Safety of rapid rituximab infusion in adult cancer patients: a systematic review
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CRD summary
This review found that rapid rituximab infusion, over 90 minutes, appeared to be safe for patients with non-Hodgkin lymphoma. The conclusions reflect the evidence presented, but given the small number of studies and patients, the use of the word ‘safe’ appears premature.

Authors’ objectives
To review the evidence on the safety of rapid rituximab infusion for adults with non-Hodgkin lymphoma or chronic lymphocytic leukaemia.

Searching
Eight bibliographic databases, including PubMed, Cochrane Central Register of Controlled Trials (CENTRAL) and CINAHL were searched, for articles from 1997, without language restrictions. The search date was not reported. Some search terms were reported. A number of other sources (listed) were searched for grey literature and unpublished studies.

Study selection
The authors stated that both experimental and non-experimental studies were eligible for inclusion. Participants had to be aged 18 years or older, have a diagnosis of non-Hodgkin lymphoma or chronic lymphocytic leukaemia, and have taken rituximab before. Studies had to compare rapid rituximab infusion (completed in ≤120 minutes) with normal infusion (>120 minutes). Studies with no comparator group were eligible. The primary outcome was the frequency and severity of acute adverse reactions.

The included studies assessed different regimens for rituximab infusion over 60 or 90 minutes. Most patients (96%) had non-Hodgkin lymphoma. Most studies used the National Cancer Institute's Common Toxicity Criteria, or Common Terminology Criteria for Adverse Events, to measure acute adverse reactions.

It appeared that two reviewers selected studies for inclusion.

Assessment of study quality
Two reviewers independently assessed study quality using standardised checklists from the Joanna Briggs Institute.

Data extraction
The rates of acute adverse reactions were extracted using standardised forms. The authors did not state how many reviewers were involved.

Methods of synthesis
Where possible, the rates of acute adverse reactions were pooled using a random-effects model. Heterogeneity was assessed using Cochran's Q and $I^2$. Publication bias was assessed using funnel plots.

Results of the review
Thirteen case series, involving 753 patients, were included.

For patients with non-Hodgkin lymphoma undergoing 90 minute infusion, the pooled rate of acute adverse reactions was 2.66% (95% CI 1.1 to 4.86; nine studies; $I^2=40.8\%$). Most adverse reactions were classified as grade one and no grade three or four reactions were reported.

Only two studies included patients with chronic lymphocytic leukaemia. They assessed 15 patients and it appeared that two developed grade one adverse reactions.

There was no evidence of publication bias.
Authors' conclusions
Rapid rituximab infusion, over 90 minutes, appeared to be safe for patients with non-Hodgkin lymphoma. There was insufficient evidence to support rapid infusion for patients with chronic lymphocytic leukaemia.

CRD commentary
The review question and inclusion criteria were generally clear; the specific study designs for inclusion were not clear. The search covered a range of sources of published and unpublished or informally published data. Methods to minimise error and bias in the review process were variably reported. Study quality was assessed, but few results were reported. All the included studies were case series and hence at a high risk of bias.

A pooled rate of adverse reactions was calculated using a standard method, and was broadly in line with the other evidence presented. The authors' conclusions reflect the evidence presented, but given the small number of studies and patients, the use of the word 'safe' appears premature.

It should be borne in mind that new evidence may have become available since the completion of this review (published in 2011; search date not reported).

Implications of the review for practice and research
Practice: The authors stated that 90-minute rapid infusion was recommended for patients with non-Hodgkin lymphoma, for the second and subsequent infusions.

Research: The authors recommended research on rapid infusion for patients with chronic lymphocytic leukaemia, and to establish the disease stages at which rapid infusion might be appropriate.

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