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Effects of different lipoprotein apheresis methods on serum protein levels

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Abstract

Background: A total plasma exchange was the first extracorporeal method to treat patients with severe hypercholesterolemia. But in the long run it has several disadvantages. The newer lipoprotein apheresis (LA) methods claim to be more selective with respect to the removal of atherogenic lipoproteins and thus are supposed to avoid an additional protein loss.
Methods: We wanted to compare the effect of these methods on serum protein concentrations (total serum protein, albumin, proteins measured with electrophoresis, immunoglobulins, fibrinogen, transferrin, and ferritin) which were checked before and after a single LA session in 75 patients. All patients underwent active LA treatment using 6 different LA methods (HELP, TheraSorb® LDL, DALI, Lipidfiltration, Liposorber D, MONET). Post-apheresis concentrations were corrected for changes in hematocrit.
Results: The slightest impact on total serum protein was observed with the whole-blood methods. Liposorber D showed the least reduction of albumin levels. All LA methods had a small effect on alpha1-globulins and beta-globulins, but alpha2-and gamma-globulins were reduced to a different extent. A major effect was seen on the immunoglobulins when filtration methods were applied. In the patients treated with MONET, both pre- and post-apheresis Immunoglobulin M concentrations were below the normal range. HELP and the filtration methods significantly reduced the fibrinogen concentrations. The filtration methods also decreased ferritin levels but the post-apheresis ferritin levels were still in the normal range.
Conclusion: All LA methods had an influence on protein concentrations. At present, these findings will not yield an individualized treatment approach for any selective LA method due to the lack of prospective comparative studies. At minimum, special attention should be paid to protein concentrations in patients suffering from protein deficit.

Keywords: Lipoprotein apheresis; Total serum protein; Albumin; Immunoglobulins; Fibrinogen; Transferrin; Ferritin

1. Introduction

Extracorporeal therapy with total plasma exchange was started for patients with homozygous familial hypercholesterolemia in 1967 [1]. This type of treatment has been performed for many years and is still used in several countries; however, it has several drawbacks: loss of proteins (usually only albumin is given as an replacement); limited efficiency of reduction of LDL-cholesterol (LDL-C) − only 50% reduction rate has been reported; marked decrease of HDL-cholesterol; a high rate of side effects (∼12%, but since most patients receive multiple treatments, 40% of patients will experience some reaction during the course of therapy) [2].

In the 1980s and 1990s several lipoprotein apheresis (LA) methods were developed. These methods claim to be more selective with respect to the removal of atherogenic lipoproteins and thus are supposed to avoid an additional protein loss.

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On the other hand, the literature hints that additional proteins besides lipoproteins are also removed [3–10]. When analyzing proteins bound to different apheresis systems, the proteins could be referred to five different functional groups: apolipoproteins, rheologically relevant proteins, inflammatory proteins, adhesive proteins and others.

We are the only center in Germany using all widely available LA methods [11,12]. Herein we compare these methods with respect to their protein lowering effect by measuring protein concentrations before and after one single apheresis session.

A special focus was set on the levels of total protein, albumin, proteins measured with electrophoresis, immunoglobulins, fibrinogen, transferrin, and ferritin.

2. Materials and methods

This study included 75 patients (46 males, 29 females; mean age 62.6 years (range 29–81 years); the majority of whom had been treated with LA for several years. All patients met the official German criteria of an indication for the treatment with LA, e. g. they suffered from a severe hypercholesterolemia and/or an elevation of lipoprotein(a) which led to cardiovascular events [12]. Apheresis sessions were performed weekly.

At the time of this evaluation, our center applied 6 different LA methods. Table 1 shows the methods and the number of patients treated with them. Details of these methods have been recently summarized [12]. In the mean the following volumes were processed during the apheresis sessions:

HELP: 3000 ml plasma
TheraSorb® LDL (TherLDL): 4400 ml plasma
DALI: 8900 ml whole blood
Lipidfiltration (LF): 3900 ml plasma
Liposorber (LipoD): 7800 ml whole blood
MONET: 3500 ml plasma

The volumes are based on recommendations by the manufacturers and are modified in each patient according to effectiveness of lipoprotein removal and sometimes due to adverse events.

Table 1
Number of males and females treated with the different LA methods.

	Males	Females
HELP	9	3
TheraSorb® LDL (TherLDL)	10	1
DALI	8	8
Lipidfiltration (LF)	8	7
Liposorber (LipoD)	9	5
MONET	2	5
Total	**46**	**29**

As a standard of care, pre- and post-apheresis measurements of lipids are performed at our center using standard methods. For this study, before and after one apheresis session additional blood was drawn in order to check protein concentrations after patients had provided informed consent.

Total serum protein was measured by biuret method and albumin by bromocresol green (BCG) method (Modular, Roche Diagnostics).

Serum protein electrophoresis (SPEP) was carried out using a Hydrasys instrument (Sebia, Lisses, France) according to the manufacturer's instructions.

Serum immunoglobulins were determined by nephelometric methods (BNII, Siemens Healthcare Diagnostics).

Plasma fibrinogen concentration was measured by Clauss method (STA-R, Roche Diagnostics).

Transferrin and Ferritin were measured by immunological turbidimetric methods (Modular, Roche Diagnostics).

In parallel, when blood was drawn to measure proteins the hematocrit was assessed before and after the apheresis sessions and all post-apheresis protein concentrations shown in this paper have been corrected for the change in hematocrit (to exclude the influence of hemodilution).

2.1. Statistical methods

For comparison of the concentrations between the subgroups before and after apheresis sessions and of the reduction rates an ANOVA (with Bonferroni post-hoc tests) was performed (SPSS 18.0).

3. Results

All lipoprotein apheresis methods reduced the total protein concentration, but differed in this effect (Fig. 1).

The lowest reduction rates were seen with the whole-blood methods (DALI and Liposorber D). Total protein levels immediately after the apheresis sessions were below the normal range (66–83 g/L) with all methods. Patients treated with the filtration methods showed significantly lower concentrations than those on whole-blood methods. It should be noted that mean pre-apheresis total protein concentrations were already below this normal range in those patients who were treated with the filtration methods (difference not statistically significant).

Albumin levels were acutely decreased by all methods as well (Fig. 2).

Here the Liposorber D showed the least effect. In contrast to total proteins, the mean post-apheresis albumin levels did not decrease below the normal range (35–52 g/L) with any of the apheresis methods.

The mean reduction rates of alpha1-globulins ranged between −3 and − 11% and were not statistically different between the lipoprotein apheresis methods. On the other hand, the reduction rates of alpha2-globulins were found to