Standard chemotherapy is superior to high-dose chemotherapy with autologous stem cell transplantation on overall survival as the first-line therapy for patients with aggressive non-Hodgkin lymphoma: a meta-analysis


CRD summary
The authors concluded that high-dose chemotherapy was associated with a disadvantage in overall survival compared with standard chemotherapy in patients with aggressive non-Hodgkin lymphoma. The authors’ conclusion reflects the evidence presented and is likely to be reliable.

Authors’ objectives
To evaluate the effectiveness of high-dose chemotherapy compared with standard chemotherapy as a first-line treatment for patients with aggressive non-Hodgkin lymphoma.

Searching
MEDLINE, EMBASE, The Cochrane Library and Science Citation Index were searched to November 2008. The reference lists of included studies and major conference abstracts were searched to identify further studies.

Study selection
Eligible for inclusion were randomised controlled trials (RCTs) of high-dose chemotherapy compared with standard chemotherapy in patients with untreated aggressive non-Hodgkin lymphoma. Trials measured overall survival at three years. Trials had to have at least 20 patients per study arm; those that contained patients with predominant follicular or lymphoblastic lymphoma were excluded.

The included patients were aged between 15 and 61 years with intermediate, high-grade, aggressive large cell-type non-Hodgkin lymphoma. A variety of chemotherapy regimens were reported across intervention and control groups.

Two reviewers independently carried out the study selection.

Assessment of study quality
Study quality was assessed using a scale (maximum 10 points, higher scores indicated better quality) which included randomisation, allocation concealment, blinding, clarity of inclusion and exclusion criteria, similarity of baseline characteristics, clarity of treatment protocol, co-interventions, outcome definition, follow-up and use of intention-to-treat analysis.

Two reviewers independently carried out the quality assessment. Disagreements were resolved by consensus.

Data extraction
Data were extracted to enable the calculation of hazard ratios (HRs) for overall survival at three years, along with 95% confidence intervals (CI).

Two reviewers independently extracted the data. Disagreements were resolved by consensus. Authors were contacted for missing data where necessary.

Methods of synthesis
Hazard ratios were pooled in a random-effects meta-analysis. Statistical heterogeneity was assessed using the Q statistic (p greater than 0.10 indicated no heterogeneity). Sensitivity analyses were conducted to explore the impact of including only trials with the following features: more than 100 patients; high quality; use of intention-to-treat analysis; randomisation before the start of treatment; drop-out rate in high-dose chemotherapy arm less than 30%; and where high-dose chemotherapy was given to the control group as a salvage treatment. Publication bias was assessed using a funnel plot and confirmed with Egger's test.

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Results of the review
Fourteen RCTs (2,412 patients) were included in the meta-analysis. Quality scores ranged from 5 to 8 (median 6) which indicated satisfactory methodological quality (full details were reported).

At three years, overall survival was significantly decreased following high-dose chemotherapy compared to standard chemotherapy (HR 1.20, 95% CI 1.05 to 1.37; 14 RCTs; no evidence of heterogeneity).

Sensitivity analyses did not affect the main findings. There was no evidence of publication bias.

Authors' conclusions
High-dose chemotherapy was associated with a disadvantage in overall survival compared with standard chemotherapy in patients with aggressive non-Hodgkin lymphoma.

CRD commentary
The review question was clear and inclusion criteria were potentially reproducible. Relevant data sources were accessed and attempts were made to minimise publication bias. Publication bias was assessed and found not to be a threat. The review process was conducted with sufficient effort to minimise error and bias, and the results of the quality assessment were detailed enough to verify the authors’ judgement. Study details were presented.

Clinical heterogeneity was apparent across intervention and control groups, but there was no statistical heterogeneity so the chosen method of synthesis seemed appropriate. The authors’ conclusion reflected the evidence presented and was likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that this review supports the use of standard chemotherapy as the first-line treatment in patients with aggressive non-Hodgkin lymphoma.

Research: The authors stated further randomised controlled trials, or a meta-analysis of individual patient data were needed to determine definitive treatment recommendations.

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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.