Adjuvant and adjunctive chemotherapy in the management of squamous cell carcinoma of the head and neck region: a meta-analysis of prospective and randomized trials

El-Sayed S, Nelson N

Authors' objectives
To assess the potential value of adding chemotherapy, in one form or another and with any sequence, to local definitive treatment (surgery and/or radiotherapy) in the radical management of squamous cell carcinoma of the head and neck region.

Searching
Various unnamed national and international medical online literature search facilities were accessed, but no search strategy or restrictions were outlined. Additional material was obtained through personal communications, and by examining meeting abstracts and reference lists from publications.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Chemotherapy and local definitive treatment (surgery and/or radiotherapy). No details of drugs or doses are given.

Participants included in the review
Patients undergoing chemotherapy and/or local definitive treatment in the radical management of squamous cell carcinoma of the head and neck region. No patient characteristics are reported.

Outcomes assessed in the review
Toxic side-effects, positive response and survival (through comparison of hazard or mortality rates) were assessed.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
For inclusion in the systematic review, studies had to address the authors objective and adhere to the study design criteria, which were not outlined in the review. Nonadherence to the protocol, and exclusion of patients after randomisation, led to exclusion from the review. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The Mantel-Haenszel summary test was used to test for differences in the occurrence of side-effects between control and experimental treatments, with sample size used as a weighting factor. In addition, survival analysis was undertaken on those randomised studies with sufficiently reliable survival data.
How were differences between studies investigated?
Subgroup analysis was performed using non-parametric rank order statistical tests to assess whether estimated relative hazard rates were associated with 3 treatment protocols, i.e. induction (neoadjuvant) chemotherapy, induction plus maintenance chemotherapy, and concurrent chemotherapy with local definitive treatment.

Results of the review
Forty-two prospective RCTs with 5,079 patients were included and used to analyse the relative risk of side-effects, response rates and control rates for the different treatments. Of these, 25 studies were used in the meta-analysis for survival (3,839 patients).

Toxicity was significantly increased when chemotherapy was added to local definitive treatment, with a relative proportion of side-effects of 2.17 (95% confidence interval, CI: 1.84, 2.56, P<0.001). In contrast, initial response (2 months post-treatment) and local control (2 years post-treatment) rates increased significantly with chemotherapy and local treatment, as evident in the relative proportion of occurrence rates of 1.13 (95% CI: 1.04, 1.21, P=0.002) and 1.27 (95% CI: 1.15, 1.40, P<0.001), respectively.

The use of chemotherapy with local treatment significantly improved survival, as reflected in the relative hazard of dying of 0.89 (95% CI: 0.81 to 0.99, p<0.05) (all 25 studies). Similarly, there was a higher rate of survival with chemotherapy and local treatment, than local treatment alone, throughout the 5 years following treatment. The relative hazard of dying varied from 0.61 after 1 year to 0.95 after 5 years (11 studies).

Further analysis of the variation in relative hazard rates between the studies, ranging from 0.41 to 2.56, revealed significant differences between the 3 chemotherapy protocols. Specifically, concurrent chemotherapy had a mean relative hazard of 0.78 (95% CI: 0.67, 0.92, P<0.005), compared to induction chemotherapy at 0.95 (95% CI: 0.83, 1.10) and induction and maintenance chemotherapy at 1.02 (95% CI: 0.91, 1.13).

Authors’ conclusions
Addition of chemotherapy to local definitive treatment has significantly increased the morbidity of treatment, as well as the chance of initial tumour response and local control. A statistically-significant improvement in survival was found for the simultaneous use of chemotherapy and local definitive treatment.

CRD commentary
The review stresses the importance of applying a rigorous approach to systematic reviews in order to achieve a complete and unbiased synthesis of evidence, but important aspects of the review process are inadequately discussed. The specific sources, restriction criteria (dates, language and type of publication), and strategy used in the literature search are not outlined.

The criteria for the validity or quality of primary studies, the application of the criteria, and the methods for extracting data from the primary studies are not discussed. Description of the primary studies lacks appropriate detail.

The statistical methods for data analysis are discussed at length, with extensive delineation of the equations, but limited definition of the components. Presentation of the results from the review were relatively clear, although CIs would have been useful for the table of individual studies. The conclusions reached appear to be supported by the evidence presented.

Bibliographic details

PubMedID
Indexing Status
Subject indexing assigned by NLM

MeSH
Antineoplastic Agents /adverse effects /therapeutic use; Carcinoma, Squamous Cell /drug therapy /mortality; Chemotherapy, Adjuvant; Data Interpretation, Statistical; Head and Neck Neoplasms /drug therapy /mortality; Humans; Prospective Studies; Randomized Controlled Trials as Topic; Survival Rate

AccessionNumber
11996000591

Date bibliographic record published
31/01/1997

Date abstract record published
31/01/1997

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.