

THERAPEUTIC APHERESIS IN THE REPUBLIC OF MACEDONIA – OUR FIVE YEARS EXPERIENCE (2000–2004)

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Abstract: Membrane plasma exchange (PE) is a mode of extracorporeal blood purification. Since 1985 membrane PE has been in regular use at the Department of Nephrology, Medical Faculty of Skopje, R.Macedonia. In this paper we report on five years (2000–2004) of single centre plasma exchange activity. We performed 540 PE treatments (108 PE/per year) on 99 patients. The M/F ratio was 40/48. The patients underwent a median of 5.45 procedures (range, 1–16). The treated patients were from different Departments. Protocols for PE depend on the disease and its severity. PE were performed 2–4 times weekly using Gambro PF 2000 N filters with an adaptation of the Gambro AK10 dialysis machine or with the Gambro Prisma machine (2 cases). Blood access was achieved through femoral vein. Substitution was made with fresh frozen plasma and/or with 20% human albumin combined with Ringer’s solution. An average amount of 2150 ml plasmafiltrate per treatment (respectively 30 to 40 ml plasmafiltrate/kg body weight) was eliminated.

Most therapeutic procedures were performed on patients from the Department of Neurology. 63.6% of all patients were referred for Myasthenia gravis and the Guillian Barre syndrome. The total number of procedures per year has remained fairly stable, corresponding to a median of 5.4 treatments/100 000 inhabitants. We observed hypocalcaemia in 8% of the patients, urticarial reactions in 7.3%, pruritic reactions in 12%, and hypotension/headache in 6.8%. No major procedural complications were seen.

Key words: apheresis, membrane plasma exchange, indications, treatment, complications.

Introduction

Membrane plasma exchange (PE) is a mode of extracorporeal blood purification. Plasma exchange offers the capability of removing molecules of different molecular weights that have accumulated in the intravascular space. During the past period PE has been used to remove different unwanted substances from the blood: toxins, metabolic substances, and plasma constituents implicated in disease, such as complement or antibodies. Plasma can be purged of nonspecific factors such as mediators of inflammation and lymphokines that contribute to the severity of a disease process without being its root cause. The indications for apheresis have changed over the years [1, 2]. The application of various forms of apheresis techniques is extending and so is their technical development [3]. The first clinical application of therapeutic PE in the world was in 1952 in a patient with Waldenstrom disease. Waldenstrom macroglobulinemia was the most frequent reason for the plasma hyperviscosity syndrome [4]. Since 1985 membrane PE has been in regular use at the Department of Nephrology, Clinical Centre, Medical Faculty of Skopje, R.Macedonia [5, 6, 7]. The number of therapeutic procedures is increasing steadily year by year. Unfortunately therapeutic apheresis in our Department is still limited to PE. In our country, depending on our health system, the costs that are coupled with plasma exchange procedure may be a cause of the restriction to a limited number of plasma exchanges and only one modality of plasmapheresis.

In this paper we report on our five years' (2000–2004) experience with plasma exchange.

Patients and methods

In the course of 5 years, (2000–2004), 540 PE treatments (108 PE/per year) were performed on 99 patients at our Department of Nephrology, Clinical Centre, Medical Faculty of Skopje. The M/F ratio was 44/55. The patients underwent a median of 5.45 procedures (range, 1–16). The patient characteristics and diagnosis are summarized in Table 1. The treated patients were from different Departments (Neurology, Nephrology, Intensive Care Unit, Haematology and Toxicology). The patients were diagnosed using standard clinical and laboratory criteria at the Departments where they were being treated. PE was considered only as an adjunct to the therapy of the underlying disease with steroids or other immunosuppressants, especially in cases with a poor outcome from using current medications.

