

## ORIGINAL PAPER

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# Plasmapheresis in Pediatric Intensive Care Unit

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## ABSTRACT

**Introduction:** Plasmapheresis also known as a therapeutic plasma exchange (TPE) is extracorporeal procedure by which individual components of plasma that are harmful or blood cells can be removed from organism by using a blood separation technology. **Aim:** To present the results of the implementation of plasmapheresis in children in the Department of Pediatric Intensive Care of Pediatric Clinic, Clinical center of Sarajevo University, Bosnia and Herzegovina. **Patients and methods:** Research (period from December 2011 to June 2016) analyzed 66 plasmapheresis (11 patients-6 plasmapheresis per patient). **Results:** Out of 11 patients, 7 (63.6%) were girls and 4 (36.4%) were boys. The average age of patients was  $11.6 \pm 3.9$  years (the youngest patient had 4 years and 7 months, while the oldest had 16 years and 10 months). Plasmapheresis were significantly more often done in the winter and summer. Underlying disease was in 54.5% of cases of neurological origin. The treatment was in form of receiving IVIG in 7 patients, or the application of mechanical ventilation in 6 patients. The most common complication was hypotension, which occurred in 45.5% of patients, followed by bleeding in 36.3%, hypercoagulability in 27.2% of patients and hematoma in 27.2% of patients. Lethal outcome occurred in 3 (27.2%) patients. **Conclusion:** Plasmapheresis represents an invasive method due to need for placement of centralized venous catheter that provides adequate blood flow during the procedure. Although complications can be serious, they are rare and are mainly related to the presence of central venous catheter, hemostasis disorders due to use of anticoagulant therapy, and hypotension of the cardiovascular system. It should be noted that for success of plasmapheresis in children multidisciplinary approach is necessary (children's nephrologist, neuropediatrician, intensive care doctor) as well as well-trained team of doctors and nurses with the acquired knowledge and skills.

**Key words:** plasmapheresis, indications, complications.

## 1. INTRODUCTION

Plasmapheresis also known as a therapeutic plasma exchange (TPE) is a procedure of plasma removal with its ineligible plasma's component (extracorporeal procedure by which individual components of plasma that are harmful or blood cells can be removed from organism by using a blood separation technology) (1, 2). It is divided into membrane and centrifugal plasmapheresis. Membrane plasmapheresis is therapeutic and it is done in the dialysis centers, and staff must be familiar with the principles of extracorporeal circulation and handling of machine called MultiFiltrate (3).

Centrifugal plasmapheresis is done on transfusion department for separation of individual components from donor blood. Plasmapheresis is used for fast reduction of titers of circulating antibodies or immune complexes, also as a useful addition to chemotherapy for the removal of circulating immunoglobulin components in multiple myeloma and other similar dysproteinemia. It is useful in the preparation of the patient for transplantation in order to prevent vascular organ transplant rejection (e.g. kidney) (3) Indications for plasmapheresis treatment are: myasthenia gravis- acute phase, secondary glomerulonephritis which does

not respond to standard treatment protocols, systemic vasculitis, hemolytic uremic syndrome, thrombocytopenic purpura, Guillain-Barre syndrome, familial hyperlipidemia, chronic demyelinating polyneuropathy, blood hyperviscosity syndrome, cryoglobulinemia, paraproteinemia, macroglobulinemia, etc. (4). In preparing the patient for therapeutic plasmapheresis following laboratory findings have to be done: differential blood count, electrolyte status, urea and creatinine, blood glucose, APTT, INR and fibrinogen. Vascular access is one of the large central veins: femoral vein, internal jugular vein and subclavian vein, which is rarely used. As substitution fluid 5% human albumin, fresh frozen plasma, other plasma derivatives (e.g. supernatant), crystalloids (0.9% NaCl, Ringer's lactate) are used. Albumin is used more than plasma due to the lower risk of allergic reactions and transmission of viral infections by plasma. Standard unfractionated heparin is the most common anticoagulant for membrane plasmapheresis (5). The most common complications when performing this procedure are: hypotension, hypokalemia, hypocalcemia (especially when fresh frozen plasma is used as a replacement fluid), muscle cramps and numbness of the extremities, a metallic taste in the mouth, allergic reactions, bacterial infections and severe suppression of the immune system. To make sure that procedure is well executed and to minimize complications following is needed: good preparation of appliance and set for plasmapheresis, substitution solution, anticoagulant therapy, respect of principles of asepsis and antisepsis, and prepared anti-shock therapy (6).

