Small cell lung cancer (SCLC) accounts for approximately 25% of all lung cancer cases,[1] and about one third of the patients with SCLC presents with limited-stage disease. Lung cancer is the third most common cause of cancer death in Korean.[2] Especially the death rate of lung cancer in the Korean has increased during the past 10 years with increased smokers.

SCLC differs from the other major histologic subtypes of primary lung cancer in that it has neuroendocrine features, grows more rapidly, spreads earlier, is more responsive to chemotherapy and radiation therapy, and has a lower cure rate. Because of the propensity to metastasize early, the lack of screening modalities, and the sensitivity to chemotherapy, the cornerstone of treatment has been combination chemotherapy.

Recently, although chemotherapy with thoracic radiotherapy increases local control and a modest survival benefit in patients with limited-stage SCLC, the optimal method of the delivery of TRT is unknown.

Thoracic radiotherapy administered single daily with etoposide/cisplatin for patients with limited-stage SCLC has been used in numerous trials with/without alternating chemotherapy with vincristine, doxorubicin, and cyclophosphamide. Patients who participated in these trials has 20% to 40% o 2- and 3-year survival rates.[3-7]

Conventional fractionation radiotherapy and chemotherapeutics could be toxic to lung by themselves. Thus, excellent anti-cancer effects were overshadowed, perhaps, by increases of the mortality and morbidity. In an attempt to overcome these disadvantages, twice daily (BID) thoracic radiotherapy (TRT) was devised.[8, 26] Irradiation of SCLC cell lines in vitro showed a radiation survival curve that the cells were sensitive to single, low doses of radiation less than 200 cGy It suggested this tumor had little capacity fo repair of sublethal doses of radiation.[9] In contrast, tumor-cell lines of other types of lung cancer, and presumably normal pulmonary tissue, are

comparatively resistant to these low doses of radiation.

Twice daily low dose chest radiotherapy has been used in multiple trials with etoposide/cisplatin chemotherapy, with median survival times of grea ter than 20 months and 2-year survival rates o 36% to 46%.[8, 10, 11]

This retrospective study was conducted to compare single daily fraction (SDF) thoracic radio therapy (TRT) with BID TRT to determine the potential benefits of BID TRT in limited-stage SCLC. Endpoints of this study were response survival, pattern of failure, and acute toxicity.

MATERIALS AND METHODS

Between November 1989 to December 1996, 78 patients with histologically proved limited-stage SCLC were treated at the Department of Thera peutic Radiology, Chungnam National University Hospital. Of these, 9 were irradiated for palliative intent, and 1 had recurrent disease. Remaining 68 patients were enrolled in this study. Patients underwent staging evaluation before the initiation of chemotherapy and thoracic radiotherapy. Pre-treatment staging included a physical examination, chest x-ray, bronchoscopy, pulmonary function assessment, computed tomography (CT) of chest liver, and adrenals, radionuclide bone scan, complete blood cell count with differential, and serum chemistry profile. Limited stage was defined as tumor confined to one hemithorax with hilar ipsilateral, contralateral mediastinal, both supracla-vicular lymph nodes, and including the pleura effusion.

By radiation fractionation regimen, there were 26 in SDF TRT and 42 in BID TRT. SDF TRT consisted of 180 cGy, 5 days a week. BID TRT consisted of 150 cGy BID, 5 days a week in 13 of 42 and 120 cGy BID, in 29 of 42. The fractiontion dose in BID TRT was decreased from 150 cGy BID to 120 cGy BID because of increased toxicity. And the twice daily fraction were separated by at least 4 hours. Total radiotherapy doses were between 5040 and 6940 cGy (median, 5040 cGy) in SDF TRT and were between 4320 and 5100 cGy (median, 4560 cGy) in BID TRT. The radiotherapy technique of both groups consisted of initial anterior and posterior opposed fields followed by two oblique or three-fields planning. The initial fields encom-passed the primary tumor with minimum margin of 2 cm and involved mediastinal nodes, but supraclavicular nodes and contralateral hilum were not irradiated routinely. The doses to the spinal cord were kept below 4500 cGy. Prophylactic cranial irradiation (PCI) was optional, but was recommended for patients who achieved a complete response. The recommended PCI dose and schedule were 2500 cGy administered in 10 fractions over 2 weeks.

