UTILITY OF DOUBLE FILTRATION PLASMAPHERESIS IN ACUTE ANTIBODY-MEDIATED RENAL ALLOGRAFT REJECTION

Alessandro Domenico Quercia, Guido Merlotti, Gabriele Guglielmetti, Marco Quaglia, Davide Medica, Vincenzo Cantaluppi

SCDU Nephrology and Renal Transplant Unit, University of Eastern Piedmont, AOU "Maggiore della Carità"; Interdepartment Transplational Research Institute for Autoimmune Disease (CAAD), Novara, Italy

WORKSHOP

Purification Therapies

LE IDEE PER LA RICERCA CLINICA

15-16 MARZO 2019

Background

Double filtration plasmapheresis (DFPP) is a special form of membrane filtration, used in the setting of ABO blood group incompatible kidney transplantation and in patients with antibody-mediated acute renal allograft rejection (AAMR).

Methods

We describe the use of DFPP *(Fig. 1)* as a component of anti-rejection treatment regimen. The evolution of patient renal function was evaluated during the hospital admission. Moreover, we developed an *in vitro* study using anti-HLA/DSA antibody on endothelial glomerular cells (HGECs) to evaluate protective effect of DFPP in microvascular injury induced by antibody-link and Complement-cascade activation. Sera of patient were stored at 0 time and before and after every DFPP session. The inflammatory state was evaluate analyzing Complement activity (C5b9), the expression of adhesion molecules VCAM-1, E-selectine and CD40 (FACS analysis) and the adhesion of PBMCs and NK cells on Matrigel-coated plates. The effect of DFPP on apoptosis were analysed using TUNEL assay (% of apoptotic cells). Moreover, were evaluated the pro-angiogenetic effects on HGECs analyzing the N° of capillary-like structures for field.

