Eur J Cancer, Vol. 26, No. 6, pp. 706–708, 1990.
Printed in Great Britain

0277-5379/90$3.00 + 0.00

Quality of Life Assessment During Chemotherapy for Non-small Cell Lung Cancer

Paula K. Maasilta, Jukka K. Rautonen, Madeleine T. Mattson and Karin V. Mattson

Quality of life was assessed by linear analogue scales for patients with non-small cell lung cancer participating in a phase I–II trial. Chemotherapy consisted of cyclophosphamide 600 mg/m² intravenously on day 1 and trimetrexate (five dose levels) intravenously on days 1–5, repeated every 21 days. Eleven subjective items were assessed by the patients. Nine of the scales related to performance, problems related to the disease itself and uncertainty about the value of treatment; two scales related to the major known side-effects of chemotherapy. Each patient completed the scales before treatment, on the last day of treatment (day 5) and once between cycles. Variation in the scores for items (e.g. for nausea or appetite) suggests that the method was useful in estimating the patient's perceived quality of life during repeated cycles of chemotherapy. Compliance was good and the method was easily accepted by both patients and nurses as part of a routine.
Eur J Cancer, Vol. 26, No. 6, pp. 706—708, 1990.

INTRODUCTION

IT HAS not been established that chemotherapy is superior to the best supportive treatment in terms of survival and quality of life of patients with inoperable non-small cell lung cancer (NSCLC) [1, 2]. When evaluating experimental chemotherapy it is therefore essential to assess the quality of survival. In a randomized trial of NSCLC, untreated controls scored slightly less well at 3 months than in two treatment groups whereas no difference between the arms was seen at 6 months. A transient improvement of quality of life despite poor objective response to therapy seemed to occur in the treated patients [3]. That NSCLC study used serial questionnaires completed by patients and staff simultaneously. There are several other methods available [4–6]. There is, however, a need for standardization of methods to assess and report on quality of life in trial patients [6]. We have tested visual analogue scales (VAS) [4] with eleven subjective items for quality of life assessment in patients with inoperable NSCLC in a phase I–II trial.

PATIENTS AND METHODS

Patients

All patients gave their informed consent and the studies were approved by the Ethical Committee of the Department of Pulmonary Medicine of the Helsinki University Central Hospital.

The eligibility criteria were: confirmed metastatic or inoperable, previously untreated, NSCLC, measurable in one or two dimensions (phase II patients): age 18–80 years; life expectancy more than 6 weeks; Zubrod performance status under 2; white cell count below 1.5×10^9/l and platelets over 100×10^9/l; and serum creatinine under 130 μmol/l, bilirubin under 40 μmol/l and aspartate aminotransferase below three times the upper limit of the normal range. Before treatment a physical examination, laboratory tests, electrocardiogram and chest X-ray were done, and the reference lesion (phase II patients) was measured.

Three of the 59 patients were not eligible for quality of life assessment because of language difficulties (1 patient) or impaired intellectual function due to brain metastases (2). One patient who agreed to participate later refused to complete any forms. These four patients were not included in the analysis.

Twenty-three patients were included in phase I and 32 phase II (Table 1). Epidermoid carcinoma was the most common histological subtype (47% of patients). One had non-disseminated disease.

Chemotherapy

In phase I trimetrexate (provided by Warner-Lambert) was administered intravenously on an escalating daily dosage schedule starting at 3 mg/m² for 5 consecutive days (4 patients), escalated gradually to 5 mg/m² (4), 7.5 mg/m² (4), 10.5 mg/m² (9) and 13.5 mg/m² (2). Every 5 day cycle of trimetrexate was preceded by cyclophosphamide 600 mg/m² intravenously on day 1. At least two cycles every 3 weeks were administered to every patient unless toxicity or disease progression intervened. The maximum number of cycles was six.

Address correspondence to: P.K. Maasilta, M.D, Department of Pulmonary Medicine, Helsinki University Central Hospital, Haartmaninkatu 4, 00290 Helsinki, Finland.
P.K. Maasilta and K.V. Mattson are at the Department of Pulmonary Medicine and J.K. Rautonen is at the Department of Pediatrics, Helsinki University Central Hospital and M.T. Mattson is at the Faculty of Science, Helsinki University, Helsinki, Finland.

Table 1. *Characteristics of patients*

	Phase I (n = 23)	Phase II (n = 32)
M/F	19/4	27/5
Mean age (yr)	61	55
Zubrod performance status		
0–1	22	32
2	1	0
Clinical stage		
I–III	8	6
IV	15	26

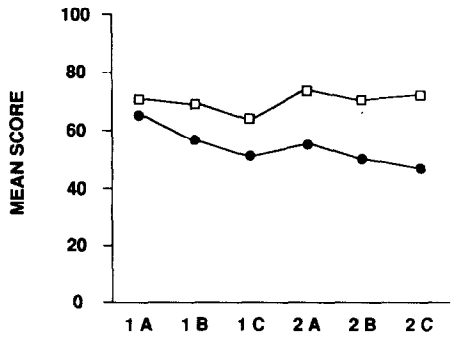

Fig. 1. Mean scores combined for all questions in phase I (solid circles) and phase II (open squares) patients. 1 = first and 2 = second cycle; A = pretreatment; B = on last treatment day and C = 1 week after treatment.