Chemotherapy consisted of CAV (cytoxan 1000 mg/m^2, adriamycin 40 mg/m^2, vincristine 1 mg/m^2) alternating with VPP (cisplatin 60 mg/m^2, etoposide 100 mg/m^2) every 3 weeks in 25 (96%) of SDF TRT and in 40 (95%) of BID TRT. Median cycle of chemotherapy was six in both group. Timing fo chemotherapy was sequential in 23 of SDF TRT and in 3 BID TRT, and concurrent in 3 of SDF TRT and in 39 of BID TRT.

Response assessment was evaluated at 1 month after completion of treatment and based on the results of chest x-ray, bronchoscopy and chest CT. Tumor responses were classified as complete response (CR), partial response (PR), and no response (NR). CR was defined as the total disappearance of all tumor by chest x-ray and/or chest CT scan. PR was defined as a more than 50% reduction in the volume of tumor. NR was defined as less than a PR or pro-gression of the cancer during treatment. Survival was calculated from the on-study date to the date of death or last follow-up. Follow-up ranged from 2 to 99 months (median, 14 months) in both groups. Survival curves were constructed using the Kaplan-Meier method. Comparisons of pro-gnostic variables in the patients were made using the Log- rank test.

Locoregional failure was considered as re-development of the tumor within the thorax and

distant metastasis included sites outside the thorax.

The acute toxicities during the radiotherapy were scored by the Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring scheme[12]. The evaluated toxicities consisted of pulmonary, esophageal, and hematologic toxicities; WBC, hemoglobin, and platelet counts.

RESULTS

1. Patients Characteristics

Patients characteristics are shown in Table 1. There were 22 men and 4 women, a median age of 58 years (range, 41 to 75 years), and 22 (85%) ECOG performance score of less than 1 in SDF TRT. There were 36 men and 6 women, a median age of 57 years (range, 32 to 75 years), and 36 (86%) ECOG performance score of less than 1 in BID TRT.

2. Response and Survival

Tumor response are shown in Table 2. Of the 26 SDF TRT, 9 (35%) achieved a CR and 14 (54%) experienced a PR. Of the 42 BID TRT, 18 (43%) achieved a CR and 23 (55%) experienced a PR. Overall response rates were 89% in SDF TRT and 98% in BID TRT, respectively. There was no significant response difference between the two arms (p=0.119). Of the all 27 CR patients, 3 refused to receive PCI.

Overall 1- and 2-year survival rates were 61%

Table 2. Tumor Response

Response*	SDF RT (n=26) No. (%)	BID RT (n=42) No. (%)	p
Complete response	9 (35)	18 (43)	
Partial response	14 (54)	23 (55)	
No response	3 (11)	1 (2)	
Response rate	23 (89)	41 (98)	0.119

*Evaluated at 1 month after completion of treatment

Table 1. Patients and Treatment Characteristics (n=68)

	SDF RT (n=26) No. (%)	BID RT (n=42) No. (%)	Total
Age (yr)			
Median	58	57	
Range	41-75	32-75	
Sex Male	22 (85)	36 (86)	58 (85)
Female	4 (15)	6 (14)	10 (15)
Performance (ECOG)			
≤ 0-1	22 (85)	36 (86)	58 (86)
> 1	4 (15)	6 (14)	10 (14)
No. of patients receiving PCI*	8 (31)	16 (38)	24 (35)
RT† dose			
Median dose	5040 cGy	4560 cGy	
Daily dose	180 cGy	120 cGy, BID, 29 150 cGy, BID, 13	
CT‡ regimen			
CAV/VPP§	25 (96)	40 (95)	
Others	1 (4)	2 (5)	
CT cycle			
Total	3-10	1-11	
Median	6	6	
CT timing			
Sequential	23 (88)	3 (7)	26 (38)
Concurrent	3 (12)	39 (93)	42 (62)

*Prophylatic cranial irradiation
†Radiation therapy
‡Chemotherapy
§Cytoxan, adriamycin, vincristine / cisplatin, etoposide

and 26.8%, respectively. Median survival was 15 months (Fig. 1). Of the 26 received SDF TRT, the median survival, 1- and 2-year survival rates were 17 months, 61.5% and 26.9%, respectively. Of the 42 received BID TRT, the median survival, 1- and 2-year survival rates were 15 months, 60.9% and 28%, respectively. There was no significant survival difference between the two arms (p=0.51)(Fig. 2). The survival was analyzed by the response. One- and 2-year survival rates were 72.7%, 35% in CR and 56.7% and 24.2% in PR, respectively, and there was borderline survival difference (p= 0.06)(Fig. 3).

