CNOP (mitoxantrone) chemotherapy is inferior to CHOP (doxorubicin) in the treatment of patients with aggressive non-Hodgkin lymphoma (meta-analysis)

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CRD summary
This review concluded that doxorubicin (CHOP) chemotherapy was more effective than mitoxantrone (CNOP) at equitoxic (myelosuppression) doses with regard to complete remission in patients with aggressive non-Hodgkin lymphoma. CHOP was associated with greater risk of adverse effects. Given several limitations, including the small number of included studies and the potential for reporting bias, the authors' conclusions may not be reliable.

Authors' objectives
To compare the safety and efficacy of mitoxantrone (CNOP chemotherapy regimen) with doxorubicin (CHOP chemotherapy regimen) in patients with aggressive non-Hodgkin lymphoma (NHL).

Searching
MEDLINE and CANCERLIT were searched for articles from 1980 onwards. Search terms were reported. Conference proceedings of the American Society of Clinical Oncology, American Society of Hematology (1980) and the European Hematology Association (1994) were handsearched. Experts in the field and pharmaceutical companies were also contacted for unpublished and ongoing data.

Study selection
Eligible studies were randomised controlled trials (RCTs) comparing mitoxantrone (10 mg/m$^2$ to 12 mg/m$^2$) with doxorubicin (50 mg/m$^2$) in the CNOP or CHOP chemotherapy regimens, including cycles repeated every three to four weeks for a total of six to eight courses in responding patients over the age of 16 years with advanced (stages II to IV) non-Hodgkin lymphoma of intermediate- or high-grade malignancy. Eligible studies were required to report tumour response (complete remission defined as complete disappearance of all disease manifestations for at least four weeks) and overall survival as the primary outcomes, and adverse effects as secondary outcomes.

Where stated, most included patients were aged 60 years or over, with median ages ranging between 47 and 71 years. Duration of follow-up ranged from two to five years.

The authors did not state how many reviewers selected studies for relevance.

Assessment of study quality
The authors did not state that validity was assessed.

Data extraction
Complete remission and overall survival rates were extracted and odds ratios were calculated with their 95% confidence intervals. The authors did not state how many reviewers extracted the data.

Methods of synthesis
Odds ratios were pooled using a fixed-effect model for complete remission. A random-effects model was used to combine overall survival due to significant heterogeneity. Two studies had overlapping patients, thus meta-analysis was performed after excluding in turn each of the studies with overlapping patients.

Results of the review
Five RCTs (n=1,005) were included in the review. There was some overlap between two studies. Excluding the smaller of the overlapping studies gave n=916. Sample sizes ranged between 15 and 205 patients.

Significantly higher complete remission rates were reported with CHOP compared with CNOP for the two meta-analysis that excluded each overlapping study in turn, CHOP odds ratio 0.55 (95% confidence interval: 0.42, 0.72,
p=0.000005) and CNOP odds ratio 0.50 (95% confidence interval: 0.37, 0.68, p=0.000005). There was no significant difference between CNOP and CHOP for overall survival.

No formal testing of side effects could be undertaken, but both regimens were equally myelosuppressive. The incidence of alopecia (four studies) and gastrointestinal toxicities (three studies) were reported to be more frequent in CHOP patients compared to CNOP patients. Three of four studies reported no difference in cardiotoxicity; one study reported significantly more patients with a non-symptomatic reduction in left ventricular ejection fraction in the CHOP compared to CNOP group (CHOP 40 per cent and CNOP seven per cent, p<0.039). Values for results data were generally not reported in the paper.

Authors’ conclusions
CHOP chemotherapy was more effective than CNOP at equitoxic (myelosuppression) doses with regard to complete remission, and non-significantly effective with regard to overall survival. CHOP was associated with greater a risk of alopecia and gastrointestinal toxicity.

CRD commentary
The review question and supporting inclusion criteria were clear. The literature search was adequate, using two electronic databases and other appropriate sources, including a search for unpublished data, thus limiting the possibility that potentially relevant papers were missed. Validity was not assessed, so the reliability of the evidence could not be assessed. The review process was not clearly described for each stage of the review, thus reviewer error and bias could not be ruled out. Appropriate methods were used to synthesise the data. The authors acknowledged that the included studies were methodologically heterogeneous. Given the small number of studies included, the small sample sizes and the potential for bias due to limited quality of review reporting, the authors’ conclusions may not be reliable.

Implications of the review for practice and research
The authors did not state any implications for practice or research.

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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.