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**Original Article**

# The Iranian Blood Transfusion, Donor Safety Program: Effect of Long-term Plasmapheresis on Plasma Proteins.

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**Abstract**

**Background:** Plasmapheresis is a well-recognised method for harvesting plasma. It was introduced in the 1950s and is currently employed worldwide. This method has been in use in Iran since 1979.

**Objective:** To evaluate the efficacy of donor safety program used at the Iranian Blood Transfusion Organization.

**Methods:** A comparison is made of the protein concentrations between the first-time and long-term plasmapheresis donors, using protein gel electrophoresis. The effect of vaccination for collection of hyper-immune plasma was also studied.

**Results/Conclusion:** Our data comprising a 10-year evaluation of the current programmes, demonstrates no significant difference between the groups studied. This indicates safety of the plasmapheresis procedures in plasma procurement.
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**Keywords** • Plasmapheresis • donor safety • blood transfusion • Iran • safety.

Iranian Blood Transfusion, Organisation: Research & Fractionation Center

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## Introduction

When manual plasmapheresis was introduced in the 1950s, the potential capacity of this approach was easy to predict. It was revealed that, plasmapheresis could be up to 50 times more effective as a "plasma producer". During 1960s, plasmapheresis was adapted for the collection of hyperimmune plasma. Over the following two decades, collection of source plasma by the commercial plasmapheresis centers increased rapidly in the U.S.[1] and other Western countries. In Iran, plasmapheresis developed as part of a program within the Iranian Blood Transfusion Organization (IBTO) which is responsible for the provision of blood services through its more than 100 centers functioning as a national network across the country. Blood, plasma, cryoprecipitates and cellular products are provided, free of charge, to all patients. Collection of plasma by plasmapheresis was initiated in 1978 in the Plasmapheresis Unit based in Tehran. This procedure was chosen as an alternative

**Table 1:** Normal ranges for total protein and protein fractions in Iranian donors

| Age | Total Protein g% | Albumin Fraction % | Albumin Fraction g% | Alpha1globulin % | Alpha1globulin g% | Alpha2 globulin % | Alpha2 globulin g% | Beta globulin % | Beta globulin g% | Gammaglobulin % | Gammaglobulin g% |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 18-20 | 6.0-8.5 | 51-70 | 3.2-5.9 | 1.0-0.4 | 0.1-0.4 | 3.0-10.9 | 0.23-0.97 | 5.5-15 | 0.5-1.4 | 10-23.0 | 0.6-1.7 |
| 21-30 | 5.5-8.5 | 51-70 | 3.22-5.5 | 0.9-4.9 | 0.1-0.39 | 2.0-11.0 | 0.22-0.97 | 6.1-15 | 0.5-1.5 | 10.0-23.0 | 0.55-1.7 |
| 31-40 | 5.8-8.5 | 51-70 | 3.38-5.48 | 0.9-5.0 | 0.1-0.39 | 3.2-11.0 | 0.22-1.0 | 6.0-15 | 0.5-1.5 | 11.3-22.8 | 0.77-1.7 |
| 41-50 | 6.0-8.5 | 51-69.9 | 3.25-5.5 | 0.9-5.0 | 0.1-0.39 | 3.0-11.0 | 0.22-0.96 | 6.4-15 | 0.5-1.5 | 10.8-22.0 | 0.72-1.67 |
| > 50 | 6.0-8.5 | 51-69.2 | 3.6-5.3 | 1.0-5.0 | 0.12-0.39 | 3.0-11.0 | 0.26-1.0 | 7.3-15 | 0.5-1.0 | 10.2-22.0 | 0.70-1.67 |

method to obtaining fresh frozen plasma (FFP) from normal, as well as hyperimmunized donors. It was used for the production of intramuscular hyperimmune gammaglobulins, as an attempt to achieve self-sufficiency in various plasma products and to meet the growing present and future need for plasma derivatives. Ever since the first published regulations by FDA in 1973,[2] the relationship between frequency of donation, volume of donated plasma and health status of plasmapheresis donors has remained controversial.[3-5] In Iran, the plasmapheresis procedures are in accordance with the guidelines outlined by Council of Europe[6] and WHO.[7] Hereby, a healthy blood donor, on the first visit, is examined by a physician, and tested for blood-borne infections (HBV, HIV, HCV), as well as protein analysis and liver function tests (LFT). In the case of donors undergoing serial plasmapheresis, the above tests are repeated at least every 3-4 months while special attention is paid to any significant fall in the serum protein level even though they might be within normal limits. According to the present protocols, the plasmapheresis donor donates an average of 500 ml plasma per donation every 2 weeks. The main objective of the present study was to ascertain that the currently used plasmapheresis practices do not expose long-term donors to any harmful effects so that this procedure can be used as an alternative or additional method to the ever-increasing need of plasma for the plasma fractionation plant, of which, the capacity has been increased to 120,000 litre per annum. Another purpose of this study was to establish the normal ranges for some biochemical parameters tested among the Iranian donor population.