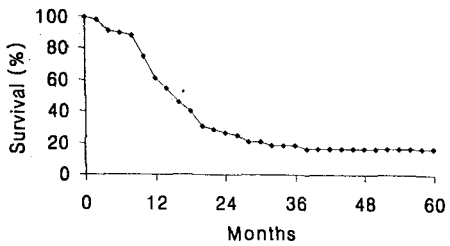

Fig. 1. Overall survival.

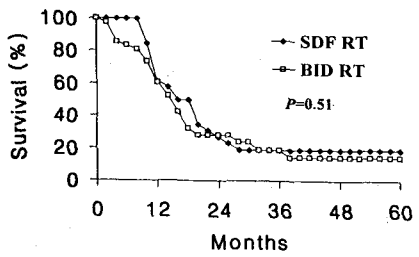

Fig. 2. Survival by fractionation schedule.
SDF RT : Once daily fraction radiotherapy
BID RT : Twice daily radiotherapy.

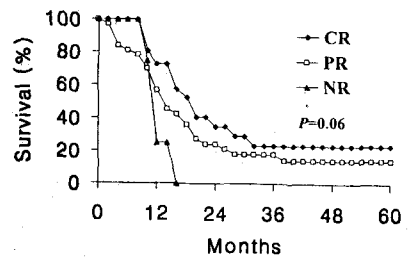

Fig. 3. Survival by response.

3. Failure Analysis

Patterns of failure are shown in Table 3. Of the patients who received the SDF TRT, 6 patients (23%) failed locoregionally, and 9 patients (35%) failed in the distant sites, and 1 patients (4% showed the combined failure. Of the patients who received BID TRT, 4 patients (9%) failed locore gionally, and 10 patients (24%) failed at distan sites, and 3 patients (7%) showed the combined failure. There was no difference in locoregiona and distant metastasis between the two arms (p= 0.125 and 0.335, respectively). The most common site of distant metastasis was the brain (15), and following incidence was liver (7), bone (4), peri cardium (2), adrenal gland (1), axillary lymph node (1), abdominal lymph node (1). In the 3 of the 24 CR patients who had received PCI, brain was the site of initial metastasis.

4. Acute Toxicities

Acute Toxicities are shown in Table 4. The pulmonary toxicity of grade 2 was 0 in SDF TRT and 1 (2%) in BID TRT. They experienced mild

Table 3. Patterns of Failure

Pattern	SDF RT (n=26)	BID RT (n=42)	Total	p
LR*	6 (23)	4 (9)	10 (15)	0.125
DM†	9(35)	10 (24)	19 (28)	0.335
LR+DM	1(4)	3 (7)	4 (6)	

*Locoregional failure
†Distant metastasis

Table 4. Acute Toxicities by RTOG Toxicity Criteria 1995

Organ/ Tissue	Grade	SDF RT (n=26) no. (%)	BID RT (n=42) No. (%)	p
Lung	0-1	26 (100)	41(98)	0.428
	2	0	1(2)	
Esophagus	0-1	26 (100)	35(83)	0.028
	2-3	0	7(17)	
WBC	0-1	20 (77)	17(40)	0.003
	2-4	6 (23)	25(56)	
Hemoglobin	0-1	25 (96)	37(88)	0.255
	2	1 (4)	5(12)	
Platelet	0-1	24 (92)	39(93)	0.930
	2-3	2 (8)	3(7)	

symptoms of dry cough. There was no difference in pulmonary toxicity between the two arms (p=0.428).

The esophageal toxicity of grade 2 and 3 was 0 in SDF TRT and 7 (17%) in BID TRT. There was significant difference in esophageal toxicity between the two arms (p=0.028).

The grade 2 to 4 leukopenia was 6 (23%) in SDF TRT and 25 (56%) in BID TRT. There was significant difference in leukopenia between the two arms (p=0.003). Grade 4 leukopenia (<1000) was developed in 1 in SDF TRT and 3 in BID TRT

The grade 2 anemia was 1 (4%) in SDF TRT and 5 (12%) in BID TRT. There was no difference in anemia between the two arms (p=0.255).

The grade 2 and 3 thrombocytopenia was 2 (8%) in SDF TRT and 3 (7%) in BID TRT. There was no difference in thrombocytopenia between the two arms (p=0.930).

