Acta Oncologica 28 (1989) Fasc. 1

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QUALITY OF LIFE DURING CHEMOTHERAPY IN NON-SMALL CELL LUNG CANCER PATIENTS

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Abstract

To evaluate the usefulness of chemotherapy in non-small cell lung cancer, objective response, length of remission and survival have been considered the main yardsticks. Subjective improvement and gain in Karnofsky performance status have attracted very little attention. Thirty-one patients with stages III and IV underwent combination chemotherapy with high-dose cisplatin, and were assessed with categorical scales and 100 mm visual analogue scales used by patients themselves to report on several symptoms of their illness. After chemotherapy 17 of 19 patients (89%) gained weight; 20 presented anorexia, 10 of those (50%) improved; 15 had pain, 7 of those (47%) were alleviated; cough was reported in 22, in 10 (45%) it was ameliorated; hemoptysis disappeared in 10 of 11 patients (91%); of the 9 patients who had dyspnea, 7 improved (78%); and astenia was attenuated in 8 of 16 patients (50%). Quality of life was reported improved in 75% of those patients who had considered themselves seriously affected prior to the treatment. When compared with Karnofsky performance status, no relationship was found (r=0.31). It is concluded that, apart from the objective response achieved, a significant proportion of patients did benefit from treatment as demonstrated by a marked relief of symptoms.

Key words: Lung neoplasms; non-small cell cancer, chemotherapy, evaluation of symptoms, quality of life.

Clinical trials in advanced non-small cell lung cancer (NSCLC) have produced varied results: partial responses ranging from 20 to 60% when regimens containing cisplatin were used (1, 2) with few patients achieving complete remission, and no median survival benefit. Furthermore, there has been some concern regarding toxicity. Hence, lack of efficacy of current chemotherapy (CT) combinations and troublesome side effects have prompted a nihilistic view of treatment in advanced NSCLC. However, in contrast to the study by Woods et al. (3), improved survival has been demonstrated after vindesine plus cisplatin compared with the best supportive care (4). In spite of this demonstrated gain in terms of survival length, some doubt remains as to whether the benefit is outweighed by the degree of toxicity. Better tolerance to CT could be obtained when ancillary aids such as antiemetic control are employed (1, 2, 5, 6). However, little emphasis has been placed on the importance of a feeling of well-being, tolerance to CT and quality of survival (7–10). Apart from measuring the degree of success by relying on objective response (OR) and survival, few attempts have been carried out to measure the subjective response with regard to quality of life reported by patients themselves, independently of an observer's assessment by way of the Karnofsky functional index. Specific instruments for subjective evaluation of response in NSCLC have been developed and their validity and reliability when compared with observer assessment have been well proven (11, 12).

In this study a series of 11 100-mm visual analogue scale (VAS) items were presented to patients for completion concerning lung cancer symptoms, anorexia, weight loss, side effects (nausea and vomiting), level of physical activity and quality of life. We tried to establish the correlation between the Karnofsky performance status (KPS) and OR, and to examine the relationship between the level of physical activity as measured by VAS and OR. With the VAS, we tested changes of symptoms, weight loss, anorexia and quality of life. Furthermore, we compared the scores obtained on categorical scales with those on VAS in measuring the side effects of CT, such as nausea and vomiting. Finally, we looked at correlations between the KPS and quality of life as well as between activity level and quality of life.

Presented at ECCO-4, Madrid, November 1–4, 1987.

Table 1

Karnofsky performance status (KPS), visual analogue scale (VAS) assessment of physical activity, and objective response

Parameter	Objective response	Fisher exact test
KPS >80%	50% (1CR, 7PR)	
KPS <80%	33% (1CR, 4PR)	p=0.56
Physical activity VAS assessment		
>80	48% (2CR, 9PR)	
<80	25% (0CR, 2PR)	p=0.24

Material and Methods

Patients were asked to answer a series of questions by placing a mark on a 100-mm line. The VAS uses a 100-mm horizontal line with 2 anchor points at the ends indicating the severity of the symptoms, '0' indicating absence of symptoms and '100' showing the maximum severity of symptoms. Ratings were scored by measuring in mm from '0' to the subject's mark. The 11 questions were represented in horizontal lines as is shown in the Figure and were designed to elicit response regarding main lung cancer symptoms: cough, dyspnea, hemoptysis, pain weakness, anorexia, physical activity level, nausea and vomiting, and a global question on quality of life.

The VAS questionnaire was answered 1 h before the first cycle of CT; a nurse explained to the patient the content of the VAS items and checked them when they were completed. The VAS examination was repeated 3 weeks after the first cycle of CT and 3 weeks after the second cycle of CT, when patients were assessed to evaluate their objective response. At that point we compared the pre-CT scores with those obtained after the second CT cycle.