## Materials and Methods

As many as 1910 regular donors of the Plasmapheresis Unit were selected for this analysis. The data for biochemical tests, carried out in the biochemistry laboratory, were also compared with their first-time donations. Normal ranges for the total protein electrophoresis fractions as well as LFTs were derived from 1900 first-time plasmapheresis donors. Total protein estimation was carried out using Biuret method[3]; ALT, AST, total and direct bilirubin levels were measured using automation reagents (Abbott I & II.) on Abbott-VP chemistry analyzer. Protein electrophoresis in all cases was carried out on agar gel protein electrophoresis plates obtained from Corning Diagnostics, U.K. and the amount of proteins in each fraction was measured by a Corning densitometer. To ascertain the accuracy and precision of the routine analysis, a protein standard produced by Sigma, U.S.A, and a normal serum control by Abbott Diagnostics were also used at all stages. Statistical analysis was performed on all the available data using SPSS software.

## Results

Table 1, demonstrates the ranges for protein parameters from the first time donors according to their age. The normal ranges obtained for each parameter were calculated according to the method

**Table 2:** Normal ranges for liver function tests in Iranian donor

| Age | No. of Donors | AST IU/ L | ALT IU/ L | T.B. mg% | D.B. mg% |
|---|---|---|---|---|---|
| < 20 | 225 | 5 - 40 | 5 – 45 | 0.20 – 1.6 | 0.09 - 0.68 |
| 21-30 | 1035 | 4 - 40 | 4 – 45 | 0.16 – 1.6 | 0.08 - 0.70 |
| 31-40 | 411 | 4 - 40 | 6 – 43 | 0.21 – 1.6 | 0.06 - 0.70 |
| 41-50 | 192 | 7 - 40 | 5 – 42 | 0.22 – 1.6 | 0.10 - 0.70 |
| >50 | 46 | 5 - 37 | 5 – 34 | 0.26 – 1.3 | 0.10 - 0.63 |

**Table 3**: Comparision of protein values in vaccinated and non. vaccinated plasma donors

| | | | Protein Fractions (%) | | | | |
|---|---|---|---|---|---|---|---|
| **Type of Donor** | **no** | **Total protein 8%** | **Alb** | **Alpha - 1** | **Alpha – 2** | **Beta** | **Gama** |
| Vaccinated for rabies | 1156 | 6.1-8.5 | 51-70 | 0.9-5.0 | 2.3 –11 | 5.5-15.0 | 10–23 |
| Vaccinated for tetanus | 416 | 6.1-8.5 | 5 -70 | 1.0-5.0 | 2.0 –11 | 6.6-15.0 | 11-22.9 |
| Normal | 176 | 6.1-8.5 | 52-70 | 0.9-4.5 | 3.0 –11 | 6.8-15.0 | 11.5–22.4 |

**Table 4:** Comparison of liver function tests in vaccinated and non-vaccinated plasma donors.

| **Type of Vaccin** | **NO. of Donors** | **AST IU/ L** | **ALT IU/ L** | **T.B. mg %** | **D.B. mg %** |
|---|---|---|---|---|---|
| Vaccinated for Rabies | 1156 | 4 – 40 | 4 – 45 | 0.16 - 1.6 | 0.06 - 0.7 |
| Vaccinated for Tetanus | 416 | 4 –40 | 5 – 38 | 0.20 - 1.5 | 0.1 - 0.7 |
| Normal | 176 | 5 – 40 | 5 – 41 | 0.21 - 1.6 | 0.09 - 0.69 |

described in NCCLS.[8] It can be observed that the normal ranges observed in the Iranian adult population does not differ significantly from ranges mentioned in clinical chemistry textbooks such as Tietz.[9] However, the only noteworthy difference was a slight increase in the upper limit of normal range observed in gamma globulin fraction of proteins (1.7 g% compared to 1.3 g%).

