Non-Hodgkin's lymphoma: meta-analyses of the effects of corticosteroids and non-steroidal anti-inflammatories

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CRD summary
This review concluded that there is little evidence to support a link between the use of corticosteroids or non-steroidal anti-inflammatory drugs and the risk of developing non-Hodgkin's lymphoma. However, the reliability of the review's findings is unclear given the poor reporting of review methods and the potential methodological weaknesses of the study data.

Authors' objectives
To evaluate the effects of corticosteroids and non-steroidal anti-inflammatory drugs or agents (NSAIDs) on the risk of developing non-Hodgkin's lymphoma (NHL).

Searching
MEDLINE and life science journals (unspecified) were searched using the National Center for Biotechnology Information search and retrieval system; search terms, but not dates, were reported.
In addition, the authors searched conference abstracts presented between 2002 and 2006 at the annual meetings of the American Society of Clinical Oncologists, the American Society of Hematology, the American Rheumatology Association and the European League Against Rheumatism. The reference lists of retrieved articles and reviews were also checked for additional studies.

Study selection
Study designs of evaluations included in the review
Case-control and cohort studies were eligible for inclusion in the review.

Specific interventions included in the review
Studies comparing the use of corticosteroids and/or NSAIDs with unexposed controls were eligible for inclusion.

Participants included in the review
Studies comparing individuals with NHL (cases) with non-NHL controls were eligible for inclusion. The majority of the studies recruited participants from the general population; one recruited rheumatoid arthritis patients and another postmenopausal women. One study excluded participants who were infected with the human immunodeficiency virus (HIV). The majority of the controls were selected from health service or hospital registries, while cases were mainly selected from tumour registries. Three studies included women only; the proportion of women included in the remaining studies varied between 43% and 55%. The mean age of the participants varied from 52 to 67 years.

Outcomes assessed in the review
Studies reporting the incidence of NHL and the incidence of exposure to corticosteroids and/or NSAIDs were eligible for inclusion. The majority of the included studies assessed exposure to corticosteroids or NSAIDs through questionnaires.

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

Assessment of study quality
The quality of the studies was assessed in terms of case ascertainment and data collection methods. The authors did not state how the validity assessment was performed.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data
extraction. The incidence of exposure versus no exposure to corticosteroids and/or NSAIDs was extracted. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each study.

Methods of synthesis
How were the studies combined?
The studies were combined using a random-effects model (DerSimonian and Laird method) to calculate pooled unadjusted and adjusted ORs with 95% CIs. Funnel plots were used to investigate the risk of publication bias.

How were differences between studies investigated?
Chi-squared tests were used to statistically assess the level of homogeneity between the studies. Sensitivity analyses were also performed to investigate the effects of study size and date of publication.

Results of the review
Eight case-control studies and one cohort study were included in the review. In total, 15,778 participants (6,897 cases and 8,881 controls) were included in the analysis of corticosteroids and 40,501 (5,794 cases and 34,707 controls) in the analysis of NSAIDs. Five studies were based in the USA, two in Sweden, one in Denmark and one in the Netherlands.

There was no evidence of an increased risk of developing NHL with either corticosteroid use (OR 1.09, 95% CI: 0.96, 1.24) or NSAID use (OR 0.93, 95% CI: 0.74, 1.14). The authors stated that the quality of the included studies was uniformly high and that there was no evidence of statistical heterogeneity or publication bias. Sensitivity analyses did not show any significant effect of study size or publication date (results not presented).

Authors' conclusions
There is little evidence to support a link between the use of corticosteroids or NSAIDs with an increased risk of developing NHL.

CRD commentary
This review answered a clear research question. The authors searched for studies in a number of databases, although the search dates were not reported and it was unclear exactly what journals were included in the search. Publication bias was assessed, but the reliability of this assessment is unclear given the small number of studies included in the review; however, some attempts were made to retrieve unpublished material through the searching of conference abstracts. Lack of detail about the review methodology, including details of the validity assessment and whether data were extracted in duplicate, make it difficult to assess and confirm the reliability of the authors' findings.

The review findings were based on data from a small number of case-control studies, which are likely to be affected by recall bias. The analysis was also limited by a lack of detail about the original studies, e.g. the drugs involved and which confounding factors had been included in the adjusted analyses. The authors acknowledged that the level of drug exposure was often not reported, thus the results were restricted to exposure versus no exposure; this makes it difficult to assess dose-related effects.

Statistical heterogeneity was considered in the analysis, but it is unclear how clinically similar the studies were with respect to the pooling of data. Finally, the generalisability of the findings to other populations may be limited since the majority of the participants were older women living in the USA.

Overall, the reliability of the review's findings is unclear given the poor reporting of review methods and the potential methodological weaknesses of the study data.

Implications of the review for practice and research
Practice: The authors stated that exposure to corticosteroids and NSAIDs does not appear to increase the risk of developing NHL.

Research: The authors did not state any implications for 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.