DISCUSSION

Over the years, several investigators have attempted to improve on the treatment results for limited-stage SCLC using a combined modality approach involving chemotherapy with thoracic radiotherapy. The theory behind this approach involves the development of drug resistance via spontaneous mutations within tumors.[13, 14] Ionizing radiation can be used to salvage local recurrences of drug refractory SCLC. Subsequently, it is theorized that drug-resistant SCLC is not completely cross-resistant with radiotherapy and the addition of radiotherapy to chemotherapy will serve to eradicate the repository of de novo chemotherapy resistant cells present in the primary tumor. As a result, there have been a number of randomized clinical trials attempting to discern a potential benefit with the addition of thoracic radiotherapy to systemic chemotherapy in patients with limited-stage SCLC. Seven prospective trials have compared chemotherapy versus radiotherapy plus chemotherapy.[15-21] Regardless of whether combined modality therapy is used in a concurrent, alternating, or sequential fashion, it appears the addition of radiotherapy improves the local control rate from about 50% to 90%. Furthermore, in three of seven trials, statistically significant improvements in response rates and survival rates were shown in favor of the combined modality approach. In our study, all patients was received combined chemotherapy with thoracic radiotherapy. However the timing of chemotherapy was different SDF TRT and BID TRT. Most patients (88%) in SDF TRT were received sequential chemotherapy, and the patients (93%) of BID TRT were received concurrent chemotherapy. So we considered that patients of SDF TRT were received sequential chemotherapy and that patients of BID TRT were received concurret chemotherapy. The overall response rate including CR and PR showed favorable results with 98% in SDF TRT and 89% in BID TRT.

There were several studies about the timing of chemotherapy plus radiotherapy. Carlson et al.[22] conducted a randomized phase III trial testing the value of late consolidative involved-field radiation therapy in the treatment of limited-stage SCLC. They concluded that the addition of late consolidative radiation therapy to induction chemotherapy in the treatment of limited-stage SCLC was well tolerated and improved local control, but did not improve time to progression or suvival rates. In the report of Jeremic et al.,[23] initial administration of BID TRT with concurrent chemotherapy seemed to produce better local control and survival rates than delayed administration. The 5-year survival rates were 30% and 15%, respectively. In the report of Coy P et al.,[24] early administration of locoregional thoracic radiotherapy with concurrent etoposide/cisplatin chemotherapy produced a 64% complete response with a median survival of 21.1 months and 2-year survival of 40%. The proportion of brain metastases was significantly higher in late administration of locoregional thoracic radiotherapy. Murray et al.[6] evaluated the importance of the timing of thoracic irradiation in the combined modality therapy of limited-stage

SCLC in a randomized trial. The chemotherapy consisted of CAV alternating on an every-3-week basis with etoposide/cisplatin. Patients were then randomized to receive early thoracic radiotherapy or late thoracic irradiation. Although complete remission rates were not significantly different between the two arms, the investigators noted overall survival were superior in the early TRT arm (p=0.008). Therefore, the currently accepted approach to the treatment of limited-stage SCLC is considered as a etoposide/cisplatin based chemotherapy with early concurrent thoracic radiotherapy. In our study, 93% (39/42) of BID TRT received early thoracic radiotherapy. Whereas only 12% (3/26) of SDF TRT received early TRT and 88% received late TRT. Although there was not statistically significance, locoregional and distant metastasis were less in the patients of BID TRT than in those of SDF TRT (Table 3).

Although there is heterogeneity in the radiosensitivity of clonogenic cells from SCLC, they are usually quite radiosensitive with the exception of the variant histology. In vitro survival curves demonstrated the lack of a shoulder for SCLC.[9] Twice daily thoracic radiotherapy has two theoretic bases. First, small fractions cause less damage to tissues having a radiobiologic shoulder, but cells without a shoulder, like small cell carcinoma, are exponentially killed with even small fractions. After allowing 4 to 6 hours for repair by normal tissues, a second dose may further kill surviving, shoulder-less small cells, but allow tumor cells in resistant phases of the cell-cycle to move to more sensitive phases. Thus, theoretically the twice daily method could be more effective against tumor and less toxic to normal tissues. A useful compromise in hyperfractionated regimens is the use of dose fractions ranging between 1.15 and 1.6 Gy, administered at least twice daily, at least 5 days per week.[25] In 1985 Armstrong et al.[26] initiated a prospective trial to evaluate the impact of twice daily thoracic irradiation without concomitant chemotherapy in limited-stage SCLC. The complete response rate after thoracic radiotherapy was higher for twice daily patients compared to the once daily patients (86% vs 61%, respectively). However, this advantage was offset by the shorter duration of thoracic control among CR patients treated with twice daily thoracic radiotherapy compared to once daily thoracic radiotherapy (32% vs 67% at 2 years). Three other trials have treated patients with limited-stage SCLC with concurrent etoposide/cisplatin induction chemotherapy and twice daily thoracic radiotherapy or alternating therapy. These trials reported median survival times of 20 to 24 months and 2-year actuarial survival rates of 36% to 45%.[10, 11, 27]