It was also noted that in adult population the values were not age-dependent. The normal range for liver function tests are summarized in Table 2.
The effect of vaccination protocols for rabies and tetanus on the protein concentrations and liver functions is shown in Tables 3 and 4, where no change is observed after completion of vaccination protocols.

Finally the effect of long-term plasmapheresis on the protein synthesizing system was studied by comparing the results of the donors who had donated 1-10 bags of plasma with those plasmapheresed for more than 100 bags. The results are summarized in Table 5, where no significant effect is observed on the protein fractions and total protein concentrations.

## Discussion

The results presented in this paper demonstrate that when 500 ml plasma is collected by plasmapheresis at bi-weekly intervals, no marked effect on protein levels and liver function occurs in the donors. Consequently, the present protocols ensure the safety of the plasmapheresis donors. As far as the blood safety is concerned, it is always safer to identify a population of healthy donors who are frequently tested for different blood-borne infections. Therefore, since this procedure requires a smaller number of donors to obtain a given quantity of plasma with particular quality specifications, a safer supply of plasma is ensured for fractionation.

Despite the disputes concerning the cost effectiveness of plasmapheresis, the general understanding is that this approach may not be cost-effective for normal plasma collection in countries aiming to reach national self-sufficiency in fractionation of plasma required for routine donations.[10] Quality of plasma for fractionation is of paramount importance in the production of safe plasma-derived products, especially coagulation factors. This quality is affected by many factors starting from donor selection, through freezing procedures and storage conditions. In a country such as Iran, on account of the presence of numerous collection centers, it is difficult to achieve a cross-country ideal and uniform quality for routine donations, plasmapheresis may prove to be a more logical

**Table 5:** Effect of long-term plasmapheresis on protein fractions of donors.

| **No. of Bags donated** | **No. donors** | **T.P g %** | **Albumin** | | **Alpha 1** | | **Alpha 2** | | **Beta** | | **gamma** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | % | %g | % | %g | % | %g | % | %g | % | %g |
| 1-10 | 575 | 6.1-8.3 | 51-70 | 3.35-5.5 | 0.9-4.9 | 0.1-0.39 | 3.2-10.9 | 0.22-0.97 | 6.1-15 | 0.54-15 | 11.4-22.4 | 0.61-1.63 |
| 10-50 | 1005 | 6.1-8.5 | 51-70 | 3.12-5.5 | 0.9-5.0 | 0.1-0.4 | 2-11 | 0.22-1.0 | 6-15 | 0.5-1.5 | 10-23 | 0.55-1.7 |
| 50-100 | 267 | 6.2-8.5 | 51-70 | 3.22-5.5 | 1.4-5.0 | 0.1-0.39 | 3.2-10.5 | 0.22-0.95 | 6.3-15 | 0.5-1.4 | 11-22.6 | 0.7-1.7 |
| >100 | 55 | 6.2-8.5 | 56.2-69. | 3.78-5.46 | 1.7-4.7 | 0.11-0.33 | 4-10.5 | 0.26-0.87 | 6.4-15 | 0.53-1.5 | 10.9-22.4 | 0.7-1.6 |

approach and more cost effective in the long run.

However, plasmapheresis is generally accepted as the method of choice for preparation of hyperimmune plasma from immunized donors for production of various hypeimmune gammaglobulins.[2, 10] The present study shows that vaccination against rabies and tetanus followed by plasmapheresis has no adverse effect on the donors. Therefore, a limited number of known donors with high levels of certain specific anti-bodies can guarantee safe plasma for rare and important products such as anti- rabies and- tetanus gammaglobulin. In this respect, the planned upgrading of this department by installing automatic facilities will reduce the two main disadvantages related to the current manual techniques, and will ensure speed and prevention of possible faulty cell returns.[2, 10]

Finally, our data also demonstrate that normal ranges for the biochemical parameters of the Iranian adult population are not significantly different from those among Western populations which is referred to in available clinical chemistry textbooks[9], therefore, Western normal ranges may be considered also valid for this country. This goes for normal ranges of AST, ALT, bilirubin and different protein fractions in the Iranian adult population.

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