Protocols for PE were different and depend on the disease and its severity. PE were performed 2–4 times weekly using Gambro PF 2000 N filters with an adaptation of the Gambro AK10 dialysis machine or with the Gambro Prizma

machine (2 cases). Blood access was achieved through the femoral vein. Substitution was made with fresh frozen plasma (FFP most often used) and/or with 20% human albumin combined with Ringer's solution. An average amount of 2150 ml plasmafiltrate per treatment (respectively 30 to 40 ml plasmafiltrate/kg body weight per treatment – approximately one plasma volume) were eliminated. Both fresh frozen plasma and human albumin were very well tolerated. We did not register any serious side-effects during the PE procedure. Most complications were mild, such as hypotension and hypocalcemia.

Results

Our centre performs an average 108 procedures per year (Table 1). Most therapeutic procedures were performed on patients from the Department of Neurology, 63.6% of all patients were referred for rapidly progressive neuromuscular syndromes: Guillain-Barre syndrome and Myasthenia gravis. The indications for PE are shown in Table 2, with separate indications for each year. The number of exchanges used to treat haematological and neurological disorders has remained constant in recent years.

Table 1 – Табела 1

Number and distribution of patients and PE procedures from 2000 to 2004
Број и дисџрибуција на болниџе и џреџманиџе со џлазмаџереза
од 2000 до 2004 џодина

Year	2000	2001	2002	2003	2004	total
No of patients	22	21	23	12	21	99
No of PE	122	129	121	55	113	540

Except in the year 2003 a stable trend of activities was found during the last five years. In 2003 there was a problem with the new offer and reimbursement of the plasma filters. The total population is about 2 milion inhabitants and has been stable through the years included in the study. The total number of procedures per year has remained fairly stable corresponding to a median of 5.4 treatments/100 000 inhabitants.

We observed hypocalcaemia in 8% of the patients, urticarial reaction in 7.3%, pruritic reactions in 12%, and hypotension/headache in 6.8% (data not shown). No patient died during the procedure and no major procedural complications were seen. Patients respond well to intravenous calcium supplementation and/or methylprednisolone. Fresh frozen plasma, less expensive than albumin, is associated with more frequent urticarial and pruritic reactions than human albumin.

Table 2 – Табела 2

Main indications for PE expressed as the number of patients during 2000–2004

Главни индикации за плазмафереза и број на болни во итекој на 2000–2004 година

Indications	2000	2001	2002	2003	2004	total
Myasthenia gravis	7	7	8	7	8	37
Guillain Barres syndrome	7	6	5	2	6	26
RPGN	2	3	1			6
SLE	3	3	1			7
TTP	1	1	3			5
Rejection after transplantation	2	1		1	2	6
HLA-ab removal before transplantation					1	1
Wegener's syndrome			2	1	1	4
Myeloma multiplex			1		1	2
Mushroom poisoning			1			1
Macroglobulinemia			1			1
Waldenstrom				1		1
Goodpasture's syndrome					1	1
HUS					1	1
Polymiozitis	22	21	23	12	21	99
Total						

RPGN, rapidly progressive glomerulonephritis; SLE, systemic lupus erythematosus; TTP, thrombotic thrombocytopenic purpura; HLA-ab, HLA-antibodies; HUS, hemolytic uremic syndrome.

Discussion/Conclusion

Our experience with plasma exchange is growing. There are many variables influencing the efficiency of PE. Reports in medical literature regarding the use of therapeutic PE have generated both enthusiasm and controversy. Despite occasional complications the method is regarded as safe. Our database has also been useful in helping us understand the risks of PE. Most complications we observed were mild, which is in accordance with reports from other centres [8, 9]. All complications were successfully controlled with crystalloid or fresh plasma infusions or citrate management. Nogales-Gaete *et al.* also observed hypotension in 10% and paresthesias in 7% [10]. The French Registry Study Group reports that the immediate complications during PE decreased by half in the last 15 years [11]. Published data from Yeo *et al.* are not encouraging. They

analysed 568 PE treatments in 54 patients; 22% patients experienced a major complication including death, and 11% died [12].

