A review of randomized controlled trials using therapeutic apheresis

Shehata N, Kourouakis C, Kelton J G

Authors' objectives
To assess the evidence for plasma exchange (apheresis), the optimum schedules for apheresis and the replacement solutions used, based on randomised controlled trials (RCTs).

Searching
MEDLINE (from 1976 to 1999) and EMBASE (from 1980 to 1999) were searched for publications in the English language; the search terms were stated. Reference lists were also checked for additional studies. Abstracts were excluded. The search was repeated in August 2001.

Study selection
Study designs of evaluations included in the review
The inclusion criteria specified RCTs as the study designs to be included.

Specific interventions included in the review
An apheresis technique was the only inclusion criterion stated for the intervention.

Participants included in the review
The inclusion criteria specified adult patients as the participants.

Outcomes assessed in the review
The inclusion criteria specified that studies report a clinical end point.

How were decisions on the relevance of primary studies made?
Two authors independently selected the papers for the review. The kappa statistic was used to measure agreement between the two reviewers.

Assessment of study quality
The authors used the 5-point assessment scale of Jadad et al. for assessing validity. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

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
How were the studies combined?
The studies were grouped in narrative analyses in the following categories: apheresis procedures in patients with neurologic disorders, dermatologic disorders, rheumatologic disorders, haematologic disorders, renal disorders, cardiovascular disorders and endocrine disorders.

How were differences between studies investigated?
The authors did not address any of the differences between the studies.

Results of the review
A total of 85 RCTs were included in the review; the number of participants was not reported.

The kappa statistic for agreement between reviewers for study selection was 0.75.

Neurologic disorders: 6 studies of 1,544 participants with Guillain-Barre syndrome found that apheresis was effective in decreasing the duration of disability and in decreasing the degree of disability in patients with this syndrome. The data supported a schedule of 3 to 5 exchanges over a period of 7 to 14 days. In 5 studies (n=180) there were no clear results for the use of apheresis in patients with myasthenia gravis. In 3 poor-quality studies (n=66), the results were that exchanges may be performed 1 or 2 times per week using albumin as the replacement fluid in apheresis, in patients with chronic inflammatory demyelinating polyneuropathy. In 6 studies (n=447) there were no clear benefits in the use of apheresis in patients with multiple sclerosis.

Dermatologic disorders: in 3 studies (n=169) therapeutic apheresis was not found to be effective in patients with pemphigus or bullous pemphigoid.

Rheumatologic disorders: in 8 studies (n=192), six of rheumatoid arthritis and two of progressive systemic sclerosis (scleroderma), apheresis was not as effective as adjunctive therapy in patients with rheumatoid arthritis. In addition, there were no benefits for the use of apheresis in patients with progressive systemic sclerosis. In 2 studies (n=140) the addition of apheresis was not shown to benefit disease activity, the relapse rate, or the number of deaths in patients with polyarteritis nodosa and Churg-Strauss syndrome. In 7 studies (n=268) therapeutic apheresis has not been found to have an additive benefit in systemic lupus erythematosus patients with active disease or renal disease.

Haematologic disorders: in 2 studies (n=129) it was found that therapeutic apheresis should be used as soon as possible following the diagnosis of patients with thrombotic thrombocytopenic purpura. The appropriate number of exchanges had not been assessed in RCTs. Daily exchanges were recommended and should be continued until neurologic symptoms disappear and there is normalisation of the platelet count and serum lactate dehydrogenase. In 4 studies (n=138) of patients with monoclonal gammopathy of undetermined significance (2 studies) or multiple myeloma (2 studies), the results were uncertain in the former group and have not been adequately assessed with RCTs in the latter group.

Renal disorders: in 7 studies (n=205) of patients with rapidly progressive glomerulonephritis, therapeutic apheresis had a small benefit of exchange. Further trials are needed to clearly define the role of apheresis in this group of patients. In the treatment of renal allograft rejection, 4 studies (n=146) found no difference in graft survival after apheresis while one trial also found that a greater number of these patients required haemodialysis compared with those in a control group.

Cardiovascular surgery: in 9 studies (n=169) overall, therapeutic apheresis with platelets significantly reduced the likelihood of exposure to at least one unit of allogeneic red cells, the mean number of allogeneic red cells transfused, and the volume of blood loss in the first 24 hours of the peri-operative period.

Endocrine disorders (familial hypercholesterolaemia): in 2 studies (n=81) there were benefits to both sets of patients, in terms of improvements on exercise stress tests in one study and a decrease in triglycerides and lipoprotein in a second group.

In trials of patients with miscellaneous diseases (sudden hearing loss, sepsis syndrome, ascites, Crohn's disease, polymyositis or dermatomyositis, burn care, schizophrenia and Raynaud's) there were insufficient data to make a determination of effectiveness for these indications.

Authors' conclusions
The authors stated that apheresis has become a very common therapeutic modality but there are only a few well-established indications for its use. This review clearly showed that better-designed RCTs are needed to further clarify the role of apheresis for the treatment of many diseases.

CRD commentary
The authors clearly stated the review question but the inclusion and exclusion criteria were quite vague. The review covered a wide range of interventions using the process of apheresis. The searches were fairly good and it appears unlikely that additional relevant studies have been missed. The process of the review, including the study selection, validity assessment and data extraction processes, appear to have been clearly reported and the authors performed a validity assessment of the included studies.

The data were tabulated in detail. Statistical analyses were not performed due to the considerable differences between the measurements used for the outcomes. A narrative summary, grouped on type of intervention and incorporating a discussion of the studies included for that intervention, was made and this presents a good overall picture of the quality and scope of the data available. Additional sensitivity analyses were not performed, nor were any statistical checks for heterogeneity. Overall, the authors’ conclusions appear to have been appropriate, even though they found there was a lack of evidence in this research area.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that better-designed, RCTs are needed to further clarify the role of apheresis in the treatment of many diseases.

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