**2. AIM**

The aim of this paper was to present the results of the implementation of plasmapheresis in children in the Department of Pediatric Intensive Care of Pediatric Clinic, UCC Sarajevo (Bosnia and Herzegovina).

**3. MATERIAL AND METHODS**

In the period from December 2011 to June 2016, on the Department of Pediatric Intensive Care of Pediatric Clinic, Clinical Center of Sarajevo University, 66 plasmapheresis were performed in 11 patients (6 plasmapheresis per patient). Occurrence of complications related to the execution procedures was monitored as well as the final outcome of the treatment. Descriptive statistics of data was performed in Microsoft Excel (version 11. Microsoft Corporation, Redmond, WA, USA), and level significance of  $p < 0.05$  was used.

**4. RESULTS**

In the period from December 2011 to June 2016, on the Department of Pediatric Intensive Care of Pediatric Clinic, UCC Sarajevo, 66 plasmapheresis were performed in 11 patients, of which 7 (63.6%) were girls and 4 (36.4%) were boys.

The average age of patients was  $11.6 \pm 3.9$  years (the youngest patient had 4 years and 7 months, while the oldest had 16 years and 10 months). There were no significant differences in age in relation to the sex of the pa-

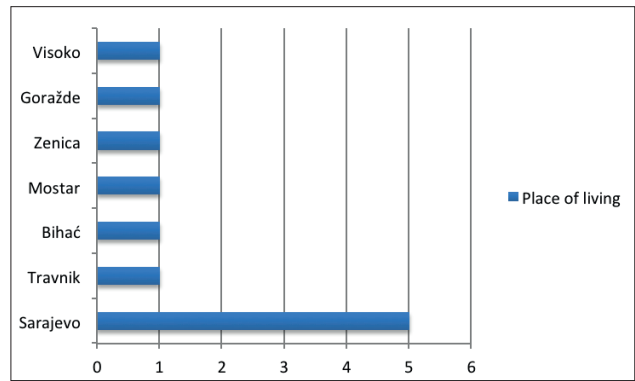


Figure 1. Patients place of living

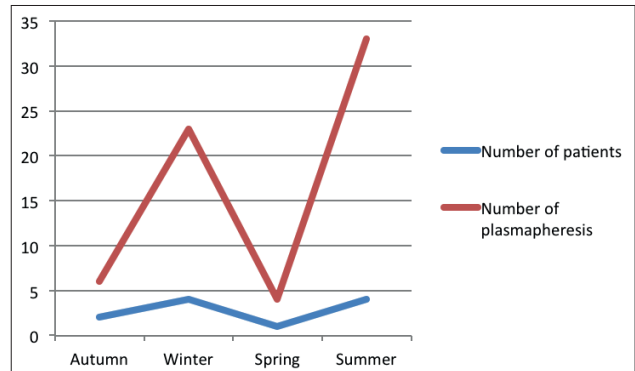


Figure 2. Correlation between number of patients and number of plasmapheresis

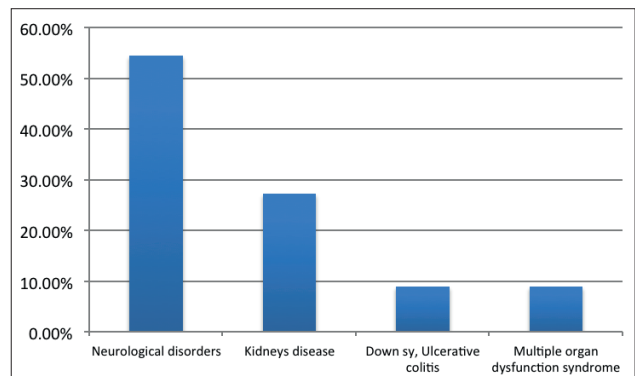


Figure 3. Underlying disease of patient

tient ( $p > 0.05$ ). Of the total number of patients, 45.4% of them came from Sarajevo (Sarajevo Canton) (Figure 1).

