DOUBLE FILTRATION PLASMAPHERESIS (DFPP) IN A PATIENT WITH WEST NILE VIRUS ENCEPHALITIS (WNE)

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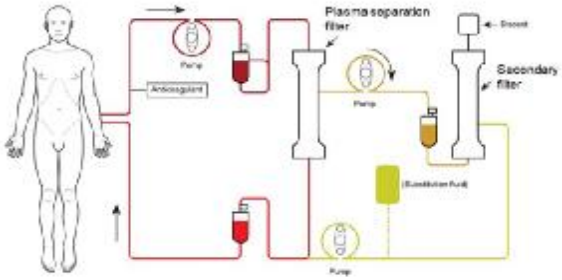
Abstract: *Double filtration plasmapheresis (DFPP) is a plasma filtration technique, the indications of the method overlapping theoretically over the conventional therapeutic plasmapheresis indications. The advantages of the method consist in the fact that it is not necessary to administer human albumin or PCC as substitution, or the amounts administered are very small. We used the method in the pathogenetic treatment of a patient, aged 59 years, diagnosed with West Nile virus encephalitis.*

INTRODUCTION

The term of "apheresis" means separation and it comes from the Greek term "apairesos" or the Roman term "aphairesis", meaning "to take away". It is a process in which blood is removed from a patient and is continuously separated into component parts, allowing a component to be retained while the remainder is returned to the patient.

Double filtration plasmapheresis (DFPP) is a cascade plasma filtration technique in two steps. After the removal of plasma out of blood, it is passed through a second filter called fractionator which has the pores of the membrane 10 times smaller than the plasmafilter (figure no. 1). This way, there will be retained high molecular weight molecules (fibrinogen, IgG, IgM, LDL-cholesterol, Lp (a), triglycerides), and viruses and the rest of the plasma can be returned to the patient. The advantages of the method consist in the fact that it is not necessary to administer human albumin or PPC as substitution, and the amounts administered are very small. The indications of the method overlap theoretically over the conventional therapeutic plasmapheresis indications. The most common situations in which it was used and studied are: the treatment of chronic hepatitis C, renal transplantation with ABO incompatibility, but also in familial hypercholesterolemia, thrombotic thrombocytopenic purpura, autoimmune neurological diseases (Guillain-Barre, myasthenia gravis etc.), rapidly progressive glomerulonephritis, blood hyperviscosity syndromes.

Figure no. 1. Principles of Double Filtration Plasmapheresis (DFPP) (1)

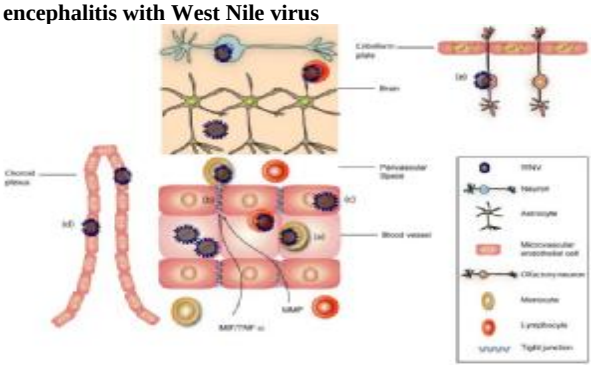


Hur M et al. ABO-incompatible kidney transplantation. 2011.

In West Nile virus encephalitis, there is an autoimmune component in the pathogenetic mechanism of disease production.(3,4,5,6,7,8,9)

In figure no. 2, Hyelim Cho and Michael S. Diamond present the autoimmune pathogenic mechanism of encephalitis with West-Niles virus.

Figure no. 2. Autoimmune pathogenic mechanism in encephalitis with West Nile virus



Hyelim Cho, Michael S. Diamond. Immune Responses to West Nile Virus Infection in the Central Nervous System. Viruses. 2012 Dec; 4(12): 3812–3830.

MATERIALS AND METHODS

DFPP treatment in practice

Figure no. 3. Machine in DFPP

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Infomed. Blood purification devices

To run a treatment we need :

- 1 machine (figure no. 3);
- 1 plasmafilter (figures no. 4, 5);
- 1 fractionator adapted to Ig (figures no. 4, 5);
- 1 tubing set (figures no. 4, 5);
- Approx. 4 liters of physiologic solution.
  - 1 session consists in filtering 1-2 plasma volumes in 1-3 hours;
  - A vascular access (venous central catheter);
  - Anticoagulation can be done with citrate or heparin.

Figure no. 4. Plasmafilter and fractionator in DFPP

Clearance of substances depends on volumes and sieving coefficients.

The volume to consider is ratio betwen the plasma treated and the total plasma volume of the patient.

Sieving coefficient (S)

$S = Cr/ Cd$

Where:

- *S* is the sieving coefficient,
- *C*r is the mean concentration mass receiving stream,
- *C*d is the mean concentration mass donating stream.