Figure 1

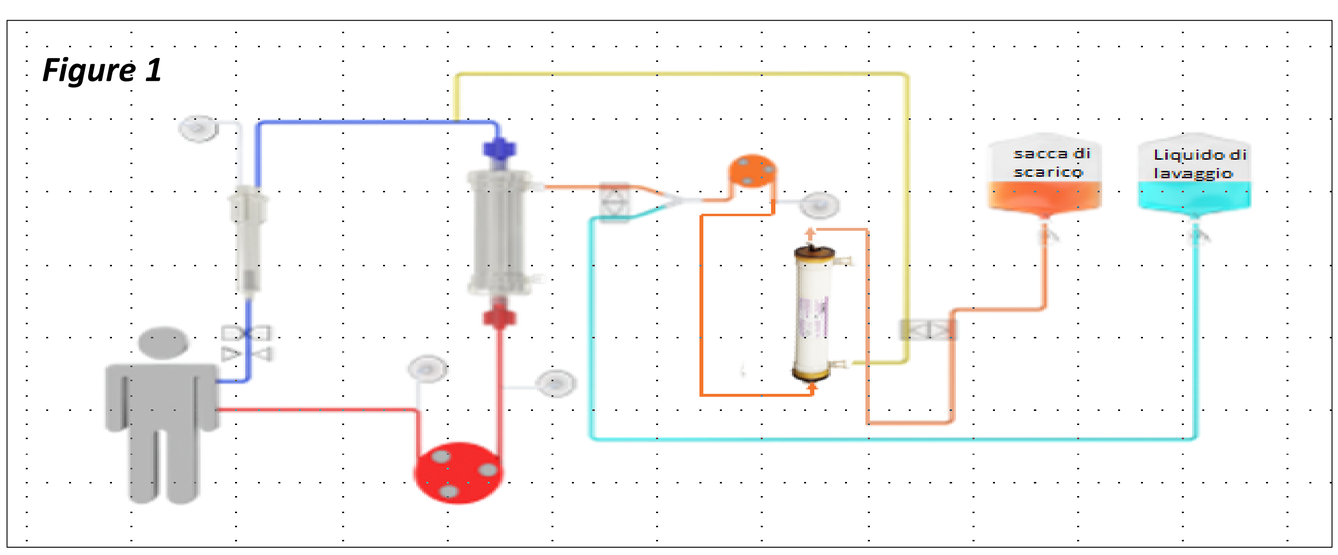


Figure 2

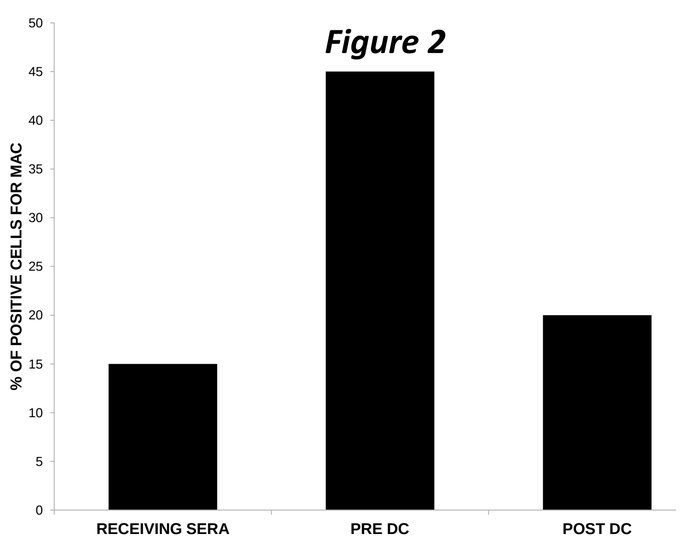


Figure 3A

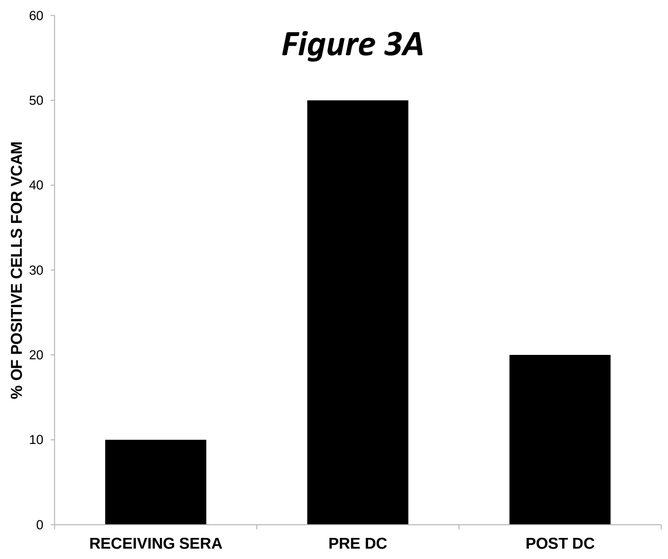


Figure 3B