The contribution of twice daily compared with single daily fractions of thoracic radiotherapy has yet to be defined. The survival of patients treated with etoposide/cisplatin plus single daily thoracic radiation is similar to that reported in trials tha used twice daily thoracic radiation. Two large studies that used etoposide/cisplatin plus concurrent single daily thoracic radiation have reported median survival and 2-year survival rates of 18 months and 40% and 15 months and 40% respectively.[4, 6] In a randomized study of Johnson et al.[28], patients with limited-stage SCLC rando mized patients to receive either once or twice daily thoracic radiotherapy with etoposide/cisplatin chemotherapy. Final results showed similar surviva for both arms. Complete response and overal response rates were 48.4% vs 56.4% and 87.1% vs 87.2%, respectively. Median survival and 2-year survival rates were 18.6 months vs 22.7 months and 43.4% vs 29%, respectively. In their study BID TRT failed to substantially improve long-term survival in limited-stage SCLC over that achieved with SDF TRT. However, the authors did not rule out the possibility of a more modest benefit in long-term survival. In our study, median surviva and 2-year survial rates were 15 months and 28% in BID TRT, 17 months and 26.9% in SDF TRT respectively. Although our study was not a rando mized study and somewhat low 2-year survival compared with Johnson et al. study, our study showed a similar result. That is, BID TRT failed to substantially improve long-term survival over

that achieved with SDF TRT.

SCLC is unique among lung cancers by virtue of histology, responsiveness to chemotherapy, and propensity for early and widespread metastases. The brain is a common metastatic target, both a presentation and at the time of disease pro gression. The development of CNS metastases has emerged as a significant clinical problem in the management of patients. At the time of initia diagnosis, 10% to 14% of patients with SCLC have brain metastases.[29, 30] At the time of death at least one third of patients harbor clinically recognized brain metastases, and more than 50% of patients have brain metastases at autopsy.[31, 32] The risk of isolated brain metastases as the first site of recurrence has been evaluated in 300 patients with SCLC who achieved a complete remission. The cumulative risk of developing brain metastases as the sole initial site of recurrence in patients not treated with prophylactic cranial irradiation was 45%, compared with 19% in those treated with prophylactic cranial irradiation. In our study, the risk of developing brain metastasis in patients treated with PCI was 12% (3/24). This result was comparable with the study of Arriagada et al.[33]

Based on the data from randomized trials, it appears that concurrent chemotherapy and TRT administration is associated with improved survival compared with other schedules. However, concurrent chemoradiotherapy is associated with increased host toxicity usually manifested as greater myelosuppression, more frequent esophagitis, and more cutaneous and pulmonary complication.[19, 20, 28, 36] In a randomized study of Johnson et al.[28] that received either once or twice daily thoracic radiotherapy with etoposide/cisplatin chemotherapy, grade 3 esophagitis was more common in BID TRT than SDF TRT (10.9% vs 25.7%). But other toxicities was virtually identical in the two arms. In our study, grade 2 and 3 esophageal toxicity and grade 2 to 4 leukopenia were more common in BID TRT (p=0.028, 0.003). This result suggested that concurrent chemotherapy with BID TRT increase more acute toxicity than SDF TRT.

CONCLUSION

In our study, the median survival and 2-year survival rates were 17 months and 26.9% in SDF TRT with sequential chemotherapy, and 15 months and 28% in BID TRT with concurrent chemo therapy, respectively. We did not observe a substantial improvement of long-term survival in the BID TRT with concurrent chemotherapy com pared with standard schedules of SDF TRT with sequential chemotherapy. The grade 2 to 3 esophageal toxicity and grade 2 to 4 neutropenia were more common in BID TRT with concurren chemotherapy. Although the acute toxicities were more common in BID TRT with concurrent che motherapy than SDF TRT with sequential chemo therapy, a concurrent chemotherapy and twice daily TRT was feasible. However further patients accrual and long-term follow-up are needed to determine the potential benefit of BID TRT in limited-stage SCLC.