Based on the results of phase I, the trimetrexate dose chosen for phase II was 10.5 mg/m^2 per day on 5 consecutive days in combination with cyclophosphamide 600 mg/m^2 on day 1. Cycles were repeated every 3 weeks. Patients were evaluable for response after two cycles. The maximum number of cycles administered was six.

Metoclopramide for nausea was provided as requested (intravenous bolus or suppositories).

Quality of life assessment

Vital signs were measured at the beginning and end of each infusion, and 30 min later. Laboratory tests were done weekly. Toxicity was assessed according to WHO grading [7] and tumours were measured every 6 weeks.

Quality of life was assessed by linear analogue scales (details of the form from P.M.). Eleven subjective items were assessed by the patients. Nine items concerned performance, problems related to the cancer and the uncertainty of improvement or cure with the treatment while two items concerned major known side-effects of chemotherapy. Each item was represented by a 10 cm line, the right-hand end always describing normality or absence of a symptom and the left-hand end the opposite. Thus the higher the score the better the quality of life. Each patient completed the form before treatment, on the last day of each cycle and 1 week after the end of each cycle.

Statistics

A paired two-tailed t-test was used to analyse the changes in the scores for each item during the chemotherapy cycles. Spearman's rank correlation coefficients were calculated to study the relation between trimetrexate dose or treatment response and the mean scores, and linear correlation coefficients to examine the association between leucopenia or thrombocytopenia and the mean scores.

RESULTS

Treatment-related toxicity

Haematological toxicity consisted of anaemia (phase I, 67%; phase II, 80%), leucopenia (67% and 28%) and thrombocytopenia (52% and 26%). Non-haematological toxicity included nausea and vomiting (67% in both phases), mucositis (30% and 44%) and urticaria or rash (22% and 21%). The frequency of leucopenia and mucositis in the phase I study were dose-related. No patient death was attributed to treatment-related toxicity.

Tumour response

In phase II, tumour responses could be evaluated in 24 out of 32 patients (75%) (7). After two cycles, one patient (4%) achieved a partial response and two patients (8%) minor responses; 18 patients (75%) had stable disease and three patients (13%) progressive disease. After six cycles, seven patients were evaluable for response: four had a partial response and the other three had stable disease. Complete responses were never seen.

Quality of life

Treatment-related toxicity or disease progression led to the withdrawal of 20 patients after one cycle. Nineteen and 11 patients, respectively, completed the scales for one and two cycles in phase I. Thirty-one, 21, 21 and six patients completed the forms for one, two, four and six cycles in phase II. The total number of analysed forms was 101 for phase I and 274 for phase II (35 out of the possible total of 410 forms were lost or never completed by the patients).

Figure 1 shows the mean scores combined for all questions in phase I and II for the first two cycles. Whilst the mean scores of patients in phase II remained steady throughout the treatment period, the scores of patients in phase I declined significantly

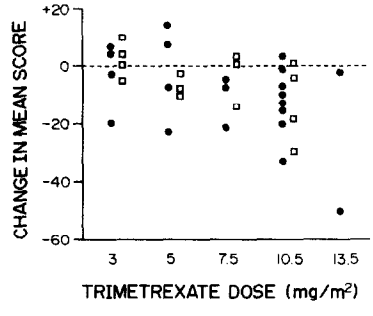

Fig. 2. Change in mean scores of all items between start of treatment and last treatment day in individual patients receiving different doses of trimetrexate during the first (solid circles) and second (open squares) cycles of chemotherapy in phase I.

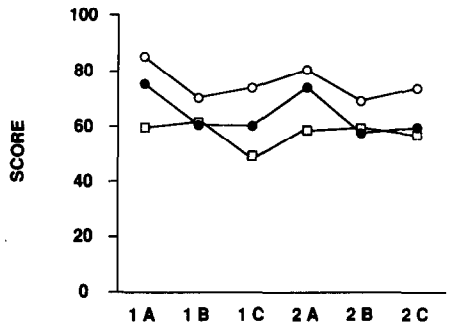

Fig. 3. The scores for nausea (open circles), appetite (solid circles) and general well-being (open squares) during the first two cycles of chemotherapy in all patients in phases I and II.

with time ($P = 0.03$). In both phases a small but non-significant improvement in the mean scores took place in the assessment done between treatments (2A in Fig. 1).

The change in mean scores before chemotherapy was compared with the last treatment day at different trimetrexate dose levels in phase I (Fig. 2). Increasing trimetrexate dose was significantly correlated ($P < 0.05$) with a decrease in the mean score for quality of life.