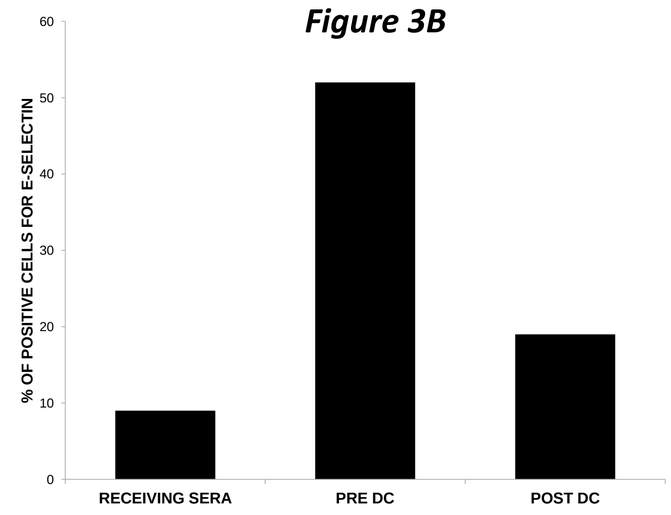


Figure 3C

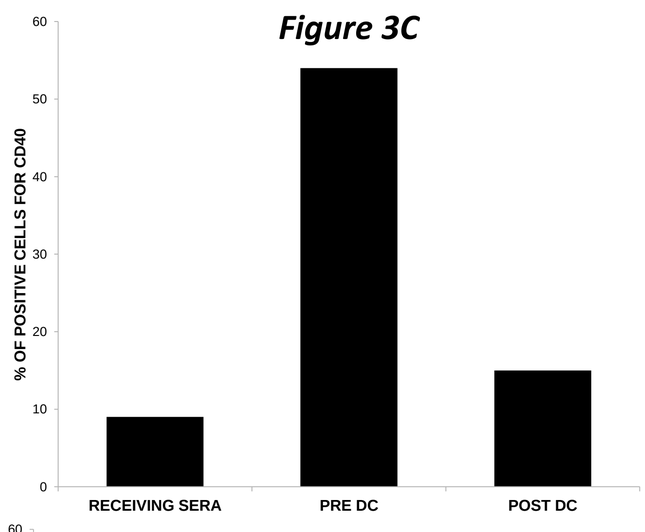


Figure 4A

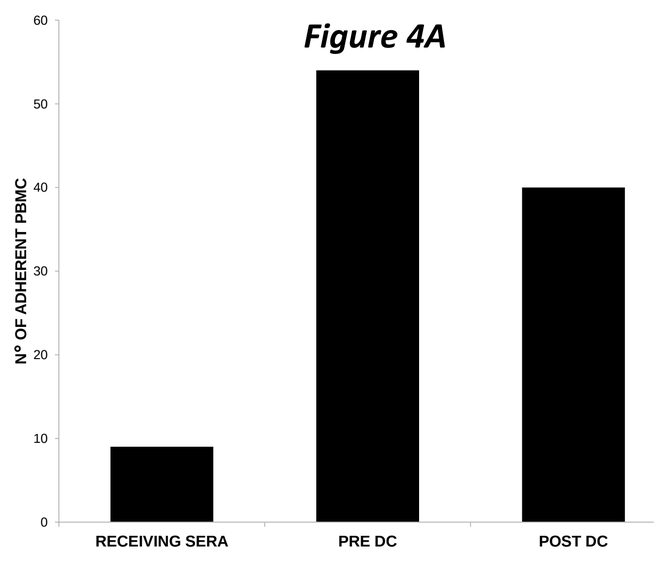
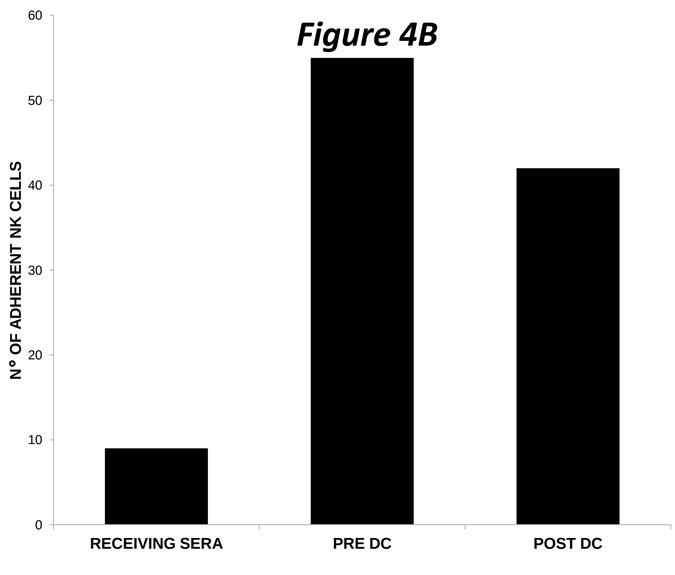