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국문 초록 =

국한성 병기 소세포폐암의 방사선치료시 분할 조사방식에 따른 치료성적

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목 적 : 국한성 병기 소세포폐암으로 복합 화학요법과 방사선치료를 받은 환자들에서 통상적 방사선치료와 다분할 방사선치료 간의 종양 관해율, 생존율, 재발율 및 부작용에 대해 비교 분석하고자 하였다.

대상 및 방법 : 1989년 11월부터 1996년 12월까지 충남대학교 병원 치료방사선과에서 국한성 병기 소세포폐암으로 치료받았던 78명 환자 중 고식적 방사선치료 및 재발성 병변으로 치료받았던 10명을 제외한 68명을 대상으로 후향성 분석을 하였다. 대상환자 중 통상적 방사선치료군(A군)은 26명, 다분할 방사선치료군 (B군)은 42명 이었다. 전체 환자의 연령, 성별 및 ECOG 활동지수는 각각 32~75세 (중앙값 58세), 남자 58명 여자 10명, ECOG 0-1이 58명 2 이상이 10명 이었으며 두군 간에 유사한 분포를 보였다. 방사선치료로서 A군은 총 조사선량 5040-6940 cGy (중앙값 5040 cGy), 180 cGy/fx 로 치료하였고 B군은 총 조사선량 4320-5100 cGy (중앙값 4560 cGy)으로 29명 (69%)은 120 cGy/fx 로, 13명 (31%)은 150 cGy/fx 로 1일 2회 조사하였다. 화학요법은 전체 68명 중 65명에서 VPP (cisplatin 60 mg/m^2, etoposide 100 mg/m^2) 요법과 CAV (cytoxan 1000 mg/m^2, adriamycin 40 mg/m^2, vincristine 1 mg/m^2) 요법을 교대로 시행하였으며, 화학요법 횟수는 A군 3-10회 (중앙값 6회), B군은 1-11회 (중앙값 6회) 시행하였다. 화학요법 시기는 A군에서 23명이 연속 화학요법을, B군에서는 39명이 동시 화학요법을 시행하였다. 예방적 전뇌조사는 두군 모두에서 완전관해 후 시행하였는데 A군 8명, B군 16명에서 조사선량 2500 cGy/10fx 로 조사하였다. 추적기간은 2-99개월 (중앙값 14개월)였다.

결 과 : 종양 관해는 완전관해율, 부분관해율이 각각 A군 35% (9/26), 54% (14/26), B군 43% (18/42), 55% (23/42)(p=0.119) 였다. 중앙생존기간 및 2년 생존율은 전체환자에서 15개월, 26.8%였고, A군 17개월, 26.9%, B군 15개월, 28% (p=0.51)였다. 전체환자 중 완전관해 및 부분관해 환자의 2년 생존율은 각각, 35% 와 24.2% (p=0.06)였다. 실패양상으로 두 군간에 국소재발 및 원격전이의 통계적인 차이는 없었다 (p=0.125, 0.335). 방사선치료중 발생한 급성합병증으로 RTOG criteria상 중등도 이상의 식도염 및 백혈구 감소가 B 군에서 더 높게 나타났다 (p=0.028, 0.003).

결 론 : 국한성 병기 소세포폐암의 복합 화학요법과 방사선치료시 종양의 부분관해 이상의 반응율이 연속화학요법을 받은 통상적 방사선 치료군과 동시화학요법을 받은 다분할 방사선 치료군 모두에서 높게 나타났다. 그러나 두 군간의 생존율에는 통계적인 차이를 보이지 않았다. 급성합병증으로서 식도염과 백혈구 감소가 동시화학요법을 받은 다분할 방사선치료군에서 더 높게났지만, 국한성 병기 소세포폐암에서 동시화학요법과 다분할 방사선치료가 적절한 치료의 한 방법이 될 수 있을 것으로 사료된다. 그러나 국한성 병기 소세포폐암에서 다분할 방사선치료의 장점을 밝히기 위하여 좀더 많은 대상환자와 추적관찰이 필요할 것으로 사료된다.