A sieving coefficient of unity implies that the concentrations of the receiving and donating stream equilibrate.(16)

DFPP sessions in the patient with West-Nile encephalitis were performed at a distance of 24-48 hours.

In DFPP, 2 filters exist with different sieving coefficients (SC): SC of Medopen 10 and SC of Medopen 30 (tables no. 1, 2).

Table no. 1. SC of Medopen 10 filter (16)

SC of Medopen 10	Removed with 1 plasma volume	Removed with 1,5 plasma volume
Albumin: 0,62	33%	48%
IgG: 0,18	52%	63%
Fibrinogen:0	63%	77%

Table no. 2. SC of Medopen 30 filter (16)

SC of Medopen 30	Removed with 1 plasma volume	Removed with 1,5 plasma volume
Albumin: 0,86	10%	14%
Fibrinogen: 0,32	48%	63%
HDL: 0,86	17%	24%
LDL: 0,02	55%	72%

In autoimmune diseases, and hence in the patient with West-Niles encephalitis, Medopen 30 filter is used to remove circulating immune complexes and antibodies.

Medopen filter 10 is useful in case of transplant rejection.

Figure no. 5. DFPP in practice

CASE REPORT

We used double filtration plasmapheresis method in the pathogenetic treatment of a female patient aged 59 years with a diagnosis of West Nile virus encephalitis.

Previous medical history of the patient revealed peripheral idiopathic immune thrombocytopenia for which she received corticosteroids in 2011.

The diagnosis on admission in August 2015 was acute meningitis, confusion syndrome, thrombocytopenia. Signs and symptoms present upon admission were: slight neck stiffness, obtundance, myalgia, cerebelous ataxia, dancing eyes.

Laboratory and paraclinical analyses showed: ESR 18 mm/h, CRP 6 mg%, platelets 120 000/mm^3, triglycerides 204 mg%, CT-Scan normal, glucose level in CSF 79 mg%, protein 0.9 g%, WBC 1040/mm^3, PMN 89%, cultures of CSF - germ free.

Etiologic diagnosis was established by the presence of West Nile virus antibodies IgM in serum and CSF.

Neurological evolution of the patient was unfavourable, from Glasgow Coma Scale (GCS) 14 points to 4 points in GCS level, despite anti-infective, neurotrophic and supportive therapy in the ICU ward. After 21 days of hospitalization, the autoimmune component of the neurological disease, secondary to viral infection, came into discussion.

DFPP procedure was initiated in three sessions every 24 hours, then a fourth session after 48h. No major incidents were reported during the procedures.

Neurological status improved, clinically significant already after the first session of DFPP up to a GCS score of 10, followed by a plateau phase in the neurological development.

DISCUSSIONS

West Nile virus encephalitis is one of the causes of Opsoclonus Myoclonus Syndrome (OMS); a synonym of this

syndrome is dancing eyes-dancing feet.

The patient in this case report shows Opsoclonus-myoclonus Syndrome (OMS).

Opsoclonus Myoclonus Syndrome (OMS), known as Opsoclonus Myoclonus Ataxia (OMA) is a neurological disease extremely rare, of unknown cause, which appears to be the result of an autoimmune process affecting the nervous system.

OMS signs and symptoms:

- Repeated, rapid eye movements in both horizontal and vertical directions (opsoclonus);
- Unsteady gait (ataxia);
- Brief, repeated, shock-like spasms of several muscles within the arms, legs (myoclonus);
- Extreme irritability;
- Reduced and fragmented sleep;
- Rage attacks;
- Difficulty articulating speech (dysarthria), or inability to speak (mutism);
- Decreased muscle tone (hypotonia).(10)

Plasmapheresis therapy has been used in Opsoclonus-Myoclonus Syndrome therapy and it has been presented in several studies.(11,12,13,14,15)

Indication of plasmapheresis in autoimmune diseases is clear and is included in international therapeutic guidelines ASFA Guidelines (J Clin Apher 2010).

Plasma exchange versus DFPP:

In plasma exchange, the plasma is discarded and replaced by fluids such as albumin or plasma.

In DFPP, the plasma is filtered to retain targeted substance such as antibodies or cholesterol before being returned to blood.(16)

Protein kinetics in therapeutic plasma exchange

- IgM is removed more efficiently than Ig G. Both re-equilibrate within 24-48 hours.(17)
- To effectively deplete total body IgG by 85%, there are needed 5 exchanges and only 2-3 exchanges for IgM.(17)
- Effect of plasma exchange is temporary (T1/2 Ig G 21 days, T1/2 IgM - 7-10 days).(17)

CONCLUSIONS

DFPP has proven its therapeutic efficacy in this case, unresponsive to the anti-infective, consolidation and supportive therapy in the ICU ward, by clinical improvement in neurological evolution after only one session.

Using plasmapheresis techniques in neurological disorders with autoimmune component secondary to infectious pathology of central nervous system needs further research.

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