Categorical scales were evaluated by a trained nurse to record nausea and vomiting 24 h after each CT cycle. KPS grading was done by a physician before the start of CT and was reassessed before each consecutive CT cycle. To establish a correlation between categorical scales, reported by a trained nurse measuring the number of emetic episodes, and severity of emesis reported by patients themselves, the number of emetic episodes was transformed into categorical values as follows: 1–2 emetic episodes was considered as 25; from 3 to 5 emetic episodes was equated with 50; from 6 to 8 was recorded as 75; and more than 8 as 100.

Eligibility criteria included histologic evidence of NSCLC, stage III and IV according to Mountain's new international classification (13) and Karnofsky performance status >50%. Staging procedures included physical examination, a blood chemistry panel, bronchoscopy, chest radiography, and upper abdominal and thoracic computerized tomography scans. Restaging included physical examination, chest radiography and upper abdominal and thoracic computerized tomography. Treatment schedules were as follows: cisplatin 120 mg/m^2 was given according to a modified Hayes' technique (6). Cisplatin doses were repeated on day 29 and then every 6 weeks. Furthermore, all patients received vindesine (3 mg/m^2) weekly for 5 weeks and then every other week, and either mitomycin C 8 mg/m^2 or ifosfamide 3 g/m^2, either of them administered only at the time of the first 3 cisplatin doses. All patients received proper antiemetic support with high-dose metoclopramide, dexamethasone and lorazepam, as previously described (2). Thirty-one patients went through the VAS test 1 h prior to beginning CT, and 3 weeks after each of the 2 first cycles of CT. VAS assessment and observers' ratings of nausea and vomiting were compared by means of the Pearson correlation coefficient (r). Furthermore, both KPS and physical activity level were compared with quality of life.

All patients receiving 2 courses of chemotherapy were

VISUAL ANALOGUE SCALES QUESTIONNAIRE

1. How much vomiting have you had during the last course of chemotherapy?.

   0 ——— 100 mm

2. How much nausea have you had during the last course of chemotherapy?

   0 ——— 100 mm

3. How much weight do you reckon have lost?

   0 ——— 100 mm

4. How is your appetite?

   0 ——— 100 mm

5. How much is pain interfering with your daily activities?

   0 ——— 100 mm

6. How much do you cough?

   0 ——— 100 mm

7. How much does breathing difficulty interfere with normal life?

   0 ——— 100 mm

8. Have you observed blood spots in your phlegm?

   0 ——— 100 mm

9. How tired do you feel?

   0 ——— 100 mm

10. How much does your disease restrict you in your daily activities?

    0 ——— 100 mm

11. What is your quality of life like now?

    0 ——— 100 mm

Table 2

Influence of chemotherapy on symptoms and quality of life

Item	Severity* Mean VAS scores (0=lowest, 100=highest)	No. of patients with symptoms		Improved %
		Before chemotherapy	After chemotherapy	
Pain	50	15	8	47
Cough	28	22	12	45
Dyspnea	48	9	2	78
Hemoptysis	38	11	1	91
Weakness	46	16	8	50
Weight loss	45	19	2	89
Anorexia	42	20	10	50
Quality of life	74	12	3	75

* Measured before the first cycle of CT.

Table 3

Relationship of symptom improvement to objective response

Item	Patients with objective response		Patients without objective response	
	No.	% improved	No.	% improved
Weight loss	(10/11)	91	(7/8)	87
Anorexia	(6/10)	60	(4/10)	40
Pain	(1/4)	25	(6/11)	54
Cough	(4/8)	50	(6/14)	43
Dyspnea	(3/4)	75	(4/5)	80
Hemoptysis	(4/5)	80	(6/6)	100
Weakness	(6/9)	67	(2/7)	28

Table 4

Reliability of patient generated VAS and observer scored categorical scales

Parameter	VAS Mean score*	Categorical scales	
		Mean score*	Pearson r
Vomiting	34	33	0.97**
Nausea	25	23	0.78**

*0=Best; 100=Worst. ** $p<0.0001$.

considered evaluable for response. Complete response (CR) was defined as disappearance of all tumor signs for at least 1 month, including negative fibrobronchoscopy with a negative biopsy. Partial response (PR) required a reduction of 50% or more of the sum of the longest perpendicular diameters of measurable disease with no lesion developing elsewhere, lasting at least 1 month. For the patients with evaluable but not bidimensionally measurable disease, a more than 75% reduction was required to qualify for PR. Stable disease was characterized by absence of remission or progression during a minimum of 3 months. Progressive disease was defined as a 25% increase of an existing lesion or the appearance of new lesions. Differences in proportion between groups were tested by the Fisher exact test.