Plasmapheresis were significantly more often done in the winter and summer (Figure 2).

Underlying disease was in 54.5% of cases of neurological origin (Figure 3).

Comorbidities with primary disease were respiratory diseases (80% bronchopneumonia, 20% acute respiratory distress syndrome) in five patients, in one patient sepsis appeared (*Candida albicans*), and in one patient measles. Vascular access significantly went through the femoral vein rather than through internal jugular vein (72.7% vs 27.2%). The treatment was in form of receiving IVIG in 7 patients, or the application of mechanical ventilation in 6 patients. The most common complication was hypotension, which occurred in 45.5% of patients, followed by bleeding in 36.3%, hypercoagulability in 27.2% of patients and hematoma in 27.2% of patients (Figure 4).

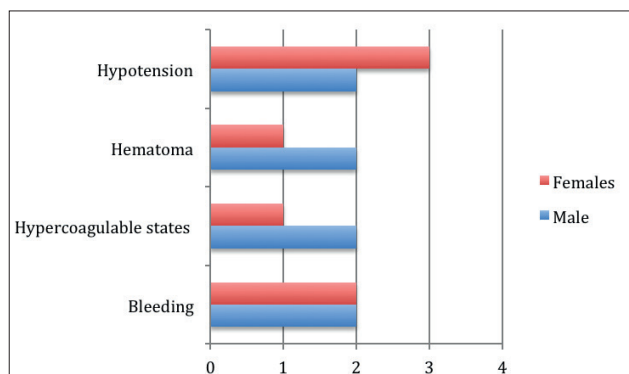


Figure 4. Number of complications

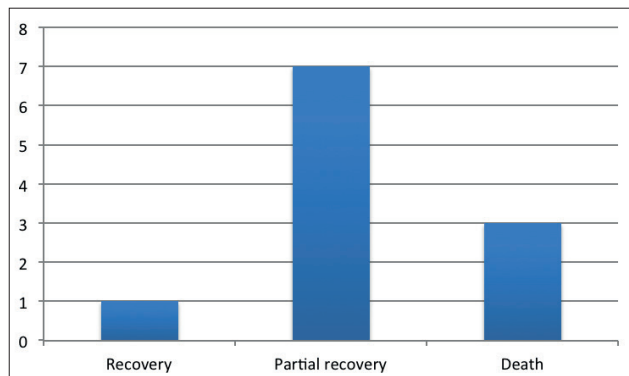


Figure 5. Treatment result

There were no significantly more frequent reporting of one complication in relation to the gender of patients.

The outcome of treatment in 7 (63.6%) patients was partial recovery, while the lethal outcome occurred in 3 (27.2%) patients, and total recovery was achieved in 1 (9%) patient (Figure 5).

## 5. DISCUSSION

As vascular access femoral vein was most commonly used (in 8 patients), internal jugular vein was used in 3 patients, while subclavian vein was not used (7). Plasmapheresis first separates plasma from the blood's cell component; in the classical plasma exchange modality, the patient's plasma is then replaced with fresh frozen plasma from a donor, this procedure is still current in different fields of medicine, as there are hematological (thrombotic thrombocytopenic purpura, Waldenström's disease), neurological (Guillain-Barre' syndrome, myasthenia gravis) and toxicological indications (several forms of mushroom poisoning, tricyclic antidepressants, transfusion reactions), as well as nephrological indications (Goodpasture's syndrome, ANCA-associated vasculitis, myeloma) for its use (8). Indications for performing plasmapheresis were myasthenia gravis in acute stage in two patients, Guillain-Barre syndrome in one, super-refractory status epilepticus in one patient, autoimmune encephalitis and mitochondrial encephalopathy with lactic acidosis and episodes that resemble stroke in one patient and liver failure of unknown origin complicated with acute renal failure and with development of multiple organ dysfunction in one patient. Also one patient had Down syndrome and ulcerative colitis with the complication of intestinal perforation that was treat-

