Erythroctapheresis, a treatment modality in hereditary hemochromatosis

Citation for published version (APA):

Document status and date:
Published: 01/01/2016

Document Version:
Publisher's PDF, also known as Version of record

Please check the document version of this publication:
• A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

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Hereditary hemochromatosis (HH) is the most common autosomal recessive disorder in the population of north European origin. The disease is characterized by increased iron absorption, leading to a progressive iron accumulation in tissues and organs with impairment of their function, especially of the liver, heart, pancreas, joints, skin and gonads as a result. The treatment, consisting of two phases (depletion and maintenance), is based on the removal of excess body iron. Start of treatment in early phase of the disease increases survival and decreases morbidity of patients. It is important to realize that life expectancy of HH patients on therapy equals that of the non-HH population but only when the disorder has been diagnosed and treated before the onset of cirrhosis and diabetes.

Despite many scientific discoveries and breakthroughs in the area of iron metabolism, treatment has remained the same for many decades. Phlebotomy is still the cornerstone in the treatment. More recently erythrocytapheresis, a technique using apheresis equipment, has become an attractive alternative. With erythrocytapheresis selectively only red blood cells (RBC’s) are removed while valuable blood components such as plasma proteins, clotting factors, platelets, are returned to the patient. In general two different approaches are applied: first, a personalized approach based on individually adjusted volume of removed RBC’s, and an approach removing a standard volume of RBC’s.

In this thesis we have systematically evaluated whether a personalized approach with erythrocytapheresis has an added value in the treatment of HH.

It was shown that personalized erythrocytapheresis leads to a significant reduction in the number of treatment procedures as well as in treatment duration in the depletion phase of treatment. Based on these results we have provided evidence for this method as treatment of choice. Indeed, our data have contributed to the advice of American Society For Apheresis (ASFA) to employ this method as a first line treatment for all HH patients.

Additionally, we have shown a significant reduction in number of treatment procedures and significant extension of inter-treatment interval using erythrocytapheresis in the maintenance phase of treatment.

Based on the data we have collected, a position paper and guide for the optimal treatment regimen for various groups of patients with HH has been written. In this guide we propose the use of erythrocytapheresis as a preferred treatment modality during both the depletion and maintenance phase of treatment.

While the scientific evidence has been generated, the next phase of implementation of erythrocytapheresis into routine care for HH patients poses several obstacles. The most important issue is related to the costs of erythrocytapheresis in comparison to phlebotomy. Our randomized trial has shown that the use of erythrocytapheresis in the depletion phase of treatment is cost effective. This is based on costs reduction resulting from a considerable decrease in the number of treatments as well as a
reduction in indirect costs related to the lower number of treatments resulting in lower travel costs and costs resulting from work absenteeism.

HH is a chronic disease and therefore treatment compliance is a highly important factor. Patient acceptance and patient preference are crucial factors in this respect. Our second randomized trial showed that erythrocytapheresis is preferred by the majority of patients (81%). This preference may also have a positive effect on compliance during the lifelong maintenance treatment.

In an observational study we demonstrated that erythrocytapheresis may lead to a better recovery of hemoglobin and hepcidin at start of the next procedure compared to phlebotomy. This may be clinically relevant and may prevent an increase in intestinal iron uptake and an ensuing vicious circle of more frequent treatment procedures. However, measurements of serum iron parameters were performed only before treatment procedures and not on a scheduled interval and therefore the outcome of this explorative study needs to be confirmed in larger prospective studies. Furthermore, it would be of great benefit for both patients and physicians when at start of depletion treatment the total number of phlebotomy and erythrocytapheresis procedures could be predicted. Such a prediction could guide patients and physicians in process of shared decision making to choose for the most effective treatment modality, and will provide insight in cost-effectiveness for insurance companies. We have designed, and presented an algorithm to predict the number of needed treatment procedures during depletion phase of treatment. This algorithm will be incorporated into a generally available app which would allow healthcare professionals to easily apply this algorithm and follow the treatment as well as patients to follow their treatment and possible have a positive effect on compliance.

In this thesis we have provided evidence that personalized erythrocytapheresis is a very efficient treatment modality with a good balance between effectiveness, tolerability and costs. These arguments are in favor of erythrocytapheresis over phlebotomy as a first line treatment in hereditary hemochromatosis.