Results

There was no significant difference in predictability of response when KPS was compared with 100-mm VAS in measuring level of physical activity. No significant difference was found between remitters with KPS >80% (8 patients out of 16) and those with physical activity >80 (11 out of 23). Neither was there any difference between remitters with KPS <80% (5 patients out of 15) and those with physical activity <80 (2 out of 8) (Table 1). The correlation between KPS and self reported level of physical activity on the VAS scale did not achieve statistical significance ($r=0.52$, $p=0.06$).

The patient generated VAS ratings provided useful assessment of subjective response with improvement of symptoms ranging from 45 to 91% as depicted in Table 2. Chemotherapy improved dyspnea, hemoptysis and weight loss in more than two thirds of the patients. About half of the patients experienced a reduction of pain and cough, or improved their feeling of strength. Quality of life was reported improved by 75% of the patients. There was an improvement of symptoms not only in patients who met objective response criteria, but even in those patients who had not achieved a PR (Table 3).

When comparing patients' VAS ratings and observers' category scales in the assessment of nausea and vomiting, good interrater reliability was found ($r=0.97$, $p<0.0001$) as shown in Table 4. Sixty-one percent of the patients

showed less than 3 emetic episodes in 24 h. No correlation was found between KPS (mean score 75) and quality of life (mean score 73) ($r=0.31$, $p=0.08$) nor between physical activity level (mean score 86) and quality of life ($r=0.10$, $p=0.58$).

Discussion

Clinical chemotherapy trials in advanced NSCLC have yielded varying results; partial response has usually been observed in less than 50% of the patients and in most studies enhanced survival has not been observed. Despite a relatively high response rate chemotherapy regimens containing cisplatin have, according to some observations, not obviously prolonged median survival and they are associated with considerable toxicity that may reduce quality of life. A pessimistic view is expressed by Woods et al. (3) who found no difference in the median survival between patients treated with vindesine plus cisplatin and chemotherapy-naive patients. In contrast, however, Rapp et al. (4) in a recent multicenter trial reported improved survival in patients treated with vindesine plus cisplatin compared to those with only good supportive care. We suggest that chemotherapy could be useful and apart from the objective response, give a more satisfying life by ameliorating symptoms. Padilla et al. (14) tried to define the qualities which render life and survival worthwhile and suggested that the quality of survival can be measured by traditional methods, such as the KPS scale (15) applied to the symptoms that afflict patients. The KPS scale records patient status on a 0 to 100 categorical scale. Although estimates obtained with this scale showed a significant correlation with objective tumor response, the scale does not give information about quality of survival. The increasing use of aggressive chemotherapy in NSCLC has been met with strong criticism, claiming that the chemotherapy is too toxic and ignores the welfare of the patient. Much effort has concerned the development of response criteria dealing with quality of life (8–10, 16–19). Linear analogue scales have been used for rating of subjective feelings (20) and a great variety of scales deriving from enquiries focused on psychiatric symptomatology has been produced. Some of these have used categorical scales in which symptoms are recorded from absent (0) to maximum (100) and others have utilized continuous analogue scales (21). Satisfactory interobserver agreement has been shown with both types of scales.

In the present trial quality of life was measured with linear analogue scale items concerning lung related symptoms, gastrointestinal toxicity, anorexia, weakness, weight loss, level of physical activity and the more general enquiry "What is your quality of life like now?". Internal consistency and test-retest variation as well as the validity and the feasibility of the method have previously been reported by Monras et al. (12).

Under these instruments Burke et al. (11) found that the majority of their patients with major objective response after chemotherapy also had improvement of their symptoms. Similarly, Osoba et al. (22) reported a 44% response rate in advanced NSCLC after etoposide, cisplatin and bleomycin and showed that the objective responses correlated with improvement of symptoms; in 51% of their patients all symptoms were temporarily controlled. In our present study the VAS items provided useful assessment of subjective response and improvement of symptoms was reported by 45 to 91% of the patients. In contrast to the Sloan-Kettering study (23) we did not find significant differences in predictability of response between KPS and VAS as concerned physical activity. In the Sloan-Kettering study (23) there was a trend towards better predictability of response with VAS than with KPS.

Despite the high dose of cisplatin, nausea and vomiting were not a major problem in our series due probably to the strong antiemetic treatment (2). Similar observations have been reported by other investigators (1).

We conclude that instruments for measuring the patients' subjective responses were useful in order to assess the real improvement of symptoms as well as the feeling of well-being and chemotherapy tolerance.

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