A review of anti-D treatment of childhood idiopathic thrombocytopenic purpura

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CRD summary
The authors concluded that a single dose of 50 μg/kg IV Rh(D) immunoglobulin G (anti-D) was effective in raising the platelet count to at least 20 x10^9/L in approximately 70% of children within 3 days, with fewer side-effects than intravenous immunoglobulin G. Given the lack of a formal validity assessment and the potential for error and bias in the review, the conclusions should be treated with caution.

Authors' objectives
To review the literature on the use of Rh(D) immunoglobulin G (anti-D) in the treatment of childhood idiopathic thrombocytopenic purpura (ITP).

Searching
PubMed was searched from inception to 6th February 2006; the search terms were reported. The reference lists of identified papers were reviewed.

Study selection
Studies of anti-D as treatment for childhood ITP were eligible for inclusion. The majority of included studies were of intravenous (IV) anti-D. Other methods of administration were infusion of in vitro opsonised erythrocytes, intramuscular injection and subcutaneous injection. The dosage ranged from 10 to 100 μg/kg. Two randomised controlled studies that used oral prednisolone or IV immunoglobulin G (IgG) as control treatments were included. Studies of children with ITP were eligible for inclusion. In the included studies there were similar numbers of children with acute ITP and chronic ITP overall, however, some trials only studied one of these groups. A small number of included children had human immunodeficiency virus (HIV)-positive ITP or were splenectomised. Some studies also included children who did not have ITP and who received other treatments, and some also included adults. Where reported, the median platelet (PLT) count at time of inclusion ranged from ≤ 13 x10^9/L to ≤50 x10^9/L. Inclusion criteria were not defined in terms of the outcomes. The outcomes reported were the median PLT count on a specific day, the number of days to reach a certain PLT count, or the number of children reaching a predefined end point such as 'no bleeding symptoms'. The inclusion criteria for study design were not clearly specified. The included studies comprised randomised controlled trials (RCTs) and studies of unspecified design.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

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

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The results were reported in a narrative synthesis. Further information was apparent from the tables. The results were discussed separately for the different forms of administration of anti-D. The results of 2 RCTs were highlighted.

Results of the review
Twenty studies (n=719) were included in the review; 422 children were treated with anti-D. Two studies were RCTs (56 children treated with anti-D). There was insufficient information to ascertain the designs of the other trials.

There were 14 studies of IV anti-D (367 children treated with anti-D). In general, 70% of Rhesus-positive non-splenectomised children with acute or chronic ITP showed a PLT count increase to ≥20 x10^9/L within 3 days after IV
anti-D treatment. In at least 60% of children the PLT count increased to ≥50 x10^9/L within 3 to 10 days. One RCT found that IV anti-D at a dosage of 25 μg/kg on 2 consecutive days resulted in a slower increase in PLT count compared with IV IgG and prednisolone (no p-values reported). Another RCT found that treatment with IV IgG resulted in a significantly higher PLT count than anti-D at 3 and 7 days post-treatment in children with chronic ITP (no p-values reported).

Adverse effects of nausea, headache, fever, chills and vomiting were reported in 3 to 15% of patients in 5 studies. One RCT found a higher incidence of side-effects in children treated with IV IgG (no p-values). Anti-D mediated haemolysis with haemoglobin decrease from 0.5 g/dL was observed in most patients in 7 studies (no statistical values provided). In one trial where anti-D was compared with IV IgG, similar levels of haemoglobin decrease were observed with IV IgG and anti-D treatments. A small number of children experienced renal failure and haemolysis. No HIV-positive thrombocytopenic children experienced excess toxicity (2 studies).

In terms of other routes of administration of anti-D, in the 2 studies that looked at in vitro opsonised erythrocytes (19 children treated with anti-D), the researchers found a similar level of efficacy in raising PLT count to that found in IV studies. Intramuscular anti-D was also found to be effective (3 studies, 34 children treated with anti-D). One study used subcutaneous administration of anti-D in 2 children and found it to be effective in raising the PLT count. No statistical information or p-values were reported for these interventions.

Authors' conclusions
A single administration of 50 μg/kg IV anti-D increased the PLT count to at least 20 x10^9/L in approximately 70% of children within 3 days. IV anti-D appears safe in children with classic ITP and shows fewer side-effects than IV IgG. However, haemolysis is a concern with IV anti-D.

CRD commentary
The research question was clearly defined for the population and intervention, but not for study design. The outcomes did not appear to be defined a priori and in some studies the end point was defined as ‘PLT increase’, which makes it difficult to evaluate the clinical impact of the intervention. Only one database was searched and it is unclear whether any attempts were made to minimise publication and language bias, therefore important data might have been missed. A formal validity assessment was not carried out and there was insufficient information on study design to determine the quality of the included studies; the reliability of the results is therefore unclear. One limitation evident from the review was the small sample size of many included studies. Given the clinical heterogeneity in the included studies, the decision to use a narrative synthesis was appropriate. However, many studies also included adults or children who did not have ITP, some of whom received other treatments. There was insufficient information about the data extraction process to determine how the data for children with ITP receiving anti-D were isolated, therefore error and bias cannot be ruled out. Furthermore, p-values were not reported where appropriate, which makes it difficult to assess the significance of the results. The authors' conclusions follow from the study results. However, inadequate reporting renders it difficult to assess the quality of the review process and, therefore, limits the reliability of the authors' conclusions.

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

Research: The authors stated that further research into subcutaneous administration of anti-D is needed.

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