Leukocytapheresis in Inflammatory Bowel Disease (Primarily Ulcerative Colitis)

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Summary and Conclusions

SBU's appraisal of the evidence

Ulcerative colitis and Crohn's disease are the most common chronic inflammatory bowel diseases. Leukocytapheresis is a method aimed at ameliorating symptoms in patients with moderately severe to severe inflammatory bowel disease.

- Few studies of sufficient quality address leukocytapheresis in the treatment of inflammatory bowel disease. No randomized studies were found on Crohn's disease. Hence, well-designed studies of sufficient size are urgently needed to determine the effectiveness of leukocytapheresis in treating inflammatory bowel disease.

- Contradictory scientific evidence* makes it impossible to establish whether the treatment results of leukocytapheresis are superior to conventional pharmacotherapy with corticosteroids or sham apheresis in treating moderately severe to severe ulcerative colitis. Studies that compare apheresis with steroid treatment suggest that the treatments yield comparable results.

- Compared to steroid treatment, apheresis has fewer and milder adverse effects during the treatment period. Knowledge is lacking concerning the potential adverse effects of leukocytapheresis in the long term, but it is well documented that long-term treatment with corticosteroids carries a substantial risk for adverse effects.

- Apheresis treatment is more expensive than conventional pharmacotherapy[1]. The scientific evidence is insufficient* to determine the cost-effectiveness of the method.

* *Criteria for Evidence Grading SBU's Conclusions, see page 2.*

1 *Does not include treatment with so-called biological/immunomodulating drugs (eg, infliximab).*

Technology and target group

Approximately 1% of the Swedish population has ulcerative colitis or Crohn's disease. In ulcerative colitis the rectum and often part or all of the colon are inflamed. Common symptoms include blood in feces, diarrhea, and urgency and increased frequency of bowel movements. In Crohn's disease, inflammation is usually localized in the small intestine and colon, but it can affect the entire gastrointestinal tract. Crohn's disease in the colon causes symptoms similar to ulcerative colitis, but substantial weight loss is more usual. A common feature of both diseases is that they often present as recurring episodes of acute attacks followed by periods that are relatively or even completely symptom-free.

Conventional treatment of acute episodes aims to make patients symptom free and usually includes cortisone medication (corticosteroids). This method, however, often involves substantial adverse effects. Surgical treatment is an option and involves removal of the inflamed parts of the intestine, mainly in severe cases. In Crohn's disease, surgery seldom yields a permanent cure, and the disease often reappears in other parts of the gastrointestinal tract.

Leukocytapheresis aims to reduce the number of white blood cells (leukocytes) to dampen the inflammatory reaction. Different apheresis techniques remove different types of white blood cells. The two most common techniques involve drawing blood via a venous catheter, pumping it through a cylinder (column) containing cellulose acetate beads (Adacolumn) or a filter of nonwoven polyester fibers (Cellsorba), thereafter returning it to the circulatory system. As blood passes through the system, leukocytes adhere to the beads or filter. Treatment takes one hour and is usually repeated once per week for 5 weeks. The biochemical mechanisms concerning how leukocytapheresis affects the course of disease remain largely unknown.

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Leukocytapheresis involves mainly adult patients. The aim of treatment is to ameliorate symptoms in acute, severe attacks of the disease, or in moderately severe to severe chronic, active disease where satisfactory effects have not been achieved from corticosteroids or other immunosuppressive therapy. The target group also includes patients who have developed steroid dependence, ie, disease recurs if steroid dosage is reduced. The number of patients who could be candidates for treatment is difficult to estimate.

Primary questions

- Is leukocytapheresis an effective complement to, or replacement for, treatment with corticosteroids to relieve symptoms from acute episodes of ulcerative colitis and Crohn's disease? Could leukocytapheresis be an option when immunosuppressive treatment has not had effects, or has been discontinued due to adverse effects?

- What does treatment cost? Is it cost-effective?

Patient benefit

The assessment includes 7 randomized controlled trials that compared leukocytapheresis with pharmacotherapy or sham apheresis. One of these trials was judged to be of high quality, and the others were of medium quality. The trials included only patients with ulcerative colitis. Five of the trials used Adacolumn and two used Cellsorba.

Results were contradictory as regards the endpoints of clinical remission (symptom free), clinical improvement, and endoscopic improvement. Hence, it cannot be established with certainty whether leukocytapheresis in moderately severe or severe ulcerative colitis leads to a better treatment result than conventional pharmacotherapy with corticosteroids or sham apheresis. Studies that compared leukocytapheresis with steroid treatment alone reported treatment effects of similar size in both groups. The only study judged to be of high quality compared leukocytapheresis with sham treatment, but showed no advantage for leukocytapheresis.

Treatment of acute episodes always aims to help patients become completely free from symptoms (achieve clinical remission) with as few adverse effects as possible. To date, the adverse effects reported to be associated with leukocytapheresis, eg, headache, nausea, and fatigue, are generally mild and transitory.

The included studies differ as regards, eg, the drugs used and the severity of disease at the outset of the study. Furthermore, the studies included two methods (Adacolumn and Cellsorba), and different evaluation systems were used to assess treatment effects. This affects the comparability of the studies and raises some uncertainty about the overall assessment. Given these disparities, the prerequisites do not exist to conduct a meta-analysis of the studies' results. However, most of the studies included in the assessment suggest that treatment with leukocytapheresis yields a result comparable to pharmacotherapy, but with fewer and milder side effects. Knowledge is lacking concerning the possible adverse effects of apheresis treatment in the long term.

Considering the current level of knowledge, it is essential to conduct well-designed and sufficiently large studies to establish the effectiveness of the method.

Economic aspects

The average cost per patient and round of leukocytapheresis treatment, using Adacolumn, can be estimated at approximately 100 000 Swedish kronor (SEK). In 2007, approximately 1250 treatments were provided for 180 patients. Using Cellsorba, the corresponding cost would be approximately SEK 80 000. To date, however, Cellsorba has been used primarily in a research context. Scientific evidence is insufficient to assess the method's cost-effectiveness.

Criteria for Evidence Grading SBU's Conclusions
Evidence Grade 1 – Strong Scientific Evidence. The conclusion is corroborated by at least two independent studies with high quality, or a good systematic overview.
Evidence Grade 2 – Moderately Strong Scientific Evidence. The conclusion is corroborated by one study with high quality, and at least two studies with medium quality.
Evidence Grade 3 – Limited Scientific Evidence. The conclusion is corroborated by at least two studies with medium quality.
Insufficient Scientific Evidence – No conclusions can be drawn when there are not any studies that meet the criteria for quality.
Contradictory Scientific Evidence – No conclusions can be drawn when there are studies with the same quality whose findings contradict each other.

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PO Box 5650, SE-114 86 Stockholm, Sweden • alert@sbu.se

This summary is based on a report prepared by SBU in collaboration with **Clas Göran Axelsson**, MD, PhD, Örebro University Hospital, Örebro and **Gunnar Järnerot**, MD, Professor Emeritus, Örebro University Hospital, Örebro. It has been reviewed by **Åke Danielsson**, MD, Professor, Umeå University/Norrland's University Hospital, Umeå and **Stefan Lindgren**, MD, Professor, Malmö University Hospital, Malmö. Project manager: **Johan Wallin**, SBU, wallin@sbu.se.

The complete report is available in Swedish.