Figure 4B



Results

A 42-years-old male who had been on hemodialysis by 1991 due to nephronoptisis and with a previously renal transplant fasted from 1995 to 2004, underwent to a 2nd deceased-donor kidney transplantation. He was HCV positive without severe hepatic injury. After transplantation, he had detrimental renal function without presence of DSA and with vPRA 86,2% cl I. His maintenance immunosuppressive regimen included tacrolimus, prednisone and MMF. Percutanous allograft biopsy revealed AAMR. Two cicles of intravenous immunoglobulin (IVIG) along with alternate day DFPP (five sessions) and two cicles of anti-CD20 (Rituximab) 1 g were applied. The patient was discharged with stabilezed graft function (Crs about 3,2 mg/dl).

The *in vitro* study demonstrated the reduction of inflammatory state and of Complement-cascade activation after DFPP treatment (reduction of % of positive cells for MAC (Fig. 2), lower expression of VCAM-1, E-selectine and CD40 (Fig. 3A-C) and reduced N° of adherent PBMCs and NK cells (Fig. 4A,B) after DFPP treatment), the reduction of apoptosis (Fig. 5) and the pro-angiogenetic effects (Fig. 6) of DFPP treatment.

Figure 5

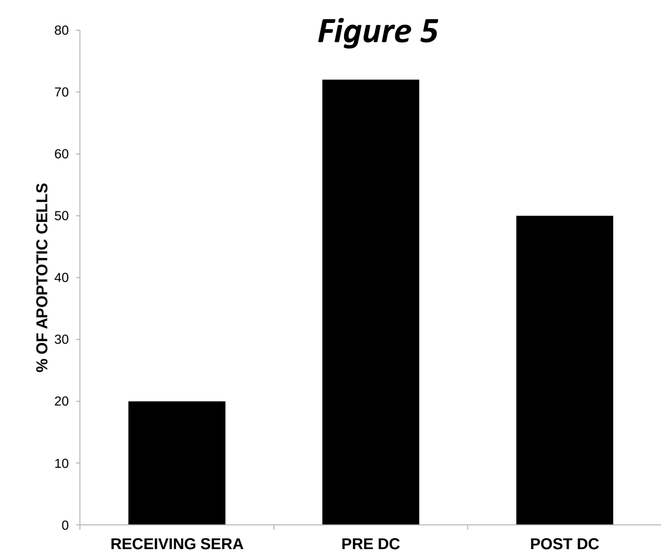
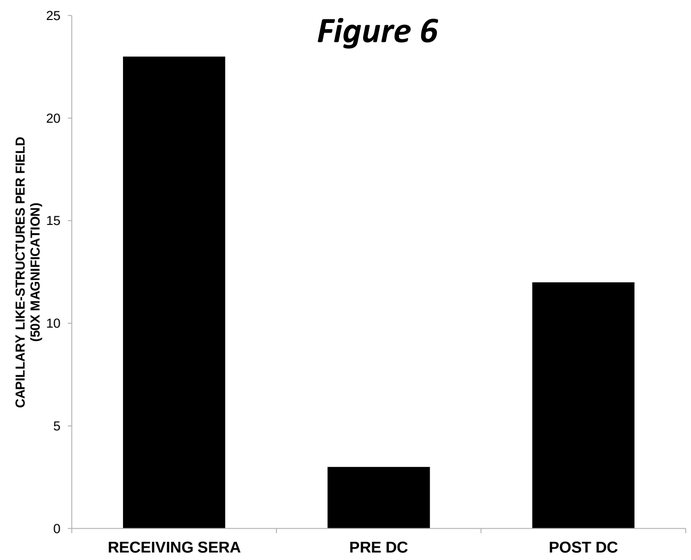


Figure 6



Conclusions

DFPP inhibit microvascular injury induced from antibody-link on endothelial cells and by activation of Complement-cascade, through antibodies against donor removal and inhibiting Complement activation and related apoptosis activation, NK cells adhesion and promoving angiogenesis preserving renal function.