Rituximab in the treatment of acquired hemophilia

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CRD summary
This review of case reports and case series concluded that rituximab appears to be an effective option for patients with acquired haemophilia for whom established therapies have failed. In view of the limitations of the evidence and methodological weaknesses of the review, the conclusions should be treated with caution.

Authors' objectives
To evaluate the use of rituximab for the treatment of acquired haemophilia.

Searching
MEDLINE (1966 to January 2006) was searched for articles written in English; the search terms included 'rituximab', 'acquired hemophilia' and 'inhibitors'. The reference lists of identified articles were also checked.

Study selection
Study designs of evaluations included in the review
No inclusion criteria for the study design were specified.

Specific interventions included in the review
Studies of rituximab were eligible for the review. In most of the included studies rituximab was given at a weekly dose of 375 mg/m²; most of the participants received 1 to 4 doses.

Participants included in the review
Eligible participants were patients with acquired haemophilia. The patients in the included studies had inhibitors to factors VIII, V or XIII, and the duration of acquired haemophilia ranged from 22 days to 10 years. All participants had shown inadequate response to a range of other therapies.

Outcomes assessed in the review
No inclusion criteria for the outcomes were specified. The outcomes most commonly evaluated in the included studies were resolution of bleeding and normalisation of clotting factor levels.

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

Assessment of study quality
The author did not state that they assessed validity.

Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data on disease characteristics and outcomes were extracted.

Methods of synthesis
How were the studies combined?
The studies were discussed in a narrative synthesis.

How were differences between studies investigated?
Some differences between the studies were described in the text and tables.

Results of the review
Fifteen case reports and case series with 38 participants were included.

In 13 studies (36 participants) of patients with acquired inhibitors to factor VIII, rituximab was effective in controlling bleeding and normalising haemostasis and factor VIII activity in all but 2 patients.

In a patient with factor V inhibitors after liver transplantation, the administration of 10 doses of rituximab resulted in normalisation of factor V activity and haemostasis.

A patient with factor XIII inhibitors given 4 doses of rituximab showed a reduction in inhibitors and a return of factor XIII activity, but an increase in inhibitor titre and a decrease in factor XIII activity occurred 3 weeks after remission.

Authors' conclusions
Despite limited data, rituximab appears to be an effective treatment for patients with acquired haemophilia in whom established therapies have failed.

CRD commentary
This review addressed a clear question. No inclusion criteria were specified for the outcomes or study designs, but this was unlikely to have affected the results given the small number of studies found. The search was limited and it is possible that some relevant studies could have been missed. Only English language studies were included and unpublished studies were not sought, thus raising the possibility of language and publication bias. Review methods were not reported, so it is difficult to assess the risk of errors and bias during the review process. Study quality was not assessed, but the author acknowledged the limitations of the available evidence. A narrative synthesis was appropriate given the small number of studies and participants included. In view of the limitations of the evidence and methodological weaknesses of the review, the conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The author did not state any implications for practice.

Research: The author stated that, in the absence of controlled trials, a number of questions remain about the optimal dosing, duration, efficacy and safety of rituximab in comparison with other established therapies for acquired haemophilia.

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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.