Figure 3 shows the data on nausea, appetite and general well-being before chemotherapy and on the last day of the first and second chemotherapy cycles in all participating patients. Chemotherapy was associated with a significant decrease in the scores for nausea ($P < 0.01$) and appetite ($P < 0.01$), but did not affect general well-being.

There was no significant correlation between the changes in white cell count, platelet count or tumour response and any of the items on the linear analogue scales.

The questions 'Does the treatment help?' and 'What have you been told about your disease?' were not answered on 25% and 5% of the forms, respectively, after the first chemotherapy cycle in all participating patients. The form with the linear analogue scales was easily accepted by patients and nurses as part of their routine. Compliance was good.

DISCUSSION

In patients with incurable cancer, quality of life is important. There are, however, no established methods to measure quality of life objectively. Several methods have been tested [4–6, 8]. We chose a modification of the visual analogue scales described by Selby *et al.* [4]. Our aim was to develop a method, acceptable to patients, that would require a minimum of extra work or financial resources and would be suitable for routine use. The lack of a 'gold standard' for quality of life makes the validity and reliability of the different methods difficult to assess. Selby *et al.* [4] found strong support from several evaluations for the validity of visual analogue scales. The questions chosen for our assessment were concerned with general well-being, with physical and social activity and with the disease and the chemotherapy. We included the patients' assessment of the treatment's effect and their awareness of their illness. To encourage compliance the items were limited to 11 and the questionnaire fitted on a single page.

Patients in phase I showed a significant decline in the combined mean scores of quality of life after the first two chemotherapy cycles, compared with no significant decline for patients in phase II. Patients in phase I were possibly more ill than those in phase II. After the first two chemotherapy cycles, patients experienced significantly more nausea and poorer appetite; but general well-being was not affected significantly. Patients tolerated treatment-related symptoms well, as has also been found previously [9]. Treatment toxicity may have been interpreted as a sign that the treatment was effective. Tumour response did not correlate with the scores for quality of life. No complete responses were seen. Patients were informed about the result of the treatment at all assessment points.

Some patients were reluctant to express their presumably negative feelings about the treatment's uncertain effect and their opinions about the amount of information they had been given; they refused to answer these questions. These are areas where it has previously been found that patients do not easily communicate [4]. There was an interesting, although not statistically significant, tendency for patients to feel that they were less informed about their disease status as the treatment progressed (data not shown). Since objective responses were not achieved in most patients, this finding may have resulted from a tendency to protect patients from bad news.

There was no control group receiving symptomatic treatment only. Therefore it was not possible to differentiate between the effect of the disease itself and that of the chemotherapy on the quality of life. The quality of supportive care may influence certain items assessed (e.g. pain and nausea).

Our assessment form was short and compliance was good. The form was easy to administer and score and thus also acceptable to nurses. This simple visual analogue scale method should be useful for quality of life assessment, especially in the comparison of different treatments. Since this method requires minimum extra work, practically no training and little time, it is suited for use in everyday practice.

1. Mulshine JL, Glatstein E, Ruckdeschl JC. Treatment of non-small cell lung cancer. Role of chemotherapy in NSCLC, low response rate, no major improvement of overall survival. *J Clin Oncol* 1986, **4**, 1704–1715.
2. Hoffman PC, Bitran JD, Clolarub HM. Chemotherapy of non-small cell bronchogenic carcinoma. *Semin Oncol* 1983, **10**, 111–122.
3. Ahmedzai S, Grzwgorzyk EA, Teather BA, Banham SW, Gregor A. Quality of life in patients with non-small cell lung cancer (NSCLC) in a randomised trial of radiotherapy+RT, and palliative treatment (Abstract). Proc 5th World Conference on Lung Cancer, Interlaken, 1988, A 182.
4. Selby PJ, Chapman J-AW, Etazadi-Amoli J, Dalley D, Boyd NF. The development of a method for assessing the quality of life of cancer patients. *Br J Cancer* 1984, **50**, 13–22.
5. Guyatt GH, Verman LB, Towsend M, Pugsley SO, Chambers L. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 1987, **42**, 773–778.
6. Donovan K, Sanson-Fisher RW, Redman S. Measuring quality of life in cancer patients. *J Clin Oncol* 1989, **7**, 959–968.
7. *WHO Handbook for Reporting Results of Cancer Treatment.* WHO offset publication, Geneva, 1979, 48.
8. Levine MN, Guyatt GH, Gent M *et al.* Quality of life in stage II breast cancer: an instrument for clinical trials. *J Clin Oncol* 1988, **6**, 1798–1810.
9. Kaasa S, Mastekassa A. Psychosocial well-being of patients with inoperable non-small cell lung cancer. The importance of treatment- and disease-related factors. *Acta Oncol* 1988, **27**, 829–835.