ed surgically (9, 10, 11). Plasmapheresis is used in the treatment of renal disease in three patients. One patient had focal segmental glomerulosclerosis with the development of chronic renal disease, second patient had mesangial proliferative glomerulonephritis and third patient had class IV lupus nephritis as part of systemic lupus erythematosus (12). The most common complications of vascular access were hematomas that occurred in three patients where femoral vein was used as vascular access. Anaphylactic reaction to the replacement fluid (fresh frozen plasma and human albumin) were not observed. Coagulation disorders like bleeding were present in four patients. In the treatment of bleeding, the process of plasmapheresis was temporarily delayed until stabilization of the hematologic state of coagulation that was suitable for performing plasmapheresis. Hypercoagulability was present in three patients, requiring the termination of plasmapheresis, and on two occasions change of way of vascular insertion. The transmission of viral hepatitis and other infections were not recorded. Infections related to central venous catheter were not detected, blood culture and culture of peak of central venous catheters were sterile. Symptomatic hypocalcemia was recorded twice and calcium gluconate was given as therapy. In both patient replacement fluid was fresh frozen plasma that contained citrate. The most common complication was hypotension, which was observed in 5 patients. For treatment boluses of crystalloids (0.9% NaCl, Ringer lactate) were given so there was no need for the inclusion of inotropic drugs (13, 14).

The final outcome of patients on which therapeutic plasmapheresis was administered was: full recovery was recorded in one patient suffering from Guillain-Barre syndrome, seven patients were partially recovered, while the death occurred in three patients. One had acute hepatic failure of unknown etiology with the development of multiple organ failure, second patient has Down syndrome with ulcerative colitis and intestinal perforation, which is surgically treated and third patient had mitochondrial encephalopathy with lactic acidosis and episodes that resemble stroke. It is important to emphasize that the outcome of death has not occurred during the execution of procedures of plasmapheresis.

It seems that TPE as a therapy has seen an increase in usage, particularly by those who take care of critically ill patients and using an evidence-based approach is the best way to standardize care and also to provide a platform for innovation to move the field forward (15). For all indications, the optimal plasma exchange protocol (number of exchanges and volumes exchanged) remains to be established through future research (16). Plasmapheresis can be considered a relatively safe method of treatment of ICU patients, but continuous observation and proper monitoring of patients provided by highly trained medical personnel are essential for its safety (17).

## 6. CONCLUSION

Plasmapheresis represents an auxiliary procedure in the treatment of potentially deadly diseases because it allows a targeted removal of causes or mediators of the

pathological process. It represents an invasive method due to need for placement of centralized venous catheter that provides adequate blood flow during the procedure. The results are now reflected in the positive outcome of treatment of Guillain-Barre Syndrome, and according to the literature of thrombotic microangiopathy. Clinical efficacy of plasmapheresis in many renal diseases is still controversial, and for better definition of plasmapheresis in the treatment of renal disease, a larger number of prospective randomized controlled trials is required. Although complications can be serious, they are rare and are mainly related to the presence of central venous catheter, hemostasis disorders due to use of anticoagulant therapy, and hypotension of the cardiovascular system. It should be noted that for success of plasmapheresis in children multidisciplinary approach is necessary (children's nephrologist, neuropediatrician, intensive care doctor) as well as well-trained team of doctors and nurses with the acquired knowledge and skills.

• Conflict of interest: none declared.

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