Quality of life in advanced non-small cell lung cancer patients receiving palliative chemotherapy: a meta-analysis of randomized controlled trials

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CRD summary
Higher global quality of life and less severe symptoms were found with carboplatin-based when compared with cisplatin-based chemotherapy in patients with advanced non-small cell lung cancer who received palliative chemotherapy. Survival rates did not differ. Limitations in reported process, the small number of included trials and uncertain trial quality make the reliability of the authors' conclusions unclear.

Authors' objectives
To assess the effect of palliative chemotherapy in patients with advanced non-small cell lung cancer on quality of life in addition to overall survival and disease-related symptoms in order to help inform selection of suitable chemotherapy regimen.

Searching
PubMed and Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched up to April 2010; search terms were reported. Reference lists were searched. Only publications in English were considered.

Study selection
Eligible studies were randomised controlled phase III trials (RCTs) that compared carboplatin-based to cisplatin-based chemotherapy in patients with pathologically confirmed advanced non-small cell lung cancer who had not previously received chemotherapy. Trials needed to report quality of life data and were required to provide longitudinal as well as explicit quality of life data measured using the European Organization for Research and Treatment of Cancer Core Questionnaire (EORTC QLQ-C30) or the Functional Assessment of Cancer Therapy-Lung (FACT-L).

Trials that compared outcomes with a historical or literature arm were excluded. Trials that did not report adequate information of the clinical assessment of the main outcomes and the randomisation process were excluded.

Quality of life outcomes focused on global quality of life and key symptom domains (fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties). Cisplatin-based chemotherapy arms included cisplatin plus paclitaxel, gemcitabine, vinorelbine or mitomycin (plus ifosfamide or vinblastine) administered every three to four weeks. Carboplatin-based chemotherapy arms included carboplatin plus paclitaxel, gemcitabine, docetaxel or mitomycin plus vinblastine administered every three or four weeks.

The authors did not state how many reviewers were involved in trial selection.

Assessment of study quality
The authors did not state that they formally assessed the quality of the included trials.

Data extraction
Estimates of effect for quality of life were to be extracted or calculated for each trial. Estimates of effect size could not be obtained for any of the included trials so one sided p-values were calculated from the two-sided p-values obtained from the published studies under the hypothesis of a favourable outcome for carboplatin-based chemotherapy. When the p-value for the difference between regimens was not provided it was calculated with a t-test using difference in quality of life scores for each regimen. In trials that did not report estimates or sufficient data to calculate estimates, a combination of all estimates (positive and negative) were assumed and corresponding one-sided p-values for all cases were calculated. Only quality of life data collected at baseline and between 12 and 17 weeks following the start of treatment were used. Relative risks and associated 95% confidence intervals (CIs) were extracted for survival and response rates. Authors were contacted for data confirmation.

Methods of synthesis
Overall quality of life estimates were calculated by pooling one-sided p-values using the inverse normal method. Survival and response rate estimates were pooled using random-effects and fixed-effect models. Results from the random-effects model were reported regardless of trial homogeneity. Relative risks greater than one reflected a favourable outcome for carboplatin-based chemotherapy. Statistical heterogeneity was assessed using the $\chi^2$ test.

**Results of the review**

Six RCTs (2,405 patients: 1,199 received cisplatin and 1,206 received carboplatin) were included in the review.

**Quality of life:** A significant effect in favour of carboplatin was found for global quality of life ($p=0.016$; three RCTs), fatigue ($p=0.007$; three RCTs), nausea and vomiting ($p=0.001$; five RCTs), appetite loss ($p=0.027$; five RCTs) and constipation ($p=0.001$; three RCTs) using one-sided p-value. When five RCTs were included, global quality of life was not significantly different between the two chemotherapy regimens.

**One-year survival and response rate:** No statistically significant difference was found between the two treatment arms for one-year survival or response rates (six RCTs; no significant heterogeneity).

**Authors’ conclusions**

Patients who received carboplatin-based chemotherapy had higher global quality of life and less severe symptoms than those who received cisplatin-based chemotherapy; survival rates at one year did not differ between the two groups.

**CRD commentary**

The review question was supported with clear inclusion and exclusion criteria. Two databases were searched and the search was restricted to trials published in English so relevant trials have been missed. It was not clear whether appropriate steps were taken to minimise error and bias during study selection and data extraction. Trial quality was not assessed formally. There was limited information about participants. Methods used to synthesise quality of life outcomes were not recommended.

Limitations in the synthesis and reported review process and uncertain quality of the included trials make the reliability of the authors’ conclusions unclear.

**Implications of the review for practice and research**

**Practice:** The authors stated that the inclusion of quality of life outcomes provided useful information regarding selection of appropriate chemotherapy regimen for patients who received palliative chemotherapy.

**Research:** The authors stated that future studies should include quality of life as an outcome measure for first-line treatment.

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