In general, the total number of procedures per year in our Department has remained fairly stable, corresponding to a median of 5.4 treatments/100 000 inhabitants. In other centres there has been a significant decrease of PE over time and other apheresis techniques are increasing. Over the years various apheresis techniques have been employed: cytapheresis (leucocytapheresis, erythrocytapheresis, thrombocytapheresis), extracorporeal photo-chemotherapy, LDL-adsorption techniques, and immunoabsorption with the protein A column. More than 50 indications have been used for apheresis treatment each year.

The most common indication for PE has been neurological disease. Neuro-muscular respiratory failure is a common complication of rapidly progressive neuromuscular syndromes. PE and intravenous immunoglobulin are the cornerstones of specific therapy for these illnesses when complicated by respiratory failure [13]. Evaluation shows a decrease in the Guillan Barre and SLE indication over the years. This is in agreement with experience from controlled studies on patients with SLE showing that the addition of pulse/synchronization apheresis to cyclophosphamide therapy does not further improve the outcome in most of the SLE patients involved in those trials [14, 15]. Controlled studies on patients with GB showed that intravenous immunoglobulin is a choice of therapy equivalent to apheresis [16]. In our centre there was no decreasing trend in the Guillan Barre syndrome mainly because intravenous immunoglobulin is an expensive modality of therapy [17, 18]. In our country the annual number of PE procedures per inhabitant is far from that of other apheresis groups [19, 20, 21, 22, 23, 24, 25, 26]. This difference may be partly explained by the fact that their data include all types of apheresis modality (not only PE). PE is useful in patients who have refractory clinical conditions and a life-threatening disease associated with undesired circulating antibodies and who are not responsive to conventional doses of corticosteroid or cytotoxic drug therapy. In future, close collaboration with other departments will be useful in order to increase the number of PE procedures and to collect more precise data. The data will be useful for the estimation of the financial resources needed for apheresis therapy, too.

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Резиме

ТЕРАПЕВТСКА АФЕРЕЗА ВО РЕПУБЛИКА МАКЕДОНИЈА – НАШЕ ПЕТ ГОДИШНО ИСКУСТВО (2000–2004)

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Мембранската плазма измена (ПИ) е начин на вонтелесно прочистување на крвта. Од 1985 г. мембранската ПИ регуларно се користи на Одделот за нефрологија на Медицинскиот факултет во Скопје, Р. Македонија. Во овој труд ги објавуваме активностите поврзани за ПИ за пет години (2000–2004) во нашиот центар. Изведени се 540 третмани на ПИ (108 ПИ/годишно) на 99 пациенти. Односот мажи/жени беше 40/48. Пациентите беа подложени средно на 5,45 процедури (распон 1–16). Третираните пациенти беа од различни

оддели. Протоколите за ПИ зависеа од заболувањето и неговата сила. ПИ се изведуваа 2–4 пати неделно, користејќи Gambro PF 2000 N филтри со адаптација на Gambro AK10 апарат за дијализа или со Gambro Prisma апарат (2 случаи). Крвен пристап беше обезбеден преку феморална вена. Свежо смрзната плазма и/или 20% хумани албумини комбинирани со Ringer-ов раствор беа користени за супституција. Се елиминираше среден износ од 2.150 мл плазмафилтрат во тек на еден третман (30 до 40 мл плазмафилтрат/кг телесна тежина).

Најмногу терапевтски процедури беа изведени на пациенти од Одделот за неврологија. 63.6% од сите пациенти беа со Myasthenia gravis и Guillian Barre синдром. Вкупниот број на процедури во тек на една година остана прилично стабилен со средно 5.4 третмани/100.000 жители. Опсервиравме хипокалцемија кај 8% од болните, уртикаријални реакции кај 7.3%, реакции на јадеж кај 12% и хипотензија/главоболка кај 6.8%. Не беа видени големи процедурални компликации.

Клучни зборови: афереза, мембранска плазма измена, индикации, третман, компликации.

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